

OPEN

Brain Trauma Foundation Guidelines for the Management of Penetrating Traumatic Brain Injury, Second Edition

Randy S. Bell, MD (CAPT (ret), MC, USN)^{1,2}, Shelley Selph, MD, MPH³, Jamshid Ghajar, MD, PhD⁴, Bizhan Aarabi, MD⁵, Angela Lumba-Brown, MD⁶, Halinder S. Mangat, MD, MSc^{4,7,8}, David W. Wright, MD⁹, Bradley Dengler, MD (LTC, MC, USA)¹⁰, Deborah M. Stein, MD, MPH¹¹, Dylan Pannell, MD, PhD (LCol, RCMS, CAF)^{12,35}, James Ecklund, MD (COL (ret), MC, USA)¹³, Stacy Shackelford, MD (Col. (ret), MC, USAF)¹⁴, Miranda Pappas, MA¹⁵, Annette M. Totten, PhD¹⁵, P. David Adelson, MD¹⁶, Rocco A. Armonda, MD (COL (ret), MC, USA)¹⁷, John Benjamin, MD, MSc (CDR (ret), MC, USN)¹⁸, Darrell Boone, MD (LCdr, RCMS, CAF)^{19,35}, Shelton Davis, MD (COL (ret), MC, USA)²⁰, Gerald Grant, MD (Lt. Col. (sep), MC, USAF)²¹, Odette Harris, MD, MPH²², Alan Hoffer, MD²³, Ryan Kitagawa, MD²⁴, Kerry Latham, MD (Col. (ret), MC, USAF)²⁰, Chris J. Neal, MD (CAPT (ret), MC, USN)²⁵, David O. Okonkwo, MD, PhD²⁶, Ross Puffer, MD (LCOL, MC, USA)²⁷, Jeffrey V. Rosenfeld, MD (MAJGEN (ret), RAAMC, ADF)^{28,29}, Guy Rosenthal, MD³⁰, Andres M. Rubiano, MD^{31,32}, Martina Stippler, MD³³, Max Talbot, MD (Col, RCMS, CAF)^{34,35}, Alex Valadka, MD³⁶, James Wright, MD³⁷, Gregory W. J. Hawryluk, MD, PhD^{2,4,38}

¹Avera McKennan Hospital and University Health Center, University of South Dakota School of Medicine, Vermillion, South Dakota, USA; ²Uniformed Services University, Bethesda, Maryland, USA; ³Department of Medicine, Pacific Northwest Evidence-Based Practice Center, Oregon Health & Science University, Portland, Oregon, USA; ⁴Brain Trauma Foundation, Palo Alto, California, USA; ⁵Department of Neurosurgery, University of Maryland School of Medicine, Baltimore, Maryland, USA; ⁶Stanford University, Palo Alto, California, USA; ⁷Department of Neurology, Kansas City University Medical Center, Kansas City, Kansas, USA; ⁸Uniformed Services University, Bethesda, Maryland, USA; (Continued on next page)

Correspondence: Gregory W. J. Hawryluk, MD, PhD, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University School of Medicine, Cleveland OH; Uniformed Services University, Bethesda, MD; Brain Trauma Foundation, Palo Alto, CA. Email: hawrylg@ccf.org

Received, July 10, 2025; **Accepted,** July 13, 2025; **Published Online,** February 16, 2026.

Neurosurgery 98:S6–S164, 2026

<https://doi.org/10.1227/neu.0000000000003738>

Copyright © 2026 Brain Trauma Foundation. Published by Wolters Kluwer Health, Inc. on behalf of the Congress of Neurological Surgeons. This is an open access article distributed under the [Creative Commons Attribution License 4.0 \(CC BY\)](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

BACKGROUND: Penetrating traumatic brain injury (pTBI) affects civilian and military populations resulting in significant morbidity, mortality, and health care costs. No up-to-date and evidence-based guidelines exist to assist modern medical and surgical management of these complex injuries.

METHODS: A preliminary literature search informed a need for updated guidelines. Methodologists experienced in TBI guidelines supported 2 co-chairs, a diverse steering committee and three expert working groups. Over half of our panelists were active service military or military veterans and they addressed twenty-six Key Questions (KQs). We searched Ovid MEDLINE®, EMBASE, and Cochrane CENTRAL from inception to August 31, 2022, reference lists, and clinical trial registries. Penetrating, perforating and tangential penetrating brain injuries were included. Predefined criteria were used to identify studies; pre-specified methods were used to assess study quality and strength of evidence for key outcomes. Effects were analyzed qualitatively and quantitatively where appropriate.

RESULTS: 125 studies provided evidence and another 80 studies provided contextual data for these guidelines. In general there was a paucity of literature and most of the identified evidence was judged to be high risk of bias due to study design. We did not identify any studies meeting inclusion criteria for 12 KQs. The highest quality evidence, rated moderate in strength, was identified for four KQs that covered: cerebral angiography vs computed tomography angiography, the relationship between bihemispheric injury in adult pTBI and mortality, the ability of the Surviving Penetrating Injury to the Brain (SPIN) score to predict mortality, and the relationship between infection and cerebrospinal fluid fistula. Evidence for most KQs came from case series.

CONCLUSIONS: The development of up-to-date evidence and consensus based clinical care guidelines and algorithms for pTBI provide guidance to care providers in the prehospital and emergency medicine, surgical and intensive care settings. Few moderately strong conclusions on the benefit of specific management strategies for penetrating brain injury could be made. Detailed reporting of patient outcomes in future studies could advance the field by providing greater evidence for specific treatments by patient population, mechanism of injury, severity of injury, and specific interventions employed.

KEY WORDS: Guidelines, Traumatic brain injury, Penetrating brain injury, Head trauma, Blast injury, Gunshot, Brain Trauma Foundation

I – DISCLAIMER OF LIABILITY

The information contained in the Brain Trauma Foundation Guidelines for the Management of Penetrating Traumatic Brain Injury (2nd Edition) reflects the current state of knowledge at the time of publication. The Brain Trauma Foundation, the Military Traumatic Brain Injury Initiative, and other collaborating organizations are not engaged in rendering professional medical services and assume no responsibility for patient outcomes resulting from application of these general recommendations in specific patient circumstances. Accordingly, the Brain Trauma Foundation and the Military Traumatic Brain Injury Initiative note that adherence to these clinical practice guidelines will not necessarily assure a successful medical outcome. The information contained in these guidelines reflects published scientific evidence at the time of completion of the guidelines and cannot anticipate subsequent findings and/or additional evidence and therefore should not be considered inclusive of all proper procedures and tests or exclusive of other procedures and tests that are reasonably directed to obtaining the same result. Medical advice and decisions are appropriately made only by a competent and licensed physician who must make decisions in light of all the facts and circumstances in each individual and particular case and on the basis of availability of resources and expertise. Guidelines are not intended to supplant physician judgment with respect to particular patients or special clinical situations and are not a substitute for physician-patient consultation. Accordingly, the Brain Trauma Foundation and the Military Traumatic Brain Injury Initiative consider adherence to these guidelines to be voluntary, with the ultimate determination regarding their application to be made by the physician in light of each patient's individual circumstances. The

views expressed in this document do not reflect those of the Uniformed Services University of Health Sciences, the Military Traumatic Brain Injury Initiative, the United States Army Medical Research and Development Command, the United States Army/Navy/Air Force/Marine Corps, the Department of Defense, and the United States Government.

II – CONFLICT OF INTEREST DISCLOSURE

Participants in the Brain Trauma Foundation Guidelines for the Management of Penetrating Traumatic Brain Injury (2nd Edition) underwent formal screening for conflicts of interest relevant to penetrating traumatic brain injury on three occasions. The first was at the outset of the project when prospective panelists were considered for inclusion in the expert working group. The second was at the in-person meeting in Bethesda, MD in September of 2023. The final occasion was just in conjunction with final approval of the document prior to submission of the work for peer review. On the first two occasions a formal paper document was completed and signed by participants. Project leadership reviewed the responses and found that no relevant conflicts of interest existed. The other authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this publication.

Panelists reported the following disclosures: Bradley Dengler contributed to this work as a part of the US government Military Traumatic Brain Injury Initiative (MTBI2) of Uniformed Services University. Stacy Shackelford contributed to this work as part of the US government US Air Force, 10th Medical Group, US Air Force Academy, CO. Deborah Stein received consulting fees from CSL Behring.

(Continued from previous page)

⁹Emergency Neurosciences, Department of Emergency Medicine, Marcus Trauma and Emergency Care Center, Grady Memorial Hospital, Emory University School of Medicine, Atlanta, Georgia, USA; ¹⁰Military Traumatic Brain Injury Initiative (MTBI2), Uniformed Services University, Bethesda, Maryland, USA; ¹¹University of Maryland School of Medicine, Baltimore, Maryland, USA; ¹²General Surgery, Department of Surgery, Sunnybrook Health Sciences Centre, University of Toronto; ¹³Inova Neuroscience and Spine Institute, Fairfax, Virginia, USA; ¹⁴Colorado Military Health System, Colorado Springs, Colorado, USA; ¹⁵Division of Informatics, Clinical Epidemiology and Translational Data Science, Pacific Northwest Evidence-based Practice Center, Oregon Health & Science University, Portland, Oregon, USA; ¹⁶WVU Medicine Department of Neurosurgery, WVU Medicine Children's Neuroscience Center, WVU Rockefeller Neuroscience Institute, Morgantown, West Virginia, USA; ¹⁷MedStar Washington Hospital Center, MedStar Georgetown University Hospital, Washington, District of Columbia, USA; ¹⁸Anaesthesia and Critical Care, Uniformed Services University, Bethesda, Maryland, USA; ¹⁹Discipline of Surgery, Memorial University, St. John's, Newfoundland and Labrador, Canada; ²⁰Walter Reed National Military Medical Center, Bethesda, Maryland, USA; ²¹Department of Neurosurgery, Duke University, Raleigh, North Carolina, USA; ²²Neurosurgery, Stanford University School of Medicine, Stanford, California, USA; ²³Department of Neurological Surgery, University Hospitals of Cleveland, Case Western Reserve University, Cleveland, Ohio, USA; ²⁴McGovern Medical School, University of Texas, Houston, Texas, USA; ²⁵Neurosurgery, Medical Center-Portland, Scarborough, Maine, USA; ²⁶Department of Neurological Surgery, University of Pittsburgh, Pittsburgh, Pennsylvania, USA; ²⁷Department of Neurosurgery, Walter Reed National Military Medical Center, Bethesda, Maryland, USA; ²⁸Department of Neurosurgery, The Alfred Hospital, Melbourne, Victoria, Australia; ²⁹Department of Surgery, Monash University, Melbourne, Victoria, Australia; ³⁰Hadassah-Hebrew University Medical Center, Jerusalem, Israel; ³¹Universidad El Bosque, Bogota, Colombia; ³²MEDITECH Foundation, Cali, Colombia; ³³Department of Neurosurgery, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts, USA; ³⁴McGill University Health Centre, Montréal, Québec, Canada; ³⁵Royal Canadian Medical Service, Canadian Armed Forces, Ottawa, Ontario, Canada; ³⁶Department of Neurological Surgery, University of Texas Southwestern Medical Center, Dallas, Texas, USA; ³⁷Department of Neurosurgery, Oregon Health and Sciences University, Portland, Oregon, USA; ³⁸Cleveland Clinic, Neurological Institute, Akron General Hospital, Fairlawn, Ohio, USA

ADF, Australian Defence Force; CAF, Canadian Armed Forces; CAPT, Captain; CDR, Commander; COL/Col, Colonel; LCdr, Lieutenant Commander; LCOL/Lt. Col./LCol, Lieutenant Colonel; MAJGEN, Major General; MC, Medical Corps; RAAMC, Royal Australian Army Medical Corps; RCMS, Royal Canadian Medical Service; ret, Retired; sep, Separated; USA, United States Army; USAF, United States Air Force; USN, United States Navy.

III – ACKNOWLEDGEMENTS

We wish to thank the United States Department of Defense and specifically the United States Army Medical Research and Development Command for funding our work (BA200139). We additionally thank the Henry Jackson Foundation and Department of Neurological Surgery at Walter Reed National Military Medical Center for their support of this work and our in-person meeting in Bethesda Maryland. We specifically wish to thank Dr. Eric Elster, Dean of the Uniformed Services University of Health Sciences for his warm welcome and institutional support. We additionally thank the Center for Neural Regenerative Medicine and the Military Traumatic Brain Injury Initiative for their kind assistance of our work and our in-person meeting. In particular we thank Drs. Bradley Dengler and Teodoro Tigno as well as Mr. Benson Akinsiku. Cristina Tecson in particular has our gratitude for her thoughtful and most capable assistance.

Numerous individuals made initial contributions to this work, which, while tremendously appreciated, were ultimately not sufficient for authorship based on pre-specified criteria. We thank Dr. Danielle Dang who provided assistance to Dr. James Ecklund.

The first edition pTBI guidelines were not created by the Brain Trauma Foundation. We thus thank the authors of the first edition of the pTBI guidelines including: Bizhan Aarabi, Tord D. Alden, J. Hunter Downs III, James M. Ecklund, Howard M. Eisenberg, Elana Farace, Robert E. Florin, John A. Jane, Jr., Mark D. Krieger, Andrew I. R. Maas, Raj K. Narayan, Alexander A. Potapov, Andres M. Salazar, Mark E. Shaffrey, Beverly C. Walters. We recognize and appreciate their creation of a high quality first edition document which served as a foundation for the 2nd edition guidelines. Permission to update the guidelines was provided by Beverly C. Walters. Our detailed review of the first edition and work to build upon that initial document has served as a strong foundation for us to build off of. We appreciate the perspectives of Drs. Bizhan Aarabi and Jim Ecklund who were authors on the first edition as well as the current second edition.

We also wish to thank medical personnel who courageously care for pTBI victims throughout all phases of care. pTBI victims generally have substantial and complex care needs throughout their recovery and beyond. These caregivers know best of all how excellent care translates to improved outcomes for these patients. We hope that our work provides medical personnel with evidence-based best practice recommendations and consensus expert opinion in the many instances where evidence is lacking. Most importantly we wish to thank those who serve, placing themselves in harms way, disproportionately falling victim to these most cruel of injuries.

The authors wish to express their most sincere gratitude to our patient representative, Joshua Cooley, and his mother, Christine Cooley. Sgt. (ret) Josh Cooley suffered a severe penetrating brain injury from an improvised explosive device while deployed to Iraq in 2005. He was initially stabilized by military neurosurgeons down range, after which he was transferred to Walter Reed for his ongoing neurosurgical care and subsequent cranial reconstruction. With the loving care of his mother, Josh made a remarkable recovery, eventually able to ride horses and sing on stage with Toby Keith. Josh and Christine attended our in-person guidelines consensus conference in September 2023, where they shared Josh's story and participated in aspects of guideline generation. One month later, and after 18 years of thriving and inspiring the countless individuals privileged to know him, Josh passed away. We are humbled by Josh's dignity, courage, and determination, and we will be forever grateful to both Josh and Christine for honoring our effort with their participation.

IV – INTRODUCTION

Penetrating traumatic brain injury (pTBI) is unique for its gravity, complexity and emergency. Physicians understand the inimitable challenge of pTBI which forces clinicians to confront unique, catastrophic and highly complex wounds with both little margin for error and great urgency for intervention. Sadly, in

ABBREVIATIONS: ABC, airway, breathing and circulation; AHRQ, Agency for Healthcare Research and Quality; AIS, abbreviated injury scale; AMR, antimicrobial resistance; AUROC, area under the receiver operating curve; AVF, arteriovenous fistula; BDI, brain death interval; BIT, brain injury time; BTF, Brain Trauma Foundation; CI, confidence interval; CNS, central nervous system; CPP, cerebral perfusion pressure; CSF, cerebrospinal fluid; CT, computed tomography; CTA, computed tomographic angiography; DSA, digital subtraction angiography; ED, emergency department; EEG, electroencephalography; EMS, emergency medical service; EPC, Evidence-based Practice Center; EVD, external ventricular drain; FB, foreign body; GCS, Glasgow Coma Scale; GCS-M, Glasgow Coma Scale-Motor Score; GFAP, glial fibrillary acidic protein; GOS-E, Glasgow Outcome Scale-Extended; GSW, gunshot wound; ICP, intracranial pressure; ICU, intensive care unit; IM, intramuscular; INR, international normalized ratio; IQR, interquartile range; ISS, Injury Severity Score; IV, intravenous; IVC, intravascular catheter; KQ, key question; LOS, length of stay; MAIS, maximum abbreviated injury scale; MAP, mean arterial pressure; MOI, mechanism of injury; MRA, magnetic resonance angiography; mREMS, modified Rapid Emergency Medicine Score; MRI, magnetic resonance imaging; MTBI², Military Traumatic Brain Injury Initiative; NBCA, N-butyl-2-cyanoacrylate; NPV, negative predictive value; NSE, neuron-specific enolase; NTDB, National Trauma Data Bank; OR, odds ratio; PAO, parent artery occlusion; PICOTS, populations, interventions, comparators, outcomes, timing, setting, and study design; PMMA, polymethylmethacrylate; PPV, positive predictive value; PT, prothrombin time; pTBI, penetrating traumatic brain injury; PTT, partial thromboplastin time; RCT, randomized control trial; REMS, Rapid Emergency Medicine Score; RR, relative risk; RTS, Revised Trauma Score; SAH, subarachnoid hemorrhage; SNP, single-nucleotide polymorphism; SOE, strength of evidence; SPIN, Surviving Penetrating Injury to the Brain; SSS, superior sagittal sinus; SWC, simple wound closure; TBI, traumatic brain injury; TEG, thromboelastography; TFL, tensor fascia lata; Ti, titanium; TICA, traumatic intracranial arterial aneurysm; TRISS, Trauma Score-Injury Severity Score; TS, transverse sinus; TXA, tranexamic acid; UCH-L1, ubiquitin carboxyl-terminal hydrolase L1 (aka PGP9.5); UFH, unfractionated heparin; VET, viscoelastic testing; VSP, vasospasm; VTE, venous thromboembolism; WHIS, War Head Injury Score; WOLST, withdrawal of life-sustaining treatments.

Supplemental digital content is available for this article at neurosurgery-online.com.

modern warfare pTBI has become a key and common wounding mechanism.¹ Few civilian neurosurgeons see enough pTBI to develop expertise or wisdom relevant to care of these challenging patients. High expertise in the management of these wounds resides with the armed forces and a handful of civilian centers which see violent injuries frequently.

Though pTBI is often thought of as synonymous with gunshot wounds to the head, pTBI encompasses any wounding mechanism in which a foreign body penetrates the skull and brain. This includes knives, tree branches, tear gas canisters, projectiles from improvised explosive devices, chopsticks, nails, unexploded ordnance and just about any other implement that you can imagine. These injuries are not only defined by the anatomy of the injury but also by the unique characteristics of the implement. White phosphorous rounds for instance, combust on exposure to air and present a particularly unique challenge to surgeons who need to remove them. Additionally, these injuries are not defined by the environment in which they are received. A penetrating head injury suffered from an explosion in the military is no different than one suffered in a civilian industrial or terrorist mediated explosion. The care provided should also be the same.

It is tremendously unfortunate that there is an epidemic of gun violence in America and other countries around the world.²⁻⁴ Gun violence is even increasing in countries in which it was exceedingly rare in the past.⁵ Civilian pTBI accounts for an estimated 20 000 deaths in the US each year with mortality in up to 90% of victims.^{2,3} Remarkably, mortality from pTBI is higher in the civilian population than in the military.⁶ The high lethality of civilian pTBI likely relates in part to the absence of protective gear and close-range mechanisms such as homicide and suicide. It may also relate to a less aggressive approach to the care of civilian patients.⁶

Ultimately, military to civilian translation has been critical to the advancements in care that we have seen in pTBI over the years. Most notably, the Vietnam war and the Lebanese conflict changed our approach to one of limited surgical debridement. Surgeons found that the neurologic morbidity inflicted on patients when an effort was made to remove all intracranial foreign bodies was not justified. Such fragments could be removed at a later time if they became the nidus of an infection. Further, a key impetus for this second edition is the finding that pTBI outcomes in recent conflicts may be better than in prior reports.^{1,7-13} It is suspected that this improvement in modern outcomes stems from a new very aggressive military care model which includes early cranial decompression and prevention of cerebrospinal fluid leak with skull base repair, aggressive detection and treatment of cerebrovascular injury as well as a multidisciplinary approach to cranial reconstruction.^{11,14,15}

There have been important advancements in brain injury care since publications of the first edition of these guidelines in 2001¹⁶ which support the need for an update and which are important to consider while reading this second edition. Perhaps most important has been increased attention to cerebrovascular injuries in both blunt TBI and pTBI.¹⁷ Rather than reactive to sequelae such as delayed hemorrhage or ischemic stroke it is now commonplace to screen patients for such pathologies and to initiate preventive

treatments when indicated. Similarly there has been advancement in and proliferation of endovascular techniques which are relevant to pTBI.¹⁴ Although open surgery for cerebrovascular lesions remains time-tested, increasingly sophisticated endovascular techniques have proliferated which offer the potential of parent vessel preservation rarely possible with open surgery. There has been advancement in prediction models for pTBI¹⁸ and advancement in neurocritical care practices. Brain oxygen monitoring has demonstrated promise¹⁹ and there has been increased recognition of the importance of cerebrovascular autoregulatory processes.²⁰ The pressure reactivity index²¹ is now widely used and complemented by the optimal cerebral perfusion pressure (CPP_{opt})²² and the possibility of other personalized treatment thresholds such as for intracranial pressure.²³

Another key impetus for this work was divergent opinions amongst neurotrauma experts on the need to screen for and treat penetrating traumatic vascular injury like pseudoaneurysms. We felt that much could be gained from the combination of a systematic review of published literature and the wisdom of world experts as to how and when such lesions should be screened for and if, when, and how they should be treated. Indeed, the feeling of our group is that the prevalence of complex vascular lesions defines pTBI and largely serves to distinguish it from blunt TBI.

The Brain Trauma Foundation (BTF) has produced guidelines for the management of TBI for over 25 years. Our first adult traumatic coma guidelines were the first guidelines ever published by a surgical specialty.²⁴ Our guidelines have been associated with a 50% reduction in mortality from TBI^{25,26} and we have addressed care for many TBI subtypes and care environments (www.braintrauma.org). Though the BTF did not produce the first edition of these guidelines¹⁶ we are grateful for permission to provide this update.²⁷ We aim to identify and disseminate best practices by identifying and synthesizing published evidence. The BTF has learned, however, that guideline users need more than an evidence report.^{20,28,29} They desire evidence synthesis and advice on how to bridge published evidence with the realities of care at the bedside. This guideline is thus the first ever BTF effort which merges evidence-based recommendations with consensus recommendations generated through a rigorous Delphi process. Indeed, the relative paucity of includable literature available for pTBI would have left little to be said if our process was restricted to the generation of recommendations based on evidence alone as the BTF has done in the past. We recognize that expert opinion has a history of being wrong in TBI care – e.g. “running patients dry” and hyperventilation are practices which were historically popular but which published literature now suggest are harmful.²⁸ We ask that readers understand the nature of the compromise inherent in providing expert opinion and to help clearly distinguish such opinion from evidence-based recommendations, they are presented in separate locations and clearly labelled as EXPERT OPINION.

Recognizing that treatment algorithms have been very popular aspects of past TBI guidelines,^{24,30,31} we felt that such treatment protocols could be of great assistance to physicians amidst the maelstrom that ensues when caring for pTBI patients and often

distract even from ingrained care protocols such as the ABCs and Advanced Trauma Life Support. Such algorithms were not included in some BTF products for a while because they are inherently not evidence-based.^{28,32} Feedback on recent BTF offerings has led us to reintroduce them. We felt that for pTBI such algorithms were best conceptualized as a common pathway which would be relevant to all patients, as well as toolkits that would be relevant for pTBI victims with specific problems.

When our work on this project first began in 2019 it was our great hope that these guidelines would never be needed – at least for wounds caused by intentional harm or international conflict. This hope was quickly dashed and our work is being completed at a time where the need for these recommendations is the greatest it has been in generations. We are aware that our draft recommendations are already being employed in ongoing conflicts prior to peer review which is an unfortunate reflection of the need for this work.

In completing this guideline project we learned a number of things. A remarkably small amount of high quality literature is available to inform pTBI care despite a relative flurry of publications stemming from the recent conflicts in the Middle East. Though many aspects of pTBI care are difficult to study, some aspects of care are readily amenable to investigation. Throughout this work we have tried to highlight the many gaps in knowledge and where we think investigations filling these gaps could easily be completed. In reality there is a great dearth of publications which are driven by a hypothesis or comparison. Too many publications are mere descriptive case series of institutional experiences with these ‘exotic’ cases that fail to meaningfully advance knowledge or patient care. It is time for the bar to be raised. Authors must aim higher and editors should reject non-informative works. Data reporting standards must be improved. Many of the studies we examined failed to report key details that would have helped us to inform our key questions. Going forward we must do better.

Ultimately, the most important patient care factor that emanated from our discussions was the belief in the supreme importance of aggressive care and avoiding nihilism. Nihilism is very common with pTBI care. Some surgeons automatically judge that a gunshot wound to the head is non-survivable despite the fact that good outcomes can be achieved in many patients if afforded the opportunity of aggressive care. The prior guidelines actually noted that, excluding those that die prior to or immediately upon reaching hospital care, outcomes of survivors of closed and penetrating brain injury at matched neurologic injury severity are the same.³³ Indeed, the impetus for the development of the Surviving Penetrating Injury to the Brain (SPIN) score was to combat inappropriately nihilistic views of some clinicians by demonstrating that good outcomes are often achievable in these patients.¹⁸ Numerous members of the military espoused the view that the good outcomes in military patients – which are achieved despite high caliber weaponry – are a result of extremely aggressive care and a lack of hesitation to provide this aggressive care.¹⁰ The avoidance of nihilism may thus be the single most important message that we wish to convey in these guidelines.

The first edition of these guidelines^{16,33} were structured similarly to the 2nd edition of the BTF’s adult coma TBI guidelines. It contained chapters on:

- Neuroimaging in the Management of Penetrating Brain Injury
- Intracranial Pressure Monitoring in the Management of Penetrating Brain Injury
- Surgical Management of Penetrating Brain Injury
- Vascular Complications of Penetrating Brain Injury
- Management of Cerebrospinal Fluid Leaks
- Antibiotic Prophylaxis for Penetrating Brain Injury
- Antiseizure Prophylaxis for Penetrating Brain Injury

It also contained a large section on prognosis³³ which examined:

- Prognostic Indicators
- Age
- Cause of Injury
- Mode of Injury
- Caliber of Weapon
- Hypotension
- Coagulopathy
- Respiratory Distress
- Level of Consciousness and Glasgow Coma Scale

The present second edition has been expanded to include sections related to prehospital and emergency care, surgical management as well as intensive care. We believe that in addition to providing more comprehensive recommendations than in the first edition there are some important areas of advancement contained herein. These pTBI guidelines support aggressive screening for and treatment of traumatic pseudoaneurysms. We recommend the use of angiography over computed tomographic angiography (CTA) in most instances. Despite old dogma that a wall-less pseudoaneurysm cannot be coiled, we note that this approach is not only viable but preferred as it preserves the parent vessel, with the caveat that coiling often needs re-treatment. We also found evidence supporting that every effort should be made to avoid a cerebral spinal fluid leak even if it requires placement of non-vascularized foreign materials, as it reduces the risk of infection and improves outcomes. We now also recommend more selective use of antibiotic prophylaxis than in the last edition. Perhaps most importantly, we recommend basing initial surgical decision making on medical futility rather than what we “think” the prognosis or ultimate outcome might be. Indeed, recent publications suggest that decisions related to withdrawal of life-sustaining therapies are being made too soon, and that even 72 h may be too soon.³⁴

We hope that our rigorous evidence-based work helps physicians and patients and that a much more robust body of literature is available to inform a future update of these guidelines. We are encouraged by new efforts to study pTBI care and believe that high quality prospective registries and trials in both military and

civilian environments have great potential to advance care. Indeed, the dearth of evidence in this domain means that even a single high quality manuscript can be very impactful as was revealed several times in developing these guidelines.

V – METHODOLOGY

The methodology presented herein reflects an evolution of established BTF practices.²⁵ While some Level 3 recommendations in early guidelines could be considered evidence-informed expert opinion, more recent efforts have removed expert opinion to align with modern standards for rigor.²⁸ Though treatment algorithms were the most popular and reproduced aspect of early guidelines,^{30,31} they were removed from recent efforts as they are inherently not evidence-based and require distinct methodology to construct with rigor.^{28,32} Though the methodologic rigor of the BTF's recent guidelines has been praised, the lack of practical advice for practitioners at the bedside has been a point of criticism.²⁸

To provide a bridge between our evidence-based recommendations and the realities of patient care, this guideline re-introduces expert opinion. We have, though, endeavored to provide a clear distinction for the reader between recommendations which are derived from evidence and statements derived from expert consensus. The recently published algorithms of the Seattle International severe traumatic Brain Injury Consensus Conference (SIBICC) provide a template for the rigorous development of a treatment algorithm.^{20,29} In an effort to be useful to clinicians who are challenged by pTBI – which generally portend a unique combination of high emergency and high surgical complexity – we additionally provide treatment algorithms which aim to provide guidance for the care all pTBI patients will need, as well as algorithmic ‘toolkits’ for specific challenges that will only be applicable to some patients. To reduce bias our methods for this work were previously published.²⁷ These methods are re-presented here. Additional methodologic details are presented in online-only appendices A to D (**Supplemental Digital Content 1** [<http://links.lww.com/NEU/F7>]), E (**Supplemental Digital Content 2** [<http://links.lww.com/NEU/F8>]), F (**Supplemental Digital Content 3** [<http://links.lww.com/NEU/F9>]), G (**Supplemental Digital Content 4** [<http://links.lww.com/NEU/F10>]) and H (**Supplemental Digital Content 1** [<http://links.lww.com/NEU/F7>])).

Key Definitions

pTBI is defined as a head injury with violation of, at minimum, the skull, the dura and brain by a foreign body. Linear non-displaced skull fractures alone, which result from a relevant wounding mechanism, are NOT included. pTBI encompasses penetrating, perforating and tangential injuries.

- Penetrating injuries involve penetration of the skull and dura with the foreign body remaining within the skull such that there is no exit wound.
- Perforating injury is characterized by a through and through injury with both entry and exit wounds.
- Tangential injury occurs when a foreign object glances off the skull commonly driving skull fracture fragments into the brain.

pTBI has previously been subclassified as high velocity missile, low velocity missile and non-missile injuries. However, because of the practical difficulty distinguishing high and low velocity missile injuries clinically, we instead subclassify pTBI mechanistically as:

1. “missile injuries” (eg. gunshot wounds)
2. “blast fragment injuries” (ie. type II Blast injury – blast over-pressure plus fragment injury)
3. “low-velocity injuries” (eg. knives).

Our working group ratified the latter classification scheme with a blinded consensus vote.

Development of an Expert Workgroup

BTF leadership, as well as civilian and military clinicians with expertise in pTBI, comprise the pTBI Expert Workgroup. Approximately half of the expert workgroup were active service military members from the United States and Canada. Of civilians constituting the remaining half, a large proportion were retired members of the armed forces. The workgroup and its efforts are led by two co-chairs with guidance from a Steering Committee. Workgroup members were selected for diversity among disciplinary expertise relevant to the management of TBI, scientific expertise, and demographic and geographic representation. Represented medical disciplines include neurosurgery, plastic surgery, neurology, general/trauma surgery, orthopedic surgery, as well as emergency medicine, physical medicine, pediatrics, prehospital care, and rehabilitation. A military medic and a patient (service member recovered from a pTBI) were included. Gender and ethnic diversity was also specifically sought. Two panelists have pediatric-focused neurosurgical practices. Workgroup members were divided into three areas of clinical focus: Pre-Hospital and Emergent Management, Surgical Management, and Medical Management. The Prehospital section might be considered a ‘Preadmission’ section as it incorporates care provided in the emergency room; it was led by ALB and DW. The Surgical section was led by BA. The Intensive Care Section was led by HM and JG. Governance was provided by a core multidisciplinary steering committee who were empowered to change any project plans or personnel with a majority vote in order to ensure successful completion of the project and a high quality product.

Systematic Review

Purpose of Review

The last iteration of the guidelines published in 2001¹⁶ outlined the best-evidence treatment recommendations for neuroimaging, intracranial pressure (ICP) monitoring, surgical management, antibiotic prophylaxis, management of CSF leak, seizure prophylaxis, and prognosis following pTBI.³³ Despite the passage of over two decades since publication and identification of the knowledge gaps, the socioeconomic and healthcare impact of pTBI remains substantial both in the United States and globally. Efforts to address pTBI have included advancements in pre-hospital and emergency care, neurocritical care, neurosurgical techniques, and rehabilitation, although the optimal treatment strategies remain undefined and no widely accepted treatment algorithms exist. pTBI has emerged as a particularly important wounding mechanism in modern military conflicts. Moreover, a new paradigm of aggressive pTBI patient care has emerged in the armed forces which is believed to be responsible for the excellent outcomes being seen as compared with civilian populations suggesting that a new effort at military to civilian translation may be beneficial.¹⁴ Even with modern care, rates of morbidity and mortality remain high in both civilian and military populations.^{2,10}

This systematic review was designed and executed to provide the evidence base for the development of an updated clinical practice guideline for the management of penetrating brain trauma for both military and civilian patients by the BTF. BTF obtained funding and convened a panel of international experts who established the scope of the project by developing the initial topics and questions for the review. The

Pacific Northwest Evidence-based Practice Center (EPC) conducted the systematic review.

Key Questions

The review is defined by 46 Key Questions (KQs) that address prehospital management, diagnosis, prognosis, critical care, and surgical management of patients with pTBI. The KQs were first drafted by the guideline panel in conjunction with the EPC review team and initially included 44 KQs (Appendix A). Over the course of the review and after discussions with the guidelines panel members, two KQs were added (and the KQ numbering adjusted) and minor edits were made to some of the existing KQs to clarify inclusion of interventions. Upon further discussions with the guideline panel members KQs 8 to 11, 21, 23, 26, and 40 were dropped due to prioritization of more important KQs, however the KQs were not renumbered. The KQs are below. Italicized KQs were dropped from this review. KQs 45 and 46 were added.

Prehospital Key Questions

Diagnosis/diagnostic accuracy

1. In patients with head injury, what is the accuracy of screening for diagnosis of pTBI (e.g., Glasgow Coma Scale [GCS], pupil response/size/symmetry, biomarkers [e.g., s100b, ubiquitin carboxyl-terminal hydrolase L1 (aka PGP9.5) [UCH-L1], glial fibrillary acidic protein [GFAP], tau, neuron-specific enolase [NSE], neurofilament/NF-1, cytokine, single-nucleotide polymorphism [SNP], electroencephalography [EEG]]), clinical exam, imaging techniques (e.g., MRI, computed tomography [CT], plain films)?
2. In patients with pTBI, what is the diagnostic accuracy of imaging to detect pseudoaneurysms?
3. In patients with pTBI, what are the benefits, harms and diagnostic accuracy of screening with cerebral angiography to diagnose traumatic intracranial arterial aneurysms and cerebral vasospasm (VSP)?
4. In patients with pTBI, when should cerebral angiography best occur and is it preferred over CT angiography (CTA)?
5. Does the diagnostic accuracy of screening for pTBI differ based on patient characteristics (e.g., age, gender, military status) or injury characteristics (e.g., mechanism of injury, location of injury)?
6. In patients with head injury and no obvious penetration of the skull, what are the benefits and harms of screening for pTBI vs no screening?
7. In patients with pTBI and the possibility of metal within the skull, what is the safety of MRI?

Prognosis

8. *In patients with pTBI, what factors related to the scene of injury (e.g., distance/time to trauma centers including rural and austere settings, prolonged field care, transport mode/factors, expertise of pre-hospital providers) impact morbidity and mortality?*
9. *What clinical characteristics (e.g., demographics, mechanism of injury, characteristics of geographic site of injury, vital signs, blood loss, neurological deficit, location of head injury, other injuries) of patients with pTBI are associated with salvageability or non-salvageability (patients or organs) that can be determined in early clinical settings including the field, the emergency department (ED), and austere environments?*
10. *What mechanisms of pTBI place a patient at higher risk for poor outcomes?*

11. *In patients with head injury, do on-scene trauma triage and assessments correctly identify pTBI patients with better or worse outcomes including death within 24 hours?*
12. In patients with pTBI, what imaging findings are associated with morbidity, mortality, quality of life, and function?
13. What is the diagnostic accuracy of instruments and models (e.g., SPIN score) in predicting survival in pTBI?

Initial management

14. In patients with pTBI, what are the benefits and harms of pre-hospital and ED resuscitation strategies (e.g., correction of coagulopathy, cardiopulmonary resuscitation, airway maneuvers, oxygen administration, cervical spine immobilization, specific fluid administration including hypertonic saline, mannitol administration, pain management, hyperventilation, posture), including the prevention of secondary injury (e.g., cerebral edema, diffuse axonal injury)?
15. In patients with pTBI, what patient and scene-related factors indicate a definitive airway is needed compared with no or non-invasive ventilation?
16. In patients with pTBI who require intubation, what are the benefits and harms of sedation and analgesia?
17. In patients with pTBI, what are the benefits and harms of on-scene wound care of head injury?
18. In patients with pTBI, what are the benefits and harms of early initiation (prehospital and ED) of antibiotic prophylaxis?
19. In patients with pTBI, what are the benefits and harms of treatment in the prehospital and ED with tranexamic acid, antiseizure prophylaxis, and pressor support?
20. In patients with pTBI, what are the benefits and harms of routine evaluation with thromboelastography and correction of coagulopathies?
21. *In patients with pTBI, what are the benefits and harms of a 24-hour or more delay in evaluation by a neurosurgeon?*
22. How should treatment be modified if field care is prolonged (>24 hours)?
23. *Do the effects of treatment for pTBI differ based on patient characteristics (e.g., age, gender, military status) or injury characteristics (e.g., mechanism of injury, location of injury)?*

Critical Care Key Questions

Intracranial pressure

24. In patients with pTBI, what are the benefits and harms of ICP monitoring?
25. In patients with pTBI, what blood pressure thresholds should be used for ICP and cerebral perfusion pressure?
26. *In patients with pTBI, what are the benefits and harms of treating intracranial hypertension (e.g., hyperosmolar therapy, lumbar drainage, ventilation therapies) in the critical care (i.e., intensive care unit) setting?*

Prophylaxis

27. In patients with pTBI, what are the benefits and harms of seizure prophylaxis, either initiated or continued, in the critical care setting?
28. In patients with pTBI, what are the benefits and harms of antibiotic prophylaxis, either initiated or continued, in the critical care setting?
29. In patients with pTBI, what are the benefits and harms of deep vein thrombosis prophylaxis?

Other

30. In patients with pTBI, what are the benefits and harms of screening for delayed vascular complications?
31. In patients with head injury, when should organ donation occur?
32. In patients with pTBI, what are the benefits and harms of rehabilitation (e.g., physical, speech, occupational therapy) and when should rehabilitation be started?

Surgery Key Questions

Timing of surgery

33. In patients with pTBI who are neurologically stable, what are the benefits and harms of delaying surgery for better operative conditions?
34. In patients with pTBI, what are the benefits and harms of urgent surgical decompression/craniectomy vs a period of observation prior to decompression?

Type of debridement

35. In patients with pTBI, what are the benefits and harms of local debridement and closure?
36. In patients with pTBI what are the benefits and harms of retained bone or metal fragments, or removal of retained/embedded objects (e.g., blade)?
37. In patients with pTBI, what are the benefits and harms of radical (brain debridement, deep fragment removal) vs conservative debridement (local irrigation and closure)?
45. In patients with pTBI, what are the benefits and harms of obtaining intraoperative cultures to determine appropriate antibiotic treatment?

Prevention of cerebral spinal fluid leaks

38. In patients with pTBI, what are the benefits and harms of watertight closure of the dura, with or without graft, to prevent cerebral spinal fluid (CSF) leak in the setting of exposure of cisterns or the ventricular system?
39. In patients with pTBI, what are the benefits and harms of CSF diversion?

Cranioplasty/facial surgery

40. In patients with pTBI, what are the benefits and harms of autologous cranioplasty vs use of alloplastic implants (i.e., titanium, methyl methacrylate, polyetheretherketone)?
41. In patients with pTBI, what are the benefits and harms of early vs delayed cranioplasty?
42. In patients with pTBI and facial injury, what are the benefits and harms of a multidisciplinary approach to pTBI surgery/management?

Traumatic cerebrovascular injury

43. In patients with pTBI, what are the benefits and harms of endovascular coil occlusion to reduce risk of rupture, in the setting of a traumatic aneurysm?
44. In patients with pTBI, what are the benefits and harms of surgical or endovascular management of venous sinus injuries to prevent venous infarction?
46. In patients with pTBI, what are the benefits and harms of surgery to reduce risk of rupture, in the setting of a traumatic aneurysm?

Search Strategies

We conducted electronic searches in Ovid MEDLINE®, EMBASE, and Cochrane CENTRAL from inception to August 31, 2022 (Appendix

A). We reviewed reference lists of systematic reviews for additional studies and the guidelines panel members provided references from their own hand searching. We also included studies from recent world conflicts that were published after the search dates as they became known to us.

Inclusion and Exclusion Criteria

Criteria were established *a priori* to determine eligibility for inclusion and exclusion of abstracts in accordance with the protocol developed by the guidelines panel. The criteria for inclusion and exclusion of studies for this systematic review are based on the KQs and PICOTS (Table 1).

For this review the population of interest was patients of any age with pTBI defined as a head injury that penetrated the dura and inflicted brain injury. This included studies of penetrating, perforating, and tangential injuries by any mechanism that addressed one or more of the KQs. Included interventions were screening for and diagnosis of pTBI, pre-hospital care, including on-scene wound care and resuscitation, medical management, including ICP monitoring and treatment, as well as seizure and antibiotic prophylaxis, and surgical management, which included management of CSF leaks, vascular injuries, and foreign body removal. We included all comparators and single arm studies with no comparator, if higher quality evidence was not available. Outcomes included accuracy of screening of diagnostic tools, mortality, neurological function, and morbidity and needed to be reported within 1 year of injury. We did not include outcomes of satisfaction, quality of life, sleep, or determining brain death. Because of the limited body of evidence it was decided *a priori* to include all study designs, including trials and observational studies that included case series and case reports when no other evidence was available. We did not include studies conducted in rehabilitation settings, but otherwise included all other settings (e.g., prehospital, battlefields, medical centers).

To ensure accuracy, all excluded abstracts were dual reviewed by two investigators. Each full-text article was independently reviewed for eligibility by two team members. All disagreements were resolved through consensus by two or three members of the systematic review team.

Study Selection

After full-text papers were retrieved and initial inclusion and exclusion screening was performed by the EPC, guideline panel members were assigned each KQ and reviewed the included articles to determine if the studies applied to their assigned KQ(s). This served as a double check of the evidence to help ensure no studies that provided evidence for any KQ were overlooked.

Risk of Bias Assessment of Individual Studies

Predefined criteria were used to assess the risk of bias (also referred to as quality or internal validity) for each individual included study, using criteria appropriate for the study design based on the Agency for Healthcare Research and Quality Methods guide, the Cochrane Back and Neck Group, and the U.S. Preventive Services Task Force (Appendix A). Each study was independently reviewed for risk of bias by two EPC members. Any disagreements were resolved through consensus. Based on the risk of bias assessment, included studies were rated as having “low,” “moderate,” or “high” risk of bias. Studies rated high risk of bias were not excluded *a priori*, but were considered to be less reliable than low or moderate risk of bias studies when synthesizing the evidence. Formal risk of bias assessment of case series and case reports was not done as these were determined to have high risk of bias due to study design.

TABLE 1. Table of Inclusion and Exclusion Criteria for PICOTS

PICOTS	Inclusion	Exclusion
Populations	All ages pTBI including blast, tangential, and perforating injury • All baseline GCS • Mixed types of brain injury with $\geq 85\%$ penetrating if results not reported individually All head injury included for KQs 1, 6, 11, 31	• Nonhuman studies • Injury limited to linear, nondisplaced skull fracture • Mixed types of brain injury with results not presented by injury type and $< 85\%$ are penetrating injury • Facial penetrating injuries, without penetrating the brain • Organ donation patients without a head injury
Interventions	Pre-hospital, prolonged field care, transport, ED, and trauma center evaluation: • Screening for and diagnosis of pTBI • Initial resuscitation and prevention of secondary injury • On-scene wound management • Cervical spine immobilization Surgical management: • Cerebrospinal leaks • Vascular injuries • Foreign body removal Medical management: • Intracranial hypertension monitoring • Intracranial hypertension treatment (hyperosmolar therapy, lumbar drainage, CPP management including BP thresholds, ventilation therapies) • Seizure prophylaxis • Antibiotic prophylaxis • DVT prophylaxis • Chemoprophylaxis for stroke prevention	• Repair of globe exclusively or ophthalmologic surgery only • Jaw, molar, dental repair only • Plastic surgery, reconstruction only • No intervention or screening
Comparators	All comparators or no comparator	No exclusion by comparator
Outcomes	• Mortality • Neurological function • Selected morbidity • Cost • Accuracy of screening or diagnostic tools (e.g., sensitivity, specificity, AUROC, etc.)	• Satisfaction • Quality of life • Sleep • Determining brain death
Timing	Outcomes up to 1-y post injury	Outcomes > 1 -y post injury
Setting	Prehospital, trauma center, medical, surgical setting in all countries. Battlefield and mass causality as well as civilian	• Rehabilitation setting
Study Designs	• All experimental study designs, observational studies including case series and case report • Epidemiological studies for salvageability • Current, well-conducted systematic reviews (may also use systematic reviews to pearl for studies searches may have missed) • Autopsy studies (KQ 7 only)	• Abstracts, comments letters, conference proceedings • Non-English language • Narrative reviews • Systematic reviews not meeting inclusion criteria • Autopsy studies for all other KQs

AUROC, area under the receiver operating curve; BP, blood pressure; CPP, cerebral perfusion pressure; DVT, deep vein thrombosis; ED, emergency department; GCS, Glasgow Coma Scale; KQ, key question; PICOTS, population, intervention, comparator, outcomes, timing, setting, study design; pTBI, penetrating traumatic brain injury.

Data Abstraction and Synthesis

For studies meeting inclusion criteria, evidence tables were constructed with the following data: study design, year, setting, country, sample size, patient characteristics (e.g., military vs civilian, age, race, mechanism of injury), and outcomes. All study data were verified for accuracy and completeness by a second team member. Additional details on data abstraction and synthesis see Appendix A.

Grading the Strength of the Body of Evidence

The strength of evidence (SOE) for each body of evidence was assessed as high, moderate, low, very low or insufficient, using the approach described in the Agency for Healthcare Research and Quality Methods Guide,³⁵ based on study limitations, consistency, directness, precision, and reporting bias. These criteria were applied regardless of whether evidence was synthesized quantitatively or qualitatively. SOE ratings reflected our confidence or certainty in the findings. For example, very low SOE means that we have very low confidence that future research will not change the findings. SOE was considered insufficient when evidence was lacking, sparse, or too conflicting such that we were unable to draw conclusions. SOE was initially assessed by one researcher and confirmed by a second. Descriptions of criteria and overall grades are described in full in Appendix A.

Development of Recommendations

The development of recommendations was the next step after the evidence was identified and synthesized and rated for risk of bias. Evidence-based recommendations are based on the quality of the body of evidence, applicability and generalizability. For topics where there is little or no research, recommendations were developed using rigorous Delphi consensus methodology.

Recommendations were assigned a level based on the quality of the body of evidence. We recognized five levels of recommendation based on the quality of the body of evidence:

- Level I recommendations are based on high quality of the body of evidence
- Level II recommendations are based on moderate quality of the body of evidence
- Level III recommendations are based on low quality of the body of evidence
- Level IV recommendations are based on very low quality of the body of evidence
- Level C: expert opinion recommendations based on consensus in the absence of research evidence

Delphi Process for Consensus

The rigorous consensus process employed in the generation of the SIBICC algorithms was replicated for this project which included overlapping leadership and participants. Blinded consensus voting was conducted to establish consensus statements complementing evidence-based recommendations. The same voting process was also used to ratify items for development of our consensus-based algorithms. As with the SIBICC algorithms,^{20,29} SurveyMonkey was used for voting prior to and subsequent to the in-person investigator meeting. At the in-person investigator meeting *Electronic Meeting Services* was hired to provide an independent consultant without medical expertise to perform the blinded voting using electronic

keypads. Panelists ratified a threshold of 80% to declare consensus as having been achieved where at least 80% of the panel participate in the vote. This is the same threshold used for consensus in the recent SIBICC effort.^{20,29} Investigators met in Bethesda in a conference center generously provided by the Henry Jackson Foundation for five days on September 4-8, 2023 for intensive in-person discussion and work to advance all aspects of the project.

Overall Results

Results specific to each KQ are presented in relevant chapters. The systematic review used in our work is available as an online-only supplement (**Supplemental Digital Content 5** [<http://links.lww.com/NEU/F11>]). Overall, a total of 6078 references from electronic database searches and manual searches were reviewed and 1923 full-text papers were evaluated for inclusion. We included a total of 125 studies in 135 publications, 29 were non-randomized studies, 85 single arm (case series) studies, and 11 case reports. A flow diagram of the search results and selection of studies is in Appendix B, a list of included studies is in Appendix C, and a list of excluded studies is in Appendix D. Evidence tables with study characteristics and detailed results are in Appendix E and risk of bias ratings for individual studies are in Appendix F.

Eighty-three studies (in 84 publications) were in civilian populations, and of these 48 were conducted in the United States; nine in South Africa; three in Brazil; two each in Canada, Colombia, Iraq, Israel, Lebanon, Switzerland, and Turkey; and one each in Afghanistan, China, Finland and Sweden, France, Iran, Italy, Palestine, South Korea, and Syria. Most civilian studies (57%, 32/56) reporting GCS scores reported the proportion of participants at specific scores or ranges of scores (e.g., GCS 3-8, GCS 9-12, and GCS 13-15) and did not report a mean or median score of the population. Fourteen studies reported mean admission GCS scores ranging from 6.7 to 14 and seven studies reported median admission GCS scores ranging from 3 to 10. One of these studies was rated low risk of bias, 23 were rated moderate risk of bias, while 58 were rated to be high risk.

Twenty-eight studies (in 36 publications) were in military populations, and of these three were conducted in the United States; three each in Iran, Turkey, and Vietnam; two each in Iraq, Syria, Croatia, and Ukraine; and one each in India, South Korea, South and North Korea, and Iraq and Iran. Similar to civilian studies, most military studies (61%, 11/18) reporting GCS scores reported the proportion of participants at specific scores or ranges of scores and did not report a mean or median score of the population. Seven studies reported mean GCS scores ranging from 7.5 to 10 and one study reported a median GCS score of 5. Two of these studies were rated moderate risk of bias, while 26 were rated high risk of bias.

Fourteen studies (in 15 publications) included both civilian and military populations; one was conducted in the United States; three in Croatia; two each in Lebanon, Israel, and Turkey; and one each in China, Egypt, Vietnam, and one Vietnam and the United States. One of these studies was rated moderate risk of bias, while 13 were rated high. As with the other populations, most of these studies (87%, 7/8) reporting GCS scores reported the proportion of participants at specific scores or ranges of scores and did not report a mean or median score of the population. One study reported a mean admission GCS score of 10 with a range from 3 to 15.

Two papers of the same population were conducted during the Lebanese conflict and the population was presumed civilian, but not

specifically reported. This study is included with the civilian counts. Eighteen civilian studies reported race, White patients ranged from 22% to 85% of the population, Black patients ranged from 15% to 92%, Hispanic patients from 0% to 84%, Asian patients from 0% to 3%, and other unspecified or unknown races from 0.8% to 23%. The studies of military personnel and mixed civilian and military patients did not report race, additional characteristics of the patients included in these studies is reported in Table 2.

The studies of civilian populations addressed 25 of the KQs, while the studies of military populations addressed 11 KQs. Mortality was the outcome reported most often in studies, with infections, seizures, imaging findings, and prediction of survival with instruments or models, also often reported. Outcomes included and reported are different based on each KQ and sample sizes for the same study may be different for KQs based on the population included for each KQ. Results are reported in order of KQ, even though some KQs may relate to each other and have substantial overlap in included studies. Since we did not renumber the KQs when some were dropped, those that were dropped are noted in their location in the sequence of KQs as a reminder.

Numerous blinded surveys were conducted in conjunction with our Delphi consensus-process. Results of 5 online SurveyMonkey surveys conducted prior to our in-person meeting are available as online-only supplemental content (**Supplemental Digital Content 6** [<http://links.lww.com/NEU/F12>], **Supplemental Digital Content 7** [<http://links.lww.com/NEU/F13>], **Supplemental Digital Content 8** [<http://links.lww.com/NEU/F14>], **Supplemental Digital Content 9** [<http://links.lww.com/NEU/F15>], and **Supplemental Digital Content 10** [<http://links.lww.com/NEU/F16>]). Results of voting conducted during our in-person meeting are also provided (**Supplemental Digital Content 11** [<http://links.lww.com/NEU/F17>] and **Supplemental Digital Content 12** [<http://links.lww.com/NEU/F18>]). Two online SurveyMonkey surveys were conducted subsequent to the in-person meeting in conjunction with the review process (**Supplemental Digital Content 13** [<http://links.lww.com/NEU/F19>] and **Supplemental Digital Content 14** [<http://links.lww.com/NEU/F20>]).

Summary of Key Findings

Twenty-six KQs were addressed in this review (Table 3): 125 studies provided evidence and another 80 studies provided contextual data from studies that did not meet criteria for inclusion but provided helpful information. Most of the evidence was of very low strength (meaning we have very low confidence in the certainty of effect) due to study design (e.g., case series, case reports) and/or few studies meeting inclusion criteria that answered the KQ (KQ31 and Appendix G). We did not identify any studies meeting inclusion criteria for 12 KQs (KQs 5, 6, 16, 17, 19, 22, 27, 32, 33, 39, 42, and 45). The highest quality evidence, rated moderate SOE (meaning we have moderate confidence that future research will not change the findings), was identified for four KQs (KQs 4, 12, 13, and 38) that covered: digital subtraction angiography vs CTA, the relationship between bihemispheric injury in adult pTBI and mortality, the ability of the SPIN score¹⁸ to predict mortality, and the relationship between infection and CSF fistula, respectively. Preliminary work on KQ26 did not demonstrate that pTBI should be managed differently than other forms of TBI and we chose not to pursue work on KQ26 further. In the course of our work KQ20 was moved to ICU section, KQ 24-25 were combined and KQ30 was combined with KQ3.

Strengths and Limitations

Evidence for head injury care is generally accepted to be lacking compared with other fields of medicine, but this is especially true for penetrating brain injury. This guideline project thus employed liberal inclusion criteria needed to identify what evidence does exist. As a result, evidence for some KQs included case series and case reports. Appropriately, such evidence enabled only uniformly low level recommendations and consensus statements. In addition, the inclusion of case reports in this guideline highlights the need for higher quality future evidence focusing on interventions and the exploration of hypotheses. Another strength is that members of the guideline panel provided an additional review of the literature, effectively double checking that no relevant studies were overlooked by the systematic review team.

TABLE 2. Characteristics of Patients in Included Studies by Population

Population	% Male ^a	Mean age, years ^a	MOI ^b	Etiology ^b
Civilian (k = 83)	0-100 (k = 75)	8.5-62 (k = 70)	k = 80 GSW: 86% (k = 69) Blast: 8.7% (k = 7) Low-velocity: 24% (k = 19)	k = 43 ^c Self-inflicted: 70% (k = 30) Assault: 84% (k = 36) Accident: 67% (k = 29)
Military (k = 28)	89-100 (k = 23)	20-35 (k = 19)	k = 28 GSW: 93% (k = 26) Blast: 75% (k = 21) Low-velocity: 18% (k = 5)	k = 28 Assault: 100%
Mixed, both (k = 14)	77-100 (k = 10)	18-34 (k = 10)	k = 11 GSW: 100% (k = 11) Blast: 54% (k = 6) Low-velocity: 9% (k = 1)	k = 4 Assault: 100% (k = 4) Accident: 33% (k = 1)

^aReported as range in studies, number of studies reporting this characteristic is presented in parentheses.

^bReported as number of studies reporting any type of the characteristic and number of studies reporting each specific type of characteristic. The percentages represent the percent of people with that characteristic of the studies reporting that characteristic (either mechanism of injury (MOI) or etiology) in each population. Studies may have reported injuries of multiple types of MOIs and etiologies.

^cSome studies reported the number of injuries from only one etiology that did not include the total population.

TABLE 3. Summary of Evidentiary Base for PICOTS Questions

KQ/Outcome # & Type of studies (N)	No. of studies: military/civilian/ Mixed	Location (Country/ Region)	Type of MOI (GSW, Blast, others)	Main Findings	Study limitations (RoB)	SOE rating
KQ 1/Diagnostic accuracy of screening for pTBI 1 NRS (179)	1/0/0	Switzerland	Stab	Sensitivity: 27.34% (19.84–35.92%); Specificity: 100% (93.02–100%); PPV: 100% (90–100%); NPV: 35.42% (33.03–37.88%); NLR: 0.73 (0.65–0.81); Accuracy: 48.04% (40.53–55.62%); pTBIs detected on X-ray vs CT: 19.5% (35/179) vs 71.5% (128/179); pTBIs missed by X-ray: 80% (93/128)	High	Very low for X-ray not being accurate at identifying pTBI
KQ 2/Diagnostic accuracy of imaging to detect pseudoaneurysms 1 retrospective NRS (45) 1 prospective NRS (73)	2/0/0	United States	GSW, stab, other	Sensitivity, specificity, PPV, NPV all 100%; AUC 1.0 for retrospective study CTA correctly identified 15% (2/13) pseudoaneurysms, misdiagnosed 15% (2/13), and missed 69% (9/13) in prospective study	Moderate	Insufficient for precise diagnostic accuracy Low for the ability of CTA to detect some pseudoaneurysms
KQ 3/Rate of identification of TICAs 8 NRS (1247 angiograms)	3/3/2	1 Iran, 1 Iran-Iraq, 1 Iraq, 1 United States, 1 Israel, 2 South Africa, 1 Lebanon	Shrapnel, stab, missile, unknown, other	8.6% of angiograms showed TICAs (range 3.6–40%)	High	Insufficient to determine the diagnostic accuracy of DSA
KQ 3/Benefits of angiography among patients with TICAs 5 NRS (1022 angiograms)	2/2/1	1 Iran, 1 Iran-Iraq, 2 South Africa, 1 Israel	Missile, shrapnel, stab, blast	65% of patients with TICAs benefitted from angiograms (treated and survived; range 55–100%)	High	Low for interventions given due to screen-detected TICA to improve the likelihood of survival
KQ 4/Diagnostic accuracy of CTA with DSA as reference standard 3 NRS (174)	3/0/0	United States	GSW, stab, other	Sensitivity 36%, 50%, and 73%; Specificity 85%, 88%, and 94%; PPV: 50%, 67%, and 89%; NPV: 62%, 83%, and 88%	Moderate	Moderate for the ability of DSA to detect a greater number of vascular injuries than CTA in GSW to the head
KQ 4/Early (within 7 d) vs late (more than 7 d) cerebral angiogram 1 NRS (181)	1/0/0	South Africa	Stab	Identification of vascular abnormalities: Early 31% vs late 41%, $P = .183$	High	Very low for no difference between late and early angiography Insufficient to determine when angiography should best occur
KQ 7/Image artifact 1 NRS (10) 1 Case report	2/0/0	1 Switzerland, 1 United States	GSW, shrapnel	MRI vs CT, severe or considerable artifact: 10% vs 70%: RR 0.14 (0.02–0.96, 1 study)	Moderate	Very low for ferromagnetic, but not other intracranial metal, associated with MRI image artifact

TABLE 3. Continued.

KQ/Outcome # & Type of studies (N)	No. of studies: military/civilian/ Mixed	Location (Country/ Region)	Type of MOI (GSW, Blast, others)	Main Findings	Study limitations (RoB)	SOE rating
KQ 7/Other safety 1 NRS (1) 1 Case report	2/0/0	1 Switzerland, 1 United States	GSW, shrapnel	No movement or heating of metal, no clinical effects	High	Very low for no detectable safety issues with MRI and ferromagnetic metal
KQ 12/Children/ Bihemispheric injury and mortality 3 pooled NRS (134) 2 NRS not pooled (153)	5/0/0	1 South Africa, 4 United States	Missile	RR 3.33 (1.80-6.14) Unpooled studies: $P < .001$; $P = .01$	High	Low for risk of mortality with bihemispheric injury (children)
KQ 12/Adults/ Bihemispheric injury and mortality 6 pooled NRS (1455)	5/1/0	1 South Africa, 3 United States, 1 Italy, 1 Turkey	Missile, shrapnel	RR 2.60 (1.38-4.88)	High	Moderate for risk of mortality with bihemispheric injury (adults)
KQ 12/Adults/ Posterior fossa and mortality 4 NRS, pooled analysis (1405)	3/1/0	2 United States, 1 Turkey, 1 Palestine	Missile, blast	RR 5.68 (1.68-19.19)	High	Low for risk of mortality with involvement of the posterior fossa
KQ 12/Adults/Epidural hemorrhage and mortality 3 NRS, pooled analysis (513)	2/1/0	2 Turkey, 1 United States	Missile	RR 1.41 (0.24-8.28)	High	Very low for mortality with epidural hemorrhage
KQ 13/SPIN score 4 NRS (858)	4/0/0	United States	GSW, stab	AUC ranged from 0.88 and 0.96	Moderate	Moderate that the SPIN score provides outstanding discriminative ability for survival
KQ 13/SPIN minus INR 2 NRS (463)	2/0/0	United States	GSW, stab	AUC 0.820 and AUC 0.948	Moderate	Low for discriminative ability for survival
KQ 13/Baylor score 2 NRS (384)	2/0/0	United States	GSW	AUC 0.876 and 0.895	Moderate	Low for excellent discriminative ability for survival
KQ 13/ABC score 2 NRS (316)	2/0/0	South Africa	GSW	AUC 0.96	Moderate	Very low for outstanding discriminative ability for survival
KQ 13/REMS 1 NRS (134)	1/0/0	Brazil	NR	AUC 0.583	Moderate	Very low for little discriminative ability for survival

TABLE 3. Continued.

KQ/Outcome # & Type of studies (N)	No. of studies: military/civilian/ Mixed	Location (Country/ Region)	Type of MOI (GSW, Blast, others)	Main Findings	Study limitations (RoB)	SOE rating
KQ 13/mREMS 1 NRS (134)	1/0/0	Brazil	NR	AUC 0.506	Moderate	Very low for poor to no discriminative ability for survival
KQ 13/WHIS 1 NRS (84)	0/0/1	Croatia	NR	AUC 0.92 (military), 0.88 (civilian)	Moderate	Very low for excellent to outstanding discriminative ability for survival
KQ 13/Maritzburg score 1 NRS (102)	1/0/0	South Africa	GSW	AUC 0.94	Moderate	Very low for outstanding discriminative ability for survival
KQ 13/Marshall score 3 NRS (257)	3/0/0	1 Columbia, 1 United States, 1 Finland/Sweden	GSW, stab, other	AUC 0.874 and 0.815	Moderate	Low for excellent discriminative ability for survival
KQ 13/Rotterdam score 2 NRS (162)	2/0/0	1 Finland/Sweden, 1 United States	GSW, stab	AUC 0.905 and 0.774	Moderate	Very low for acceptable to outstanding discriminative ability for survival
KQ 13/Stockholm score 1 NRS (75)	1/0/0	Finland/Sweden	GSW, stab	AUC 0.85	Moderate	Very low for excellent discriminative ability for survival
KQ 13/Helsinki score 1 NRS (75)	1/0/0	Finland/Sweden	GSW, stab	AUC 0.90	Moderate	Very low for outstanding discriminative ability for survival
KQ 13/St. Louis score 1 NRS (71)	1/0/0	United States	GSW	AUC NR; Sensitivity 94.12%; Specificity 75.68%; PPV 78.05%; NPV 93.33%	Moderate	Very low for a moderate PPV and high NPV in children
KQ 13/mGCS + ISS 1 NRS (101)	1/0/0	United States	GSW	AUC 0.951	Moderate	Very low for outstanding discriminative ability for survival
KQ 14/Resuscitation strategies (correction of coagulopathy) 1 NRS (89)	1/0/0	United States	GSW	Coagulopathic patients at presentation who survived 24 h: 40 Mortality, corrected coagulopathic vs uncorrected: 25% (1/4) vs 38% (8/21), $P = .29$	Moderate	Insufficient
KQ 15/Definitive airway 1 NRS (50 with airway data)	1/0/0	United States	GSW	Definitive Airway (Intubation) Intubated in field: 40 (80%) Not intubated in field: 10 (20%) Ground direct: 1 (17%) Helicopter direct: 27 (96%) Referred mode NR: 13 (76%)	High	Very low that patient or scene-related factors indicate whether a definitive airway is needed

TABLE 3. Continued.

KQ/Outcome # & Type of studies (N)	No. of studies: military/civilian/ Mixed	Location (Country/ Region)	Type of MOI (GSW, Blast, others)	Main Findings	Study limitations (RoB)	SOE rating
KQ 18/Infection 2 NRS (139)	1/0/1	United States	GSW, blast, stab, other	Results for 1 study not provided by whether or not the patient received prophylactic antibiotics; in the other study only 2 patients did not receive antibiotics	High	Insufficient
KQ 20/Mortality 1 NRS (3)	1/0/0	United States	Missile	Mortality: 100%	High	Very low for poor clinical outcomes
KQ 20/Hemorrhage cessation 1 NRS (3)	1/0/0	United States	Missile	Hemorrhage cessation: 100%	High	Very low that cessation of refractory hemorrhage may be achieved with recombinant activated Factor VII
KQ 24/CNS infection 1 NRS (763)	1/0/0	United States	GSW, low-velocity	CNS Infection, ICP monitor placement vs no ICP monitor placement: OR 2.27 (1.18-4.4), $P = .01$	Moderate	Very low for increased risk of cerebral infection with ICP monitoring
KQ 24/Discharge disposition 2 NRS (675) 1 study in children (209) 1 study is propensity-score matched adults (466)	2/0/0	United States	GSW, low-velocity	Propensity score-matched adults: no differences between ICP and no ICP monitoring on discharge disposition (data not clear) ICP monitor placement in children not associated with discharge disposition (vs no ICP monitor placement) OR 0.707 (0.196-0.864)	Moderate	Low for no difference in discharge disposition with or without ICP monitoring
KQ 24/Mortality 2 NRS (675) 1 study in children (209) 1 study is propensity-score matched adults (466)	2/0/0	United States	GSW, low-velocity	Propensity-score matched in adults Mortality rate with use of ICP monitor vs no monitor: 30.9% vs 40.8%, OR 0.65 (0.44-0.95) Study not propensity-score matched in children ICP monitor placement associated with lower mortality (vs no ICP monitor placement) OR 0.267 (0.082-0.864), although the survivorship benefit was not seen for patients with GCS 9-15	Moderate	Low for lower mortality with ICP monitoring
KQ 24/ICU stay 1 NRS (466) Propensity-score matched adults	1/0/0	United States	GSW	Propensity-score matched adults: 15 d with ICP monitoring vs 7 d without ICP monitoring, $P < .001$	Moderate	Low that ICP monitoring is associated with increased length of ICU stay
KQ 25/Mortality 2 NRS (330)	2/0/0	United States	GSW	$N = 297$: Median max ICP in survivors ($N = 15$): 22 mmHg (IQR 16-34 mmHg); Median Max ICP in those who died ($N = 11$): 33 mmHg (IQR, 21-95 mmHg), $P = .082$ $N = 33$: 8 patients died with ICPs >40 mmHg; 1 died of pneumonia with ICP <30 mmHg; 8 survived: 3 had all ICPs <20 mmHg, 2 had ICPs <30 mmHg with treatment; 4 had ICPs >40 mmHg despite treatment	Moderate	Very low for ICP threshold of 20mmHg is associated with lower risk of mortality
KQ 25/Function 2 NRS (330)	2/0/0	United States	GSW	$N = 297$ Median max ICP in those with good functional outcome: 22 mmHg (IQR 13-27 mmHg) Median max ICP in those with poor functional outcome: 26 mmHg (IQR 18-37 mmHg), $P = .240$ $N = 33$ At 6 mo: 2/4 surviving patients with ICP >40 mmHg had severe disabilities and 2/4 had moderate disabilities	Moderate	Very low for ICP threshold of 20mmHg is associated with improved function

TABLE 3. Continued.

KQ/Outcome # & Type of studies (N)	No. of studies: military/civilian/ Mixed	Location (Country/ Region)	Type of MOI (GSW, Blast, others)	Main Findings	Study limitations (RoB)	SOE rating
KQ 28/Prophylactic antibiotics 5 NRS (1249)	5/0/0	3 United States, 1 Colombia, 1 South Africa	Low-velocity, GSW	No significance difference in infection rate in 4 of 5 studies; lower infection rate in 1 study of non-GSW in South Africa. Other 4 studies were GSWs 3 in United States, 1 in Colombia.	High	Low for no difference with or with prophylactic antibiotics as part of critical care
KQ 28/Duration of prophylactic antibiotics 1 NRS (22)	1/0/0	United States	GSW	No sig. difference in infections or all cause 30-d mortality	Moderate	Insufficient
KQ 29/Clotting events 1 NRS (67)	0/1/0	Afghanistan	GSW, blast	30-d mortality: 3% vs 9%, aRR 1.50 (0.07-34.0) DVT or PE: 12% vs 17%, aRR 0.88 (0.20-3.93) Worse ICH: 16% vs 29%, aRR 0.56 (0.17-1.85) Incident-worsened ICH: 16% vs 17%, aRR 0.76 (0.21-2.79) Non-elective reoperation: 3% vs 9%, aRR 0.72 (0.06-8.70)	Moderate	Very low that early DVT prophylaxis results in little change in likelihood of VTE incidence while 30-d mortality, intracranial hemorrhage and emergent reoperation not increased
KQ 30/Timing of repeat vascular imaging 9 NRS (90)	5/2/2	1 Iraq, 4 United States, 1 Israel, 1 Iran-Iraq, 1 Lebanon, 1 Turkey	Blast, GSW, low-velocity	Interval between initial vascular imaging and follow-up imaging varied from 6 d to over 1 y	High	Insufficient
KQ 30/Difference between initial and repeat vascular injury imaging findings 9 NRS (90)	5/2/2	1 Iraq, 4 United States, 1 Israel, 1 Iran-Iraq, 1 Lebanon, 1 Turkey	Blast, GSW, low-velocity	Bell: 4 pTBI patients experienced intracranial aneurysm rupture (days 6, 14, 23, 32); 4 pTBI patients required retreatment (2 patients who also experienced aneurysm rupture and 2 patients who did not); 9/10 untreated intracranial vessels with vascular injury in pTBI patients experienced resolution of injury without treatment; including all patients with intracranial and/or extracranial vascular injury (N = 47), average time delay for aneurysm interval size increase was 24 d (range 8-75 d) Dawoud: Cerebral vascular injury on initial CTA: 28/63 (44.4%); 6 patients with no vascular injury on initial CTA had no vascular injury on repeat CTA; 1 patient with no vascular injury initially had TICA on follow-up CTA; of 6 patients with vascular injury on initial CTA, 4 patients had similar findings on repeat imaging and 2 patients had new findings (vasospasm of ACA and PCA and thrombus of superior sagittal sinus) on follow-up CTA; 2 patients with vascular injury on initial CTA had a negative follow-up CTA; follow-up angiogram on 1 patient with a negative CTA was also negative; follow-up angiogram of 2 patients with vascular injury on initial CTA had no new findings Cerebral vascular injury on initial CTA: 28/63 (44.4%) Cohen: Had aneurysm on initial screening (N = 9); successfully treated TICA (N = 9); presumed repeat imaging demonstrated that; had negative results on initial screening (N = 15); follow-up imaging yielded no additional aneurysms (second angiogram 2-4 wks after admission) Haddad: Patient A: first angiogram not conclusive, second angiogram TICA; Patient B: first angiogram not conclusive, second angiogram TICA; Patient C: TICA on MCA branch not seen on first angiogram but seen on second angiogram. In two cases TICA had increased in size. Yoon: 50% of vascular injuries was missed on initial read of imaging (radiologists had various experienced levels, images were also retrospectively reviewed by senior radiologists); 1 patient had inconclusive CTA, vascular injury found on DSA; 4 patients with no vascular injury on initial vascular screening were found to have vascular injury on follow-up (3 pseudoaneurysms, 1 occlusion); 2 diagnosed on repeat CTA, 2 diagnosed on angiogram	High	Low that repeat vascular imaging may yield different findings from initial imaging (e.g., new or unrecognized vascular injury, worsening or improved injury, resolution of injury)

TABLE 3. Continued.

KQ/Outcome # & Type of studies (N)	No. of studies: military/civilian/ Mixed	Location (Country/ Region)	Type of MOI (GSW, Blast, others)	Main Findings	Study limitations (RoB)	SOE rating
				Ozkan Arat: Patient A: TICA on CTA, 1-y FU angiogram: aneurysm decrease in size and lobulation; Patient B: TICAs on DSA, 8-d FU DSA showed interval enlargement; Patient C: Carotid angiogram revealed a carotidocavernous fistula, 6-mo follow-up carotid angiography showed occlusion of right ICA and collateral flow; Patient D: CTA showed dissecting aneurysm of MCA; 2-mo follow-up CTA showed patent MCA and occlusion of aneurysm; Patient E: CTA showed pseudoaneurysm of distal ACA, 21-mo MRA showed no recurrence after coiling Rostomily: Patient A: ICA pseudoaneurysm on initial angiography; 5-wk follow-up angiogram revealed enlargement of pseudoaneurysm; postop angiograph after bypass grafting of ICA showed patent graft; Patient B: Initial angiography showed pseudoaneurysm of ICA; after craniotomy, 4-wk angiography showed enlarge pseudoaneurysm; died 2 d before planned bypass Amirjamshidi: Findings on repeat angiography: Spontaneous healing (N = 6); Other findings: Patient A: Initial angiogram showed small traumatic aneurysm (A2); 8-d follow-up angiogram showed expansion of the TA; Patient B: Initial angiography negative; 35-d follow-up angiography showed extracavernous carotid aneurysm, Hunter ligation of ICA attempted, patient died, autopsy showed fractured bone at base of skull with tear of extracavernous carotid artery, wrong artery ligated; Patient C: initial angiogram showed traumatic aneurysm; 10-d follow-up angiogram showed expansion of the aneurysm; 3rd angiogram showed shrinkage; 4th angiogram (about 34 d from initial angiogram showed re-expansion; Patient D: initial angiogram showed carotid cavernous sinus fistula; 18-d follow-up results not reported Sweeney: Patient A: Initial CTA showed partial occlusion of distal right A2; 2-wk follow-up CTA showed patent distal right A2 with no pseudoaneurysm; 3-mo follow-up CTA showed no pseudoaneurysm; Patient B: initial CTA showed no large-vessel occlusion; 2-wk postoperative angiogram showed no pseudoaneurysm and filling of vasculature tree; 1-y follow-up CTA was normal		
KQ 31/Mortality, organ rejection 3 NRS (472)	3/0/0	2 United States, 1 Israel	GSW, NR	Donated >4 organs vs ≤4 organs Mean (SD) time from admission to declaration of death 34.98 (44.20) h vs 52.79 (72.68) h, $P = .02$ Median <97 h from injury to declaration of brain death vs ≥97 h 10-y survival of recipient: 58% vs 78%, $P = .102$; HR 1.12 (0.80-1.44) Mean (SD) total rejection score: 0.45 (0.38) vs 0.39 (0.36), $P = .46$	Moderate	Very low that more organs are transplanted when independent donor goals of cardiac ejection fraction greater than 45% and $\text{PaO}_2:\text{FiO}_2$ greater than 300 are met
KQ 31/Number of organs donated 1 NRS (297)	1/0/0	United States	NR	Donated >4 organs vs ≤4 organs Ejection fraction >45%: 91.1% vs 65.5%, $P < .001$ $\text{PaO}_2:\text{FiO}_2$ ratio >300: 79.7% vs 36.2%, $P < .001$	Moderate	Very low that a shorter time from brain trauma to brain death is associated with more organs donated but not associated with recipient mortality or organ rejection

TABLE 3. Continued.

KQ/Outcome # & Type of studies (N)	No. of studies: military/civilian/ Mixed	Location (Country/ Region)	Type of MOI (GSW, Blast, others)	Main Findings	Study limitations (RoB)	SOE rating
KQ 34/Mortality/Poor outcome 6 NRS (294)	3/1/2	1 China, 2 United States, 1 Iraq, 1 Italy, 1 Libya	Missile, blast,	N = 56, mortality: 3.5% Patients debrided within 8 h more likely to recover (undefined) vs those debrided >8 h after injury: 82.1% vs 26.7%, $P < .001$ N = 89, mortality Early surgery: 37% (10/27); Late surgery: 0% (0/6); No surgery: 82% (46/56); $P < .001$ N = 33, 6-mo GOS Poor outcome (GOS 1-3): Early surgery: 100% (16/16); Delayed surgery: 0 Good outcome (GOS 4-5): Early surgery: 82% (14); Delayed surgery: 18% (3); $P = .10$ N = 37, good outcome (not defined) <5 h: 50% (5); 5-8 h: 63% (14); >9 h: 80% (4); $P = .2$ N = 44, mortality: 40.1% (18/44) Time to surgery from injury: # cases, survived, died: Within 3 h: 2, 1, 1; mortality 50%; Within 6 h: 33, 19, 14; mortality 42.4%; >6 h: 9, 6, 3; mortality 33.3% N = 35, mortality: 22.8% (8) Time to surgery from injury and mortality <24 h: 1; 24-72 h: 3; >72 h: 4; Lower mortality when operated on within 24 h, $P = .044$	High	Very low that early surgical intervention may reduce the likelihood of death/ other poor outcome in more severely injured patients compared with delayed surgery
KQ 35/Local Debridement and Closure 4 NRS (217)	3/0/1	1 Lebanon, 1 Iran, 1 United States, 1 Iraq	GSW, shrapnel	When used as curative treatment for patients with less serious pTBI, results in generally good outcomes. Limited information on harms, some reports on complications.	High	Very low that local debridement and closure are associated with good outcomes for appropriate patients
KQ 36/Retained Fragments 12 NRS in 15 articles (3905) (12 studies because the 3 Aarabi, Rish, and Salazar are the same)	10/3/2	1 Ukraine, 1 Afghanistan, 2 United States, 1 Palestine, 1 Colombia, 1 Turkey, 2 Lebanon, 3 Iran, 1 Iraq, 2 Vietnam	Blast, GSW, low-velocity	More studies find no harm, that is rates of infection and other outcomes are not different for patients with fragments. However, a minority of studies do. While there are likely explanations, they are spread across time periods and multiple studies are enough to reduce confidence in the overall findings	High	Low that patients with retained fragments have similar infection rates and other outcomes compared with patients without retained fragments
KQ 37/Radical vs conservative debridement Radical 9 series in 11 articles (N = 3243)	3/7/1	1 Ukraine, 1 Slovenia, 1 Brazil, 2 Vietnam, 1 United States, 3 Iran, 1 Korea, 1 Lebanon	Shrapnel, GSW	Series report similar rates of mortality, infection and post injury seizures.	High	Low that radical and conservative debridement results in similar outcomes in adult pTBI
KQ 37/Radical vs conservative debridement Conservative 5 series in 6 articles (N = 956)	0/6/0	1 Syria, 3 Turkey, 2 Lebanon	Blast, GSW	Series report similar rates of mortality, infection and post injury seizures.	High	Insufficient for child pTBI
KQ 38/Infection and fistula 4 NRS (2206)	0/2/2	1 Iran, 1 Vietnam, 2 Turkey	GSW, fragment, NR	RR 30.18 (14.34-63.53)	High	Moderate that infection risk is greater with CSF fistula vs no fistula

TABLE 3. Continued.

KQ/Outcome # & Type of studies (N)	No. of studies: military/civilian/ Mixed	Location (Country/ Region)	Type of MOI (GSW, Blast, others)	Main Findings	Study limitations (RoB)	SOE rating
KQ 41/Early vs delayed cranioplasty 2 NRS (599)	0/2/0	2 United States	Blast, GSW	1 study reports no association of timing with outcomes; 1 found fewer complications when repair is after 1 y	High	Very low that the timing of cranioplasty is associated with outcomes
KQ 43/Bleeding 3 NRS (16) 6 case reports (6)	7/2/0	1 Iraq, 1 Israel, 3 United States, 1 China, 1 Ukraine, 1 Canada, 1 France	Blast, GSW, low-velocity	For largest case series (N = 12 treated with coil) Rupture: 18% Recurrence: 27% Retreatment: 36% (retreatment with coil or clip) Results varied for smaller case series and case reports	High	Very low that coil embolization of TICA may reduce risk of further bleeding outcomes or need for retreatment
KQ 44/Endovascular management of venous sinus injuries/ mortality 1 NRS (94) 2 case reports (2)	2/0/1	1 Vietnam and United States, 1 Syria, 1 United States	GSW, shrapnel, unknown	Overall mortality by injury site. Cohort 1 (1968-1970, N = 78). Anterior superior sagittal sinus (SSS): 5% (1/22); Posterior SSS 43% (15/35); Transverse sinus 33% (1/3) Mortality by repair type. Primary repairs 0% (N = 0); Venous grafting: 0% (N = 0), Anterior SSS ligation: 4% (1/27) Case report: successful repair of sinus injury; discharged postop day 5 Case report: preservation of neurological function, assume survival	High	Very low that operative repair of venous sinus injuries is feasible and may improve survivability
KQ 44/Endovascular management of venous sinus injuries/ preservation of patency 1 NRS (94) 2 case reports	2/0/1	1 Vietnam and United States, 1 Syria, 1 United States	GSW, shrapnel, unknown	Sinus patency: 94 Primary repairs: 100% (N = 5/5) Venous grafting: 83.3% (N = 5/6) The lone sinus thrombosis occurred in a patient with venous grafting Case report: restoration of proximal and distal sinus flow/patency	High	Very low that operative repair of venous sinus injuries may increase sinus patency
KQ 44/Endovascular management of venous sinus injuries/ prevention of venous infarction 1 case report	1/0/0	1 Syria	Shrapnel	Case report: no venous infarction	High	Insufficient
KQ 46/Favorable outcome 6 NRS (62)	3/2/1	1 Iraq, 1 Lebanon, 1 Iran, 2 South Africa, 1 United States	Missile, blast, low-velocity	N = 15. Outcome after trapping and excision: Good: 45%; Fair: 18%; Poor: 9%; Died: 18; Outcome after unspecified surgery: Poor: 100% (1/1) Outcome after no operation: Fair 50% (1/2); Poor: 50% (1/2) N = 8. GCO score after surgery: 2.85; GCO score in patient who did not have surgery: 1 N = 11. Surgery: 6; all "did well". No surgery: 4 died of SAH; 1 lost to follow-up N = 6. Surgery: 2; successfully operated; No surgery: 2; 1 died, 1 resolved N = 5. Surgery: 1; unfavorable outcome (GOSE 3), discharged to long-term care hospital; No surgery: 4; unfavorable outcome N = 1. Ventriculostomy, craniotomy for clipping; GOS score: 1 N = 16. Rupture with surgery: 12.5% (1/8); Rupture without surgery: 12.5% (1/8)	High	Very low that surgery in the setting of TICA may lead to more favorable outcomes than no surgery

ABC, admission blood pressure, brain spillage presence or absence of consciousness; ACA, anterior cerebral artery; aRR, adjusted risk ratio; AUC, area under the curve; CI, confidence interval; CNS, central nervous system; CT, computed tomography; CTA, computed tomography angiography; DSA, digital subtraction angiography; DVT, deep vein thrombosis; GCO, Glasgow Coma Outcome; GOS, Glasgow Outcome Scale; HR, hazard ratio; ICA, internal carotid artery; ICH, intracranial hemorrhage; ICP, intracranial pressure; IQR, interquartile ratio; ISS, Injury Severity Score; KQ, Key Question; MCA, middle cerebral artery; mGCS, modified Glasgow Coma Scale; mmHg, millimeters of mercury; mREMS, modified Rapid Emergency Medicine Score; MRI, magnetic resonance imaging; NLR, negative likelihood ratio; NPV, negative predictive value; NRS, non-randomized study; PE, pulmonary embolism; PPV, positive predictive value; pTBI, penetrating traumatic brain injury; REMS, Rapid Emergency Medicine Score; RoB, risk of bias; RR, risk ratio; SD, standard deviation; SOE, strength of evidence; SPIN, Surviving Penetrating Injury to the Brain; SSS, superior sagittal sinus; TA, traumatic aneurysm; TICA, traumatic intracranial aneurysm; US, United States; WHIS, War Head Injury Score.

An important limitation of this work is the lack of high quality evidence for most KQs, requiring undesirable reliance on case series and case reports to fill in the gaps. Not surprisingly, no randomized trials were identified in this population. We identified moderate strength evidence for only four KQs, as noted above. The remaining evidence was considered low or very low strength or was insufficient to support any conclusions.

Another limitation is that most of the studies of pTBI were retrospective. In general, retrospectively collected data may be subject to recall and selection bias and represent a convenience sample that may not be representative of all patients who experience pTBI. Additionally, much of the evidence in pTBI comes from studies in military populations comprised of healthy young men. Older patients with significant comorbidities may have distinct outcomes when treated similarly to military fighters and could potentially benefit from a distinct treatment strategy.

Gaps and Implications for Future Research

There was no evidence or very limited evidence for many of the KQs. This is largely due to the fact that pTBI is a rare injury that is often encountered in austere environments. This makes it difficult to study these patients or to prospectively accrue enough patients in a few months or years. It can also be difficult to ethically treat similarly-presenting patients too differently.

Given that most evidence in pTBI comes from case series, it is important that as much information from these series be gleaned as possible. In future studies with a mixed population (e.g., penetrating head injury vs

closed head injury) patient outcomes should be reported separately by type of injury and in as much detail as possible to increase its usability. Future studies need to report results by the severity and/or mechanism of patient injury (e.g., Glasgow Outcome Scale score, missile injury vs blast injury). Additionally, studies employing multiple treatments or management strategies (e.g., fluid administration, use of blood products, airway maneuvers) need to also report patient outcomes by the specific treatments patients received. For example, many studies reported overall mortality as an outcome, but did not link mortality to any treatment or injury characteristic. Providing patient outcomes by population, injury, and intervention characteristics may enable findings from similar studies (e.g., with similar populations, mechanism of injury, injury severity, and treatment strategies) to be pooled, which may result in stronger conclusions on the benefits, harms, or timing of any particular intervention or management strategy.

Summary and Conclusions

In order to provide useful clinical practice guidelines for pTBI we supplemented a traditional evidence-based approach with rigorous methods of identifying expert consensus. Few moderate strength conclusions related to specific management strategies for penetrating brain injury could be made. Detailed reporting of patient outcomes in future studies could advance the field by providing greater evidence for specific treatments by patient population, mechanism of injury, severity of injury, and specific interventions employed.

VI - PREHOSPITAL AND EMERGENCY CARE EVIDENCE-BASED RECOMMENDATIONS AND EXPERT CONSENSUS STATEMENTS

Section Leads: Angela Lumba-Brown and David W. Wright

VI-1 – Airway Management

D. Pannell, S. Shackelford

Recommendations

Level I-IV

There is insufficient evidence to support an evidence-based recommendation for what patient and scene-related factors indicate a definitive airway is needed compared with no or non-invasive ventilation.

Level C – Expert Consensus (Delphi Voting)

In the absence of direct scientific evidence, EXPERT CONSENSUS concluded that:

- A prehospital definitive airway (endotracheal intubation) should be initiated to improve outcomes when the Glasgow Coma Scale (GCS) is < 8, the airway is compromised due to associated maxillofacial trauma, or with longer transport times to the hospital. Definitive airway should be performed by appropriately trained prehospital personnel and with the use of accompanying O₂ saturation monitoring, ETCO₂ monitoring, and frequent blood pressure monitoring. (96.7% consensus)
- Practitioners should adhere to the recommendations of the Prehospital Guidelines for the Management of Traumatic Brain Injury - 3rd Edition³⁶ and Brain Trauma Foundation (BTF) 4th edition adult Severe Traumatic Brain Injury (TBI) guidelines²⁸ concerning prehospital and emergency department resuscitation strategies. (100% consensus)
- Select patients with penetrating TBI should undergo lateral decubitus positioning and close monitoring of oxygenation and ventilation or prehospital definitive airway placement. Select patients include those with wounds into the oropharynx associated with significant hemorrhage and airway compromise. (96.7% consensus)

No evidence or expert opinion supported distinct recommendations based on patient gender, age, wounding mechanism, or military vs civilian context.

Introduction

Prehospital airway management for patients with TBI has undergone intensive study. However, the published literature offers limited information to support recommendations specifically tailored to penetrating traumatic brain injury (pTBI). pTBI patients often present with specific conditions, such as open wounds that may extend into the oropharynx, accompanied by bleeding that could compromise the airway, especially in individuals who are obtunded. Additionally, open wounds penetrating the cranial vault may lead to massive external bleeding, hypovolemic shock, and an inability to tolerate positive pressure ventilation prior to achieving bleeding control and resuscitation with blood products. Exposure of the neck for penetrating injuries, and prompt removal of cervical collars without clinical or computed tomography (CT) evidence of cervical spine injury are important considerations.

Prior Guideline Recommendations

The previous edition of the pTBI guidelines¹⁶ did not address what patient and scene-related factors indicate a definitive airway is needed compared with no or non-invasive ventilation. All recommendations of the *2023 Prehospital Guidelines for the Management of Traumatic Brain Injury - 3rd Edition*³⁶ also apply to pTBI, with the additional considerations related to external bleeding as listed above. Note that the *2023 Prehospital Guidelines for the Management of Traumatic Brain Injury - 3rd Edition*³⁶ do not recommend intubation for all TBI patients in the prehospital environment.

Scientific Foundation

There are no prospective studies of airway management specific to pTBI. One study met inclusion criteria for inclusion as evidence for this topic (Table 4). This study by Kaufman et al³⁷ studied gunshot wounds (GSW) to the head and reported intubation rates by whether the patient was admitted directly to the

TABLE 4. Evidentiary Base for Patient or Scene Factors Related to Definitive Airway Placement

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Patient or Scene-related factors	Results	Study risk of bias
Kaufman, 1986 ³⁷ (NRS) United States Civilian GSW	136 (95%) out of 143 with penetrating skull injury Male: 83% Mean age: NR GCS 12-15: 15% GCS 9-11: 10% GCS 6-8: 14% GCS 3-5: 61% Referred from another hospital: 52% Direct admit: 46% Hours from injury to arrival 0-1: 8.4% 1-2: 45% 2-3: 10% >3: 7% Unknown: 29%	With known intubation: 35% (50/143) Ground direct: 6 Helicopter direct: 27 Referred mode NR: 17	Definitive Airway (50 with intubation) Intubated in field: 40 (80%) Not intubated in field: 10 (20%) Ground direct: 1 (17%) Helicopter direct: 27 (96%) Referred mode NR: 13 (76%)	High

GCS, Glasgow Coma Scale; GSW, gunshot wound; MOI, mechanism of injury; NR, not reported; NRS, non randomized study.

treating hospital or referred from another hospital and whether the patient was transported via ground or helicopter.³⁷ This study was a retrospective review of 143 cases of gunshot wounds to the head treated by neurosurgery in one hospital in Houston, Texas between January 1980 and June 1982 that were entered into a national trauma registry. Whether patients were intubated or not before arriving at the hospital emergency department (ED) was known for 50 (35%) of the patients. Of these, most (80%) were intubated before arriving. Patients arriving directly by helicopter were more likely to be intubated (96%) than patients arriving by ground transportation (17%) or patients referred from another hospital (76%) who arrived by either mode of transport.

Six additional studies in patients with pTBI are noted which did not meet criteria for formal inclusion as evidence for this topic. These studies report intubation for various reasons (being comatose or obtunded,³⁸⁻⁴¹ not following commands,⁴² respiratory distress,^{41,43} and low Glasgow Coma Scale score⁴⁴) but did not provide any detail that allowed inclusion as evidence.

Another retrospective study reported that airway control was often required in GSW to the face (29.5% of 247 patients were intubated in the ED) but less than 10% of patients in this study also had a brain injury (not specified whether closed or penetrating) and the airway status for these patients was not reported separately.⁴⁵ Three reports of single cases provide minimal additional information in descriptions of definitive airways in initial management.^{39,46,47}

Discussion

The management of patients with pTBI presents unique challenges compared to those with non-penetrating TBI. Given

the complexity and critical nature of these injuries, especially when open wounds extend into the oropharynx or penetrate the cranial vault, leading to potential airway compromise and hemorrhagic shock, the Prehospital Guidelines for the Management of Traumatic Brain Injury - 3rd Edition offers essential guidance.³⁶ These guidelines emphasize the importance of early intervention to prevent hypoxia, hyperventilation, and hypotension, which are pivotal in improving outcomes for pTBI patients.

The prior pTBI guidelines did not specifically address the factors indicating the need for a definitive airway in pTBI patients, highlighting a gap in the literature. However, the recommendations provided, based on existing studies and expert consensus, offer a framework for managing these critical conditions. Specifically, the guidelines underscore the importance of continuous oxygenation, monitoring, and appropriate airway management techniques to mitigate the severe consequences of pTBI. Scientific evidence, including retrospective studies on GSW to the head and the use of airway control in facial GSW, underscores the prevalence of intubation in these scenarios. These findings, albeit limited, point to the necessity of a definitive airway in certain pTBI cases, particularly in the context of comatose or obtunded states, respiratory distress, and low GCS scores.

Expert Opinion

A critical aspect of managing pTBI involves decisions related to airway management. Despite the lack of strong evidence to recommend specific patient and scene-related factors to determine the need for a definitive airway over no or non-invasive ventilation, several key insights emerge from the literature and expert consensus. For instance, a definitive prehospital airway is likely to enhance

outcomes in situations where prehospital providers are proficient in airway placement, when the GCS score is below 8 due to pTBI, in the presence of maxillofacial trauma compromising the airway, or during longer transports to medical facilities. Implementing oxygen saturation and ETCO₂ monitoring, along with frequent blood pressure monitoring, is advised as soon as possible after the injury and prior to establishing a definitive airway.

The expert consensus further clarifies practices in the absence of direct evidence. Adherence to the Prehospital Guidelines for the Management of Traumatic Brain Injury³⁶ is recommended, along with specific interventions for pTBI patients. For example, cervical collars are deemed unnecessary in isolated pTBI without clinical or CT evidence of cervical spine injury. Additionally, in cases of significant hemorrhage and airway compromise, especially with wounds into the oropharynx, lateral decubitus positioning, close monitoring, or prehospital definitive airway placement may be necessary. In situations of hemorrhagic shock or massive external bleeding, controlling the bleeding and resuscitation with

blood products precede the initiation of intubation as long as an airway can be maintained.

Future Directions

Future studies of TBI patients should clearly report the number of blunt vs penetrating TBI patients included and consider reporting specific characteristic of each sub-population as well as the outcome of each along with the outcome of the overall population. As sub-populations may not achieve statistical significance, it is also important to implement multi-center collaborative studies comparing the early treatment of both blunt and penetrating TBI patients. There is a need for randomized control trials (RCT) and comparative studies to evaluate the effectiveness of different airway management strategies (e.g., supraglottic airway devices vs endotracheal intubation) specifically in pTBI patients. This research should consider patient outcomes, the feasibility of implementation in prehospital settings, and the training required for emergency medical personnel.

VI-2 – Resuscitation Strategies

B. Dengler, D. Boone, D.W. Wright

Recommendations

Level I-IV

There is insufficient evidence to support an evidence-based recommendation specific to penetrating brain injury for ED care strategies (e.g., correction of coagulopathy, cardiopulmonary resuscitation [CPR], airway maneuvers, oxygen administration, cervical spine immobilization, specific fluid administration including hypertonic saline, mannitol administration, pain management, hyperventilation, posture), including the prevention of secondary injury.

Level C – Expert Consensus (Delphi Voting)

In the absence of direct scientific evidence, EXPERT CONSENSUS concluded that:

- Practitioners should adhere to the recommendations of the Prehospital Guidelines for the Management of Traumatic Brain Injury - 3rd Edition³⁶ and the BTF 4th edition TBI guidelines²⁸ concerning prehospital and emergency department resuscitation strategies. (100% consensus)
- Cervical collars are not required in isolated penetrating brain injury in patients without clinical or CT findings of cervical spine injury. (100% consensus)
- In patients with signs of hemorrhagic shock or massive external hemorrhage, the primary focus should be on hemorrhage control and resuscitation using whole blood or equivalent blood products. (100% consensus)
- Massive bleeding into the oropharynx often requires a definitive airway prior to packing the oropharynx with a hemostatic dressing or gauze packing. (93.3% consensus)

No evidence or expert opinion supported distinct recommendations based on patient gender, age, wounding mechanism, or military vs civilian context.

Introduction

pTBI presents unique challenges for prehospital and ED healthcare providers, who are tasked with implementing a range of

resuscitation strategies aimed at stabilizing the patient and minimizing secondary injury. These strategies include, but are not limited to, correction of coagulopathy, CPR, airway management,

oxygen administration, cervical spine immobilization, specific fluid administration (e.g., hypertonic saline, mannitol), pain management, hyperventilation, and posture adjustment. The goal of these interventions is not only to address the immediate life-threatening conditions but also to prevent further brain damage, such as cerebral edema and neuronal loss.

Despite the critical importance of these resuscitation strategies in the management of pTBI, there is a notable lack of evidence to support the superiority or optimal combination of these treatments. The complexity of pTBI cases, coupled with the variability in injury mechanisms and patient conditions, makes it challenging to conduct large-scale, randomized controlled trials that could provide high-quality evidence. The available literature on pTBI resuscitation strategies reveals a mixed picture. Some studies suggest potential benefits of certain interventions, such as the use of mannitol and hypertonic saline for the management of cerebral edema, or aggressive resuscitation with blood products in patients with coagulopathy. However, these findings are often limited by small sample sizes, retrospective designs, and the inherent confounding factors associated with trauma care, where sicker patients are more likely to receive intensive interventions.

Prior Guideline Recommendations

The previous version of these guidelines¹⁶ did not address the benefits or harms of prehospital and ED resuscitation strategies or the impact on the prevention of secondary injury in pTBI patients.

Scientific Foundation

No studies were identified meeting inclusion criteria that addressed the benefits and harms of resuscitation strategies for patients with pTBI in prehospital or ED settings, comparing those who received interventions to those who did not. A single non-randomized study published by Mansour et al involving 89 U.S. civilians with GSW to the head compared ED patients presenting with coagulopathy to those without⁴⁸ (Table 5). Coagulopathy was defined by an international normalized ratio (INR) greater than 1.3, platelet count below 100 000/ μ L, or partial thromboplastin time over 37 seconds. This study analyzed patient characteristics and outcomes between those diagnosed with coagulopathy after initial resuscitation, without specifying the resuscitation strategies used. It reported significantly higher mortality rates among patients with coagulopathy (73% vs 25%, $P < .001$), but this association disappeared after adjusting for Glasgow Coma Scale-Motor score (GCS-M) in a multivariable logistic regression (odds ratio 1.34, 95% CI, 0.22 to 8.10, $P = .75$). Among patients with coagulopathy at presentation who survived at least 24 hours, a comparison between those who corrected their coagulopathy within 24 hours and those who did not showed no statistically significant difference (75% vs 38%, $P = .29$) in survivability. The study was underpowered, relevant to interpretation of the results.

Nine studies were identified that reported on the use of one or more resuscitation strategies (e.g., intubation, blood transfusion, hyperosmolar therapy) and their outcomes in terms of mortality or

Glasgow Outcome Scale (GOS) scores. Three of these studies specifically examined the administration of mannitol, with mixed findings related to mortality and unfavorable outcomes among patients with GSWs to the head from various contexts, including the Syrian civil war and incidents in the United States and India. One study by Kaufman et al ($N = 143$) of U.S. civilians with GSWs, seven of which were not penetrating, reported 38% of those who survived were administered mannitol compared with 56% of those who died.³⁷ They noted in most cases the patients had been previously hypotensive. No other information on resuscitation strategies was reported. The second study by Can et al ($N = 104$), of patients in the Syrian civil war with sniper GSWs to the head, reported giving all patients hyperosmolar therapy, including mannitol and 3% hypertonic saline, in the ED for cerebral edema and reported a mortality rate of 36%.⁴⁹ They also reported 26% of the patients required endotracheal intubation and of those 63% (17/27, $P < .01$) died. The third study by Wani et al ($N = 26$), of patients (unclear if civilian, military, or a mix) in India with GSWs or blast injuries to the head, followed a standard protocol for resuscitation in the ED of airway, breathing, and circulation (ABC), reported all patients received mannitol 1 g/kg, and reported 92% (24/26) had an unfavorable outcome (GOS ≤ 3).⁵⁰

Two studies of civilians in South Africa with isolated GSWs to the head reported following the Advanced Trauma Life Support (ATLS®) principles. One by Glapa et al ($N = 72$) intubated 75% (48/64) of patients with pTBIs (89%, 64/72) and reported 79% died compared with 25% who died of those who were not intubated when they arrived at the hospital ($P = .0002$).⁵¹ The other study by Kong et al ($N = 102$) placed a cervical collar on all patients, 26% by emergency medical service (EMS) personnel and the remaining 74% in the ED. The study reported no cervical spinal injuries in any of the patients and all were cleared to remove the cervical collars. The mortality rate was 22% in the study.⁵²

Two studies compared the administration of aggressive resuscitation products. One study by Joseph et al ($N = 132$) of civilians in the United States with pTBIs due to GSWs compared those who survived with those who did not and reported survivors used more blood products (57% vs 34%, $P = .05$), hyperosmolar therapy (53% vs 31%, $P = .03$), and prothrombin complex concentrate (PCC) ($P = .06$) but there was no difference in use of vasopressors (41% vs 35%, $P = .6$) in survival.⁵³ The study also reported the use of aggressive management in their institution increased from 30% in 2008 to 70% in 2011. The other study by Singh et al ($N = 96$) was of patients with missile injuries to the head from terrorist attacks, assaults, accidents, or self-injuries in India and reported following a protocol at the clinician's discretion, in hemodynamically unstable patients and patients with coagulopathy. Authors reported more patients survived than died when given blood products (55% vs 30%, $P < .05$), hypertonic saline (51% vs 26%, $P < .05$), and ionotropes (39% vs 29%, $P < .5$).⁵⁴

A study by McNickle et al ($N = 241$) of civilians in the United States with GSWs to the head and face reported EMS placed spinal motion restriction on 50% of the patients before arriving at the ED

TABLE 5. Evidentiary Base for Outcomes After Correction of Coagulopathy

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Comparisons	Results	Study risk of bias
Mansour, 2021 ⁴⁸ (NRS) United States Civilian GSW: 100%	N = 89 Male: 83% Median age: 27 y (range 21-35) Black: 92% White: 5% Hispanic: 3% Median GCS at presentation: 6 (range 3-14) Assault: 83% Self-inflicted: 9% Accidental: 8%	Coagulopathic patients: 40 Non coagulopathic patients: 49	Mortality: 73% (29/40) vs 25% (12/49), $P < .001$ Survival in patients with coagulopathy who survived ≥ 24 h, who were still coagulopathic vs no longer coagulopathic: 38% (8/21) vs 75% (3/4), $P = .29$	Moderate

GCS, Glasgow Coma Scale; GSW, gunshot wound; h, hours; MOI, mechanism of injury; NRS, non randomized study.

and an additional 2% had collars placed in the hospital.⁵⁵ Cardiopulmonary resuscitation by EMS was done in 19% of patients and they intubated 46% prior to arriving at the hospital. The mortality rate in the overall study was 57%, mortality was not reported based on resuscitation strategies. The study did report six patients with collars placed by EMS were identified with cervical spine fractures, two died, and one underwent spine surgery and survived but was admitted to a long-term acute care facility after discharge.

A study by Ospina-Delgado (N = 95) of civilians in Colombia with GSWs to the head reported more patients who were intubated in the ED (36%, 34/95) compared with those who did not require or need reintubation (64%, 61/95) died (53.5% vs 46.5%).⁵⁶ However, there are discrepancies between the text and the table. Seven studies reported using a protocol but did not elaborate on details or provide outcome comparisons.^{57–63}

Despite these findings, the studies discussed are confounded by the fact that patients with more severe pTBI are more likely to require multiple resuscitation strategies and have worse outcomes, making it difficult to assess the benefits and harms of any specific strategy. Furthermore, the study comparing successfully corrected coagulopathy to unsuccessfully corrected coagulopathy provided insufficient evidence to determine the benefits and harms of coagulopathy correction in pTBI, suggesting that larger studies are needed to potentially demonstrate increased survivability.

Discussion

It is almost certain that management and resuscitation strategies employed in prehospital and ED setting impact the screening, diagnosis, and outcome of patients with pTBI, however the degree of impact and the interaction between the different strategies remains unknown. These strategies are also crucial for patient stabilization and minimizing secondary injuries such as cerebral edema and diffuse axonal injury and encompass a wide range of interventions,

including but not limited to the correction of coagulopathy, CPR, airway management, oxygen administration, cervical spine immobilization, specific fluid administration (notably hypertonic saline and mannitol), pain management, hyperventilation, and posture adjustments. Despite the critical importance of these interventions, the existing literature provides insufficient evidence to strongly recommend specific ED strategies tailored for pTBI, reflecting the complexity and variability inherent in pTBI cases.

Expert Opinion

The unanimous recommendation for practitioners to adhere to the Prehospital Guidelines for the Management of Traumatic Brain Injury³⁶ as well as the BTF's 4th edition adult coma guidelines²⁸ underscores the importance of established protocols and guidelines in ensuring consistent and informed care for pTBI patients. The guidelines presented here, developed through comprehensive reviews of the literature and expert interpretation of available data, provide a foundation for decision-making in the absence of high-level evidence specific to penetrating brain injuries. They cover a wide range of resuscitation strategies, including airway management, ventilation, circulation support, and the management of coagulopathy, among others, tailored to the unique challenges presented by traumatic brain injuries.

The consensus statement regarding the non-requirement of cervical collars in cases of isolated penetrating brain injury without clinical or CT evidence of cervical spine injury addresses a specific and common practice in the management of pTBI and reflects a balance between potential benefits and harms of cervical spine immobilization in this patient population. Given the low likelihood of cervical spine injury in isolated penetrating brain injuries and the potential for complications associated with unnecessary immobilization, this consensus provides clear guidance that can streamline patient care and avoid unnecessary interventions.

Since the initial evidence table search, new data has emerged supporting the use of whole blood for resuscitative hemorrhagic shock in the prehospital setting. Although not specific to penetrating TBI, this evidence has been included as a “consensus” to ensure the guidelines remain relevant and the document stays up to date.

Future Directions

There is a pressing need for well-designed RCTs that compare different resuscitation strategies in pTBI patients. These studies should aim to include diverse patient populations and injury mechanisms to ensure broad applicability of the findings. Priority areas might include the effectiveness of mannitol vs hypertonic saline in managing cerebral edema, the benefits of early coagulopathy correction, and the impact of advanced airway management techniques on patient outcomes. Many resuscitation strategies are considered standard of care and will not be amenable to standard RCTs in trauma settings, however robust prospective observational studies can provide valuable insights into the real-world effectiveness of various resuscitation interventions. These

studies should focus on systematically collecting data on patient characteristics, treatment protocols, and outcomes to identify best practices and areas needing improvement. This could involve studying the genetic, physiological, and clinical factors that influence patient responses to different resuscitation strategies, with the goal of tailoring treatments to individual patient needs and improving outcomes. Future studies should compare the effectiveness of different combinations of resuscitation strategies to identify the most effective protocols for specific patient subgroups or injury types. This research could inform the development of more nuanced and effective clinical guidelines. Understanding the long-term outcomes of pTBI patients who receive various resuscitation strategies is crucial for assessing the enduring impacts of these interventions. Future research should include follow-up studies that evaluate functional outcomes, quality of life, and long-term mortality rates. Investigating the organizational, financial, and logistical aspects of delivering resuscitation care to pTBI patients can provide insights into how healthcare systems can better support the delivery of effective and efficient trauma care.

VI-3 – Diagnosis of pTBI: Exam, Biomarkers, Imaging

B. Dengler, A. Lumba-Brown

Recommendations

Level I-III

There is insufficient evidence to support a strong, moderate or weak strength recommendation about the accuracy of using clinical exam and/or biomarkers for pTBI screening and diagnosis.

Level IV

- Given limited accuracy, routine plain x-rays are not recommended in the screening of pTBI.

Level C – Expert Consensus (Delphi Voting)

In the absence of direct scientific evidence, EXPERT CONSENSUS concluded that:

- CT scanning is recommended to screen patients for pTBI. (100% consensus)

No evidence or expert opinion supported distinct recommendations based on patient gender, age, wounding mechanism, or military vs civilian context.

Introduction

pTBI has one of the highest case fatality rates among all injury types. Mortality rates exceeding 90% have been reported for patients with GSW to the head in some studies. pTBI is not always obvious, as can be the case with nail gun injuries and when a stabbing implement is removed after causing injury. Consequently, it is crucial to screen patients for penetrating head

wounds upon their arrival at the ED to prevent morbidity and mortality later during their hospital stay. Screening methods vary and can include standard CT scans, plain radiography, and physical examinations. The exploration of new and evolving technologies, such as blood-based biomarkers is still in its early stages, with insufficient evidence to assess their efficacy fully. Thus, imaging modalities and physical examinations remain the

TABLE 6. Evidentiary Base for Diagnostic Accuracy of Screening With X-Ray Plain Film to Identify pTBI

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results ^a	Study risk of bias
Exadaktylos, 2002 ⁸² (NRS) Switzerland Civilian Stab: 100% (51% knives, 17% pangas, 3.3% screwdrivers, 3.3% glass bottles, 1.7% iron files, 1.1% fork and spoons, 0.5% wooden stick)	179 with stab wounds to the head Male: 93.8% Mean age: 31 y (range 15 to 71) GCS <9: 12.5% GCS 15: 11.7%	All underwent X-rays: 179 Reference standard: head CT: 179	Sensitivity: 27.34% (95% CI 19.84-35.92%) Specificity: 100% (95% CI 93.02-100%) PPV: 100% (95% CI 90-100%) NPV: 35.42% (95% CI 33.03-37.88%) NLR: 0.73 (95% CI 0.65-0.81) Accuracy: 48.04% (95% CI 40.53-55.62%) pTBIs detected on X-ray vs CT: 19.5% (35/179) vs 71.5% (128/179) pTBIs missed by X-ray: 80% (93/128)	High

CT, computed tomography; GCS, Glasgow Coma Scale; MOI, mechanism of injury; NLR, negative likelihood ratio; NPV, negative predictive value; NRS, non-randomized study; PPV, positive predictive value; pTBI, penetrating traumatic brain injury.

^aAssuming no false positives on skull radiographs.

most thoroughly researched and effective tools for the initial screening of pTBI.

Prior Guideline Recommendations

The first edition of the pTBI guidelines did not address the use of screening modalities.¹⁶ The prior guidelines did address the use of CT scan for the evaluation of patients with penetrating brain injury. They stated:

“CT scanning of the head is strongly recommended to evaluate the patient with penetrating brain injury. In addition to the standard axial views with bone and soft tissue windows, coronal sections may be helpful in patients with skull base or high convexity involvement. Plain radiographs of the head can be helpful in assessing bullet trajectory, the presence of large foreign bodies, and the presence of intracranial air. However, when CT scanning is available, plain radiographs are not essential and are not recommended as a routine.”

This recommendation was made at the option level based on 23 class III studies.^{38-40,61,64-81} These studies were all retrospective in nature and describe the merits and limitations of available diagnostic imaging studies, but do not directly discuss the imaging modalities affect on outcomes. Those 23 studies were excluded from consideration in these guidelines based on the methodology used. The 23 studies cited in the last guideline did not include a diagnostic accuracy which was the basis of the key question under consideration. Additionally, many of those earlier studies were from the pre-CT era or compared plain films to CT. There were no studies that compared CT to another “gold standard” thus eliminating them as possible considerations for a key question defined by diagnostic accuracy. It also deserves mention that in the first edition of these guidelines numerous CT findings were associated with poorer prognosis which provides further support for the importance of CT imaging.

Scientific Foundation

Only one study, published by Exadaktylos et al, was identified as meeting inclusion criteria that was pertinent to the key question on attempting to identify the best tools for screening and diagnosis of pTBI in the prehospital and ED setting⁸² (Table 6). The non-randomized study included 179 patients with stab wounds to the head, attending a trauma unit in Switzerland. They performed anterior-posterior and lateral view skull radiographs on all patients who later underwent head CT to diagnose penetration of the skull. The study reported skull X-rays identified 35 penetrating skull injuries, while follow-up CT identified 128. Assuming X-ray did not identify any false positive penetrating injuries (i.e., penetrating injuries on X-ray that were later identified as non-penetrating on CT), resulted in a sensitivity of X-ray of 27.34%, specificity of 100%, positive predictive value of 100%, and negative predictive value of 35.42%. This study is rated high risk of bias given unclear reporting with a need to assume no false positive cases. This study provides very low strength evidence that X-ray plain films are not accurate at identifying trauma patients who have a penetrating injury.

Seven non-randomized studies, not meeting inclusion criteria because they did not report diagnostic accuracy data, are reported here for completeness.^{10,58,83-87} The studies ranged in sample size from 30 to 7762; four studies (57%) included over 600 patients, with the other three including less than 100.^{58,85,87} All but one study was conducted in civilian populations;¹⁰ four in the United States, and one each in Germany, Turkey, and Austria.

Six studies reported the Glasgow Coma Scale (GCS) score by those with penetrating and those without penetrating head injuries, four reported this as a percent meeting specific GCS scores or ranges of scores, while one reported median scores⁵⁸ and the other appears to report mean scores (though the study does not report the unit of measure)⁸⁵ (Table 7). All studies reported more patients with pTBI

TABLE 7. GCS Scores for pTBI vs Blunt Head Injuries

Author, year	GCS score (% pTBI vs % blunt)
Demetriades, 2004 ⁸⁴ N = 760	3: 30% vs 7% 4-8: 18% vs 10% 9-12: 6% vs 10% 13-15: 47% vs 74%
Peek-Asa, 2001 ⁸⁶ N = 795	3-5: 47.3% vs 24.1% 6-8: 17.3% vs 21.3% 9-12: 11.8% vs 17.1% 13-15: 23.6% vs 37.5%
Dubose, 2011 ¹⁰ N = 604	3-8: 30% vs 18% 9-13: 4.6% vs 4.5% 14-15: 42% vs 51% Unknown: 23% vs 27% $P < .001$
Petridis, 2011 ⁸⁷ N = 30	3-8: 70% vs 0 9-15: 30% vs 100% $P < .05$

GCS, Glasgow Coma Scale; pTBI, penetrating traumatic brain injury.

GCS scores of 3, 3 to 5, or 3 to 8 and more patients with blunt head injuries had GCS scores of 9 to 15, 13 to 15, and 14 to 15; two studies reported these differences as statistically significant. One study reported a higher median GCS score in those with blunt injuries compared with pTBI (median, blunt vs pTBI: 15 vs 11, $P < .05$) and another reported higher mean (implied mean, unit not reported) GCS scores at admission with blunt injuries compared with pTBI (mean GCS, blunt vs pTBI: 11.3 vs 3.3, $P < .05$).

TABLE 8. Head AIS Scores for pTBI vs Blunt Head Injuries

Author, year	Head AIS score (% pTBI vs % blunt)
Demetriades, 2004 ⁸³ N = 7762	1-2: 25% vs 61% 3: 15% vs 16% 4: 33% vs 14% 5: 25% vs 8% 6: 2% vs 0 Head AIS ≥ 4 : 59% vs 22%, $p = \text{NR}$
Dubose, 2011 ¹⁰ N = 604	3: 41% vs 70% 4: 31.5% vs 24% 5: 24% vs 6.2% 6: 2.8% vs 0 Head AIS ≥ 4 : 59% vs 30%, $P < .001$
Demetriades, 2004 ⁸⁴ N = 760	Head AIS ≥ 4 : 83% vs 70%, $P < .001$

AIS, Abbreviated Injury Severity; NR, not reported; pTBI, penetrating traumatic brain injury.

Three studies reported the head AIS score by those with penetrating and those without penetrating head injuries and reported more patients with pTBIs had a head AIS score of ≥ 4 (pTBI vs blunt: 59%-83% vs 22%-70%, $P < .001$ in 2 studies,^{10,84} P -value not reported in 1 study, Table 3).⁸³

Two studies ($N = 816$) reported the Injury Severity Score (ISS) for those with penetrating and those without penetrating head injuries (Table 8). The first by Demetriades et al ($N = 760$) reported there was no difference in scores between types of head injury (mean ISS, pTBI vs blunt: 27 vs 26, $P = .18$ overall and $N = 497$, 22 vs 23, $P = .92$ when excluding those who were dead on arrival or had extracranial injuries.⁸⁴ The second study by Icer et al ($N = 56$) did not report statistical significance (median ISS, pTBI vs blunt: 25 vs 9).⁵⁸ The Icer study ($N = 56$) also reported the Revised Trauma Score (RTS) and Trauma Score-Injury Severity Score (TRISS), with no differences in median scores between those with pTBI and those without (RTS, pTBI vs blunt: 30 vs 26; TRISS, pTBI vs blunt: 91 vs 99.2).⁵⁸ In addition, the Icer study ($N = 56$) reported no differences in pupil light reflex between those with pTBI and those without.⁵⁸ Demetriades et al ($N = 760$) reported no differences in the rate of hypotension between those with pTBI and those without (systolic blood pressure < 90 mm Hg, pTBI vs blunt: 12% vs 10%, $P = .37$).⁸⁴

Discussion

The management and initial assessment of patients with suspected pTBI in the field, austere environments, or even in the ED presents significant challenges. The lack of specific tools for the screening and diagnosis of pTBI beyond standard trauma evaluations underscores a critical gap in emergency medical care. Despite the high mortality rates associated with pTBI, particularly those resulting from GSW to the head—where mortality rates can exceed 90%—there remains a substantial need for improved diagnostic and screening methodologies.

The importance of considering pTBI in any patient with an altered mental status or when a detailed history is not obtainable cannot be overstated. pTBI, especially, can be elusive and difficult to identify without a thorough and specific examination. The risk of overlooking such injuries is catastrophic, necessitating a high index of suspicion and a meticulous physical examination. This is true not only in uncontrolled field settings but also within the more structured environment of an ED.

Currently, imaging modalities such as CT scans and plain radiography, along with physical examinations, are the most reliable and researched methods for the initial screening of pTBI. These techniques, however, may not always be readily available in prehospital or austere settings, highlighting the urgent need for portable, efficient, and effective diagnostic tools.

Emerging technologies, including blood-based biomarkers, hold promise for the future of pTBI diagnosis. Nonetheless, these innovations are still in the nascent stages of development, with insufficient evidence to fully validate their efficacy. The potential of such technologies could revolutionize the way pTBI is diagnosed, especially in environments where traditional imaging equipment is not accessible. The discussion around the need for specific tools for pTBI screening and diagnosis in the field and austere environments, as well as in emergency settings,

is not just academic—it is a matter of life and death. The current evidence base is lacking in robust studies that evaluate the effectiveness of various modalities and tools for this purpose. The high case fatality rates associated with penetrating head wounds demand an aggressive approach to screening and diagnosis, emphasizing the importance of ongoing research and innovation in this field.

Expert Opinion

Although the literature lacks evidence supporting the use of CT scans for screening penetrating brain injuries, the group consensus was that it was practical, given that all patients undergo scanning in the ED. Furthermore, CT scans yield significant information about intracranial damage, unparalleled by other methods. Screening for penetrating brain injury with plain films identified one study with a high risk of bias, showing 100% specificity. However, its utility as a screening tool is undermined by the low sensitivity (27%), suggesting its use should be limited and these limitations noted. Plain x-rays can provide information on the

presence and location/trajectory of intracranial objects that are radio-opaque and it also lacks the scatter which can impede the interpretation of CT scans. Plain x-rays therefore have a limited role in the workup of pTBI, particularly when it is immediately available and CT imaging is not. Physicians must, however, have a keen awareness of the limitations of x-rays as articulated above.

Future Directions

Future studies should focus on evaluating the accuracy of various screening tools and diagnostic methods in identifying pTBI. This includes traditional assessments like the Glasgow Coma Scale and pupil response, as well as potential biomarkers (e.g., s100b, UCH-L1, GFAP, tau, NSE, neurofilament/NF-1, cytokines, SNP, EEG) that could offer novel insights into brain injury. Additionally, the effectiveness and precision of imaging techniques such as MRI, CT scans, and plain films in detecting pTBI need thorough investigation. Comparing these modalities against established standards will help elucidate their reliability and feasibility, especially in settings where resources are limited.

VI-4 – Diagnosis of pTBI: Screening Relevant to Patient Characteristics and Occult Penetrating Injuries

D. M. Stein, D.W. Wright, D. Boone, A. M. Rubiano

Recommendations

Level I-IV

There is insufficient evidence to provide an evidence-based recommendation on whether patient characteristics (e.g., age, gender, military status) or injury characteristics (e.g., mechanism or location of injury) affect the accuracy of screening for pTBI. Additionally, there is insufficient evidence regarding the potential benefits or harms of screening for pTBI in patients with head injury but no obvious skull penetration.

Level C – Expert Consensus (Delphi Voting)

In the absence of direct scientific evidence, EXPERT CONSENSUS concluded that:

- Head CT may be beneficial in identifying penetrating injury when the diagnosis of penetrating brain injury is uncertain. (100% consensus)
- A high index of suspicion for penetrating brain injury should be maintained when no obvious external signs of brain penetration are present and when CT scan is not available for confirmation. (96.6% consensus)

No evidence or expert opinion supported distinct recommendations based on patient gender, age, wounding mechanism, or military vs civilian context.

Introduction

Though the diagnosis of pTBI is often obvious, there are instances in which such injuries can be subtle or occult. For instance, this can occur when a stabbing instrument is removed

after penetration or in rare cases of penetration through the oropharynx, underscoring the importance of maintaining a high index of suspicion for such injuries. Moreover, definitive diagnosis at the time of injury may not always be possible, particularly in

austere conflict zones or other challenging settings. Numerous case studies have documented the detection of pTBIs through CT scans, even in cases without obvious penetrating injuries or when clinical evaluations are incomplete.

The role of clinical and injury characteristics in raising suspicion for pTBI and improving diagnostic accuracy has not been extensively studied. Characteristics such as patient demographics (e.g., age, gender, military status) and the mechanism and location of the injury may significantly impact the identification process. In austere or conflict environments, mass casualty situations, or cases involving multisystem trauma, wounds can be easily overlooked. Factors such as hair coverage, helmets, or bleeding scalp injuries can obscure wounds, while small entrance wounds—particularly in non-ballistic injuries like knife wounds with both entry and exit points—may show minimal visible signs of penetrating trauma, further complicating diagnosis. Therefore, screening CT imaging upon a patient's arrival at a facility equipped with advanced diagnostic technology plays a crucial role in definitely identifying such injuries.

A review of existing literature highlights a significant lack of studies examining how patient and injury characteristics influence the diagnostic process for pTBI. Non-randomized studies, primarily conducted in civilian populations across various countries, often fail to report diagnostic accuracy data, making it difficult to draw definitive conclusions. These findings underscore the pressing need for additional research to address these knowledge gaps and improve diagnostic practices for pTBI.

Prior Guideline Recommendations

The previous edition did not address the diagnostic accuracy of screening for pTBI based on patient characteristics or injury characteristics¹⁶ or the use of screening modalities.¹⁶ As previously discussed, the prior guidelines did address the use of CT scan for the evaluation of patients with penetrating brain injury. They stated:

“CT scanning of the head is strongly recommended to evaluate the patient with penetrating brain injury. In addition to the standard axial views with bone and soft tissue windows, coronal sections may be helpful in patients with skull base or high convexity involvement. Plain radiographs of the head can be helpful in assessing bullet trajectory, the presence of large foreign bodies, and the presence of intracranial air. However, when CT scanning is available, plain radiographs are not essential and are not recommended as a routine.”

This recommendation was made at the option level based on 23 class III studies.^{38-40,61,64-81} These studies were all retrospective in nature and describe the merits and limitations of available diagnostic imaging studies, but do not directly discuss the imaging modalities effect on or association with outcomes. Those 23 studies were excluded from consideration in these guidelines based on the methodology used. The 23 studies cited in the last guideline did not assess diagnostic accuracy which is the key question currently under consideration. Additionally, many of

those earlier studies were from the pre-CT era or compared plain films to CT. There were no studies that compared CT to another “gold standard” thus eliminating them as possible considerations for a key question defined by diagnostic accuracy.

Scientific Foundation

No studies were identified that assessed benefits or harms of screening vs no screening for pTBI in patients with head injury and no obvious penetration of the skull. Case reports^{88,89} suggest that screening with CT can identify penetrating objects in the absence of obvious penetrating injuries. Additionally, one non-randomized study by Exadaktylos et al (N = 179) found that CT can identify pTBIs that were not evident on x-ray (72% identified with CT vs 20% with x-ray alone),⁸² and multiple case series demonstrate that CT can identify retained or penetrating foreign bodies, bone fragments, wound tracts, and other evidence of penetrating brain injury in patients without obvious penetrating injuries or in which assessment for penetrating injuries prior to imaging was not reported.^{69,90-97} These studies indicate that CT scan may be beneficial in identifying penetrating injury when the diagnosis of pTBI is uncertain.

With respect to the risk for sustaining a pTBI which may be a consideration in screening practices, four studies (N = 2244) report mixed results on differences in ages between those diagnosed with pTBI and blunt injuries. Two studies (N = 1364) reported younger mean ages in patients with pTBI compared with patients with blunt injuries (military population, mean age, pTBI vs blunt: 25 vs 27 years, $P = .0352$ and civilian population, mean age pTBI vs blunt: 29 vs 40 years, $P < .001$), whereas the study in Austria (N = 85) reported older mean ages with penetrating injury (mean age, pTBI vs blunt: 52.7 vs 37.9 years).⁸⁵ One study (N = 795) reported percentages by age ranges, with younger patients more likely to have a penetrating injury (age, pTBI vs blunt: 16-29 years: 66.4% vs 38.1%; 30-49 years: 23.6% vs 38.1%; ≥50 years: 10% vs 23.8%).⁸⁶ One study (N = 760) that reported mean ages, also categorized patient ages as less than 55 years vs 55 years and older and found significantly more patients with pTBI were younger than 55 years compared with blunt injuries (age, pTBI vs blunt: ≤55 years: 93% vs 79%; >55 years: 7% vs 21%, $P < .001$).⁸⁴ Age is thus an inconsistent risk factor for pTBI.

Of four studies that reported differences in rates of males injured compared with females, three studies (N = 2159) report more males with head injury among pTBI patients compared with those with blunt injuries (% males, pTBI vs blunt: 87.3% vs 81.2%;⁸⁶ 37% vs 18%, $P = .001$;⁸⁴ 98.7% vs 94.6%, $P = .010$),¹⁰ while the study in Austria (N = 85) reported more males in those with blunt injuries compared with pTBIs (% males, blunt vs pTBI: 91.6% vs 76%).⁸⁵

One study reported that of those with intentional injuries (N = 469), more had pTBIs compared with blunt injuries (intentional, pTBI vs blunt: 63.5% vs 37.1%, p value not reported),⁹⁸ while the study in Austria (N = 85) reported more self-inflicted injuries were blunt (self-inflicted, blunt vs pTBI: 53.6% vs 46.4%).⁸⁵ A

third small study (N = 30) reported a significantly higher rate of suicide in those with pTBIs compared with blunt injuries (suicide, pTBI vs blunt: 33.3% vs 3.8%, $P = .006$).⁵⁸

Two studies (N = 851) reported more pTBIs in those sustaining injuries from firearms (firearms, pTBI vs blunt: 93.6% vs 0.7%),⁸⁶ bullets (bullets, pTBI vs blunt: 83.3% vs 19.2%, $P < .001$),⁵⁸ and high-velocity weapons (high-velocity, pTBI vs blunt: 73.3% vs 0, $P < .001$)⁵⁸ compared with those with blunt injuries. As well as in those with lateral as opposed to anterior/posterior injury in one study (lateral injury, pTBI vs blunt: 36.7% vs 11.5%, $P = .03$).

No studies meeting inclusion criteria provided information on how diagnostic accuracy of screening for pTBI differed based on patient or injury characteristics. Six non-randomized studies, not meeting inclusion criteria due to lack of diagnostic accuracy, provide limited information supporting expert consensus on the rate of characteristics associated with pTBI and non-penetrating head injuries.^{10,58,84-86,98}

Discussion

The evidence available is insufficient to support any evidence-based recommendation regarding the impact of patient or injury characteristics on the accuracy of pTBI screening or diagnosis, indicating a significant gap in research. The studies that were identified and discussed above do not meet the inclusion criteria for providing diagnostic accuracy data, but suggest the prevalence of certain characteristics among patients with pTBI vs those with blunt head injuries. Studies were subject to high bias and provided mixed results on age differences between patients diagnosed with pTBI vs blunt injuries.

While no studies meet inclusion criteria to support the benefits or harms of screening vs not screening for pTBI in settings without apparent skull penetration, numerous case reports document identification of pTBI with CT imaging when it had not been previously diagnosed. With this in mind, 100% consensus was achieved with respect to obtaining a CT head when diagnosis of pTBI is uncertain. No visibly apparent skull penetration would qualify as the prototypical example. The authors acknowledge that CT scan is not always available, and therefore additionally recommend a high index of suspicion for pTBI, given appropriate or suspicious history, when CT confirmation cannot be obtained.

Expert Opinion

It is our opinion that rapidly and accurately identifying patients with pTBI is critical for providing best care and achieving best outcomes. A high index of suspicion must be maintained for the

possibility of occult penetrating injuries and a policy of liberal screening - preferably with CT imaging - is encouraged. Difficult decisions regarding patient transfers may be required in care environments lacking diagnostic tools. Several promising point of care technologies such as blood-based biomarkers or infrared scanning technologies may soon provide adjunctive diagnostic information in environments lacking imaging or advanced imaging capabilities. Despite the significant limitations of X-ray imaging for pTBI, it can identify the presence and position of radio-opaque intracranial foreign bodies which can be valuable when scatter obscures CT imaging and it thus continues to have a limited role in pTBI.

Future Directions

Studies are needed which compare outcomes of patients with head injuries who undergo early screening for pTBI vs those who do not. These studies should aim to quantify the association with clinical outcomes, early detection rates, and potential harms such as radiation exposure, false positives, and unnecessary interventions. This includes long-term outcomes of screening, including neurocognitive and functional status, quality of life, and other complications. Ethical considerations would of course constrain methodologies that could be considered for relevant prospective studies. Another consideration is the need to investigate whether specific patient subgroups (e.g., based on age, gender, mechanism of injury, or initial clinical presentation) should receive stronger consideration for screening. This could help to avoid delays in diagnosis and may assist tailoring recommendations to specific populations or injury contexts. There may be important, distinct associations in military vs civilian environments.

Future research should inform which patients who are at elevated risk of occult pTBI. Large-scale, multicenter studies on diverse populations that thoughtfully analyze the impact of 1) patient demographics and 2) injury specifics in relation to the diagnostic accuracy of pTBI screening would be beneficial. Future studies should explore phenotypic differences in pTBI presentation and the relationship with injury detection.

Studies that specifically explore the utility and challenges of screening for pTBI in resource-limited/austere environments, as well as conflict zones are needed. Research should also focus on the development and validation of portable, efficient, and effective diagnostic tools for occult pTBI. This could include portable imaging technologies, point-of-care testing devices, or blood-based biomarkers that offer rapid and reliable diagnosis in the field.

VI-5 – Imaging of Neurovascular Injury in pTBI

D. M. Stein, G. Grant, D. Pannell, A. M. Rubiano, R. S. Bell

Recommendations

Level I

There is insufficient evidence to support a strong recommendation about the diagnostic accuracy of imaging to detect pseudoaneurysms.

Level II

- In patients with pTBI and a high index of suspicion for cerebrovascular injuries, digital subtraction angiography (DSA) should be performed as soon as feasible to detect traumatic aneurysms, as rupture is associated with worse outcomes.

Level III

- Following pTBI, treatment of traumatic intracranial arterial aneurysms (TICA) detected by screening improves the likelihood of survival.
- As traumatic intracranial aneurysms may develop in a delayed fashion, vascular imaging should be repeated to improve outcomes by identifying such TICAs prior to rupture. There is insufficient evidence to indicate the optimal timing for either initial or repeat vascular imaging in order to rule out cerebral vascular injury.
- CTA has the ability to detect some TICA as compared with the gold standard, digital subtraction angiography (DSA), and should be used as an initial screening modality.

Level C – Expert Consensus (Delphi Voting)

In the absence of direct scientific evidence, EXPERT CONSENSUS concluded that:

Timing

- For patients with pTBI, a CTA should be ordered to evaluate for vascular injury at the time of initial CT on presentation (100% consensus).
- In patients with pTBI, repeat vascular imaging should be obtained between 7-21 days post injury or prior to patient discharge from hospital (100% consensus).

CTA vs DSA

- If there is a high clinical suspicion for vasoospasm (VSP), DSA should be considered over CTA to enable urgent endovascular treatment. (92% consensus)
- DSA should be obtained in cases where vascular injury cannot be ruled out on CTA due to streak artifact from retained metallic fragments or where in-driven bone fragments or foreign bodies are adjacent to intracerebral vasculature (100% consensus).
- DSA should be performed in patients with CTA confirmed vascular injury (100% consensus).

Benefits, Harms, Accuracy

- The following characteristics are associated with higher risk of vascular injury, and should be considered when deciding about urgency and prioritization of vascular imaging (100% consensus):
 - wound trajectory through or adjacent to major brain vasculature
 - violation of multiple dural compartments
 - facio-orbito-pterional entry wounds
 - presence of intracerebral hematoma

No evidence or expert opinion supported distinct recommendations based on patient gender, age, wounding mechanism, or military vs civilian context.

Introduction

pTBI frequently results in cerebrovascular injuries, leading to conditions such as TICA, arteriovenous fistula, and cerebral VSP, which if untreated, can significantly increase morbidity and mortality risks.^{99,100} The rupture of TICAs in particular can cause catastrophic intracranial hemorrhage, often resulting in death. Early detection is thus crucial as it enables planning of often complex surgical or endovascular interventions, considering the size and location of the lesions. However, these lesions can develop in delayed fashion, making delayed imaging crucial. Despite the critical nature of early and accurate detection, there has been a historical absence of guidance for the optimal imaging modality and timing for vascular imaging in pTBI.

CTA offers a quick and accessible means for imaging the intracranial vasculature, yet DSA remains the more sensitive and specific gold standard, despite its lower availability and more invasive nature. The management of cerebrovascular injuries is complicated by the potential for delayed TICAs, which can develop subsequent to initial imaging.^{99,101} These pseudoaneurysms, disrupting all vessel wall layers and contained only by clot, pose severe risks upon rupture. Early and accurate diagnosis is key to enabling effective endovascular and surgical treatments, underscoring the importance of repeated imaging with appropriate timing to improve patient outcomes.

The current guidelines endeavor to inform the optimal means of diagnosing and treating vascular injury from penetrating trauma. This section focuses on the evidence related to diagnosis, addressing three key areas: (1) the accuracy of DSA and CTA in pTBI, (2) the benefits and harms of DSA, and (3) the optimal timing of initial and delayed vascular imaging.

Prior Guideline Recommendations

The prior penetrating head injury guidelines addressed the “Neuroimaging in the Management of Penetrating Brain Injury”¹⁰² and the “Vascular Complications of Penetrating Brain Injury.”¹⁰³ Concerning Neuroimaging, a total of 24 articles were included as direct evidence to support recommendations made at the level of option. Only two of the 24 articles^{66,101} addressed the utility of diagnostic cerebral angiography in the setting of pTBI. The remaining 22 articles cited as direct evidence addressed the utility of CT and plain skull x-rays in pTBI. The routine performance of CTA was not addressed. These two papers supported the recommendation, at the level of Option (Level III/IV), that a cerebral angiogram should be performed in patients where vascular injury is suspected, including those with wound trajectories near the Sylvian fissure, supraclinoid carotid, and cavernous or other venous sinuses. It was also stated that unexplained or delayed subarachnoid hemorrhage or other hematoma should also prompt the performance of catheter DSA.

Scientific Foundation – Accuracy of CTA and DSA

Three studies (N = 174) found the sensitivity of CTA, with DSA as the reference standard, to be 36%, 50%, and 73% for

cerebral artery injury in a civilian setting in the United States with most patients victims of GSWs (86%, 86%, and 89%, Table 9).¹⁰⁴⁻¹⁰⁶ Bodanapally et al (N = 45) reported lower sensitivity with CTA when metal artifacts were present (67%).¹⁰⁵ This study also reported a range of sensitivities across three different readers (64% to 73%, no metal artifacts). Specificity was 85%, 88%, and 94% across the same three studies, with no change associated with metal artifacts. The range of specificities across three readers in one study was 84% to 100%.²⁰ Positive predictive value (PPV) of CTA for arterial injury was 50%, 67%, and 89% and ranged from 74% to 100% across three readers; NPV was 62%, 83%, and 88% and ranged from 77% to 85% across three readers.^{104,105,107} In one study, the number of DSAs needed to identify one patient with a treatment-requiring lesion not found on CTA was 5.6.¹⁰⁷

Diagnostic accuracy of CTA varied across studies (especially sensitivity), across readers within one study, and whether or not metallic artifacts were present. These studies provide moderate strength evidence that DSA detects a greater number of vascular injuries than CTA in the setting of GSW to the head. These studies also provide conflicting, and therefore insufficient evidence on the precise diagnostic accuracy of CTA to detect pseudoaneurysms using DSA as a reference standard, although there is low strength evidence to say that CTA may identify some pseudoaneurysms. Meyers, et al speculates that this difference in findings may be due to selection bias in retrospective studies compared with prospective studies that may overestimate the benefit of CTA.¹⁰⁷

Scientific Foundation – Benefits and Harms of DSA

Ten studies meeting inclusion criteria for formal use as evidence reported results of cerebral angiography in patients with pTBI, with a total of more than 1320 angiograms conducted (number not reported in one study)^{99,105,107-114} (Table 10). Eight studies were case series, and did not compare angiography to another method of diagnosis (though one of these reported autopsy results in patients who died);¹¹⁴ two studies,^{105,107} also described in Key Question 2, compared cerebral angiography with CT angiography. Three studies were conducted in the United States, three in South Africa, and four in Middle Eastern countries; populations were military in three studies, civilian in five, and mixed in two. Most patients were young men (average proportion male 90% and average mean age 25.5 years across studies), and the range of the average baseline GCS scores was 8.3 to 11 across five studies that reported this severity measure. Several other studies were excluded that reported very few angiograms and/or vascular lesions or had unclear reporting of clinical outcomes.^{104,115-119}

Benefits

The primary benefit from screening for TICAs and cerebral VSP is the potential for lifesaving/morbidity-reducing intervention(s) that would not have occurred without screening. The rate at which TICAs were identified varied across seven studies,^{99,105,107-111,113}

TABLE 9. Evidentiary Base for Cerebrovascular Imaging Studies

Author, year (Study design)				
Country				
Civilian/Military				
MOI	Baseline characteristics	Intervention	Results	Study risk of bias
Ares, 2019 ¹⁰⁴ (NRS) United States Civilian GSW: 86%	Male: 91% Mean age: 32 Patients had penetrating head and/or neck injury	CTA and DSA (N = 56) DSA gold standard	Intracranial injury (internal carotid artery, posterior circulation, arteriovenous fistula) Sensitivity: 0.50 Specificity: 0.88 PPV: 0.50 NPV: 0.88	Moderate
Bodanapally, 2014 ¹⁰⁵ (NRS) United States Civilian GSW: 89% Stabbing: 9% Other: 2%	Male: 78% Age: 31 y Severity: NR Mean time between CTA and DSA: 7.4 h	CTA and DSA ^a (N = 45) DSA gold standard	Detection of arterial injuries without metal artifacts Sensitivity: 0.727, 95% CI 0.498-0.893 Specificity: 0.935, 95% CI 0.786-0.992 PPV: 0.889, 95% CI 0.653-0.986 NPV: 0.829, 95% CI 0.664-0.934 AUC: 0.83, 95% CI 0.726 to 0.936 With metal artifacts present Sensitivity: 0.667, 95% CI 0.447-0.836 Specificity: 0.943, 95% CI 0.837-0.990 PPV: 0.889, 95% CI 0.684-0.980 NPV: 0.805, 95% CI 0.715-0.845 Range across 3 readers (no metal) Sensitivity: 0.636 to 0.773 Specificity: 0.839 to 1.00 PPV: 0.737 to 1.00 NPV: 0.765 to 0.848 AUC: 0.77 to 0.86	Moderate

TABLE 9. Continued.

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Study risk of bias
Meyer, 2024 ¹⁰⁷ (NRS) United States Civilian GSW: 86.3% Stab wound: 11% Nail gun: 1.4% Crossbow: 1.4%	Male: 76.7% Mean age: 35 y Mean GCS: 9.5 (range 3-15)	CTA and DSA All patients received both (N = 73)	Mean GOS: 4 (range 1-5) Diagnostic accuracy of CTA for cerebrovascular injury (including TICA, arterial occlusions, dural venous sinus occlusion, dural arteriovenous fistula, carotid cavernous fistula) Sensitivity: 0.364, 95% CI 0.204-0.549 Specificity: 0.85, 95% CI 0.702 to 0.943 PPV: 0.667 NPV: 0.618 NNT: 5.6	Moderate

AUC, area under the receiver operating characteristic curve; CTA, computed tomographic angiography; DSA, digital subtraction angiography; GSW, gunshot wound; MOI, mechanism of injury; NNT, number needed to treat; NPV, negative predictive value; NR, not reported; NRS, non-randomized study; PPV, positive predictive value.

^aUnclear why results of only 32 DSA/CTA pairs reported for diagnostic accuracy of CTA for TICAs, vs 48 total obtained.

from 3.6% in a military population in Iran (8 TICAs in 223 angiograms) to 40% in an Israeli study of civilian and military patients (10 TICAs in 25 angiograms); the weighted average across studies was 8.6%. When identified, TICAs were usually treated (55% to 100% of patients with TICAs treated in 7 studies;^{99, 108-113} some untreated patients recovered spontaneously, some refused treatment, and some died. Between 55% and 100% of patients with angiography identified TICAs (with or without other cerebrovascular abnormalities) underwent surgery or endovascular intervention and survived (5 studies,^{108-111,113} weighted average 65% treated). These studies provide low strength evidence that interventions to treat TICA found during screening improve the likelihood of survival.

Five studies reported Glasgow Outcome Scale (GOS) scores for patients with TICAs, on a scale from 1 to 5 with higher scores representing better outcomes. Mean GOS ranged from 3.1 to 4.4 (severe to moderate disability) across three studies; in the fourth, 66% had scores of 4 or 5 (moderate to low disability). In the fifth most recent study, mean GOS ranged from 1-5 with a mean of 4.¹⁰⁷ Three studies also reported VSP,^{99,111,114} with rates between 2.7% and 54% of angiograms; the study with a rate of 54%⁹⁹ reported treating all identified lesions, but did not describe treatment outcomes. The other four studies did not report treatment for VSP.

Harms

The primary harms of screening for TICA and VSP are any increase in morbidity/mortality due to the screening process

(cerebral angiography), as well as any increase in morbidity/mortality due to any intervention provided because of a positive screen. The data on harms of screening and harms of treatment due to screening are sparse. One study stated there was “no procedure-related morbidity or mortality” and no groin complications.¹¹⁰

Diagnostic accuracy

Two studies reported information relevant to the diagnostic accuracy of cerebral angiography. Because cerebral angiography is most often considered the reference standard for detection of intracerebral vascular lesions, we did not identify studies reporting true diagnostic accuracy outcomes for angiography, and we did not assess strength of evidence for these outcomes. One study described a U.S. civilian population, with 45 patients who received both cerebral angiography and CTA.¹⁰⁵ Several reviewers assessed CTA results retrospectively, with a final reading adjudicated by a fourth reviewer. The adjudicated CTA result identified the same seven TICAs as the cerebral angiogram. However, the initial clinical CTA reading identified five TICAs vs seven seen on cerebral angiography.

A study from South Africa found one patient with a TICA among 15 undergoing cerebral angiography.¹¹⁴ The same lesion was found at autopsy in this patient; in addition, an autopsy found a ruptured TICA in another patient 11 days after injury, in whom an angiogram on admission had been normal. It is unclear whether the initial angiogram missed an aneurysm present then,

TABLE 10. Evidentiary Base for Cerebral Angiography to Diagnose Traumatic Intracranial Aneurysms and Vasospasm

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Study risk of bias
Aarabi, 1988 ¹⁰⁸ (NRS) Iran Military Shell fragments: 73.7% Missiles: 6.7% Undetermined projectile: 19.6% Penetrating: 61% (100% of TICAs) Tangential: 21% Perforating: 6% Unclassified: 12%	Among 255 pTBIs: Male: 99% Mean age: 21 y (22 among TICAs) Among 8 with TICAs: Mean GCS: 9.9	Cerebral angiography, most transfemoral (N = 223)	Benefits: 8 patients with TICAs (3.6%) 7 treated with surgery, 5 survived (potential benefit in 63%) 1 recovered without surgery (12.5%) Mean GOS: 3.4 Harms, diagnostic accuracy: NR	High
Amirjamshidi, 1996 ¹⁰⁹ (NRS) Iran-Iraq Military Missile injuries not further described; combatants in Iran-Iraq war	Among patients with TICAs: Sex: NR Mean age: 20 y Severity: NR	Cerebral angiography (N = 519, 49 unselected/screening)	Benefits: 28 TICAs in 26 patients (5.0% of patients) 16 treated and survived (potential benefit in 62%) 7 healed spontaneously (27%) 3 patients died (none treated) Harms, diagnostic accuracy: NR	High
Bell, 2010 ⁹⁹ (NRS) United States Military MOI among 34 patients with pTBI: Blast: 73.5% GSW: 20.6% Knife: 2.9% Unknown: 2.9%	Among 47 patients with any craniocervical injury and with vascular injuries: Male: 100% Mean age: 25.8 y Mean GCS: 8.8 Mean ISS: 24	Cerebral angiography (N = 162 with pTBI and angiography)	Benefits: 30 TICAs identified in 23 patients (14% of patients) 12 patients treated endovascularly (52%) 5 treated with surgery (22%) 6 not treated (26%) Among 47 patients with any craniocervical injury and with vascular injury Traumatic vasospasm found and treated in 54% of patients with TICAs Mean GOS: 3.1 Harms, diagnostic accuracy: NR	High

TABLE 10. Continued.

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Study risk of bias
Bodanapally, 2014 ¹⁰⁵ (NRS) United States Civilian GSW: 89% Stabbing: 9% Other: 2%	Among 45 pTBI patients with TICAs: Male: 78% Mean age: 31 y Severity: NR	DSA (cerebral angiography) CT angiography, helical All patients received both studies (N = 48 DSAs and CTAs ^a in 45 patients; 3 repeat studies)	Benefits: 7 TICAs detected (16% of patients) Diagnostic accuracy Sensitivity of CTA for pseudoaneurysms (adjudicated CTA reading): 100% (7 detected by both CTA and DSA) Sensitivity with initial CTA reading: 71% (5 detected by CTA, 7 detected by DSA) Harms: NR	Moderate
Cohen, 2008 ¹¹⁰ (NRS) Israel Civilian and military Terrorist bombing: 30% Combat explosion: 40% GSW: 20% Stabbing: 10%	Among 10 pTBI patients with TICAs: Male: 80% Mean age: 18.2 y Mean GCS: 8.3 Screening (based on tract) in 80%, clinical indication in 20%	Cerebral angiography, ultrasound-guided femoral artery puncture (N = 25 with pTBI)	Benefits: 10 TICAs identified (40% of patients) Endovascular treatment performed during diagnostic angiography in all 10 patients (100%) Aneurysm excluded from circulation in all 10 patients (benefit in 100%) No delayed bleeding (mean 2.6 y follow-up) Mean GOS: 4.4 Harms: "No procedure-related morbidity or mortality," no groin complications Diagnostic accuracy: NR	High

TABLE 10. Continued.

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Study risk of bias
du Trevou, 1992 ¹¹¹ (NRS) South Africa Civilian Stabbing (knife, screwdriver, sharpened stick; 48% unknown object)	250 with intracranial stab wounds, object withdrawn: Male: 91% Mean age: 27 y Mean GCS: 11 GCS <8 (coma): 25%	Cerebral angiography, Seldinger technique (N = 181)	Benefits: 24 TICAs identified in 21 patients (12%) 16 had surgery with good outcome (potential benefit in 76%) 2 refused surgery, outcome NR 2 had spontaneous resolution 1 died from primary injury Vasospasm identified: 19 patients (10%) 10 resolved by second angiogram 3 refused second angiogram, good outcome 5 died, severe primary injuries Outcome NR in 1 GOS 1 (death): 26% 4 or 5: 66% Harms, diagnostic accuracy: NR	High
Haddad, 1991 ¹¹² (NRS) Lebanon Civilian and military (militia) Shrapnel: 93% GSW: 7%	Among 15 patients with missile pTBI and TICAs: Male: 100% Mean age: 22.5 y Severity: NR Screening in 67% (routine pre- or post-operative), clinical decline in 33%	Cerebral angiography (N = NR)	Benefits: 19 TICAs identified in 15 patients (2 also had vasospasms) 13 had surgery, with good or fair outcome in 53% and death or another poor outcome in 47% Harms, diagnostic accuracy: NR	High
Kieck, 1984 ¹¹³ (NRS) South Africa Civilian Stabbing (mostly knives)	Among 109 with stab wounds: Male: 93% Age <30 y: 79% Severity on admission Coma: 11% Major neurologic deficit: 20% Minor neurologic deficit: 19% Cranial nerve palsy: 7.3% Neurologically intact: 42%	Angiography (N = 74)	Benefits: 11 patients with TICAs (15%) 6 treated with surgery, "all did well" (potential benefit in 55%) 4 died without surgery 1 lost to follow-up 2 with delayed vasospasms (2.7%), treatment NR; 1 with GOS 5, 1 with GOS 2 Harms, diagnostic accuracy: NR	High

TABLE 10. Continued.

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Study risk of bias
Nathoo, 2000 ¹¹⁴ (NRS) South Africa Civilian Transcranial or transorbital stab injuries (82% knives)	17 patients with brainstem injuries: Male: 94% Mean age: 28.6 y Mean GCS: 8.53	Cerebral angiography (N = 15) Cranial autopsy in patients who died (N = 13)	Benefits, harms: NR Diagnostic accuracy: Angiography: TICA in patient 5 (6.7%; surgery with clipping, death from sepsis) Vasospasm in patient 12 (6.7%; later infarct, patient died) Autopsy: TICA in patient 5 Ruptured TICA in patient 7, death 11 days after injury; cerebral angiography at admission normal	High
Meyer, 2024 ¹⁰⁷ (NRS) United States Civilian GSW: 86.3% Stab wound: 11% Nail gun: 1.4% Crossbow: 1.4%	73 pTBI patients with DSA: Male: 76.7% Mean age: 35 y Mean GCS: 9.5 (range 3-15)	CTA DSA All patients received both (N = 73)	Mean GOS: 4 (range 1-5) Pseudoaneurysm diagnosed by DSA: 13 Pseudoaneurysm missed by CTA: 9 (69%) Pseudoaneurysm misdiagnosed by CTA: 2 (15%) Accurately diagnosed by CTA: 2 (15%)	Moderate

CT, computed tomography; CTA, computed tomographic angiogram; DSA, digital subtraction angiography; GCS, Glasgow Coma Scale; GOS, Glasgow Outcome Scale; GSW, gunshot wound; ISS, injury severity score; MOI, mechanism of injury; NR, not reported; NRS, non-randomized study; pTBI, penetrating traumatic brain injury; TICA, traumatic intracranial aneurysm; VSP, vasospasm.

^aUnclear why results of only 32 DSA/CTA pairs reported for diagnostic accuracy of CTA for TICAs.

or whether the TICA developed during the 11-day interval between admission and death.

One study from Turkey did not meet inclusion criteria (62% with intracranial injury [and some of those injuries may not have been penetrating] which is less than the inclusion cutoff of 85% with penetrating injury when study findings are not reported by penetrating vs nonpenetrating injury), but reported 115 patients with missile head injuries who received conventional angiography; 82 patients had magnetic resonance angiography (MRA) as well as angiogram.⁹⁶ Cerebral angiography identified traumatic pseudoaneurysms in 21 patients, of which MRA detected three and missed 18; angiography identified 23 patients with vasospasm, of which MRA detected five. It was unclear whether every patient with TICA or VSP identified on angiogram also had an MRA; however, the authors concluded that DSA was preferable to evaluate these lesions.

Another study that did not meet inclusion criteria (75% with pTBI) retrospectively reviewed the charts of patients from the Iraq war and reported that 47% of 57 patients were found to have VSP (mean duration 14.3 days) identified by CTA.¹⁰⁰ Most of these injuries were blast-related (82%). This study found that

intracranial vasospasm was associated with TICA (48% of patients had both a TICA and vasospasm, $P = .05$) and mortality (15% of patients with vasospasm died vs 0% without vasospasm, $P = .029$), as well as hemorrhage ($P = .03$) and number of lobes injured ($P = .0012$). Discharge GOS was worse in patients with vasospasm (2.78 vs 3.68, $P = .002$). Ten patients (37%) were treated with medical management including hypertensive, hypervolemic, and hemodilution therapy as needed; 17 patients (63%) also received endovascular interventions including micro-balloon angioplasty. GCS scores improved with medical management alone and with medical management plus endovascular therapy. There is thus insufficient evidence to determine the diagnostic accuracy or harms of cerebral angiography and low strength evidence that screening for TICA with cerebral angiography improves the likelihood of survival.

Scientific Foundation – Timing of initial and repeat vascular imaging

One study (N = 181) from South Africa of victims of stab wounds to the head reported outcomes in patients who underwent

angiography within 7 days of injury or after 7 days (Table 11). They reported no statistically significant difference in the identification of vascular injury ($P = .183$) between early and late angiography, although a higher proportion of patients were found with vascular injury in the group ($N = 51$) who underwent angiography after 7 days (41% vs 31%).¹¹¹ This study provides very low strength evidence of no difference between early and late angiography. Of the 21 patients with TICA, there was one death in the group who underwent late angiography (1/6 [17%] vs 0/15 [0%]). However, due to the small number of patients with TICA and very few deaths, it is not possible to determine if angiography before or after 7 days of injury is preferred, although the study authors concluded that angiography should occur as soon after admission as possible.

Nine case series were included which addressed benefits and harms of screening for delayed vascular complications and included both military and civilian populations. Most injuries were blast-related or GSWs. The three largest case series included 26 patients with pTBI and 60% blast-related intracranial vascular injury in Iraq.^{99,111} Thirteen U.S. patients with GSWs,¹²⁰ and 24 mostly civilian patients in Israel¹¹⁰ and are discussed below. The time to second vascular imaging varied across the nine studies. All studies were rated high risk of bias due to study design.

In one case series ($N = 26$), all patients received DSA and repeat angiography.⁹⁹ Of those 26 patients, four experienced a TICA rupture, one each on days 6, 14, 23, and 32. Additionally, most intracranial vessels that were not treated (9/10) experienced resolution of their vascular injury. When including patients with intracranial vascular injury or extracranial vascular injury, the mean time to aneurysm interval expansion was 24 days (range 8 to 75 days).

A second case series ($N = 13$ patients with GSWs and follow-up CTA) reported 44.4% vascular injury on initial CTA.¹²⁰ Mean time to repeat CTA was 6.8 days. Of those 13 patients, seven had no vascular injury on initial CTA and six of those patients had no vascular injury on follow-up. However, one patient had a TICA on repeat CTA. Of the six patients with vascular injury on initial CTA, four had similar findings on follow-up CTA. However, two patients had new findings on repeat CTA (VSP of anterior cerebral artery and posterior cerebral artery and thrombus of superior sagittal sinus). Additionally, two patients with vascular injury on initial CTA had a negative follow-up CTA. Three patients had follow-up angiograms (1 with no vascular injury and 2 with vascular injury on initial CTA) and follow-up imaging had similar findings.

A third case series ($N = 24$ with repeat imaging; details provided for 9 TICA patients).¹¹⁰ reported nine patients with TICA on initial angiogram, all of whom were successfully treated; it is presumed that follow-up vascular imaging with angiography or CTA demonstrated resolution or improvement. Of 15 patients with no TICA on screening angiography, no new TICAs were detected on repeat imaging.

These studies plus the smaller case series reported in the table provide low strength evidence that repeat vascular imaging may yield different findings from initial imaging (e.g., new or unrecognized vascular injury, worsening injury, improved injury [with or without treatment], resolution of vascular injury).^{109,112,121-123} There is insufficient evidence to determine the best interval between initial and follow-up vascular imaging, with most studies reporting a repeat imaging interval between 1 and 5 weeks, although longer intervals are also reported.

Discussion of Evidence

Evidence for CTA vs DSA to detect cerebrovascular injury from pTBI

The importance of timely and accurate diagnosis of traumatic pseudoaneurysms following pTBI is significant, given their high risk of growth and rupture with an associated high mortality rate. The discussion around the best screening modality for detecting cerebrovascular injuries post-pTBI highlights the complexity and urgency of this medical challenge. Traumatic pseudoaneurysms represent the most common histologic type observed after pTBI, necessitating urgent management to prevent life-threatening consequences. The treatment of pTBI induced traumatic cerebrovascular injury will be addressed in Sections VII-6, VII-7, and the Management Algorithm. This section addresses issues related to imaging of cerebrovascular injury specifically.

Historically, the guidelines for managing penetrating brain injuries have recommended vascular injury screening using angiography, particularly in cases where the trajectory of the wound suggests an increased risk of vascular injury.^{102,103} However, advancements in diagnostic imaging and a lack of consensus in the literature have led to a debate over the optimal screening regimen, timing of imaging, and specifically between use of CTA and DSA.

The scientific foundation, one prospective study and two retrospective studies led to a level II recommendation in support of DSA for high-risk patients.^{104,105,107} However, the data reported in the prospective study were insufficient to calculate sensitivity and specificity of CTA to detect pseudoaneurysms due to the possibility of one individual having multiple pseudoaneurysms and other methodological concerns which limited the impact of the study. The retrospective studies evaluated the diagnostic accuracy of CTA against DSA and showed high sensitivity, specificity, and predictive values for detecting pseudoaneurysms when both modalities were in agreement. Yet, the initial interpretation of CTA results missed a significant proportion of traumatic intracranial arterial aneurysms, and missing data for a third of the CTA-DSA pairings reduces confidence in these results. This highlights the potential limitations of relying solely on CTA for initial diagnosis without considering DSA for confirmation, especially in ambiguous cases.

While both CTA and DSA offer valuable insights into cerebrovascular injuries post-pTBI, the decision on which modality to employ should be guided by the specific clinical context, including the availability of technology, expertise, and the patient's condition.

TABLE 11. Evidentiary Base for Screening for Delayed Vascular Complications

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Study risk of bias
Bell, 2010 ⁹⁹ (NRS) United States Military Blast: 60% GSW: 25% Knife: 8%	N = 47 pTBI patients with vascular injuries Male: 100% Mean age: 25.8 y Mean admission GCS: 8.8 Mean ISS: 24	pTBI patients with intracranial vascular injury detected on DSA (N = 26) All patients received follow-up angiography N = 47 with intracranial and/or extracranial vascular injury Average time to primary angiogram: 10 d Average time to treatment: 16 d	pTBI patients experienced intracranial aneurysm rupture: 4 (days 6, 14, 23, 32) pTBI patients required retreatment: 4 (2 who also experienced aneurysm rupture and 2 who did not) Untreated intracranial vessels resolved without treatment: 90% (9/10) Average time delay for aneurysm interval size increase (N = 47 with intracranial and/or extracranial vascular injury): 24 d (range 8–75)	High

TABLE 11. Continued.

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Study risk of bias
Dawoud, 2021 ¹²⁰ (NRS) United States Civilian GSW: 100%	N = 63 Male: 81% Median age: 36 y White: 62% Black: 33% Asian: 2% Severity: NR Bihemispheric: 25.4%	Initial screening for vascular imaging was CTA (N = 63) Patients with follow-up CTA: 13 Patients with follow-up angiogram: 3 Mean time to repeat CTA: 6.8d	Cerebral vascular injury on initial CTA: 44.4% 6 patients with no vascular injury on initial CTA had no vascular injury on repeat CTA; 1 patient with no vascular injury initially had TICA on follow-up CTA; of 6 patients with vascular injury on initial CTA, 4 patients had similar findings on repeat imaging and 2 patients had new findings (VSP of ACA and PCA and thrombus of superior sagittal sinus) on follow-up CTA; 2 patients with vascular injury on initial CTA had a negative follow-up CTA Follow-up angiogram on 1 patient with a negative CTA was also negative; follow-up angiogram of 2 patients with vascular injury on initial CTA had no new findings	High
Cohen, 2008 ¹¹⁰ (NRS) Israel Mostly civilian Blast: N = 7 GSW: N = 2 Umbrella: N = 1 Other: NR	N = 25 with pTBIs (13 with TICAs) Male: 77% Median age: 18.4 y (range 0.5–31) Median GCS: 7 (range 5–11)	All pTBI patients had angiography (N = 25) Had repeat vascular imaging (CTA or angiography; N = 24)	Had aneurysm on initial screening: 9 Successfully treated TICA (presumed repeat imaging demonstrated that): 9 Had negative results on initial screening: 15 Follow-up imaging yielded no additional aneurysms (second angiogram 2–4 wks after admission)	High

TABLE 11. Continued.

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Study risk of bias
Amirjamshidi, 1996 ¹⁰⁹ (NRS) Iran-Iraq Military GSW: 100% (presumed)	N = 29 pTBI patients Male: 100% (presumed) Mean age: 20 y (range 15–27) Severity: NR	Had initial angiography (N = 26) Had repeat angiography (N = 10)	Findings on repeat angiography Spontaneous healing: 6 Other findings: Patient A: Initial angiogram showed small traumatic aneurysm (A2); 8-d follow-up angiogram showed expansion of the TA Patient B: Initial angiography negative; 35-d follow-up angiography showed extracavernous carotid aneurysm, Hunter ligation of ICA attempted, patient died, autopsy showed fractured bone at base of skull with tear of extracavernous carotid artery, wrong artery ligated Patient C: Initial angiogram showed traumatic aneurysm; 10-d follow-up angiogram showed expansion of the aneurysm; 3rd angiogram showed shrinkage; 4th angiogram (about 34 d from initial angiogram) showed re-expansion Patient D: Initial angiogram showed carotid cavernous sinus fistula; 18-d follow-up results not reported	High

TABLE 11. Continued.

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Study risk of bias
Haddad, 1991 ¹¹² (NRS) Lebanon Military/Civilian Shrapnel: 93% Spent bullet: 7%	N = 15 pTBI patients Male: 100% Mean age: 22.5 y (range 6–57) Severity: NR	All patients had TICA on initial or follow-up angiogram (N = 15) Had repeat angiograms (N = 3) Time to repeat angiogram: 18 d for 2 patients, NR for 1 patient	Patient A: First angiogram not conclusive, second angiogram TICA Patient B: First angiogram not conclusive, second angiogram TICA Patient C: TICA on MCA branch not seen on first angiogram but seen on second angiogram In 2 cases TICA had increased in size	High
Ozkan Arat, 2015 ¹²⁴ (NRS) Turkey Civilian Knitting needle: 2 Shotgun: 2 Pencil: 1	N = 5 Male: 60% Median age: 15 y (range 2–16)	Varied initial and follow-up imaging (see results)	Patient A: TICA on CTA, 1-y follow-up angiogram: aneurysm decrease in size and lobulation Patient B: TICAs on DSA, 8-d follow-up DSA showed interval enlargement Patient C: Carotid angiogram revealed a carotidocavernous fistula, 6-mo follow-up carotid angiography showed occlusion of right ICA and collateral flow Patient D: CTA showed dissecting aneurysm of MCA; 2-mo follow-up CTA showed patient MCA and occlusion of aneurysm Patient E: CTA showed pseudoaneurysm of distal ACA, 21-mo MRA showed no recurrence after coiling	High

TABLE 11. Continued.

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Study risk of bias
Rostomily, 1997 ¹²² (NRS) United States Civilian GSW: 100%	N = 2 with pseudoaneurysm of ICA Male: 100% Ages: 24 and 34 y Severity: NR	Both patients had initial angiography	Patient A: ICA pseudoaneurysm on initial angiography; 5-wk follow-up angiogram revealed enlargement of pseudoaneurysm; postop angiograph after bypass grafting of ICA showed patent graft Patient B: Initial angiography showed pseudoaneurysm of ICA; after craniotomy, 4-wk angiography showed enlarge pseudoaneurysm; died 2 d before planned bypass	High
Sweeney, 2011 ¹²⁵ (NRS) United States Civilian Knife: 100%	N = 2 Male: 50% Ages: 21 and 31 y	See results	Patient A: Initial CTA showed partial occlusion of distal right A2; 2-wk follow-up CTA showed patent distal right A2 with no pseudoaneurysm; 3-mo follow-up CTA showed no pseudoaneurysm Patient B: Initial CTA showed no large-vessel occlusion; 2-wk postoperative angiogram showed no pseudoaneurysm and filling of vasculature tree; 1-y follow-up CTA was normal	High

TABLE 11. Continued.

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Study risk of bias
Yoon, 2022 ¹²³ (NRS) United States Civilian GSW: 100%	N = 73 pTBI patients Male: 90.4% Median age: 43.4 y Median GCS: 6 Median ISS: 21	Received initial CTA, MRA, or DSA (N = 59) Total with cerebral vascular injury on initial or follow-up imaging (N = 14) Total with repeat imaging (N = NR)	Vascular injuries missed on initial read of imaging (radiologists had various experienced levels, images were also retrospectively reviewed by senior radiologists): 50% Inconclusive CTA, vascular injury found on DSA: 1 patient No vascular injury on initial vascular screening, found to have vascular injury on follow-up: 4 patients (3 pseudoaneurysms, 1 occlusion) Diagnosed on repeat CTA: 2 Diagnosed on angiogram: 2	High
du Trevou, 1992 ¹¹¹ (NRS) South Africa Civilian Stabbing (knife, screwdriver, sharpened stick; 48% unknown object): 100%	N = 250 with intracranial stab wounds, object withdrawn Male: 91% Mean age: 27 y (range 8 mo to 70 y) GCS: NR Parietal: 42%	Initial angiography within 7 d (N = 130) Initial angiography after 7 d (N = 51)	Identification of vascular abnormalities between early and late angiography ($P = .183$): Early angiography: 31%; of the 15 patients with traumatic aneurysms, 14 were operated and survived; 1 patient had a small intracavernous aneurysm managed conservatively Late angiography: 41.2% had vascular abnormalities; of the 6 patients with traumatic aneurysms, 2 were successfully operated on, 2 refused surgery, 1 died, and 1 patient was managed conservatively	High

ACA, anterior cerebral artery; CTA, computed tomographic angiography; DSA, digital subtraction angiography; GCS, Glasgow Coma Scale; GSW, gunshot wound; ICA, internal carotid artery; ISS, Injury Severity Score; MCA, middle cerebral artery; MRA, magnetic resonance angiography; NR, not reported; PCA, posterior cerebral artery; pTBI, penetrating traumatic brain injury; TA, traumatic aneurysm; TICA, traumatic intracranial aneurysm.

Given the high stakes of missing or delaying the diagnosis of a traumatic pseudoaneurysm, a conservative approach involving the use of the most accurate and reliable diagnostic tools available is warranted. Screening for traumatic pseudoaneurysms should be conducted as soon as feasible, with a preference for DSA where practical, given its role as a reference gold standard. However, in settings where DSA is not readily available or feasible, CTA serves as a critical tool, with the understanding that follow-up or confirmatory testing may be necessary. The ultimate goal is to ensure the prompt and accurate detection of these potentially life-threatening injuries to facilitate timely and appropriate management.

Benefits and harms of DSA

The discussion of the diagnostic accuracy of DSA and CTA above underlines the importance of accurate screening and detection. It can be argued that the most significant harm of DSA is in not performing one. Missing a traumatic aneurysm that subsequently ruptures is a worst case scenario, and in skilled hands entirely preventable. In context, the prior pTBI guidelines provided recommendations at the lowest level for that work, or Option (Level III/IV), which admitted low level evidence with expert opinion. The currently available evidence (Level III) related to this question supports screening for traumatic intracranial aneurysms with DSA to improve survival. Coupled with the Level II recommendation supporting DSA over CTA in high-risk patients with pTBI, this subject represents one of the most potentially impactful areas of this guidelines effort.

Because DSA is considered the reference standard for cerebrovascular imaging, it is possible to assess the diagnostic accuracy of CTA in comparison (see above). There currently is no reference standard for DSA, and therefore no evidence backing its gold-standard designation.

Timing of vascular imaging

The question of when to perform vascular imaging following a penetrating brain injury is one that is incompletely addressed by current includable evidence. That said, there may be none more important. The incidence and natural history of traumatic aneurysms from pTBI has been studied and is, at least in part, known.^{99,101,108,112} We know that TICA's can form immediately or in a delayed fashion following pTBI. We know that TICA's can grow over time and rupture if not treated. The discomfort associated with the idea that some TICA's can heal or resolve without treatment is palpable, and yet does not diminish this possible outcome in limited circumstances. We now can say, based on evidence that resulted in a level III recommendation, that because traumatic aneurysms do change or perhaps develop in a delayed fashion, repeat vascular imaging should be obtained. The question concerning exactly when to perform the first imaging study and when to perform repeat imaging will be addressed by expert consensus in the absence of direct evidence.

Expert Consensus

A key impetus for updating the pTBI guidelines was diverse views in the field related to screening for and treating TICAs. Here

we provide evidence-based and consensus recommendations aimed at identifying and promoting best care practices. In response to gaps in direct scientific evidence that include the optimal timing for initial and repeat vascular imaging and specific clinical indicators for pTBI, an expert consensus developed with Delphi voting (Level C) offers guidance on the utilization of DSA and CTA in specific scenarios. The consensus underscores the importance of precise diagnostic approaches in managing pTBI, reflecting unanimous agreement (100% consensus) on several key recommendations including the high risk pTBI features that should prompt DSA. These include injuries with a wound trajectory that intersects or lies adjacent to major cerebral vasculature, violations involving multiple dural compartments, facio-orbito-pterional entry wounds, or the presence of an intracerebral hematoma. In situations where CTA is unable to conclusively rule out vascular injury (nearly all cases)—often due to interference from streak artifacts caused by retained metallic fragments or bone fragments/foreign bodies near intracerebral vasculature—DSA is recommended to ensure accurate diagnosis. For patients whose CTA results have confirmed vascular injuries, obtaining a DSA is advised to further investigate and plan appropriate interventions. Our panelists feel that DSA has numerous important advantages over CTA including improved sensitivity and specificity along with the ability to treat identified pathology. We acknowledge that it does have procedural risks which CTA does not.

Upon the initial CT scan for patients with pTBI, a CTA should be conducted to screen for any vascular injuries, providing a comprehensive understanding of the extent of damage from the outset. It is suggested that repeat early vascular imaging be performed between 7 to 21 days following the injury or before the patient's discharge from the hospital. This recommendation aims to identify any delayed vascular complications – in particular TICA – that are known to arise in delayed fashion.

An additional recommendation concerning vasospasm associated with pTBI was also made. Direct evidence meeting inclusion criteria concerning vasospasm was lacking. Referencing the section on treatment (Section VII-6, Treatment of Traumatic Pseudoaneurysms), the clinical significance of pTBI induced vasospasm remains somewhat uncertain.¹ The clinical associations outlined above were enough to formulate a recommendation that, should vasospasm be suspected, a diagnostic cerebral angiogram should be performed to facilitate intervention should the clinician choose to do so (92%).

These expert consensus recommendations highlight a strategic approach to diagnosing and managing vascular injuries in pTBI, emphasizing the critical role of DSA and CTA in ensuring timely and effective care.

Future Directions

It is imperative to conduct further research comparing CTA and DSA in patients with pTBI to discern their relative efficacies, sensitivities, and specificities. As advancements in CTA technology

continue to enhance its diagnostic accuracy, it's conceivable that DSA's role might diminish due to its invasive nature and associated higher morbidity risks. Moreover, in-depth investigations into the progression of vascular lesions post-pTBI are crucial for establishing the most opportune time for diagnostic imaging. These studies will not only refine our understanding of lesion development but also aid in refining the most effective timing for imaging, thereby optimizing patient outcomes. Other studies should focus on the development and validation of advanced imaging modalities or techniques that surpass the current limitations of CTA and DSA, particularly in sensitivity, specificity, and the ability to minimize artifacts from metallic fragments. Research into machine learning

algorithms that can improve image interpretation and reduce variability among readers could also be transformative. There is also a significant gap in understanding the optimal timing for initial and repeat imaging to detect vascular injuries post-pTBI. Longitudinal studies that track the progression of vascular injuries over time could provide invaluable insights into when these injuries manifest and evolve, potentially leading to more timely interventions. The development of biomarkers for vascular injury that could predict the development of TICA or AVF after pTBI would be powerful. Such biomarkers could facilitate earlier identification of patients at high risk of developing these vascular complications, guiding more targeted imaging and intervention strategies.

VI-6 – Prediction Models

B. Dengler and D. M. Stein

Recommendations

Level I

There is insufficient evidence to support a strong recommendation about the diagnostic accuracy of instruments and models in predicting survival in pTBI.

Level II

- The SPIN score accurately informs the probability of survival in retrospectively studied populations of patients with pTBI.

Level III

- A SPIN score incorporating INR predicts survival more accurately than one computed without coagulopathy data.
- The Baylor score has utility in discriminating retrospectively studied patients who will survive pTBI vs those who will not.
- The Marshall score can provide excellent discriminative ability for survival of pTBI patients in retrospective analysis.

Level IV

- The ABC score, Maritzburg score, Helsinki score, Stockholm score and GCS plus ISS all have outstanding discriminative ability for survival following pTBI based on retrospective analyses.
- The WHIS provides excellent to outstanding discriminative ability in retrospective analysis in predicting survival in military populations with ballistic pTBI and in civilian populations with nonballistic pTBI.
- The Rotterdam score can provide acceptable to outstanding discriminative ability in retrospective analysis to predict survival following pTBI.
- The St. Louis Scale has a moderate PPV and a high NPV to detect survival in retrospective analysis following pTBI.
- The REMS and mREMS provide poor to no discriminative ability to predict survival following pTBI.

Level C – Expert Consensus (Delphi Voting)

Independent of the validity of any prediction model, in the absence of direct scientific evidence, EXPERT CONSENSUS concluded that:

- Aggressive care and the avoidance of nihilism are central to achieving the best possible outcomes in pTBI patients. (100% consensus)
- Current predictive models for pTBI should NOT be used to guide initial treatment decisions in pTBI patients and should not supersede expert opinion on prognosis because they are based on retrospective analyses of patients and have not been tested in a prospective format. (100% consensus)

No evidence or expert opinion supported distinct recommendations based on patient gender.

The St. Louis Scale for Pediatric Gunshot Wounds to the Head specifically investigated patients under the age of 19.

Only the WHIS was specifically evaluated in military and civilian populations and stratified by wounding mechanism.

Introduction

Penetrating TBI has one of the highest case fatality rates of all types of injury. Mortality rates in excess of 90% for patients with GSW to the head have been reported in some series.¹²⁶ However, true natural history data for pTBI is lacking. Given the issues of therapeutic nihilism in patients with pTBI, it is not surprising that reported rates are so high as the perception of a poor prognosis can become a self-fulfilling prophecy. Tools that allow health care teams to accurately predict mortality, or survivability, are badly needed. The ability to accurately predict who may survive their injury allows for better allocation of resources and ability to communicate accurately with families. Over approximately the past ten years, an increased body of literature has developed and validated a variety of instruments and models that might help predict survivability following pTBI. The various models use a combination of patient characteristics, injury characteristics, physical exam, radiographic findings, and laboratory values to derive prognostic models for survival following pTBI (Table 12).

Prior Guideline Recommendations

Previous versions of the guidelines did not investigate instruments and models to predict morbidity and mortality following pTBI. However, an extensive section of the first edition of these guidelines, published in 2001, compiled evidence supporting a wide variety of variables as prognosticators in pTBI.³³ Age, intentionality (i.e. self-inflicted vs assault/homicide), anatomic wounding trajectory (i.e. perforating vs tangential tracts), hypotension, coagulopathy, respiratory distress, low GCS score, presence of fixed dilated pupils, elevated intracranial pressure, and anatomical features of injury on CT were all found to correlate with mortality and/or poor functional outcome. Many of these features are utilized in the instruments and models described above as variables used to calculate the predictive scoring.

Scientific Foundation

Fourteen studies (15 publications, N = 1988 with penetrating injuries) assessed the diagnostic accuracy of instruments and models for predicting survival or mortality in pTBI^{18,56,127-139} (Table 13). Four studies evaluated the Surviving Penetrating Injury to the Brain (SPIN) score;^{18,128,133,138} three studies (4 publications) evaluated

the Baylor cranial gunshot wound prognosis score;^{133,134,138,139} two studies assessed the ABC score;^{129,136} and one study each evaluated the Rapid Emergency Medicine Score (REMS)/modified REMS (mREMS);^{127,132} the War Head Injury Score (WHIS);¹³² the St. Louis Scale for Pediatric Gunshot Wounds to the Head;¹³⁰ the Maritzburg Score,¹³⁵ a novel model using age, Glasgow Coma Scale (GCS) score, non-reactive pupils, and posterior fossa or bihemispheric trajectory,¹³¹ and another novel model based on motor GCS and Injury Severity Score (ISS) score.¹³⁸ Additionally, three studies assessed four models that limited criteria to CT findings.^{56,133,137}

As is generally accepted, an AUC of 0.5 suggests no discrimination 0.7 to 0.8 is considered acceptable, 0.8 to 0.9 is considered excellent, and more than 0.9 is considered outstanding.¹⁴⁰ All studies included civilian subjects, while one study also included a separately analyzed military group.¹³² Mean age ranged from 14 to 41 years, and the proportion of males ranged from 80% to 96%. Seven studies were conducted in the United States, three studies (2 populations) were conducted in South Africa, with one study each conducted in Croatia, Brazil, Finland/Sweden, and Colombia. Baseline mean or median GCS ranged from 3 to 12 in four studies reporting summary baseline GCS measures.^{18,128-130} The instrument with the largest amount of data was the SPIN score (4 non-randomized studies, N = 858), which was developed using a combination of GCS, pupil response, gender, suicidal intent, whether or not the patient was transferred from another hospital, ISS, and Internalized Normalized Ratio (INR).^{18,128,133,138} Total SPIN scores can range from 4 to 52, with higher scores indicating a greater likelihood of survival. The initial study using the SPIN score (N = 413) yielded an area under the receiver operating characteristic curve (AUROC) of 0.962 in discriminating between individuals with pTBI who are likely to survive vs those who are not.¹⁸ Most individuals (98%) with a SPIN score of 35 or greater survived. Validation studies of the SPIN score (cutoff: not reported) indicated similar discriminative ability; one study (N = 87) reported an AUROC of 0.960,¹³³ one study (N = 257) reported an AUROC of 0.880,¹²⁸ and an AUROC of 0.962 was reported in another study (N = 101).¹³⁸ One study (N = 362) reported an AUROC of 0.820 using the SPIN score omitting the INR.¹²⁸ while a second study (N = 101) reported an AUROC of 0.948 for the same measure.¹³⁸ Discrimination abilities were similar when survival to 6 months was

TABLE 12. Prognostic Variables Included in Published pTBI Prediction Models

Patient characteristics		Injury characteristics	Physical exam	CT findings	Laboratory values	Other
ABC		Brain spillage	BP, consciousness			
Baylor	Age	Bullet trajectory	GCS, pupillary exam			
GCS plus ISS			GCS			ISS
Helsinki			Various features			
Maritzburg		Brain spillage	motor GCS			
Marshall			Various features			
REMS/mREMS		Mechanism	GCS, HR, RR, BP			
Rotterdam			Various features			
SPIN	Gender	Intentionality	GCS, pupillary exam		INR	Transfer from another facility
St. Louis		Bullet trajectory, lobes of injury	pupillary exam			
Stockholm			Various features			
WHIS			GCS			ISS

AUC, area under the curve; BP, blood pressure; GCS, Glasgow Coma Scale; HR, heart rate; INR, international normalized ratio; IQR, interquartile ratio; ISS, Injury Severity Score; MOI, mechanism of injury; mREMS, modified Rapid Emergency Medicine Score; NPV, negative predictive value; NR, not reported; NRS, non-randomized study; PPV, positive predictive value; pTBI, penetrating traumatic brain injury; REMS, Rapid Emergency Medicine Score; RR, respiratory rate; SPIN, Surviving Penetrating Injury to the Brain; WHIS, War Head Injury Score.

examined. These studies provide moderate strength evidence that the SPIN score provides excellent to outstanding (based on AUC values) ability to discriminate between individuals with pTBI who are likely to survive and those who are not. Two studies provide low strength evidence that the SPIN score minus INR can discriminate slightly less well than the full SPIN score.

The Baylor score (range 1 to 5 with higher scores indicate greater likelihood of mortality) is based on GCS, pupil response, age, and bullet trajectory. One study (N = 297) reported discriminative ability of 0.8756,¹³⁴ and another study (N = 87) reported an AUROC of 0.895. These studies provide low strength evidence that the Baylor score has excellent discriminative ability to determine pTBI patients likely to survive and those who are not.

The ABC score, based on admission blood pressure (A), brain spillage (B), and presence or absence of consciousness (C), yielded an outstanding discriminative ability (AUROC 0.968), in one study reporting AUROC (N = 102).¹²⁹ Another study (N = 214) did not provide diagnostic accuracy information but reported the proportion of patients who died having each ABC score, from 4% mortality with an ABC score of 0 to 78% mortality with an ABC score of 5.¹³⁶ The first study provides very low strength evidence that the ABC score has outstanding discriminative ability.

The REMS is based on GCS, age, heart rate, respiratory rate, and mean arterial pressure (MAP) (range 0 to 26 with higher scores indicating greater likelihood of mortality, cutoff not reported) performed much less well in one study (N = 134), with AUROC 0.583 indicating little discriminative ability to determine likelihood

of mortality vs survival.¹²⁷ The modified REMS (mREMS), which uses systolic blood pressure instead of MAP and includes mechanism of injury, demonstrated no discriminative ability (AUROC 0.506).¹²⁷ This study provides very low strength evidence that the REMS and mREMS provide poor to no discriminative ability.

The WHIS is based on the GCS and ISS score, and was used in one study that reported results for a military population with ballistic pTBI (N = 43) and a civilian population with non-ballistic pTBI (N = 41).¹³² Using a cutoff score of 10, the WHIS yielded an excellent discriminative ability with an AUROC of 0.88, a sensitivity of 88%, and a specificity of 76% in the civilian sample, and an outstanding AUROC of 0.92, a sensitivity of 100%, and a specificity of 78.8% in the military sample. This study provides very low strength evidence that the WHIS provides excellent to outstanding discriminative ability based on population.¹³²

The Maritzburg score, based on the motor GCS and brain spillage, was discussed in the same population as the ABC score above that reported AUROC (N = 102), and had outstanding discriminative ability to determine those likely to survive vs those likely not to survive (AUROC 0.94).¹³⁵ This study provides very low strength evidence of outstanding discriminative ability for mortality/survivability of the Maritzburg score.^{132,135}

The Rotterdam score, the Marshall score, the Stockholm score, and the Helsinki score rely solely on findings from head CT. The Marshall score is based on the degree of cerebral swelling (i.e., midline shift, compression of basal cisterns) and the presence/size of contusions/ hemorrhages. The Rotterdam score also includes

TABLE 13. Evidentiary Base for the Diagnostic Accuracy of Instruments to Predict Mortality or Survival After pTBI

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Instrument	Results	Study risk of bias
Barbosa, 2022 ¹²⁷ (NRS) Brazil Civilian MOI: NR	Among 134 pTBIs Mean GCS: 8.9 Mean MAIS: 2.8	REMS mREMS	REMS: AUC 0.583 (95% CI 0.488–0.678) mREMS: AUC 0.506 (95% CI 0.404–0.609)	Moderate
DeCuyper, 2016 ¹³⁰ (NRS) United States Civilian GSW: 100%	Among 71 pTBIs Male: 80% Mean age: 14 y Mean GCS: 7.4 (SD 5.0)	St. Louis	St. Louis: AUC NR Sens: 94.12% (95% CI 80.29–99.11%) Spec: 75.68% (95% CI 58.80–88.20%) PPV: 78.05% (95% CI 62.38–89.42%) NPV: 93.33% (95% CI 77.89–98.99%)	Moderate
Gressot, 2014 ¹³¹ (NRS) United States Civilian GSW: 100%	Among 119 pTBIs Male: 87% Mean age: 26 y GCS 3–4: 60% GCS 5–15: 39%	Novel scoring system using age (>35 y), GCS score (3 or 4), nonreactive pupils, and posterior fossa or bihemispheric trajectory	Score ≥5: diagnostic accuracy measures NR; patients with scores of 3–5 had a 75% mortality rate and patients with scores of 0–1 had a 25% mortality rate (50% mortality in patients with score of 2)	Moderate
Johnson, 2022 ¹³⁸ (NRS) United States Civilian GSW: 100%	Among 101 pTBIs Male: 90.7% Mean age: 35 y Median GCS: 4 (range 3–9)	SPIN SPIN omitting INR Novel scoring system: mGCS + ISS	Survival to hospital discharge, complete cases: 101 SPIN: AUC 0.962 (95% CI 0.929–0.994) SPIN omitting INR: AUC 0.948 (95% CI 0.906–0.991) mGCS + ISS: AUC 0.951 (95% CI 0.906–0.995) Survival to 6 mo, complete cases: 28 SPIN: AUC 0.963 (95% CI 0.928–0.998) SPIN omitting INR: AUC 0.952 (95% CI 0.908–0.989) mGCS + ISS: AUC 0.937 (95% CI 0.880–0.994)	Moderate
Kelly, 2021 ¹³⁹ Yengo-Kahn, 2021 ¹³⁴ (NRS) United States Civilian GSW: 100%	Among 297 pTBIs Male: 85% Mean age: 38 y GCS 3–4: 76% GCS 5–8: 4.4% GCS >8: 19%	Baylor	AUC 0.8756 (48 h) AUC 0.807 or 0.775 (6 mo) among those who survived the initial 48 h (discrepancy in text of article)	Moderate
Kong, 2018 ¹³⁵ (NRS) South Africa Civilian GSW: 100%	Among 102 pTBIs Male: 92% Mean age: 29 y Mean GCS: 12	Maritzburg	AUC 0.94 (95% CI 0.88–1.0) Sens: 73% Spec: 98%	Moderate
Kong, 2018 ¹²⁹ (NRS) South Africa Civilian GSW: 100%	Among 102 pTBIs Male: 92% Mean age: 29 y Mean GCS: 12	ABC	AUC 0.968 (95% CI 0.941–0.996) Sens: 82% (95% CI 60–95%) Spec: 96% (95% CI 89–99%) PPV: 86% (95% CI 66–96%) NPV: 85% (95% CI 86–99%)	Moderate

TABLE 13. Continued.

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Instrument	Results	Study risk of bias
Lindfors, 2019 ¹³⁷ (NRS) Civilian Finland/Sweden GSW: 68% Nail gun: 13% Sharp object: 13% Other: 5%	Among 75 pTBI Male: 91% Age: 41 y GCS 3–8: 53% GCS 9–12: 13% GCS 13–15: 32% Missing GCS: 1%	Marshall Rotterdam Stockholm Helsinki	6-mo mortality: 75 Marshall AUC: 0.815 (95% CI 0.715–0.914) Rotterdam AUC: 0.774 (95% CI 0.669–0.879) Stockholm AUC: 0.850 (95% CI 0.827–0.973) Helsinki AUC: 0.90 (95% CI 0.762–0.938) Actively treated patients 6-mo mortality: 59 Marshall AUC: 0.75 (95% CI 0.612–0.888) Rotterdam AUC: 0.654 (95% CI 0.509–0.799) Stockholm AUC: 0.783 (95% CI 0.653–0.912) Helsinki AUC: 0.816 (95% CI 0.694–0.939) 6-mo unfavorable outcome (GOS 1–3): 75 Marshall AUC: 0.887 (95% CI 0.802–0.971) Rotterdam AUC: 0.846 (95% CI 0.774–0.947) Stockholm AUC: 0.871 (95% CI 0.776–0.967) Helsinki AUC: 0.868 (95% CI 0.787–0.949)	Moderate
Mikati, 2019 ¹²⁸ (NRS) United States Civilian GSW: 98% Knife: 1.1% Other object: 0.55%	Among 362 pTBIs Male: 85% Mean age: 32 y Median GCS: 4 (IQR 3–9)	SPIN (N = 257) SPIN omitting INR (N = 362)	SPIN: AUC 0.88 SPIN omitting INR: AUC 0.82	Moderate
Muehlschlegel, 2016 ¹⁸ (NRS) United States Civilian GSW: 93% Knife: 2.7% Other object: 4.2%	Among 413 pTBIs Male: 87% Mean age: 33 y Median GCS: 3 (IQR 3–12)	SPIN	AUC 0.962	Moderate
Mukerji, 2022 ¹³³ (NRS) United States Civilian GSW: 100%	Among 87 pTBIs Male: 92% Mean age: 28.5 y Mean GCS: NR	SPIN Baylor Rotterdam Marshall	SPIN: AUC 0.96 Baylor: AUC 0.895 Rotterdam: AUC 0.905 Marshall: AUC 0.874	Moderate
Ospina-Delgado, 2018 ⁵⁶ (NRS) Columbia Civilian GSW: 100%	Among 95 pTBIs Male: 91.5% Mean age: 28 y GCS ≤8: 64.2% 9–12: 6.3% 13–15: 28.4% Unknown: 1% Tangential: 9.4% Unknown: 16.8%	Marshall	Marshall Score and mortality I, II, III: 20.2% IV: 15.2% V–VI: 1.3%	Moderate

TABLE 13. Continued.

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Instrument	Results	Study risk of bias
Stoffel, 2009 ¹³⁶ (NRS) South Africa Civilian GSW: 100%	Among 214 pTBIs Male: 85.5% Mean age: 30 y Conscious on admission: 39%	ABC	Mortality by ABC score 0: 4% 1: 11% 2: 22% 3: 40% 4: 61% 5: 78%	Moderate
Turina, 2001 ¹³² (NRS) Croatia Military/Civilian MOI: NR	Among 84 pTBIs Male: 96% Mean age: 33.9 y Mean GCS: NR	WHIS	WHIS, military AUC: 0.92 Sens: 100% Spec: 78.8% WHIS, civilian AUC: 0.88 Sens: 88% Spec: 76%	Moderate

AUC, area under the curve; GCS, Glasgow Coma Scale; INR, international normalized ratio; IQR, interquartile ratio; MAIS, maximum abbreviated injury scale; MOI, mechanism of injury; mREMS, modified Rapid Emergency Medicine Score; NPV, negative predictive value; NR, not reported; NRS, non-randomized study; PPV, positive predictive value; pTBI, penetrating traumatic brain injury; REMS, Rapid Emergency Medicine Score; SPIN, Surviving Penetrating Injury to the Brain; WHIS, War Head Injury Score.

midline shift and the degree of basal cistern compression but does not include the presence of contusion and limits other criteria to the presence of an epidural mass lesion and intraventricular blood/traumatic subarachnoid hemorrhage (SAH). The Stockholm score is based on SAH in convexities, basal cisterns, intraventricular hemorrhage, midline shift, epidural hemorrhage, diffuse axonal injury, and dual-sided subdural hematoma. The Helsinki score is based on the presence of subdural hematoma, intracerebral hematoma, epidural hematoma, hematoma volume, intraventricular hemorrhage, and compression of basal cisterns. One small study (N = 87) reported the discriminative ability of the Marshall and the Rotterdam scores (Marshall: AUROC 0.874; Rotterdam: AUROC 0.905) for determining the likelihood of survival or not.¹³³ Another small study (N = 75) reported the ability of all four CT-based instruments to discriminate between 6-month mortality vs survivability: Marshall AUROC 0.815; Rotterdam AUROC 0.774; Stockholm AUROC 0.850; Helsinki AUROC 0.900.¹³⁷ The Helsinki score (reference score) outperformed the Marshall score ($P = .046$) and the Rotterdam score ($P = .003$), but not the Stockholm score ($P = .089$). Among treated patients only (N = 59), the discriminative ability dropped somewhat: Marshall AUROC 0.750; Rotterdam AUROC 0.654; Stockholm AUROC 0.783; Helsinki AUROC 0.816.¹³⁷ Again, using the Helsinki score as the reference, the Helsinki score performed better than the Rotterdam score ($P = .037$), but not the Marshall score ($P = .362$) or the Stockholm score ($P = .390$). All scores (N = 71) had similar discriminative ability for unfavorable outcome, defined as Glasgow Outcome Scale score 1 to 3 AUROCs 0.800 to 0.887.¹³⁷ One

study (N = 95, includes 9 tangential TBI and 19 patients with unknown TBI status) did not provide diagnostic accuracy data but did report mortality by Marshall score: I-III 20.2%, IV: 15.2%; V-VI 1.3%.⁵⁶ These studies provide: low strength evidence that the Marshall score can provide excellent discriminative ability; very low strength evidence that the Rotterdam score can provide acceptable to outstanding discriminative ability; very low strength evidence that the Stockholm score can provide excellent discriminative ability; and very low strength evidence that the Helsinki score can provide outstanding discriminative ability.

The St. Louis scale for pediatric GSW to the head is based on pupil response, bullet trajectory, and lobes of injury. One study (N = 71) did not report discrimination ability of the St. Louis scale, but reported that with a cutoff score of 5 or above the scale had a sensitivity of 94.12%, specificity of 75.68%, PPV of 78.05%, and a negative predictive value (NPV) of 93.33%.¹³⁰ This study provides very low strength evidence that the St. Louis Scale has a moderate PPV and a high NPV.

Another study (N = 101) reported outstanding discriminative ability using the continuous motor GCS plus ISS score (AUROC 0.951).¹³⁸ When assessing the model's ability to discriminate between survival and mortality at 6 months, the same study (N = 35) reported an AUROC of 0.937. This study provides very low strength evidence that GCS plus ISS can provide outstanding discriminative ability.

A novel scoring system developed by Gressot et al, (N = 119) using age (>35 years), GCS score (3 or 4), nonreactive pupils, and posterior fossa or bihemispheric trajectory was found to correlate

with mortality outcomes; while measures of diagnostic accuracy were not reported, patients with scores of 3 to 5 had a 75% mortality rate and patients with scores of 0 to 1 had a 25% mortality rate (50% mortality in patients with score of 2).¹³¹ As measures of diagnostic accuracy were not reported in this study, we did not rate the strength of evidence.

Discussion

Although many of the instruments described above have good accuracy for determination of survivability following pTBI, all are imperfect, especially when predictions for a single patient are considered. *A key limitation of these studies, however, is that all models have thus far only been subject to retrospective validation. This creates the risk of reinforcing overly pessimistic perspectives, as the true natural history of pTBI remains unclear due to the influence of care withdrawal practices.* The SPIN score is currently the most studied and validated model although numerous models performed well in initial investigations.

Understanding the limitations of the current prognostic models is, indeed, essential. Predictive modeling is based on probabilities across a population and therefore carry inherent inaccuracies when applied to individual patients especially in the acute post-injury time-frame. Additionally, the type of data used to generate these models must be considered. As most modern pTBI patients die from withdrawal of life-sustaining therapy, prognostic models are not based on true natural history data but instead a perception of a bad outcome. It is also important to consider the relationship between prediction models and the risk of the self-fulfilling prophecy that may arise from their application. The SPIN score was developed with an interest in reducing nihilism, demonstrating that patients with pTBI can achieve acceptable outcomes with aggressive care.¹⁸ By contrast, however, the use of prognostic calculators has, at times, been linked to clinical decisions that may be overly influenced by deterministic assumptions.¹⁴¹

It should also be noted that this key question focused only on survival and not on functional outcome which is clearly a subject of critical importance to patients and their families. It is critical to frame family meetings with discussions of functional outcomes which are as important, if not more important, than just survival in determining the extent of the care rendered. Care should be taken in discussion with families when issues of survival or functional outcome are considered. As a general rule, the terms survivability - which indicates likelihood of whether the patient will live or die - and salvageability - which is related to a likelihood of a poor functional outcome - may be considered.

Expert Opinion

The use of prognostic calculators generated a substantial amount of discussion amongst our panelists and, in particular, there was great concern that the predictions they generate could be

used or misused to limit care of patients who might have a chance of an acceptable outcome.³⁴ Our panelists expressed concerns about overly negative perspectives within neurotrauma broadly, noting that such challenges are particularly pronounced in the context of pTBI. Concern was expressed that many clinicians currently judge care for those with a gunshot wound to the head as automatically futile despite the fact that many of these patients can have good neurological outcomes. Indeed, in considering the fact that military patients have better outcomes than civilian patients¹⁰ despite higher caliber weapons in combat, it is believed that the highly aggressive approach taken to pTBI in the military is likely the key factor underlying this difference. Admittedly, the high lethality of suicide-related pTBI is likely also a factor.

Although there is very little published data regarding nihilism,^{34,142} our group felt a strong need to combat inappropriate therapeutic nihilism despite our limited ability to write evidence-based guidelines on the topic. Acknowledging that the TQIP guidelines recommend at least 72 h of aggressive care before making withdrawal of life sustaining therapy decisions, our group felt that this timepoint may be premature given that important neurological improvements are often seen after this time point.

Our group ultimately felt that existing prognostic calculators should not be used to drive care-limiting decisions. While the information inherent to prognostic calculations can provide a helpful benchmark and can have utility in educating substitute decision-makers, the imprecision of these tools in the care of an individual patient must be considered.

Future Directions

Prognostication has been a major recent advance in TBI care. There will be a perpetual push to develop increasingly accurate yet simpler models that are accurate earlier and earlier in the course of care.¹⁴³ As models become more accurate it may be reasonable for them to play a greater role in patient care decisions. Machine learning algorithms, for example, are starting to out-perform regression models¹⁴³ and are anticipated to advance pTBI prognostication in the near future.

The enthusiasm to develop prediction models has not been equaled by efforts to delineate how to use prognostic information. What is a good outcome? What is an acceptable chance of achieving a good outcome? How accurate does a prognostic calculator need to be to support routine clinical use?¹⁴² A tremendous amount of additional research is needed in this regard. Implicit in the term nihilism is the assertion that physicians play a key role in medical decision-making in critically ill patients. The extent to which decision-making in these patients is made by physicians vs well-informed substitute decision-makers is also very deserving of discussion. It would also be beneficial for prognostic models to incorporate longer-term functional outcomes as opposed to only short-term survival.

VI-7 – Safety of MRI

D. W. Wright, A. Lumba-Brown

Recommendations

Level I-IV

There is insufficient evidence to support an evidence-based recommendation for the safety of diagnostic brain MRI in pTBI patients with identified or suspected metallic intracranial foreign bodies.

Level C – Expert Consensus (Delphi Voting)

In the absence of direct scientific evidence, EXPERT CONSENSUS concluded that:

- MRI of the brain should not be obtained in pTBI patients with unknown or ferromagnetic intracranial foreign bodies. (100% consensus)
- Non-ferromagnetic metals can be contaminated with ferromagnetic metals so MR imaging represents a potential hazard and should be avoided for any patient with intracranial metal following a penetrating brain injury. (100% consensus)
- Injuries in which the foreign body is known to be non-metallic, MRI may be considered. (100% consensus)

No evidence or expert opinion supported distinct recommendations based on patient sex, age, wounding mechanism, or military vs civilian context.

Introduction

MRI is distinguished for its superior resolution over Computed Tomography (CT) in imaging most soft tissues, particularly the brain, making it highly effective in scenarios involving penetrating trauma. It excels in delineating ballistic trajectories, assessing the extent of soft tissue damage, and identifying retained foreign objects, while also eliminating the risk of exposure to ionizing radiation—a notable advantage in situations requiring frequent imaging. MRI's multiplanar imaging capabilities further enhance its utility by obviating the need for patient repositioning, thereby facilitating prompt and accurate assessments crucial for determining the severity of injuries, prognostication, and developing surgical or therapeutic strategies. This is especially vital in neuroimaging, where the choice between MRI and CT can significantly influence patient outcomes due to their respective safety and efficacy profiles. However, despite the advantages of MRI, the practical challenges related to its availability and the time constraints often make CT a more feasible option for immediate assessment.

The intense magnetic fields inherent to MR imaging introduces potential risks in the presence of ferromagnetic materials within the body, such as bullet fragments or shrapnel in penetrating cranial injuries. These materials can move or generate heat, posing risks of further serious injury. The majority of evidence supporting these concerns comes from experiments with gel and post-mortem models,⁷⁹ which may not fully replicate clinical scenarios. Nevertheless, MRI's

ability to provide superior resolution for evaluating brain tissue damage and identifying non-metallic objects underscores its potential, necessitating a thorough literature review to assess the safety and efficacy of MRI in such critical conditions.

The concern for retained ferromagnetic fragments was evaluated in studies by Oliver and Kabala,⁸¹ Smith et al⁷⁹ and Teitelbaum et al.⁸⁰ In addition to artifact and image distortion, ferromagnetic missiles can also rotate and deflect in response to magnetic torque. However, the literature has not reported any patient suffering additional injury caused by MRI. In certain situations when the presence of metal fragments is not a consideration, MRI can be valuable. For example, whereas penetrating wood may be poorly visualized on CT scan, MRI can better reveal the projectile and associated tissue damage. The role of other imaging studies, such as intraoperative ultrasound, MRA, stereotactic imaging techniques, positron emission tomography, and single-photon emission CT in the acute management of pTBI has not yet been defined.

Prior Guideline Recommendations

Prior guidelines indicate that MRI has a limited role in the acute management of pTBI upon assimilation of very low evidence from the 1990s.¹⁶ The first edition stated that:

“Routine MRI is not generally recommended for use in the acute management of missile-induced PBI. MRI may have a role in

evaluating injuries from penetrating wooden or other nonmagnetic objects. The utility of other imaging modalities such as intraoperative ultrasound, positron emission tomography, single-photon emission CT, and image-guided stereotaxis in the acute management of PBI has not yet been studied and recommendations cannot be made.”

Scientific Foundation

Two studies met criteria for inclusion as evidence which included humans with penetrating intracranial trauma undergoing MRI^{80,144} (Table 14). The studies had extremely low numbers of subjects and were categorized as moderate to high risk of bias. The first study was a forensic analysis of individuals with fatal GSW to the head (N = 10), examined *postmortem* with both CT and MRI¹⁴⁴; the second was of patients with retained bullets or shrapnel, regardless of location, undergoing MRI, only one of whom had intracranial shrapnel.⁸⁰ Both studies reported image artifacts with both MRI and CT. The artifact was considered a safety issue because it could result in missed diagnosis. MRI images were less likely than CT images to have artifacts, categorized as severe (10% vs 50%) or considerable (0% vs 20%) in the study of 10 forensic cases (relative risk 0.14, 95% confidence interval 0.02 to 0.96 for severe and considerable combined). The one case with severe artifact on MRI was the only one with a ferromagnetic bullet (which was intact), and no movement or heating was detected. In the study reporting one patient with intracranial metal, the MRI showed artifact that obliterated the image around the shrapnel fragment, and suggested it was ferromagnetic. However, the MRI also detected additional metal fragments not seen with X-ray or CT, and the MRI procedure reportedly was not associated with adverse clinical effects. Together, the two studies provide very low strength evidence to base any recommendations.

Discussion

The first edition¹⁶ pTBI guidelines recommended CT as the primary imaging modality for suspected pTBI, due to concerns about potential movement of metallic objects in the strong magnetic field of an MRI machine.¹⁰² CT can be performed rapidly, is widely available and effectively demonstrates intracranial metal and blood as well as bony injury. MRI remains a secondary option, especially if no metallic fragments were confirmed or if more detailed imaging of brain tissue was needed post-initial assessment.

Previous recommendations were based on evidence from two studies using non-human models.¹⁰² While these studies were excluded from the current guidelines because they did not meet the inclusion criteria, they must not be disregarded completely. These animal models demonstrated substantial heat and movement of the ferrous fragments in simulated brain tissue as well as

difficulty in the prediction of which ballistic fragments contain ferrous material.

There is very low strength evidence from two retrospective studies of moderate-high risk of bias that included only 11 subjects total, 10 of which were in post mortem patients, and only 1 in living human subjects. More data is needed to inform the role and safety of MRI for pTBI.

Expert Opinion

CT is the workhorse cranial imaging modality in neuro-trauma because of its speed and because it readily allows detection of surgically relevant findings such as blood and midline shift of the brain. While MRI can play an important role in delineating the anatomy and trajectory of intracranial foreign bodies which are radiolucent on CT such as wood, there are few indications for considering an MRI following pTBI in patients with metallic fragments. Potential harms of MR imaging include inducing motion of the fragment causing further injury to the brain, as well as heating of the fragment to injurious temperatures. There may be a desire to obtain MR imaging in pTBI patients where there is concern for acute stroke or in a more chronic setting to rule out a brain tumor. Our review of the literature found evidence that ferromagnetic contamination is common in metals believed to be non-ferromagnetic. On this basis we feel it is safest to view all metallic foreign bodies as high risk for MR imaging. In some cases need for MR imaging could be a reason to consider removal of a metallic foreign body. In discussions amongst our panelists we note that several reported successfully obtaining MR imaging when there was a strong indication for doing so. Ultimately, however, we came to a unified view that MR imaging is ill advised for any patient with intracranial metallic foreign bodies.

Future Directions

Future research on the use of MRI in the setting of pTBI with potential metallic intracranial foreign bodies should address the safety, feasibility of imaging protocols, and the efficacy of diagnostic outcomes. Given the significant safety concerns, it is unlikely that in-human prospective studies directly comparing the safety and diagnostic outcomes of acute MRI vs those of CT in pTBI patients with known or suspected metallic intracranial foreign bodies would be ethically endeavored. Robust post-mortem models in the acute setting may provide further information as well as animal models. However, there is potential equipoise in some settings where movement and/or heat generation of the metal fragment during MRI might be more acceptable, or produce less harm (e.g. location in non-eloquent regions of the brain, fragments embedded in bone). Both of these scenarios would require knowledge of these fragments prior to MRI, presumably by CT

TABLE 14. Evidentiary Base for Safety of MRI in Patients with Intracranial Metal

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Study risk of bias
Gascho, 2019 ¹⁴⁴ (NRS) Switzerland Civilian GSW: 100%	10 forensic cases (examined after death) No patient characteristics reported	MRI, 3-Tesla scanner (N = 10) CT, 128-slice scanner (N = 10) Both studies conducted in all 10 cases Not abstracted: 1 case in which bullet did not penetrate intracranial tissue	Image artifact severity Severe (IV/IV): 10% (1/10) ^a vs. 50% (5/10) Considerable (III/IV): 0% (0/10) vs. 20% (2/10) RR 0.14, (95% CI 0.02–0.96) for severe or considerable artifact	Moderate
Teitelbaum, 1990 ⁸⁰ (Case report) United States; patient injured in Central America "Guerrilla activity" Shrapnel	Male: 100% Age: 49 y Severity: NR 1 patient with intracranial metal (of 7 reported); "minute shrapnel fragment," "presumably steel"	Plain radiograph (lateral) and CT (axial) (N = 1) MRI, 0.5-Tesla, axial (N = 1)	Plain radiograph identified "minute shrapnel fragment", confirmed intracranial by CT MRI image artifact: "black hole" artifact obliterated image around the shrapnel fragment, suggested ferromagnetic composition MRI identified additional metallic particles, with artifact (number unclear; 2 or 3), not seen on radiograph or CT "No discomfort or neurologic or vascular sequelae resulted from MR imaging"	High

CT, computed tomography; GSW, gunshot wound; MOI, mechanism of injury; MRI, magnetic resonance imaging; NA, not applicable; NR, not reported; NRS, non-randomized study.

^aThis case was the only one with a ferromagnetic bullet and for which other outcomes were reported: no movement of bullet was detected, and no thermal injury was seen at autopsy

or other modality. In these cases of study, there is a need for developing and validating imaging protocols that minimize the risk to patients with metallic foreign bodies. This includes the use of low-field MRI, sequences designed to limit heating and displacement of metal fragments, protocols for rapid identification of adverse events and studies to explore technological advancements in MRI that may reduce the risks associated with metallic fragments.

Leveraging existing data from trauma registries and retrospective analyses to better understand the prevalence of adverse events associated with MRI in this patient population could help in identifying specific risk factors associated with negative outcomes. Addressing ethical considerations, including the development of informed consent processes that clearly communicate the potential risks and benefits of MRI in this context is crucial for ensuring that patients can make informed decisions about their care.

VII – SURGICAL EVIDENCE-BASED RECOMMENDATIONS AND EXPERT CONSENSUS STATEMENTS

Section Lead: Bizhan Aarabi

VII-1 A – Urgency of Neurosurgery: Emergent Surgery vs Observation

J. V. Rosenfeld, D. O. Okonkwo, B. Aarabi

Recommendations

Level I-III

There is insufficient evidence to support a strong, moderate strength or weak recommendation for urgent surgical decompression/craniectomy vs a period of observation prior to decompression.

Level IV

In severely injured penetrating traumatic brain injury (pTBI) patients, we recommend performing a craniectomy or craniotomy early when indicated to reduce the likelihood of death or poor outcome.

Level C - Expert Consensus (Delphi Voting)

In the absence of direct scientific evidence, EXPERT CONSENSUS concluded that:

- Patients with pTBI who are medically salvageable with a surgical indication should undergo urgent surgery to reduce morbidity and mortality. Surgical planning should be individualized and the availability of resources needed for safe surgery must be ensured. (100% Consensus)

There is no evidence or expert opinion consensus to support distinct recommendations based on patient gender, age, wounding mechanism, or military vs civilian context.

Introduction

Nearly all pTBI patients have an open wound and possibly high intracranial pressure (ICP) and require surgery as soon as feasible. It is generally accepted that this surgery should occur emergently or at least urgently in most circumstances. For instance, patients with craniocerebral TBI due to gunshot wounds (GSW) or blast fragment injuries generally require debridement and dural repair. Patients impaled by sharp foreign bodies usually require emergent surgery to remove the foreign body, and to debride and close the wound.¹⁴⁵ Many factors can delay surgery, however. The surgery for pTBI patients may require mobilization of personnel and resources not readily available. These resources may not be present on site or after hours. Importantly, delays to reach a neurosurgeon or an advanced (Level I) trauma center are common for casualties in war and disaster zones and in remote or resource-poor

environments. This therefore raises the question of whether surgical exploration, debridement, decompression and repair of dura can be delayed if the injury is not immediately life threatening. Would such a delay be inconsequential or could it lead to harms related to cerebral spinal fluid (CSF) fistulas, infection rate and ultimately quality of life? One must also consider that timing of surgery also depends on the general status of the patient, hemodynamic stability, other injuries, as well as physician judgment. Severe life-threatening polytrauma is more likely in the context of multiple GSW or blast injuries. Blast trauma includes injury from the blast energy, penetrating injury from projectiles, blunt injuries from secondary impacts and burns. These complex and challenging injuries affecting multiple body regions demand multidisciplinary care led by a general trauma surgeon. In pTBI, delays in surgery resulting from initial judgements of a poor prognosis may also induce

unnecessary harm if the initial determination of poor prognosis is later reversed. Mass casualty events in military or civilian hospitals can also limit the availability of operating rooms and staff. The trauma surgeon triages the urgency of surgery for the patients. It is often advantageous for the patient to have a damage control laparotomy or orthopedic surgery for limb trauma and craniotomy/craniectomy performed simultaneously by two teams, thus conforming to the principles of damage control neurosurgery.^{146,147} With all of this in mind, a literature review was conducted to compare outcomes of early vs delayed therapy and six relevant studies were identified as providing relevant evidence.

Prior Guideline Recommendations

The prior penetrating head injury guidelines addressed “Surgical management of penetrating brain injury.¹⁴⁸” Timing of surgery was addressed by the evaluation of four civilian studies.^{73, 77,149,150} None of these four studies was carried forward into these updated guidelines. There was a paucity of evidence related to timing of surgical intervention in military environments.

In the previous edition it was recommended as an option:

“...to operate as soon as the indications for surgery are recognized. If simple wound care is elected, this should be performed expeditiously to prevent the complications associated with CSF contamination. If intracranial surgery is indicated, this should be performed promptly. If intra-cranial findings are equivocal regarding need for immediate neurosurgical intervention, follow-up CT scanning and intracranial pressure (ICP) monitoring should be strongly considered as adjuncts to determining the need for and timing of surgical intervention.”

The first edition noted that it was difficult to differentiate the effects on outcome of the timing of surgery from those resulting from rapid field triage and resuscitation. It was also noted that although authors often state that early surgery (ES) is desirable, no solid evidence supports this practice. In the first edition, identified patients undergoing late surgery (LS) were markedly different from those treated early preventing solid conclusions about the actual timing of surgery.

Scientific Foundation

Six studies were determined to meet quality and other criteria for inclusion in the evidentiary base (Table 15).

Wei et al provided a non-randomized, retrospective cohort study, which identified civilian/military patients in China with cranial GSW and blast injuries.¹⁵¹ The authors identified 56 patients from 1966 until May 2009 and performed a retrospective analysis of outcomes. Surgical intervention in this cohort included debridement, hematoma evacuation, and decompressive craniectomy and the authors noted this was performed as early as possible. Surgical intervention was performed within 8 hours of injury in 39 patients (69.6%) and beyond 8 hours of injury in 15 (8.9%). Two of the 56 patients died (one extensive brain injury, 1

multiple organ failure). The authors report that patients who underwent surgical intervention within 8 hours of injury were more likely to recover (undefined) than those who received debridement after 8 hours (82.1% vs 26.7%, $P < .001$).

Helling et al provided a second non-randomized retrospective study performed in the United States (2 urban trauma centers in Kansas City, Missouri) which examined the association of ES, LS, and no surgery (NS) with outcomes in a population of patients ($N = 89$) with cranial penetrating GSW.⁷² Early and LS were defined as less than 24 hours and greater than 24 hours, respectively. Reasons provided for delayed surgery were an initial determination of poor prognosis or minor injuries. The study period spanned 1987 to 1989 and was retrospective by design. Twenty-seven patients underwent ES, six underwent LS, and 56 underwent NS due to clinical findings and presumptive poor prognosis as determined by local neurosurgeons. The authors report a statistically significant difference in mortality for the groups (ES [$N = 10$, 37%], LS [$N = 0$, 0%], NS [$N = 46$, 82%], $P < .001$). It should be noted that the mean Glasgow Coma Scale (GCS) score of the groups differed (ES [7.86 ± 4.72], LS [12.17 ± 4.10], and NS [5.59 ± 4.42]). Patients in the NS group were the most severely injured and the least severely injured were in the LS group. There were fewer patients with GCS scores 3 and 4 in the ES group ($N = 11/27$) compared with the NS group ($N = 37/56$). However, there were more survivors in the ES group ($N = 4/11$) compared with the NS group ($N = 1/37$) amongst those patients with GCS 3 or 4 ($P = .007$). No patients in the LS group died; however, the mean GCS of this cohort was much higher at presentation. There was one infection (brain abscess) and this occurred in a patient who underwent LS.

A third non-randomized, retrospective study from Ecker et al examined the impact of early vs delayed decompressive bilateral or bicompartamental craniectomy in a U.S. military population ($N = 33$).¹¹ The median age of the population was 24 years (range 19 to 46 years) and median GCS 5 (range 3 to 14). Nineteen patients underwent bifrontal decompression (58%), eight underwent bi-hemispheric decompression (24%), and six underwent both supra- and infratentorial decompression (18%). Eighty-eight percent of injuries in this cohort were due to blast injury and 12% from GSW. All but three patients underwent early decompression prior to evacuation. Poor outcome was defined as Glasgow Outcome Score (GOS) 1 to 3 at 6 months and at 1 to 5 years. At 6 months, 16 patients in the ES group had poor outcomes as compared with none in the LS group. Among good outcomes at 6 months, three (18%) patients underwent delayed surgery and 14 (82%) underwent ES ($P = .10$). Among patients for whom GOS were available at 1 to 5 years, 12 patients had a poor outcome and 18 had good outcome. Of the patients with poor outcome, 100% underwent ES ($N = 12$). Of those patients with good outcome 16 (89%) underwent ES and two (11%) underwent delayed surgery ($P = .36$). *Importantly, no time from injury to surgery were defined for early or delayed surgery by the authors.*

Dolachee et al provide a fourth prospective and retrospective, non-randomized study of civilian injuries in Iraq ($N = 39$).⁶³ The

TABLE 15. Evidentiary Base for Early and Late Decompression/Craniectomy in pTBI

Author, year	Baseline characteristics	Intervention	Results	Risk of bias
Wei, 2013 ¹⁵¹ <i>Turk Neurosurgery</i>	Total population (N = 56) GSW (66%) and Blast (33.9%) Male: 89% Mean age: 24.1 (range 2-52) y Admission GCS GCS 3-5: 8.9% GCS 6-8: 80% GCS 9-12: 7.1% GCS 13-15: 3.6% Penetrating wound: N = 11 (19.6%) Blind tract wound: N = 41 (73.2%)	Surgery (N = 54; 96.4%) Surgery <8 h of injury: N = 39, 68.9% and surgery >8 h of injury: N = 15, 8.9% Debridement and foreign body removal: N = 40, 71.4% Debridement and partial foreign body removal: N = 12, 21.4%	Total cohort mortality: 2, 3.5% Patients receiving debridement within 8 h more likely to recover (undefined) than those receiving debridement >8 h after injury (82.1% vs 26.7%, $P < .001$).	High
Helling, 1992 ⁷² <i>The J of Trauma</i>	Total population (N = 89) Male: 91% Mean age: 31 y (range 13-73) GCS: ES: 7.86 ± 4.72 Civilian GSW: 100% LS: 12.17 ± 4.10 NS: 5.59 ± 4.42	ES (<24 h; N = 27), LS (>24 h; N = 6), NS (N = 56)	Mortality ES: 10/27, 37% LS: 0/6, 0% NS: 46/56, 82% $P < .001$	High
Ecker, 2011 ¹¹ <i>J Neurosurg</i>	Total population (N = 33) Male: 100% Median age: 24 y (range 19-46) Median GCS 5 (range 3-14) GSW: 12% Blast: 45% Projectile: 48%	Early (not defined) vs delayed (not defined) decompressive craniectomy (N = 33) Bifrontal: N = 19, 58% Bihemispheric: N = 8, 24%Supra and Infratentorial: N = 6, 18%	6-mo GOS Poor (GOS 1-3): 16 Good (GOS 4-5): 17 Poor Outcome (GOS 1-3) Early Surgery: 16, 100% Delayed Surgery: 0 Good Outcome (GOS 4-5) Early Surgery: 14, 82% Delayed Surgery: 3, 18% $P = .10$ 1-5 y GOS Poor: 12 Good: 18 Poor Outcome (GOS 1-3) Early Surgery: 12, 100% Delayed Surgery: 0 Good Outcome (GOS 4-5) Early Surgery: 16, 89% Delayed Surgery: 2 11% $P = .36$	High

TABLE 15. Continued.

Author, year	Baseline characteristics	Intervention	Results	Risk of bias
Dolachee, 2019 ⁶³ <i>Int J of Research in Pharma Sciences</i>	Total civilian population (N = 38) Male: 90% Blast/shell: 18% GSW: 61% Other: 20% Mean age: NR GCS 13-15: 41% GCS 9-12: 43% GCS 5-8: 13% GCS Unavailable: 3%	Association of surgical timing with good and poor outcome in pTBI at time points from injury: <5 h (N = 10) 5-8 h (N = 22) >9 h (N = 5) Craniotomy: 7.7% Craniectomy: 92.3%	Good Outcome (not defined) <5 h: 5, 50% 5-8 h: 14, 63% >9 h: 1, 20% Poor Outcome (not defined) <5 h: 5, 50% 5-8 h: 8, 36% >9 h: 4, 80% P = .2	High
Siccardi, 1991 ¹²⁶ <i>Surgical Neurol</i>	Total civilian population (N = 44) GSW: 100% Characteristics of 314 patients reported but not for the 44 included patients who had surgery	Surgical Intervention (N = 44): debridement of necrosis, removal of in-driven fragments, evacuation of hematoma, hemostasis, watertight dural closure.	Mortality: 40.1%, N = 18/44 Time to surgery from injury: # cases, survived, died: Within 3 h: 2, 1, 1, mortality 50% Within 6 h: 33, 19, 14, mortality 42.4% >6 h: 9, 6, 3, mortality 33.3%	High
Sertbas, 2020 ¹⁵² <i>Trauma (UK)</i> GSW: 100%	Total population (N = 35) Male: 100%, Civilian GSW: 100% Mean age: 27 y GCS 12-15: 37% GCS 7-12: 34% GCS 3-7: 28%	Surgical intervention: Duraplasty: N = 29, 82% Decompressive craniectomy: N = 21, 60% Hematoma evacuation: N = 20, 57% Bone fragment removal: N = 20, 57%	Mortality: 8, 22.8% Time to surgery from injury: <24 h: 1 24-72 h: 3 >72 h: 4 Lower mortality when operated on within 24 h (P = .044)	High

ES, early surgery; GCS, Glasgow Coma Scale; GOS, Glasgow Outcome Score; GSW, gunshot wound; LS, late surgery; NRS, non-randomized study; NS, no surgery; pTBI, penetrating traumatic brain injury.

investigators examined the association of surgical timing with outcomes. Time to surgery from injury was defined as less than 5 hours (N = 10), 5 to 8 hours (N = 22), and 9 hours or more (N = 5). Surgical intervention included craniotomy or craniectomy, debridement, hemostasis, and watertight dural repair. The authors report good outcome for five patients (50%) in the less than 5 hours cohort, 14 (63%) in the 5 to 8 hours cohort, and one (20%) in the 9 hours or more cohort. Poor outcomes were reported in five patients (50%) in the less than 5 hours cohort, eight (36%) in the 5 to 8 hours cohort, and four (80%) in the 9 hours or more cohort (P = .2). It should be noted that no clear definition was provided for good or poor outcome, although GOS was referenced.

In a fifth non-randomized, retrospective study, Siccardi et al examined time to surgery from injury in a population of civilians (N = 44) in Italy with GSW.¹²⁶ Time intervals from injury to surgery were within 3 hours, within 6 hours, and greater than 6

hours. Surgical intervention included debridement of necrosis, removal of in-driven fragments, evacuation of hematoma, hemostasis, and watertight dural closure. Of patients who underwent surgery within 3 hours (N = 2), one patient survived and one patient died (50% mortality). Of patients who underwent surgery within 6 hours (N = 33), 19 survived and 14 died (mortality 42.4%). Of patients who underwent surgery greater than 6 hours from time of injury (N = 9), six survived and three died (mortality 33.3%).

Sertbas et al is the sixth non-randomized, retrospective study included as evidence.¹⁵² It examined the impact of duration of time between injury and surgery on morbidity and mortality in a military/civilian (civil war) population in Libya with craniospinal GSW. Data for morbidity was reported in aggregate for cranial and spinal GSW and could not be included. The association of time to surgery on mortality for patients with cranial GSW (N = 35) was examined. Surgical intervention included duraplasty (N =

29, 82%), decompressive craniectomy (N = 21, 60%), hematoma evacuation (N = 20, 57%), and bone fragment removal (N = 20, 57%). The mortality for the overall cohort was 22.8% (N = 8). Time intervals from injury to surgery which were examined were less than 24 hours, 24 to 72 hours, greater than 72 hours. Mortalities by time from injury to surgery were: one in less than 24 hours, three in 24 to 72 hours, and four in greater than 72 hours. For patients with cranial GSW the authors report a significantly lower mortality when operated on within 24 hours ($P = .044$).

In summary, the six studies identified consisted of GSW and blast injury,^{11,63,151} and GSW alone.^{72,126,152} Three of these studies are civilian,^{63,72,126} two are mixed civilian and military,^{151,152} and one is military.¹¹ Military and civilian trauma systems are different particularly in the prehospital resuscitation and evacuation systems, and therefore are not equivalent when assessing medical evidence. As a result, generalizations related to outcome may not apply. The decision for early vs LS in these six reviewed articles varies. Some patients with severe pTBI were deemed to have a poor prognosis and were relegated to late or NS.⁷² This skews results in favor of performing ES for better outcomes. Patients with higher mean GCS were relegated to the LS group and this also skews the results.⁷² In the military setting, delays in casualties reaching neurosurgical care also resulted in LS being performed. The timing of surgery in these six articles varies considerably. What is characterized as ES in these six articles ranges from <3 hours to <24 hours, and in Ecker et al is undefined.¹¹

All six of these studies were judged to be at high risk of bias. Together they provide very low strength of evidence (SOE) that early surgical intervention may reduce the likelihood of death/other poor outcome in more severely injured patients compared with delayed surgery and highlight a lack of agreement for what timeframe constitutes early vs delayed. Associations with other outcomes could not be determined due to the methods of reporting data (not by time to surgery) in the included studies. These six non-randomized observational studies had a high risk of evidentiary bias because of variability in the cohort size and composition, the non-standardized definition of ES and some patients being relegated to have NS. Surgical techniques were also not standardized. Studies conducted in war zones and low and middle income countries^{63,151,152} cannot be easily compared to studies conducted within high income civilian trauma systems.^{11,72,126} It is unsurprising that no randomized trials of the timing of surgery in pTBI have been identified in the literature given the emergent nature of this issue. Moreover, important differences between characteristics of patients treated early vs late are undoubtedly important confounds.

Though not taken formally as evidence, we additionally noted other relevant studies that merit discussion. Shackelford et al reported a retrospective series of 486 military combat casualties from Iraq who had combat-related brain injury and had a craniectomy, and found that postoperative mortality was significantly lower when craniectomy was initiated within 5.33 hours of

injury.¹ 209 (43%) of patients had pTBI (168[35%] had GSW, 239[49%] explosives, and 79[16%] other). This 5.33 hour time point informed our consensus statement on the timing of surgery. These results have also encouraged the aggressive surgical management of combat casualties with pTBI. Aarabi et al in a series of 964 patients from the Iran-Iraq war, reported that the incidence of infection was lower when surgery was carried out in the first 24 hours rather than NS or evacuation to a more distant base hospital with further delay.¹⁵³

Discussion

For patients with closed or blunt TBI, early evacuation of surgical lesions has become standard practice. Evidence based guidelines have been published for the surgical management of TBI.¹⁵⁴ It is recommended that patients with acute subdural hematoma and acute epidural hematoma, where surgery is indicated, be operated as soon as possible.^{154,155} However, these guidelines do not include pTBI. Moreover, the 'four hour rule' was developed from a series of 82 patients with closed TBI and acute subdural hematoma. The mortality increased to 90% compared with 30% if surgery was delayed >4 hours. Functional survival was achieved in 65% of patients (GOS $\geq$ 4) in patients having surgery <4 hours.¹⁵⁶ However, management paradigms for closed TBI are not directly applicable to patients with pTBI.

Patients with craniocerebral pTBI are usually treated acutely as there is inherently an open wound, which requires early debridement and closure; there is often significant brain swelling with pathological midline or trans-tentorial/foramen magnum shifts; CSF leaks require acute repair to prevent infection; and early decompression of large or expanding hematomas may be indicated. Lin et al highlighted the need for urgent surgery for severe craniocerebral GSW, and the concept that "time is brain". They described four patients with cranial GSW who had a GCS < 5 on admission. Three had surgical decompression within one hour of injury. They were functionally independent at one year. One patient initially had a delayed decompression at day 7 and recovered to be wheelchair dependent.^{145,157} Decompression/craniectomy is indicated in patients with pTBI and brain swelling/hematoma. Craniotomy may be performed for more localized trauma or where brain swelling/hematoma is not significant or not likely to worsen.

Current military casualty care positions surgical facilities within the area of combat operations such that ES (within 3 to 4 hours) is undertaken. The injured soldier, once stabilized, is then evacuated to a facility with a higher level of care. Delays in transporting the injured soldier for neurosurgery may occur due to various operational constraints. These may include damage control general surgery performed in a forward hospital where there is no neurosurgery, or restrictions in aeromedical transport opportunity or availability. Civilian trauma systems have evolved to transport a casualty rapidly to a trauma center where ES including neurosurgery can be achieved.

Based on the included studies reviewed and Shackelford et al, the consensus opinion of our expert panel is that surgery be performed acutely, or within 5 hours.¹ The 5.33 hours reported

by Shackelford et al was rounded to 5 hours by consensus to provide practical guidance on the urgency of surgery. Notably, the Shackelford paper was not formally included as evidence for this topic as fewer than 85% of the patients in the study suffered a pTBI (47%) though its findings were judged to be highly relevant by the panel. We emphasize that the time to surgery <5 hours is the goal, and is not mandatory. The *Committee on Surgical Combat Casualty Care position statement: Neurosurgical capability for the optimal management of brain injury during deployed operations* was developed by the US military for the care of combat casualties, but also was designed to apply to civilian trauma systems. The recommendation is that provision should be made for casualties to access neurosurgical care as soon as possible, but within 5 hours of injury.¹⁵⁸ Earlier surgery is recommended to prevent CSF leakage and chances of infection (also refer to KQ 35).

If the clinical picture is unclear, initial local debridement, closure and observation with an ICP monitor if indicated +/- multimodal monitoring is recommended to guide treatment. Decompressive craniectomy may be indicated if the patient deteriorates. If there is no mass lesion and no evidence of elevated ICP, but there are bony fractures that require repair, it is recommended these be addressed as a typical depressed skull fracture to prevent infection and neurologic worsening.

Expert Opinion

Early intervention is standard of care for many neurologic emergencies such as stroke and spinal cord injury. Similarly, pTBI requires urgent surgical care in most instances. The human brain is a privileged organ, which is immersed in CSF and protected by scalp, skull and pachy/leptomeninges. pTBI violates this natural integrity, which should be repaired as soon as possible to prevent infection. Brain compression is a frequent secondary insult in these patients and must too be addressed rapidly. The expert consensus statement provided here stresses the need for urgent surgery to improve outcomes and reduce the risk of death. In providing this judgement our panelists were informed by their personal experience as well as the body of literature – particularly the included studies and the work of Shackelford et al. We also note the *Committee on Surgical Combat Casualty Care position statement: Neurosurgical capability for the optimal management of brain injury during deployed operations* which was developed by the US military for the care of combat casualties, but also was designed to apply to civilian trauma systems. The military's position expressed in this document is that provision should be made for casualties to access

neurosurgical care as soon as possible, but within 5 hours of injury.¹⁵³

We wish to additionally note that our expert panelists expressed unanimous support (100% consensus) for this 5 h time frame for neurosurgical management in blinded Delphi voting. We believe that systems of care and individual providers must make a concerted effort to ensure that needed resources are available to facilitate safe neurosurgery for pTBI victims within a 5 h time frame. Unnecessary delays undoubtedly harm these patients. We also recommend that 5 hours be considered a reasonable cutoff time for ES in future research based on the Shackelford et al investigation.¹ Surgery >5 hours from the time of injury may be unavoidable in some instances where there are systemic constraints or a neurosurgeon is lacking at the primary center. Accordingly, we emphasize our view that while a time to neurosurgery <5 hours is the goal, it is not mandatory.

There does appear to be equipoise in two scenarios regarding timing of surgical intervention: 1) presence of an open wound and retained foreign body in a neurologically intact patient, and 2) the patient who presents with no intracranial pathology (for example, from a tangential penetrating injury), and the need for wound washout. In both of these scenarios, prompt but not emergent interventions seem reasonable. There is not adequate data to provide a “safety cutoff” time. In these cases it would be recommended to intervene as soon as safe and clinically feasible.

Future Directions

While the literature that exists on this topic is very limited, it is recognized that a prospective randomized controlled trial on surgical timing would be not only difficult but also likely unethical. As such, careful and detailed prospective nonrandomized observational studies could help with timing of surgery in pTBI patients, being military or civilian.

To improve the quality of the pTBI evidence for early vs LS, there is a need to establish a widely agreed upon definition of early vs LS. As improved classification of pTBI emerges over time it is possible that patients with different characteristics (severity and types of pTBI patients based on mechanism of injury, clinical status, imaging, laboratory investigations and serum biomarkers) will reveal that some patients require surgery more urgently than others. There is a need to define surgical techniques with more precision and to better describe trauma system factors including extent of prehospital resuscitation. Relevant studies would be assisted by standardized outcome assessments following pTBI including GOSE, Modified Rankin Score, Quality of Life instruments, epilepsy status, infection, patient reported outcome measures and duration of follow-up.

VII-1 B – Urgency of Neurosurgery: Delaying for Better Operative Conditions

M. Talbot, M. Stippler, R. Kitagawa, B. Aarabi

Recommendation

Level I-IV

There is insufficient evidence to support an evidence-based recommendation related to delaying surgery for better operative conditions.

Level C - Expert Consensus (Delphi Voting)

In the absence of direct scientific evidence, EXPERT CONSENSUS concluded that:

- Patients with penetrating brain injury who are neurologically stable should be transferred to a facility with neurosurgical expertise as soon as feasible. (100% Consensus)

No evidence or expert opinion supported distinct recommendations based on patient gender, age, wounding mechanism, or military vs civilian context.

Introduction

In high-income countries, especially in urban settings, patients with pTBI can be transferred to neurosurgical centers where surgery can be performed promptly after resuscitation and cross-sectional imaging. In contrast, when pTBI occurs in remote or austere locations, clinicians are faced with a dilemma. Surgery can be performed early in the evacuation chain, but often in more difficult conditions. Alternatively, transfer to a fully equipped neurosurgical center may result in significant delays before reaching surgical care.

Prior Guideline Recommendations

The 2001 pTBI clinical practice guidelines recommended that surgery be performed promptly when a surgical indication is present.¹⁴⁸ The authors did not investigate the benefits and harms of delaying care to obtain better operative conditions for neurologically stable patients.

Scientific Foundation

The systematic review did not identify any studies that specifically documented the benefits and harms of delaying surgery to obtain better operative conditions in neurologically stable patients. However, some observational studies that did not meet the inclusion criteria provide indirect evidence to inform our recommendation (Table 16).

A study conducted in South Africa by Leibenberg et al¹⁵⁹ highlights that delays in care may result in fatal outcomes for patients with pTBI. The retrospective study describes an

approach in which care was deliberately delayed in an attempt to preserve resources.¹⁵⁹ One hundred and twenty-five patients were included in the study. Emergency surgery was only performed for obstructive hydrocephalus or significant hematomas. Patients without these indications had superficial wound debridement and closure in the emergency department (ED) and were transferred to a critical care unit with limited resources. Delayed surgery was offered to patients who survived the initial phase of supportive care. Twenty-seven patients (21.6% of the entire cohort) underwent surgical treatment at a mean of 11 days post-injury. Emergency surgery was performed in only three patients. Delayed surgical debridement was performed in the remaining 24 patients, six of which required multiple debridements for infection. The mortality rate was 69.6% for the entire cohort (87/125) and 7.4% (2/27) in patients who underwent surgery. Fifty-six patients died within 8 hours of admission. The infection rate was 26% in the 38 patients who survived. The most notable finding was a mortality rate of 25% (7/28) in patients with an admission GCS of 13-15, including three who died from uncontrolled ICP. The authors concluded that their management strategy led to a high mortality rate, even in patients with an admission GCS $\geq$ 13.

A study of combat-related pTBI published by Aarabi et al found that surgery performed at higher echelons of care was associated with a reduced rate of infection. This retrospective study reported the outcomes of 964 patients with pTBI sustained in the Iran-Iraq war.¹⁵³ Five hundred patients underwent an initial neurosurgical procedure at a base hospital, located near the

TABLE 16. Infection Rates Reported by Aarabi et al. During the Iran-Iraq War¹⁵³

	n	Infection rate (%)
First surgery at tertiary hospital	414	5
First surgery at base hospital without secondary operation	224	13.8
First surgery at base hospital + reoperation at tertiary hospital	276	16.3

Iran-Iraq geographical border, and were subsequently transferred to a major provincial hospital (i.e., a tertiary neurosurgical center) close to 200 miles inside mainland Iran. In the remaining 414 patients the initial neurosurgical procedure—with a radical approach to debridement—was performed at the same major provincial hospital. The mean time between wounding and surgery at the provincial center was 55.9 hours. The time between wounding and surgery at the base hospital was not reported, but, for perspective, the senior author reported on a smaller pTBI cohort earlier in the war in which the time to surgery at the base hospital was 19.1 hours compared to 66.5 hours at the provincial center.¹⁶⁰ Fifty-five percent of the 500 patients who had surgery at a base hospital required revision surgery at provincial hospital because the initial procedure was deemed inadequate. The indications for re-operation included (1) retained bone fragments, (2) inadequate debridement of the scalp or brain (3) intracranial hematoma, and (4) cerebrospinal fluid leakage. Fifty patients did not undergo debridement at either the base hospital or provincial center. The major finding of this study is that patients who had their index procedure at the provincial (tertiary) hospital had a lesser incidence of infection than patients who were first operated at the base hospital, despite a greater delay before surgery (Table 1). A multivariate regression analysis that incorporated, *inter alia*, the mechanism and the anatomic extent of injury found a statistically significant odds ratio for infection of 2.5 in patients who underwent primary surgery at a base hospital and did not require reoperation. Patients who underwent primary surgery at a base hospital and required a subsequent operation had an odds ratio for infection of 1.9, which did not reach statistical significance.

Another study of combat-related pTBI published by Singh et al also found a high rate of reoperations for patients operated in austere conditions.¹⁶¹ The series included 60 patients injured by explosive fragments (n = 48) and missiles (n = 12). Thirty patients were initially treated at forward hospitals while thirty were transferred directly to a command hospital in the rear. The average time between wounding and surgery was 36 hours. Six of eight patients (75%) who had surgery in forward locations required a second surgery at the command hospital due to an “inadequate” initial procedure. The authors do not provide enough information to determine whether these patients had planned reoperations as part

of a damage control approach or required a secondary surgery due to complications. The neurologic status of patients operated at each location is also not reported separately, making it difficult to extrapolate to the specific subset of neurologically stable patients.

In contrast, Arendall et al published a study of pTBI associated with air sinus injury that suggests that ES in relatively austere conditions is not always detrimental.⁶⁵ The study included 120 patients with pTBI sustained during the Korean War. During the initial phase of the war, patients were transferred to an American military hospital in Japan for neurosurgical care. As the conflict progressed, neurosurgeons were deployed to field hospitals and mobile army field hospitals in Korea to provide quicker access to surgery. The infection rate was 5% when surgery was performed less than 12 hours after injury, 43% for surgery between 12-24 hours, and 33% for surgery performed later than 24 hours despite the presumably harsher operative conditions in the field.

Discussion

For this key question (KQ), operative conditions were considered to include the operating theatre, surgical equipment, and surgical expertise. Therefore, better operative conditions would be obtained, in most cases, by a transfer to a higher level of care. The current section does not address delaying surgical intervention for medical issues or associated injuries. The role of subspecialists is addressed in another section.

The scientific literature provides limited evidence about the benefits and harms of delaying surgery to obtain better operative conditions for pTBI patients who are neurologically stable. The studies summarized above do not meet inclusion criteria for formal inclusion as evidence as they do not describe the operative conditions with enough detail to inform our recommendations. In addition, the literature relevant to our recommendations spans over 70 years - a period of significant change in neurosurgery, critical care, microbiology, and combat casualty care.

The theoretical risks of delayed surgery include infection and neurologic deterioration secondary to hemorrhage or edema. However, there is little evidence that performing surgery in poor conditions will prevent these adverse outcomes. In military operations, medical treatment facilities located close to the point of injury may be limited to surgical theatres with poor lighting, contaminated surfaces, and rudimentary equipment. In addition, neurosurgical expertise and advanced imaging are rarely present in these facilities.

Expert Opinion

Due to the complex nature of surgery for pTBI, we believe that the quality of the initial neurosurgical procedure is more important than its timing for neurologically stable patients. We therefore recommend that these patients be urgently evacuated to a neurosurgical center, and that surgery, if indicated, be performed promptly. The evidence does not allow us to establish precise recommendations for an acceptable delay before surgery for

neurologically stable patients. Delays in transfer should be minimized as even patients with a high Glasgow Coma Score who appear neurologically stable can deteriorate, with catastrophic results.

Future Directions

This research question is unlikely to be amenable to clinical trials. Therefore, our main recommendation for future investigators is to capture as much data as possible to allow comparison between studies and secondary analyses. We acknowledge that data collection is challenging during armed conflict and express our gratitude to present and future clinicians who document their experience.

Specifically, to further advance our understanding of the implications of delaying surgery for stable patients with pTBI, future investigations should aim to:

1. Document the delay between wounding and surgery.
2. Document the initial GCS.
3. Document specific outcomes such as mortality, infection, and unplanned reoperations for neurosurgical procedures performed in austere or remote locations.
4. Document the outcome of neurosurgical procedures performed by non-neurosurgeons.
5. Establish a pTBI registry with data collection methods compatible with low-resource environments.
6. Review prospectively collected data of war-related pTBI to provide comparative analyses between patients receiving surgery in forward (military) surgical facilities and those treated initially at higher echelons of care.⁶⁵
7. Make accessible complete datasets to allow for secondary analyses at a future pTBI consensus conference.
8. Describe the operative conditions. This should include, when possible, details about the facility (e.g., field hospital, mobile surgical team), operating room equipment, operating room lighting, pre-operative imaging, tactical conditions, and the specialty of the operating surgeon.

VII-2 – Local Wound Debridement and Closure

B. Aarabi, J. V. Rosenfeld

Recommendations

Level I-III

There is insufficient evidence to support a strong, moderate strength or weak recommendation related to primary local wound debridement and closure in patients with pTBI.

Level IV

Local wound debridement is appropriate in patients with penetrating brain injury with good neurological status, minimal brain and soft tissue disruption as well as minimal wound contamination.

Level C - Expert Consensus (Delphi Voting)

In the absence of direct scientific evidence, EXPERT CONSENSUS concluded that:

- In demanding circumstances such as mass casualties, in a conscious patient with penetrating brain injury and no intracranial bleeding, wound debridement and careful closure of a scalp laceration is recommended. (90% Consensus)
- It is recommended that casualties undergoing local wound debridement and closure be treated with short-term antibiotic(s) and have computed tomography (CT) scan of the head between 3-6 weeks to rule out abscess formation at the site of the penetrating projectile. (96.7% Consensus)

No evidence or expert opinion supported distinct recommendations based on patient gender, age, wounding mechanism, or military vs civilian context.

Introduction

pTBI is by default an open wound with a tendency to expose intracranial structures as well as the cerebrospinal fluid to infectious organisms. It has therefore been the common perception of trauma surgeons that there is a need to debride the tract, close the dura water-tight and repair the scalp.^{67,153,162-164} In 1991, however, during the Lebanese Civil War, Taha¹⁶⁵ treated 32 patients by simple wound closure and reported an acceptable risk of infection and CSF leakage. This has led to a consideration of circumstances in which local wound debridement and closure may reasonably be performed or perhaps even preferred with a view that this finding may be relevant to both military and civilian care environments.

Prior Guideline Recommendations

In the first edition of these guidelines this topic was discussed in the surgical section under the title “*Less Aggressive Debridement in Military Circumstances*”.¹⁴⁸ The application of this concept ranged from simple wound closure to very superficial debridement.^{61,69,70,74,165,166} Only Taha et al¹⁶⁵ reported simple wound closure in 32 patients of which one patient developed a brain abscess following surgery. Since 2001, four non-randomized studies¹⁶⁷⁻¹⁶⁹ have been added to the literature.

Scientific Foundation

For this KQ we included studies reporting local debridement and closure of wounds performed in an emergency room, at bedside, or in the field, but not in an operating room as part of a surgical intervention. We also included studies where this was presumed to be curative treatment and excluded studies where local debridement and closure were used only for patients not expected to survive.

There were no randomized trials or prospective cohort studies identified that addressed the benefits and harms of local debridement and closure as treatment for pTBIs. We identified five studies meeting inclusion criteria that provided information about patient outcomes and the indications for this treatment strategy, including one retrospective cohort study that compared outcomes for patients who received simple wound closure with those who received surgery¹⁶⁷ and two studies where all patients received local debridement (Table 17).

One nonrandomized study reported by Krueger et al¹⁶⁷ viewed all cases of GSW to the head from a single large trauma center in Florida from 2008 through 2018. Included patients were civilians older than 18 years of age who sustained a new, acute gunshot wound with suspected or confirmed dural penetration. Patients were excluded if they were transferred from other hospitals; had injuries that were not from a firearm; did not survive initial resuscitation; had an initial GCS score of 3 or 4 and nonreactive pupils; or died or had confirmed brain death within 48 hours of admission. Sixty-seven patients were included: 17 were treated with simple wound closure

(described in the Table) and 50 with surgery. The neurosurgeons made the treatment choice. The patients were clinically different: those who received surgery had a statistically significantly higher incidence of mass effects and involvement of frontal sinuses. While not statistically significant, the surgery patients had a lower mean GCS and more had fixed pupils. While this suggests the operated patients had more severe injuries, their outcomes, including mortality, Glasgow Outcome Scale-Extended (GOS-E) at 30-, 60-, and 90-days, infections, CSF fistulas, and seizures, were not significantly different. However, it is important to note that six (35.3%) of the patients who received simple wound closure and 14 (28%) who received surgery were lost to follow-up, and their results could change the conclusions in a study this size. In addition, the sample size may not provide sufficient power to detect clinically important differences.

A case series from Amirjamshidi et al¹⁶⁹ reported long-term follow-up data on 99 patients of 191 victims of the Iran-Iraq conflict who were treated at two centers affiliated with Tehran University of Medical Sciences.¹⁶⁹ These patients ranged in age from 13 to 55 years and all were male. Patients received no initial surgical interventions for pTBIs obtained in battlefield areas due to shrapnel and shell fragments. Patients who had a GCS score of 8 or higher, no rapid deterioration in consciousness, and a small entrance wound of less than 2 to 3 cm were candidates for local treatment. Patients were treated with wound cleaning, local debridement, stitches, and dressing at a field hospital. They were then transferred to a medical center where better X-rays and CT scans were taken and cases were reviewed by the attending surgeon. Sixty-two cases had CSF leakage, or the wound was under tension, requiring more superficial debridement of the skin, bone, and any contused brain tissue; however, the attending surgeon determined more extensive debridement was not necessary. Patients were then admitted, treated with antibiotics for 2 weeks, and had at least two additional CT scans. Mean follow-up was almost 8 years, in which time 91% of patients had good outcomes and were able to perform their usual job/activities, 4% were severely disabled, and 5% had died of their injuries or meningitis. None of the patients had brain abscesses, epilepsy, or hematomas. Outcomes were not significantly different for the 37 patients who did not require additional superficial debridement after transfer compared with the 62 patients who did.

In another series reported by Taha et al,¹⁶⁵ 32 patients from conflict zones in Lebanon with shrapnel (84%) or gunshot injuries (16%) were treated within a mean of 3 hours after injury,¹⁶⁵ in an emergency room, with superficial entry wound debridement and wound closure without drainage. Patients had to have a GCS greater than 10, an exam within 6 hours of the injury, a small entry wound, no exit wound, and to meet other criteria related to missile tract and hematomas (Table 17). Patients ranged in age from 3 to 51 years with a mean age of 32 years. Most (19 of 32) patients had an initial GCS of 15. At follow-up (mean 3.5 years after injury) there were no deaths and no neurological deficits. Only one

TABLE 17. Evidentiary Base for Local Debridement and Closure for Penetrating Brain Injury

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Risk of Bias
Krueger, 2023 ¹⁶⁷ (NRS) United States Civilian Single trauma center GSW: 100%	N = 67 Male: 83.6% Mean age: 32.9 y Initial mean GCS: 9.9	17 (25.4%) simple wound closure (SWC): bedside, sterilized procedure field, wound irrigation with iodine solution, wound inspection and removal of any easily accessible foreign bodies or bone fragments, tightly approximating the superficial tissues with a nonabsorbable suture, and covering with sterile dressings 50 (74.6%) surgery Treatment at discretion of physician, SWC vs surgery patient Incidence of mass effect: 17.6 vs 62%, $P = .002$ Involvement of frontal sinus: 0 vs 28%, $P = .01$ Mean GCS: 10.9 vs 9.6, $P = .27$ Nonreactive pupils: 5.9% vs 14.9%, not significant	Follow-up, mean # of days SWC: 61.9 (SD 78.2) Surgery: 174.9 (SD 359.2) Lost to follow-up SWC: 6 (35.3%) Surgery: 14 (28%) SWC vs surgery Mortality: 17.6% (3/17 vs. 14% (7/50); OR 1.3, 95% CI 0.3-5.8, $P = .76$ Good neurological outcomes (GOS-E ≥ 5) 30 d: 36.4% vs 34.3% 60 d: 28.6% vs 30.8% 90 d: 37.5% vs 46.2% Mean GOS-E at hospital discharge: 5.1 vs 4.7, $P = .56$ Infections: 5.9% (1/17) vs 12% (6/50), $P = .67$ CSF fistulas: 11.6% (2/17) vs 6% (3/50), $P = .60$ Seizures: 17.6% (3/17) vs 18% (9/50), $P > .99\%$	High
Kadhim, 2020 ¹⁶⁸ (NRS) Iraq Civilian Falling bullets: 100%	N = 30 Male: 63% Median age: 17.5 y (range 8-55) GCS 13-15: 66% GCS 9-12: 10% GCS 6-8: 7% GCS 3-5: 17% Injury Unilobar: 13 Multilobar or bihemispheric: 6 Through deep midline structures: 10 Transventricular with IVH: 7 SAH: 4	19 local wound care only 5 local wound care + extraction of extra cranial bullets 6 more extensive surgery Indications Local wound care unless surgery needed due to Depressed fracture related to bullet Indriven bone chips	Follow-up: 6 mo after hospitalization Reported for local wound care for this KQ GOS 5: 42% (8/19) Initial GCS: 12-15 GOS 4: 26% (5/19) Initial GCS: 4, 5, 8, 13, 14 GOS 3: 11% (2/19) Initial GCS: 12 GOS 1/died: 21% (4/19) Initial GCS: 5-6	High

TABLE 17. Continued.

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Risk of Bias
Amirjamshidi, 2003 ¹⁶⁹ (NRS) Iran Military/civilian-battlefield areas Metal shrapnel: 98% Grenade fragments: 2%	N = 99 patients treated for low-velocity wounds without surgery and followed for up to 9 y Male: 100% Mean age: NR (range 13-55 y) GCS 13-14: 48% GCS 10-12: 41% GCS 8-10: 10% Injury site Parietal: 31% Temporal: 20% Occipital: 5% Suboccipital: 2% Orbitofacial: 2%	Treatment (at field hospital) Wound cleaned and dressed or skin debrided, 2-4 stitches 1 dose antibiotic 250 diphenylhydantoin and 8-16 mg dexamethasone by IV Indications, patients With GSC $\geq$ 8 No rapid deterioration in consciousness Small entrance wound Treatment at secondary hospital X-ray and CT 62 to OR for CSF leak or wound under tension Superficial debridement of skin, bone, and local contused brain tissue IV antibiotics for 2 wk $\geq$ 2 CT scans Diphenylhydantoin 125 mg $\times$ 2 d for 1 y	Mean follow-up: 98 mo (range 90-124) Good = back to work: 91% (90/99) Poor = severe disability: 4% (4/99) Bad = dead due to severity of injury and meningitis: 5% (5/99) Mortality: 5% (5/99) No hematoma, brain abscess, epilepsy Outcome did not vary by whether superficial debridement was needed at second hospital ($P = .23$)	High
Taha, 1991 ^{a,165} (NRS) Lebanon Civilian/conflict zone (presumed, not specified) Fragments: 84% GSW: 16%	N = 32 Male 87.5% Mean age: 23 y (range 3-51) GCS 15: 19 GCS 14: 5 GCS 13: 3 GCS 12: 2 GCS 11: 2 Not reported: 1	Superficial entry wound debrided and closed without drainage in ER within 6 h (mean 3 h after wounding, with a range of 0.5-6 h) Indications GSC >10 Exam within 6 h of injury Entry wound <2 cm with or without visible cerebral tissue and with or without indriven bone No exit wound Missile tract did not traverse the proximal Sylvian fissure No epidural or subdural hematoma No intracerebral hematoma that enlarged on serial CT or at least 4 cm in diameter	Mean follow-up: 3.5 y (range 1-7.5) Mortality: 0 Neurological deficits: 0 Complications 1 (3.1%) seizure ^b and left hemiparesis 20 d after injury Brain abscess, excised and 3 wk of cefotaxime given 2-mo follow-up: no abnormalities	High
Suddaby, 1987 ¹⁷⁰ (NRS) Canada Civilian GSW .22 caliber: 100% Suicide attempts: 88%	N = 49 Male: 88% Mean age: 30.4 y (range 8-92) GCS 12-15: 20.4% GCS 8-11: 12.2% GCS ≤ 7 : 65.4%	36 local superficial wound care in ER prior to admission 13 taken to OR 6 emergency craniotomy for ICH 4 surgery for ICH (2 died) 2 craniotomy of subdural hematoma (2 died) 1 local wound debridement in OR	Mortality rate 61% (30/49) Complication rate 18% ^c 1 brain abscess 5 CSF leaks 1 meningitis 1 hydrocephalus 1 late epilepsy	High

CSF, cerebrospinal fluid; CT, computed tomography; ER, emergency room; GCS, Glasgow Coma Scale; GOS-E, Glasgow Outcomes Scale-Extended; GSW, gunshot wound; ICH, intracerebral hemorrhage; IVH, intraventricular hemorrhage; OR, operating room; SD, standard deviation; SDH, Subdural hematoma; SWC, simple wound closure.

^aIncluded in first edition of guideline.

^bText specifies 1 case with seizure, case 21; Table 1 indicated case 7 also had a seizure.

^cArticle says 16% in text; table suggests 9/49 = 18%.

patient (3.1%) had complications including a seizure and then a brain abscess that was excised; however, 2 months later the patient had no abnormalities.

In two other studies, the cases were defined by the mode of injury, but the majority of patients were managed with local debridement and closure.^{168,170} Kadhim et al¹⁶⁸ in a non-randomized study reported care and outcomes for 30 patients treated for injuries from falling bullets, when guns are shot into the air often as part of celebrations. The patients were treated at one teaching hospital in Baghdad, Iraq.¹⁶⁸ Patients ranged in age from 7 to 55 years with a median age of 17.5 years and 63% were male. Two thirds (66%) had an initial GCS of 13 to 15, and in another 10% of patients their initial GCS was 9 to 12. Nineteen patients were treated with local wound care, five had extra cranial bullets extracted, and six needed extensive surgery. Local wound care was the standard treatment unless a bullet caused a depressed skull fracture or indriven bone chips. Follow-up was limited to 6 months after hospitalization. At follow-up, 42% of patients who received local wound care had a GOS score of 5 (good recovery). Twenty-six percent (5/19) were GOS 4 (moderate disability) including patients with initial GCS of 4, 5, 8, 13, and 14. Two patients (11%) had a GOS 3 at the end of follow-up. Four patients died (21%), but it is important to note these patients all had an initial GCS of 5 or 6.

Another series from Suddaby et al¹⁷⁰ from one hospital in Canada, included 49 patients treated for .22 caliber GSW. These were predominately suicide attempts (88%). The mean age of the patients was 30.4 years old, but they ranged from 9 to 92 years old and 88% were male. Patients were assessed in the ED and 36 were provided local wound care and then admitted, while 13 were taken to the operating room for surgical interventions. Unfortunately, the study authors did not report patient outcomes separately by type of treatment. We have included the outcomes and the study in the Table as it was included in the prior guideline and to highlight that this study included patients who were more seriously injured (64.5% have GCS $\leq$ 7) and had a much higher mortality rate (61%). However, as the results are not separated, we did not include it in our assessment of the strength of the body of evidence.

One nonrandomized study and three case series provide very low SOE that local debridement and closure are associated with good outcomes for appropriate patients.¹⁶⁷⁻¹⁷⁰ However, the rigor of the studies limits and little information is provided on

potential harms. The small number of studies/reports suggest that there may be publication bias, as it is at least possible that this approach to care has been tried more frequently, likely out of necessity, but that negative results may not have been published.

Discussion

In military or civilian pTBI from low velocity shell fragments or shot gun pellets, as described in the report by Kadhim et al,¹⁶⁸ the foreign body carries at least 70 joules (J) of energy,¹⁷¹ enough to lacerate scalp, penetrate skull and enter the brain without causing a temporary cavity. In Carey's feline experiments, ordinary pressure waves with a magnitude of several atmospheric pressure were needed to produce temporary cavities.¹⁷² Under such circumstances there may be focal deficit without a major drop in the level of consciousness. Such penetrations carry the risk of introducing contaminating bacteria into the brain or cerebrospinal fluid.^{160,173,174} Our consensus recommendation based on the past guidelines and the recent literature is a short-term course of antibiotics, limited superficial debridement, and closure of soft tissues and skin. These patients are followed with contrast enhanced CT scans to look for the very low probability of abscess formation.

Expert Opinion

Do all penetrating injuries need radical or conservative tract debridement? New very low and low strength evidence adds to that considered in the 2001 guidelines to support local wound debridement and closure as a viable option for select victims of pTBI. The concept is much more meaningful in mass casualties and when low energy pellets accidentally penetrate skull and non-eloquent brain and cause no deficit. In such circumstances a short term course of antibiotics following local debridement and closure of scalp and re-evaluation of the brain tract by contrast CT seems to be an acceptable recommendation.

Future Directions

Wound management studies in low velocity pTBI patients seem feasible and ethically acceptable. Prospective observational studies at a time when mass casualties harm a large number of patients could shed some light into the risk of deep brain infections or seizures when tract exposure and debridement in an operating room is not performed.

VII-3 A – Extent of Debridement: Radical vs Conservative Debridement

R. Kitagawa, D. O. Okonkwo, B. Aarabi

Recommendations

Level I-II

There is insufficient evidence to support a strong or moderate strength recommendation related to the extent of debridement in pTBI.

Level III

Conservative debridement involving less dissection of the brain is preferred over radical debridement as the latter approach is not associated with superior outcomes and risks greater injury to the brain.

No evidence or expert opinion supported distinct recommendations based on patient gender, age, wounding mechanism, or military vs civilian context.

Introduction

Cranial penetrating wounds are inherently contaminated and at a minimum require debridement and closure. The rationale for aggressive debridement is to decrease the incidence of intracranial infection, seizures, and other complications. However, more brain dissection may lead to increased morbidity and potentially mortality. The degree of neurosurgical debridement and removal of devitalized brain, bone fragments, and foreign bodies in pTBI has evolved over time. The modern definition of conservative debridement includes the removal of visible and easily accessible fragments of bone and foreign bodies that are encountered during the process of hematoma removal and hemostasis. In contrast, radical debridement involves an attempt to remove all devitalized brain and foreign materials including debridement of the entire missile tract, often with the use of image guidance (stereotactic navigation, ultrasound, or x-rays). This radical resection may also involve return to the operating room for further foreign body removal if retained lesions are present on postoperative imaging.

Initially neurosurgeons favored radical debridement believing it was necessary to reduce the risk of infection. Practice shifted, however, when multiple studies from the Vietnam war era demonstrated significant complications from aggressive debridement while conservative measures had relatively low incidence of infections (3-6% in the studies quoted in these previous guidelines).^{68,70,74,175} From the perspective of seizure prevention, bone fragment removal did not correlate with decreased seizure incidence, and although some studies showed that the presence of metallic fragments correlated with increased seizure risk, it was unclear if fragment removal decreased this risk.^{61,70}

Prior Guideline Recommendations

The first edition of these guidelines addressed the question of extent of debridement in detail.¹⁴⁸ Unfortunately, as acknowledged by the authors, relevant studies were not rigorous limiting the conclusions that could be drawn. Based on this evidence, however, the authors recommended against aggressive removal of bone and foreign bodies for the purpose of preventing infections or seizures due to the increased risk of complications. The increased risk of infection was highly correlated with CSF leakage as will be addressed elsewhere in these guidelines.

Scientific Foundation

No randomized trials or non-randomized cohort studies were identified that directly compared patient outcomes when treatment involved radical vs conservative debridement for penetrating brain injuries. Studies included in the last guideline (n = 8) and additional case series (n = 10) were identified in this new search that provide outcomes for patients who received either radical or conservative debridement (Table 18).

Debridement type as reported in studies published across several years and locations was not standardized, and therefore no universal definition of radical and conservative debridement was used. To resolve this, we reviewed the description provided in several case series with a subgroup of members of the guideline panel and confirmed inclusions and assignments. For this summary, conservative is defined as debridement of the brain limited to fragments that can be seen and are easily accessible. No attempt is made to remove all or remote fragments or to follow the entire

TABLE 18. Evidentiary Base for Radical vs Conservative Debridement

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Risk of Bias
Radical debridement				
Pilipenko, 2020 ¹⁷⁶ (NRS) Ukraine Military Shrapnel: 84.5% Bullet: 15.5%	N = 81 Male: 100% Mean age: 34.8 y (range 18-56) GCS: mean 10 (range 4-15)	"Our approach is to perform a thorough surgery with a balanced brain debridement which, on the one hand, is aimed at maximal removal of bone fragments, detritus, and available metal foreign bodies, and on the other hand, includes the most careful, sparing attitude to brain tissue and subsequent treatment in a specialty neurosurgical profile intensive care unit with extensive experience in treating neurosurgical patients."	Follow-up at discharge Mortality: 13.6% (11) 5 from meningitis (5/11) 6 from multiple organ failure (6/11) GOS 4-5: 70.4% (57/81) GOS 3: 16.0% (13/81) Infection purulent: 14.8% (12/81) Meningitis: 12.6% (10/81) Follow-up at 6 mo and 1 y Post-traumatic epilepsy was significantly associated with bone fragments left in brain matter ($P < .05$) frequency not reported 21.4% (51/70) had post-traumatic epilepsy	High
Strojnik, 2004 ¹⁷⁹ (NRS) Slovenia Civilian GSW: 100%	N = 37 All patients Male: 94.6% Mean age: 43.3 y (range 10-78) Post resuscitation GCS 15: 1 GCS 8-14: 16 GCS 4-7: 13 GCS 3: 7	N = 26 (70.3%) operated "The dural opening was then enlarged and eventual hematomas were evacuated. Suction debridement of the brain around the tract was performed until viable tissue was seen. Complete removal of the driven-in bone and missile fragments was considered ideal. Gentle finger insertion into the tract with circumferential palpation often disclosed the driven-in bone. No attempt was made to remove bone fragments that were not readily assessable (contra-lateral side, risk of blood vessel injury...)"	Operated patients only At hospital discharge Mortality: 30.8% (8/26) GOS 4/5: 34.6% (9/26) GOS 2/3: 24.6% (6/26) GOS by GCS GCS 15 GOS 4/5: 100% (1/1) GCS 8-14 GOS 4-5: 37.5% (6/16) GOS 2-3: 37.5% (6/16) Died: 18.8% (3/16) GCS 4-7 GOS 4-5: 15.4% (2/13) GOS 2-3: 23.1% (3/13) Died: 30.8% (4/13) GCS 3 Died: 14.3% (1/7) Retained bone fragment: 53.9% (14/26) Second operation: 1 Meningitis: 21.4% (3/14) Brain abscess: 14.3% (2/14)	High

TABLE 18. Continued.

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Risk of Bias
Martins, 2003 ¹⁸⁰ (NRS) Brazil Civilian GSW: 100%	N = 319 Male: 93% Mean age: 26 y (range 3-72) Dura not pierced: 17% (54/319) N = 265 GCS 13-15: 22.3% (59) GCS 9-12: 12% (32) GCS 6-8: 18.5% (49) GCS 3-5: 47.2% (125) Mortality rate all cases of penetrating wounds: 65%	N = 156 aggressive surgical protocol 5 identified as no dura penetration during surgery 151 patients were submitted to surgery "Surgical treatment was indicated for patients with penetrating wounds with GCS > 3 and with GCS = 3 but without clinical evidence of brain stem compromise. A large craniotomy with proper exposure of the damaged dura and brain tissue, including the entrance wound, was accomplished. When there was an exit wound, the same procedure was done at this level. The surgical treatment included the resection of necrotic tissue; vigorous cleaning of the foreign bodies (missile) and bone fragments; drainage of hematomas; and appropriate repair of dura, bone, and soft tissues."	For surgery At hospital discharge Mortality rate: 39.7% (60/151) GOS 2: 3.3% (5/151) GOS 3: 4% (6/151) GOS 4: 10% (15/151) GOS 5: 43.0% (65/151) Mortality and GOS by initial GCS GCS 13-15 mortality: 9% GOS 2: 0 GOS 3: 0 GOS 4: 5% GOS 5 86% GCS 9-12 mortality: 22% GOS 2: 3.5% GOS 3: 7% GOS 4: 28.5% GOS 5 39% GCS 6-8 mortality: 62.5% GOS 2: 5% GOS 3: 10% GOS 4: 10% GOS 5: 12.5% GCS 3-5 mortality: 92.5% GOS 2: 7.5% GOS 3: 0 GOS 4: 0 GOS 5: 0 Complications 30 cases pneumonia (20%), 7 deaths CSF leaks: 2 pre op, 7 post op and 3 with meningitis; 1 death 4 abscess, all treated 3 surgical wound infections Meningitis: 5.3% (8 cases)	High
Carey M, 1974 ⁶⁸ (NRS) Vietnam Military-U.S. MOI: NR	N = 103 Male: 100% Age: NR	"In Vietnam, the need for thorough brain debridement with complete removal of all indriven bone was a Command Policy. Retained bone fragments were regarded as infective in themselves and also as indicators of incompletely debrided, devitalized brain. Many patients underwent multiple debridement procedures in Vietnam or at rear hospitals to remove all traces of retained bone."	11.7% (12/103) surgical mortality after evacuation from war zone Post debridement any complications 34% 31/91 survivors 16% retained bone fragments 15% infection 2% CSF leaks or dehiscence	High

TABLE 18. Continued.

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Risk of Bias
Grahm, 1990 ⁴⁰ (NRS) United States Civilian GSW: 100%	N = 100 Male: 84% Mean age: 35 y (range 8-87) Attempted suicide: 63% Assault: 24% Accident: 3% Unclear: 10% GCS 13-15: 22% GCS 9-12: 12% GCS 6-8: 8% GCS 3-5: 58%	N = 43 operated/debridement "The penetration and exit sites on the dura were debrided and opened widely to allow complete access to the underlying damaged brain. Necrotic brain, hematomas, and accessible missile and bone fragments were removed. The bullet tract was followed to its exit site, if possible."	Operative mortality: 23% (10/43) 3 from noncerebral causes 7 from cerebral causes during initial hospitalization Complications 2 CSF leaks—controlled 2 meningitis resolved with antibiotics Other outcomes reported for entire sample, not subgroup with debridement	High
Aarabi 1990 ¹⁶⁴ (NRS) Iran Military Shell fragments: 72.1% GSW: 11.8% Not determined: 16.1% Note: populations overlap by some undetermined number in these three articles by Aarabi.	N = 435 survived Male: 99% Mean age: 21 y GCS 13-15: 63% GCS 9-12: 13% GCS 6-8: 13% GCS 3-5: 11%	364 followed for 6 mo "The exploration of craniocerebral missile wounds was as complete as possible. The gross total removal of the necrotic brain was accomplished in every case up to normal looking white and gray matter. When the surgeon was sure that the tract was free of all foreign material, the dura mater was debrided..."	6 mo follow-up Died: 16.3% (71)* Severe disability: 5% (22) Moderate disability: 46.7% (203) Good recovery: 32% (139) Deficits in survivors Motor: 34.6% (154) Visual field: 13.7% (61) Cranial nerve: 12.1% (54%) Speech: 6.1% (2) *Note: GOS is reverse coded in article; 5 is death, 1 is good outcome	High
Aarabi, 1998 ¹⁵³ (NRS) Iran Military Shell fragments: 69% Missiles: 9.4% Undefined projectiles: 21%	N = 964 operated patients Male: 99.7% Mean age: 21 y GCS 13-15: 67% GCS 9-12: 12% GCS 6-8: 11% GCS 3-5: 7.7% GCS unknown: 2.7%	500 surgery at base hospital; 414 at Namazee hospital "Procedures at the Namazee Hospital were radical, with the intention of removing most of the pulped brain and foreign bodies followed by watertight closure of the dura and scalp."	105 (11%) patients with infections 82 meningitis 20 abscesses	High
Aarabi B, 2000 ¹⁷⁷ (NRS) Iran Military Shell fragments: 71% Missiles: 10% Not determined: 19%	N = 489 Male: 99.5% Mean age: 21 y GCS 13-15: 73.8% GCS 9-12: 13.9% GCS 6-8: 7.9% GCS 3-5: 4.2%	"The procedure was radical and complete. All visible hematoma and pulped brain with superficial foreign bodies were removed, but the inaccessible deep metal fragments were left intact."	Follow-up: mean 39.4 mo (range 6-154) 32% (157) developed epilepsy GOS 5: 35.8% (175) GOS 4: 58.7% (287) GOS 3: 5.5% (27) GOS 2: 0	High

TABLE 18. Continued.

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Risk of Bias
Arendall, 1983 ⁶⁵ (NRS) Korea Military, U.S. and Korean Forces Shell fragments: 61% GSW: 17% MVA: 14% Various: 3% Undetermined: 5%	N = 163 pTBI with air sinus wounds Male: 100% Age: NR Single sinus: 71% Multiple: 29%	147 craniotomy (16) or craniectomy (131) 16 treated conservatively after having undergone debridement and closure of the scalp laceration. (Note: this in 9.8% of the population so we can retain the study) "Devitalized brain tissue was resected and the missile tract was debrided. All indriven bone fragments and all accessible metallic fragments were removed. The affected sinus was exenterated in 106 cases as has been described and advocated by Bishop."	Mortality: 4.9% (8/163) NR for only the 147 with surgery Complications CSF fistula: 26 10 developed infections 13 reoperated to repair Total infections: 29% (47) Reoperations: 30 cases Total reoperations: 47.8% (78) 31 for retained metal or bone 20 y follow-up 23% post traumatic epilepsy	High
Haddad, 1978 ¹⁷⁸ (NRS) Lebanon Military/Civilian Shrapnel: 60% Bullet: 35%	N = 219 Male: 82% Age range: fetus to 70 y	164 underwent surgery "Debridement is most important and should be thorough. It should include removal of all devitalized tissue and foreign bodies whenever possible. After evacuation of all clots present and debridement of the macerate and severely contused brain, the line of demarcation becomes obvious. The unhealthy brain tissue is extremely edematous and can be easily suctioned. [...] we found no untoward effect from retained bone fragments. Although we spared no effort in each case to remove all the bone fragments... We did not attempt to remove metallic fragments unless they were encountered or found to be moving in roentgenographic studies"	Mortality: 27.4% (45/164)	High
Hammon, 1971 ^{a 175} (NRS) Vietnam Military GSW: 10.7% Fragment: 87.3% Misc: 2%	N = 1732 surgical debridement (others near terminal) Male: NR Age: NR	"The tract of the missile was followed to its depth, the walls of the tract debrided with suction, and all in driven debris removed. The debrided area was re-inspected and palpated to assure total debridement; the preoperative skull films were consulted frequently for localization of visible indriven bone fragments and the penetrating missile. When the missile had entered a ventricle, this ventricle was opened surgically and all debris and hematoma removed..."	Total mortality: 11.43% U.S. Military: 9.74% GSW: 22.73% Fragment: 7.64% Misc: 22.58% All others: 14.48% GSW: 29.63% Fragment: 13.32% Misc: 25.00%	High
Conservative				
Jamous, 2019 ¹⁸¹ (NRS) Syria Military Blast: 75% GSW: 25%	N = 44 Male: 88.6% Age: mean 25 y (range 11 mo to 63 y) Mean GCS: 8 (range 3- 15)	"All patients had surgical wound debridement and closure of the dura. Superficial foreign bodies and bone fragments were usually removed when cleaning and debriding the scalp wound. Deep foreign bodies were usually left in place to avoid unnecessary brain damage." Decompressive craniectomy: 43% (19)	Follow-up: mean 6 mo (range 1-15) Mortality: 25% GOS 5: 57% (25) GOS 4: 18% (8) GOS 3: 0 GOS 2: 0 GOS 1: 25% (11)	High

TABLE 18. Continued.

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Risk of Bias
Cosar, 2005 ¹⁸² (NRS) Turkey Military Shrapnel: 67% GSW: 33%	N = 400 Male: 99% Mean age: 23 y (range 4-52) GCS 14-15: 28 GCS 11-13: 124 GCS 8-10: 152 GCS 5-7: 88 GCS <5: 8	"The margins of the missile tract in the bone were minimally (approximately 1.5 cm) debrided and the size of the craniotomy/craniectomy was dictated by the underlying brain damage. [...] Superficial necrotic brain tissue, bone and shrapnel fragments were removed. Deep bone and metal fragments or those in intraventricular locations were left in place."	Follow-up: mean 2 y (range 6 mo–6 y) Mortality rate overall: 7.75% (31/400) By initial GCS: GCS 14-15: 0 (0/27) GCS 11-13: 2.4% (3/125) GCS 8-10: 4.6% (7/151) GCS 5-7: 15.5% (14/90) GCS <5: 100% (7/7) By GOS score GOS 5: 33.8% GOS 4: 50% GOS 3: 7.3% GOS 2: 1% GOS 1: 8% Infections: 5.5% (22/400) Abscess: 40.9% (9/22); 5 with CSF fistula, 4 without Meningitis: 31.8% (7/22)	High
Gonul, 1999 ¹⁸³ (NRS) Military Turkey Shrapnel: 65% GSW: 35%	N = 288 Male: 100% Mean age: 22 y (range 4-45) GCS 14-15: 20 GCS 11-13: 90 GCS 8-10: 109 GCS 5-7: 65 GCS <5: 4	All had surgery and removed visible palpable fragments. Necrotic cerebral tissue was debrided. Bone and metal fragments in deep or intraventricular locations left in place.	Follow-up: mean 2 y (range 3 mo to 3 y) Mortality overall: 7.3% (21/288) Mortality by initial GCS GCS 14-15: 0 GCS 11-13: 2.2% (2) GCS 8-10: 3.6% (4) GCS 5-7: 18% (12) GCS <5: 75% (3) GOS 5: 35.1% (101) GOS 4: 50% (144) GOS 3: 6.9% (20) GOS 2: 0.7% (2) GOS 1: 7.3% (21) Complications Retained deep fragment: 26.7% CSF fistula: 4.5% (13 cases) Infections: 3.8% (11 cases; 2 without CSF fistula)	High
Gonul, 1997 ¹⁷⁰ (NRS) Military Turkey Shell fragments: 66% GSW: 34%	N = 148 Mean age: 22 y (range 4-45) Penetrating: 56% Perforating: 20% Tangential: 24%	"Preoperatively visible and palpable intracranial bone and metal fragments were removed in the first operation. Necrotic cerebral tissue was debrided. Bone and metal fragments in a deep or intraventricular location were not removed."	Mortality: 8% (12) 7.3% (11) CSF fistula 7/11 developed CNS infections 5.9 y follow-up (N = 43) 51% (22) retained bone fragments on CT, no CNS infections	High

TABLE 18. Continued.

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Risk of Bias
Brandvold, 1990 ^{a,61} (NRS) Lebanon Military Shrapnel: 72% Stones: 2.5% GSW: 16% Tangential, but indriven bone: 9%	N = 113 Started with 116; 3 dropped when charts did not reveal dural penetration Mean age: 21.6 y (range 2-52) GSC ≤10: 48%	75% (85) treated with surgery "Removal of gross contamination with minimum manipulation of cerebral tissue. No effort was made to locate or remove in-driven bone or metal fragments visualized on the preoperative CT scan; only those fragments presented during gentle irrigation and hemostatic maneuvers were removed. Retractors were not placed into the missile tract and suction was applied to brain tissue only sparingly."	Died: 26% (30) Died with admission GCS >5: 13% GOS at hospital discharge* Good: 41% (46) Moderate or severe disability: 27% (31) Persistent coma: 5% (6) *Note: GOS is coded 1 for good and 5 for dead CSF leaks: 29 patients CNS Infections: 11% Meningitis: 8% (9 patients, 7 with prior CSF leaks) Sepsis: 9 cases Severe pneumonia: 8 cases 46 Israeli citizens 18-25 y at time of injury attempted follow up Follow-up data for N = 43: mean 5.9 y No neurologic deterioration 4 required assistance 26 evidence of retained fragments 1 meningitis, no CSF leak 22% delayed seizures	High
Levi L et al, 1990 ^{a,74} (NRS) Lebanon Military Shrapnel: 75% GSW: 13% Stone fragments: 2.5%	N = 116 GCS: 13-15: 45% (52) GCS: 9-12: 14% (16) GCS 5-8: 15% (18) GCS 4: 12% (14) GCS 3: 14% (16)	83% (96) treated with surgery Surgical procedures included meticulous debridement with a watertight closure of the dura. Mass lesions were excised but only in driven fragments that were easily accessible were removed. Distant or unencountered particles were left behind in order not to increase tissue damage.	Death: 26% (30/116) Cerebral injury: 66% (20/30) Intracranial infection: 7% (2/30) Other multi-organ failure: 27% (8/30) GOS at hospital discharge Good recovery: 42% (49) Moderate disability: 21% (24) Severe disability: 6% (7) Coma: 5% (6) Follow-up data for N = 49: median 6 y 1 meningitis, 18 mo post injury 10 seizure disorder controlled with 1 drug 24 retained fragments on CT 0 brain abscess Note these patients are the same as with Brandvold above, except Levi retained the 3 that were dropped.	High
Miner, 1990 ⁴² (NRS) United States Civilian GSW: 100% Attempted suicide: 33%	N = 33 children and adolescents Male: 70% Age range: 8 mo to 15 y GCS 9-15: 15% GCS 6-8: 21% GCS 3-5: 64%	"The basic surgical procedure was the removal of all devitalized brain tissue and accessible foreign bodies."	Mortality: 58% (19/33) 10 died in ER or within 24 h 6 mo GOS 5: 6% (2) GOS 4: 27% (9) GOS 3: 9% (3) GOS 2: 0 GOS 1: 58% (19)	High

CSF, ER, emergency room; GCS, Glasgow Coma Scale; GOS, Glasgow Outcome Scale; GSW, gunshot wound; IVH, intraventricular hemorrhage; NRS, nonrandomized study; OR, operating room; SDH, subdural hematoma.

^aIncluded in first edition of guideline.

wound tract. Using fingers or imaging to locate fragments was also considered radical. Standard of practice has shifted over time from favoring radical removal in an effort to prevent infections and potentially prevent seizures, to favoring conservative approaches to balance removing contaminants with causing further brain injury.

Case series were excluded in which either (a) no information was provided about the approach to debridement or the information was not detailed enough to allow classification or (b) the series included a mixture of cases that were treated with different approaches to debridement without reported outcomes separated by the debridement type.

Radical Debridement

We identified 11 articles that reported patient results when debridement was radical, including three reports from a large series that include overlapping cases from the Iran-Iraq War. Six of these case series report on military/war zone injuries and three examine civilian injuries.

The most recent military case series (Pilipenko, et al¹⁷⁶) reported 81 patients treated in Ukraine where as much bone and foreign matter as possible was removed from the brain using what the authors describe as a balanced approach that considers the fragment location and neurosurgical expert opinion. A study that followed U.S. soldiers injured in the Vietnam War⁶⁸ reported outcomes from 103 patients who were treated under a policy in which all fragments were viewed as infectious and were removed. These patients may have had multiple surgeries to remove all traces of retained bone as well.⁶⁸ The three articles by Aarabi, et al included subsets of patients operated on during the Iran-Iraq War and examined different outcomes, reported different follow-up periods, and had different samples of patients.^{153,164,177} A series from the Korean War (Arendall et al) included only injuries that included the air sinuses⁶⁵ and involved radical debridement that removed bone and metallic fragments. A study in Lebanon¹⁷⁸ (Haddad et al) included 219 military and civilians injured and reported outcomes for the 164 who underwent thorough debridement. The earliest published study included is a large case series including 1732 military and civilian patients treated in Vietnam with radical debridement.

These six military studies are similar in that a majority of injuries were caused by shrapnel or shell fragments while 10% to 35% were GSW. The mortality rates for four of the studies ranged from 11% to 16% (11.2%,¹⁷⁵ 11.7%,⁶⁸ 13.6%,¹⁷⁶ 16.3%¹⁶⁴) with more extreme mortality values in two studies; 4.9% in the Korean War series that included a small number of cases of local debridement⁶⁵ and 27.4% in the case series that included a mixed population treated in the Lebanese conflict.¹⁷⁸ Two studies report that approximately three quarters of the patients (70.4%¹⁷⁶ and 78.7%¹⁶⁴) have good outcomes defined as a GOS score of 4 or 5. Four studies report infection rates ranging from 11%¹⁵³ to 29%.⁶⁵ Two studies include long term follow-up and reported

that 32%¹⁷⁷ and 23%⁶⁵ of patients developed post traumatic epilepsy.

The radical debridement in civilian population series are all studies of GSW to the head. In a series of 37 patients in Slovenia,¹⁷⁹ 70.3% (N = 26) were treated with surgical debridement that aimed for complete removal of all fragments. A study in Brazil (Martins, et al) included 151 gunshot victims¹⁸⁰ all who were treated with radical debridement including patients with low Glasgow Coma Scale (GCS) scores as long as they did not have clinical evidence of brain stem compromise. In a study of 100 patient with gunshot wound in the United States (Graham et al), 43 were treated with surgical debridement that involved opening entrance and exit sites and following the bullet tract.⁴⁰

The civilian studies all had mortality rates that were similar (30.8%,¹⁷⁹ 37.9%,¹⁸⁰ 23%⁴⁰) and generally higher than in the studies of military patients. The two studies that measured GOS reported relatively high levels of good recovery or moderate disability (34.6%¹⁷⁹ and 53%¹⁸⁰ of patients with GOS 5 or 4). The same types of infections were not reported across all three of these studies; however, the number of any kind of reported infection was small.

Conservative Debridement

We included seven studies of conservative debridement. These included six articles that report military or war zone patients; one in Syria (Jamous et al),¹⁸¹ three in Turkey,^{70,182,183} and one group of patients in Lebanon described in two articles.^{61,74} One study (Miner, et al) is a small case series of pediatric patients treated for gunshot wound in one urban medical center in the United States.⁴²

The mortality rates were lower in the series from Turkey (7.75%,¹⁸² 7.3%,¹⁸³ and 8%⁷⁰) than in the series from Syria (25%)¹⁸¹ and from Lebanon (26%).^{61,74} The infection rates were also low in the Turkish samples (rates for any infection of 5.5% with 9 abscess;¹⁸² 3.8%;¹⁸³ and 4.8%⁷⁰ of the sample who developed CSF fistula who also developed central nervous system [CNS] infections), and higher in the series from the Lebanese conflict (11% developed CNS infection including 8% with meningitis).⁶¹ One series (Brandvold, et al), reported that 22% of 43 patients who were available for long-term follow-up experienced post traumatic seizures.⁶¹ The one small study (N = 33) of pediatric patients (Miner, et al) reported a high rate of mortality (58%) with almost a third of patients (10 patients) dying in the emergency room or within 24 hours of injury.⁴² Six-month outcomes included good recovery for 6% (GOS 5), moderate disability for 27% (GOS 4) and severe disability for 9% (GOS 3).⁴² As these case series span over 30 years and include different environments and populations, caution should be exercised in making comparisons across these series. Each series report important outcomes including mortality, GOS, infection, or seizures, but these results can be attributed to many other factors that differ across the series other than the level of debridement.

Given this heterogeneity and the lack of direct comparison of radical and conservative debridement in any one study, we conclude that there is low SOE that radical and conservative debridement results in similar outcomes in adult patients with penetrating brain trauma and that there is insufficient evidence to come to a separate conclusion about debridement in pediatric patients.

Discussion

The extent of debridement has been extensively discussed and is an important subtopic in pTBI as it is based on the surgeon's clinical judgment. This characteristic makes studying this topic via trials challenging and results in a lack of relevant high-quality data. Thus, current neurosurgical practice has evolved out of the variety of experiences reported in the literature.

Indeed, the treatment of penetrating head injury has evolved over time. Because of the unique incidence of pTBI in military conflicts, military-civilian translation has played a critical role in how debridement practices have evolved. The earlier studies from the Vietnam and Korean Wars advocated for aggressive debridement and removal of all foreign bodies including repeat operations for retained lesions with the goal of preventing infection and perhaps seizures as well. Ultimately concerns for increased morbidity and potentially mortality from the manipulation of viable tissue led to changes in practice. From the seizure perspective, the incidence is highly variable and only correlated with retained metallic foreign bodies. However, it remains unclear if removal would decrease the risk.

With more modern series, limited debridement was not associated with a higher risk for infection and did not increase mortality. These series included both conflict related injuries and peacetime pTBI. Evidence of benefit would be needed to justify surgery that is more injurious to the brain; as available evidence does not suggest

such benefit, we provide a Level III recommendation to avoid aggressive removal of bone fragments and foreign bodies for the purpose of preventing infection and seizures.

There are limitations to the data. All of the cases are retrospective reviews with heterogeneous patient populations. There are no studies directly comparing the two approaches, and the degree of debridement in each individual study is difficult to compare. It is important to consider that available literature focuses on metallic foreign bodies. Metal can have antibacterial properties and it is thus possible that there is greater need to aggressively remove other materials such as wood.

Expert Opinion

Our investigators feel that the contemporary approach of minimal debridement is the best current approach in pTBI and that dissection through brain to remove retained fragments should only be performed if infection develops at a deep fragment site. A more aggressive debridement may still be appropriate in some circumstances, such as with a highly contaminated wound. The role of antibiotics in preventing infection in the setting of retained fragments or contaminated wounds is not known with certainty and is discussed in another section of this guideline. Our investigators also feel that although the data presented here focuses on adult patients, there is no basis or rationale for considering a different approach in children.

Future Directions

While it would be important to study diverse pTBIs, rare injuries such as those involving non-metallic objects or low velocity pTBI would be more difficult to study. Under these circumstances, radical debridement may be appropriate, but given current practice, evidence would be required to support such a determination.

VII-3 B – Extent of Debridement: Retained Foreign Bodies

C. J. Neal, J. V. Rosenfeld, B. Aarabi

Recommendations

Levels I-II

There is insufficient evidence to support a strong or moderate strength recommendation regarding risks of infection due to retained bone or metal fragments in pTBI.

Level III

Routine surgical removal of residual retained bone and metal fragments is not necessary following pTBI.

Level C – Expert Consensus (Delphi Voting)

In the absence of direct scientific evidence, EXPERT CONSENSUS concluded that:

- A foreign body (FB) that is protruding from the skull, such as a knife or an arrow, that penetrates the brain should be removed in a controlled environment, such as the operating room, after appropriate studies have been performed to determine the position of the object, the degree of brain injury and the adjacent structures that need to be evaluated or monitored upon removal. (100% consensus)
- Removal of symptomatic fragments migrating within the skull should be considered. (100% consensus)
- If a foreign body is present at the site of an intracranial infection it should be removed, if possible, to reduce the risk of recurrent infection. (100% consensus)

No evidence or expert opinion supported distinct recommendations based on patient gender, age, wounding mechanism, or military vs civilian context.

Introduction

The risk posed by retained bone or metal fragments after a pTBI has guided the degree of initial surgical debridement and the perceived need for reoperation.^{7,61,68,70,73,75,150,161,164,165,169,170,176-178,182,184-196} Independent of the extent of debridement, here we seek to inform the relative risks and benefits of removing metallic and bony foreign bodies vs those of leaving them *in situ*. Even if an extensive debridement of a pTBI was performed, fragments may be left behind after surgery. Seizure and infection have been the most common outcome measures used to judge the risk of retained intracranial fragments.^{61,70,164,165,176,177,185,186,188,190,193,194} We are considering here, in part, whether re-operation to remove fragments left behind should be considered. Here we also consider the removal of protruding foreign bodies and how this is best conducted. The purpose of this clinical question is to determine benefits and harms of removing retained bone or metal fragments vs those of leaving them, independent of the extent of a debridement that is performed.

Prior Guideline Recommendations

The prior guidelines did not specifically address the question of benefits and harms of retained fragments.¹⁶ The discussion of

retained fragments and their potential complications was framed around the degree of debridement. The prior guidelines recommended debridement of penetrating cranial wounds and in the setting of mass effect, the removal of safely accessible fragments.¹⁴⁸ The routine removal of fragments not easily accessible or reoperation with the sole purpose of removing retained fragments were not recommended. These recommendations were Options based on Class III evidence.¹⁴⁸

Scientific Foundation

This KQ considers the balance of benefits and harms when inadvertently retained, inaccessible or deep fragments of bone or metal from a penetrating brain injury are removed vs when they are not. The response to this question is related to decisions about: whether primary surgery or debridement should aggressively attempt to remove all fragments during initial treatment (addressed in KQ 37); and when only local debridement may be appropriate (addressed in KQ 35). In addition to the decisions made during initial treatment, this question is also relevant to whether later or additional surgery to remove fragments identified on imaging should be performed in the absence of conditions or symptoms such as infection.

Several studies reported whether patients had retained metal or bone fragments after initial treatment, but in many cases the presence of retained fragments was a descriptive variable and not all studies include data on patient outcomes related to retained fragments. When outcomes were included, the most frequently reported outcome was infection, but seizures, mortality, function, and toxicity were also reported in at least one identified study. In many cases, the impact of retained fragments was not the primary focus of the study. When the overall study sample size was small, the subgroup with retained fragments was often limited to very few or no patients with the reported outcomes. Given that we identified over 90 studies that mentioned retained fragments, we included only studies with an initial sample size of at least 45 people with penetrating brain injuries. At least 17 papers in the prior pTBI Guidelines discuss retained metal or bone fragments. Ten of these papers have been carried forward to contribute to the evidence base for this KQ^{61,68,70,73,150,164,165,177,193,194} (Table 19).

Additionally, we reviewed and present the studies by the year the patients were injured and initially treated, because the standard of practice shifted following the US experience in the Vietnam War, from removing all fragments to reduce the likelihood of infection to a less aggressive approach that suggested it was better to not remove fragments if they were deep or difficult to reach (Table 20). Removal of deep fragments might risk damage to more brain tissue, which could outweigh the potential for infection and other negative outcomes.

In total we included 31 articles. These reported results from 26 studies and patient cohorts (three studies are based on the same registry from the Vietnam War,¹⁹²⁻¹⁹⁴ three reports are of different outcomes using data of overlapping cases from the Iran-Iraq War),^{164,177,185} and two studies included the same military personnel in Croatia.^{195,196} Several included studies were not designed to assess the impact of retained fragments and, while studies had to report a patient outcome to be included, authors may not have reported sufficient data to allow a comparison of outcomes for patients with penetrating brain injuries with vs without retained fragments. There is a subset of 13 studies that either reported a comparison (outcomes with retained vs no retained fragments) or reported data that allowed us to calculate a rate for the patients with and without retained fragments and test the difference in the rates.^{7,61,70,164,165,176,177,184-186,188,190,193,194}

The results of these 13 studies are reported in Table 19 and are used as the basis for our SOE assessment. Following this, Table 20 is the evidence table for this question and contains more detail on all 26 studies.^{7,61,68,70,73,75,150,161,164,165,169,170,176-178,182,184-190,192-197}

Treatment since 2000s

Six studies were included for SOE analysis (6 total studies^{7,176,186-188,190}). The first 6 studies in Table 19 and one additional study in Table 20 (for a total of 7 studies) report results for patients treated since 2000.

Three studies reported that outcomes were not statistically significantly different for patients with and without retained fragments. The largest study by Harmon et al followed 763 civilian patients from 17 trauma centers in the United States who survived at least 72 hours and reported 7% of those with retained fragments and 5% without developed CNS infections (not statistically significant).¹⁸⁸ A second study by Darwazeh et al of 520 Palestinian civilians reported a lower but not statistically different rate of local and systemic infections for patients with retained fragments (6.8% vs 9.4%).¹⁸⁶ In a third study by Larkin et al of 80 U.S. military personnel injured in Afghanistan, the proportion of patients with and without retained fragments with a GOS score of 4 or higher was not significantly different at any of the three follow-up times (6 months, 1 year, and 2 years after injury).⁷

Two studies from this period reported worse outcomes for patients with retained fragments. A study by Pilipenko et al of military injuries in Ukraine that employed comparatively radical debridement as part of treatment for patients who were mostly injured by shrapnel (84.5%) found patients with retained bone fragments were significantly more likely to have an infection during their hospitalization and significantly more likely to have post-traumatic epilepsy when followed for a year after discharge.¹⁷⁶ While the odds ratios are significant for both outcomes, the 95% CIs are wide, (e.g., 1.4 to 28.8) indicating that the estimates are not precise due to the relatively small sample size (N = 81). A study by Jimenez et al of civilian patients in Colombia with GSWs reported a high rate of intracranial infections overall (25%) and a significantly higher rate for patients with retained fragments (45.8% vs 12.9%) compared with patients without retained fragments.¹⁹⁰

Another study examined records of all U.S. military personnel injured with a penetrating brain injury in Afghanistan and Iraq between 2009 and 2014, but who were evacuated and treated in U.S. hospitals. The authors found that 73.6% (N = 78) of the 106 patients had retained fragments.¹⁹⁸ These included a combination of types (27 with bone, 10 with metal, and 40 with both, and 1 type was missing). Overall, 11.3% of the patients developed a CNS infection during their hospitalization, but as all of the patients with an infection had a retained fragment, the infection rate for patients with fragments was 15.4% and significantly higher than 0% for the patients with no fragments. However, the infection rate did not vary significantly by types of fragments. Meningitis or ventriculitis was the type of infection seen in 83.3% of the patients (N = 10).

The final study in this time period by Fathalla et al reported that of 102 civilian and military patients treated at various locations in Egypt, among 52 survivors with 1-year follow-up data, none with retained fragments suffered from lead toxicity.¹⁸⁷ However, this article did not report the number of survivors with and without retained fragments.

Treatment in 1980s and 1990s

5 studies for SOE in 7 articles were included (11 total studies in 14 articles^{61,70,161,164,169,177,182,184,185,189,195,196,199}). All of the

TABLE 19. Summary of Studies Reporting Data for Outcomes With and Without Retained Fragments

Years of treatment	Author, year N	Outcome	Results for retained fragments (bone or metal) vs none, type of fragment	Notes on patients and study
2014-2017	Pilipenko, 2020 ¹⁷⁶ 81	Infection Epilepsy	OR 6.4 (95% CI 1.4-28.8), bone OR 7 (95% CI 12.0-40.9), bone	Military, Ukraine. Focus on reporting results of surgical approach including comparatively radical debridement.
2010-2013	Larkin, 2018 ⁷ 80	GOS≥4	69.4% vs 77.3%, $P = .69$, fragment type NR	U.S. military, Afghanistan. Report long-term outcomes.
2009-2014	Meister, 2023 ¹⁹⁸ 106	CNS infections	Infection incidence of 15.4% (12/78) with retained fragment vs 0 (0/28) without retained fragment, bone, metal, or both	U.S. military injured in Afghanistan or Iraq, evacuated to Germany and treated in United States
2006-2016	Harmon, 2019 ¹⁸⁸ 763	CNS infections	7% vs 5%, $P = .37$, fragment type NR	Civilians, United States. 17 trauma centers. Data from study on antibiotics.
2000-2010	Darwazeh, 2018 ¹⁸⁶ 520	Infection, local or systemic	6.8% vs 9.4%, $P = .34$, bone or metal	Civilians, Palestine. Study to identify factors affecting outcomes.
2000-2010	Jimenez, 2013 ¹⁹⁰ 160	Intracranial infections	45.8% vs 12.9%, $P < .00001$ OR 7.5 (95% CI 3.0-18.4), bone or metal	Civilians, Colombia. Study to identify risk factors for infection.
1992-1994	Gönül, 1997 ⁷⁰ 148	Infections	4% vs 7%, $P = .44$, bone or metal	Military, Turkey. Study to identify risk factors for infection.
1982-1985	Brandvold, 1990 ⁶¹ 43	Infections Seizure	0 vs 5.9%, $P = .22$, no fragment 19.2% vs 29.4%, $P = .50$, bone or both	Military, Lebanon. Follow-up to determine outcomes of treatment which included use of CT and conservative debridement.
1981-1988	Taha, 1991 ¹⁶⁵ 403	Infections	20.6% vs 1.8%, bone including with CSF fistula 4% with fragments and no CSF fistula	Lebanon. Likely civilian in area of conflict but not clear. The study focuses on the 30 cases with infection but provides some data on a larger group that includes patients with and without fragments.
1980-1988	Aarabi, 1989 ¹⁸⁵ , 1990 ¹⁶⁴ , 2000 ¹⁷⁷ 310 (each study has a slightly different sample)	Infection Seizures Good outcome	7.2% vs 2.7%, $P = .085$, bone, metal, or both 40.37%, bone; 4.00%, metal; NS different for both vs none 81.3% vs 79.9%, $P = .87$, bone or metal	Military, Iran. Series of articles reviewing different outcomes from overlapping sample of cases.
1980s NR	Elzayat, 1986 ¹⁸⁴ 170	Seizures	3.2% vs 2.9%, $P = .92$, metal	Likely military or mixed. Described as frontline hospital in Iraq during Iran-Iraq War.
1967-1970	Rish, 1981 ¹⁹³ 1121	Brain abscess Mortality with brain abscess	6.4% vs 2.5%, $P = .006$, bone 82% vs 42.3%, $P = .14$, bone	U.S. military, injured in Vietnam.
1967-1970 ^a	Salazar, 1985 ^{a,194} 421	Seizures	63% vs 50%, NS, bone 59% vs 42%, $P < .05$, metal	U.S. military, injured in Vietnam.

CI, confidence interval; CNS, central nervous system; CSF, cerebrospinal fluid; CT, computed tomography; GOS, Glasgow Outcome Scale; NR, not reported; NS, not significant; OR, odds ratio; vs, versus.

^aSame patients as Rish.

TABLE 20. Evidentiary Base for Removal of Retained Intracranial Fragments: Included in Studies by Years of Treatment

Author, year (Study design) Years of treatment Country Civilian/Military MOI	Baseline characteristics	Fragments	Outcomes	Study risk of bias
Meister, 2023 ¹⁹⁸ (NRS) 2009-2014 United States Military Missile: 37.7% Blast: 56.6% Other: 5.7%	N = 106 with 78 having retained fragments Male: 100% Median age: 25 y (range 22-29) 23 patients did not undergo a neurosurgical procedure	27 with retained bone 10 with retained metal 40 with both 1 missing type	11.3% of the patients developed a CNS infection during their hospitalization, but as all of the patients with an infection had a retained fragment, the infection rate for patients with fragments was 15.4% and significantly higher than 0% for the patients with no fragments. Infection rate did not vary significantly by type of fragments. No discussion on rate of epilepsy. Other factors that affect presence of infection include ventriculostomy placement and presenting GCS. 10/12 infections were meningitis/ventriculitis	High
Pilipenko, 2020 ¹⁷⁶ (NRS) 2014-2017 Ukrainian Military Shrapnel: 84.5% Bullet: 15.5%	N = 81 Male: 100% Mean age: 34.8 y (range 18-56) Mean GCS at admission: 10 (range 4-15) GCS $\geq$ 4 at admission required for inclusion	22 with metal retained 33 all metal removed 9 bone retained 5 had reoperations 3 small fragments 1 deep seated, near the middle cerebral artery	Retained bone fragments Infection (purulent-septic complications) during hospitalization: 14.8% (12/81) All patients Mortality: 5 from meningitis—fragment status NR Significant association with retained bone fragments ($P = .008$) frequency NR With vs without bone fragments: OR 6.4 (95% CI 1.4-28.8) Post-traumatic epilepsy at hospital discharge, and 6 to 12 months; through clinic visits and phone interviews: 21.4% (15/70) Significant association with retained bone fragments ($P < .05$) frequency not reported With vs without bone fragments: OR 7 (CI 12.0-40.9) Retained metal fragments No association with infection or epilepsy ($P > .05$)	High
Fathalla, 2018 ¹⁸⁷ (NRS) 2011-2018 Egypt Various facilities (40% inside war zone; 60% civilian) Military GSW: 59% Blast: 41%	N = 102 Male: 98% Mean age: 25 y Admission GCS GCS 3-5: 36.3% GCS 6-12: 31.4% GCS 13-15: 32.3%	Number with fragments NR; no information on types of fragments reported	Complications in 52 survivors at 1 y None with retained fragments had lead toxicity No other outcomes reported by whether patient had retained fragments	High

TABLE 20. Continued.

Author, year (Study design) Years of treatment Country Civilian/Military MOI	Baseline characteristics	Fragments	Outcomes	Study risk of bias
Larkin, 2018 ⁷ (NRS) 2010-2013 Afghanistan United States Military, U.S. GSW: 28% Blast: 73%	N = 80 Male 100% Mean age: 24.9 y (range 19-40) Mean admission GCS (N = 64) 8.5 GCS 3-5: 48% GCS 6-15: 52%	36 (45%) retained fragments No additional information provided about fragments 44 (55%) no retained fragments	Good GOS (≥ 4) with retained fragments vs no retained fragments 6 mo: 55.6% (20/36) vs 70.5% (31/44), $P = .41$ 1 y: 69.4% (25/36) vs 77.3% (34/44), $P = .69$ 2 y: 75% (27/36) vs 79.5% (35/44), $P = .82$ Results reported as reported in article GOS for patients with retained fragments, good (≥ 4) vs poor (< 4) 6 mo: 56% (20/36) vs 44% (16/36), $P = .24$ 1 y: 69% (25/36) vs 31% (11/36), $P = .45$ 2 y: 75% (27/36) vs 25% (9/36), $P = .79$	High
Harmon, 2019 ¹⁸⁸ (NRS) 2006-2016 United States 17 trauma centers Civilian GSW: 90% Knife: 6% Nail gun/hammer/arrow: 4%	N = 763 survived >72 h Male: 85% Mean age: 35 y (range 18-90) White: 45% Black: 42% Hispanic: 5% Asian: 1% Other: 7% Mean ISS: 24 (range 1-75) Dural penetration Diffuse: 60% Local: 40%	479 (63%) retained foreign body No additional information provided about foreign bodies (i.e., type, location, size)	CNS infections: 7% (51) With retained foreign body: 35 infections (7%); 444 none Without retained foreign body: 16 infections (5%); 268 none; $P = .37$ <i>Follow-up period/time to infection not clearly stated. Seems to be during hospitalization.</i> 63% of infections were 10 d or more after injury Focus of study was antibiotics. Whether foreign bodies where present was not included in multivariable model as it was not significant in bivariate analysis.	High
Darwazeh, 2018 ¹⁸⁶ (NRS) 2000-2010 Palestine Civilian Metal bullets: 67.5% Rubber bullets: 26.7% Shrapnel: 5.8% Tangential: 73.9% Penetrating: 22.3% Perforating: 3.8%	N = 520 Male: 90.4% Age range: 6 mo to 75 y Adults age: mean 33.5 y (N = 380; 73%) Children age: mean 10.2 y (N = 140; 27%) Admission GCS GCS 3-5: 10% GCS 6-7: 8.5% GCS 8-10: 15.6% GCS 11-15: 65.9%	190 (37%) deep retained metal or bone fragments found on follow-up CT. No information provided about this subgroup of patients	Follow-up mean: 7.7 mo (range 3-12) Infection (local or systemic including meningitis, brain abscess and sepsis): 44 With fragments: 6.8% (13/190) Without fragments: 9.4% (31/330), $P = .34$ Authors of article state: "no significant statistical association between retain fragments and increased infection rate." No other outcomes	High
Jimenez, 2013 ¹⁹⁰ (NRS) 2000-2010 Colombia Civilian GSW: 100%	N = 160 Male: 91% Mean age: 29 y (range 15-61) Admission GCS GCS ≥ 9 : 66% GCS ≤ 8 : 34% GCS ≥ 7 : 92.5%	59 (37%) postsurgical intra parenchymal fragments on CT (either bone or metal) 101 none	Follow-up mean: 39 mo (range 3-92) Intracranial infections including: meningitis, cranial osteitis, epidural abscess, subdural empyema, cerebritis, brain abscess, or ventriculitis: 25% (40/160) With fragments: 45.8% (27/59) Without fragments: 12.9% (13/101), $P < .0001$; OR 7.5 (95% CI 3.0-18.4) Other factors associated with infection: projectile trajectory through paranasal sinus or oral cavity and prolonged hospital stay.	Moderate

TABLE 20. Continued.

Author, year (Study design) Years of treatment Country Civilian/Military MOI	Baseline characteristics	Fragments	Outcomes	Study risk of bias
Singh, 2003 ¹⁶¹ (NRS) 1999 India Military Shrapnel: 71.7% GSW: 20.0% IEDs: 8.3%	N = 60 Male: 98.3% Mean age: 25 y (range 19-40) GCS 13-15: 13% GCS 8-12: 50% GCS 5-8: 24% GCS 3-5: 13%	22 (37%) retained bone fragments 18 (30%) metal fragments - Not clear if these are unique patients or if patients had both types	50 surviving patients followed up to injury: mean 6 mo (range 3-9) Brain abscesses: none on follow-up with or without retained fragments No other outcome reported by retained fragments	High
Cosar, 2005 ¹⁸² (NRS) 1992-2002 Turkey Military Shrapnel: 67% GSW: 33%	N = 400 Male: 99% Mean age: 23 y (range 4-52) GCS 14-15: 7% GCS 11-13: 31% GCS 8-10: 38% GCS 5-7: 22%	130 (33%) bone and metal fragments in deep locations and eloquent brain areas after surgery on CT Treated conservatively and surgery only if infection noted	Follow-up mean: 2 y (range 6 mo to 6 y) Infections all: 5.5% (22/400) Authors state fragments did not seem to increase infection, but do not provide data 2 patients developed epilepsy in acute phase; neither had retained fragments	High
Erdogan, 2002 ¹⁹⁹ (NRS) 1992-1999 Turkey Military/Civilian GSW: 100% Bullet: 32.3% Shrapnel: 67.7%	N = 374 Male: 99.2% Mean age: 22 y (range 4-48) Initial GCS GCS <5: 1.3% GCS 5-7: 22.5% GCS 8-10: 38% GCS 11-13: 31.2% GCS 14-15: 7%	119 (32%) retained deep bone or metal fragment postop	Follow-up mean: 24 mo (range 3-36) Infections 5 cases with fragments and without CSF fistulas 13 cases with CSF fistulas (unclear if these are in patients with or without retained fragments) Data not provided to calculate infection rates with and without fragments. Data not provided linking fragments to other outcomes.	High
Gönül, 1997 ⁷⁰ (NRS) 1992-1994 Turkey Military Shell fragments: 66% GSW: 34%	N = 148 Male: NR Mean age: 22 y (range 4-45) GCS: NR	51 (34%) bone and metal fragments on CT after first debridement	Follow-up mean: 12 mo (range 5-18) Infections all: 6% (9/148) With retained fragments: 4% (2/51) Without retained fragments: 7% (7/97) $P = .44$ Seizure disorders, no correlation found with bone fragments (data NR)	High

TABLE 20. Continued.

Author, year (Study design) Years of treatment Country Civilian/Military MOI	Baseline characteristics	Fragments	Outcomes	Study risk of bias
Tudor, 2005, ¹⁹⁵ 1998 ¹⁹⁶ (NRS) 1991-1995 Croatia Military Shell fragments: 74.3% GSW: 25.7%	N = 176 Male: 94.3% Mean age: 29.5 y (range NR) Admission GCS GCS <8: 45.8% GCS ≥8: 54.2%	72 (41%) intracranially retained foreign bodies on postop CT Metal: 45 (62.5%) Bone: 11 (15.27%) Both: 16 (22.2%) No foreign bodies: 104	Follow-up unclear Infections: 28 CNS: 15 (8.52%) Superficial: 13 (46.4%) With foreign bodies: 57% Without foreign bodies: 38% (frequencies not provided; difficult to ascertain from figures) Early seizures reported, but no detail related to foreign bodies Good outcomes (simplified GOS-moderate disability and good recovery) With foreign bodies: 68% (49/72) Without foreign bodies: 68% (71/104)	High
Jankovic, 2000 ¹⁸⁹ (NRS) 1991-1995 Croatia Military (86.4%) Civilian (13.6%) MOI: NR	N = 176 Male: NR Age: NR Mean admission GCS (N = 156): 10 (range 3-15)	No data provided	Follow-up unclear: appears to be during hospitalization Infection, statistically significant association between remaining bone fragments and the occurrence of infection (Chi square = 9.42, $P = .002$, data NR). All patients with CNS infection and retained foreign bodies had ≥2 other risk factors (GCS ≤5, extensive brain injuries, CSF fistula, craniobasal penetrating injuries) CNS infections and sepsis were the most common causes of mortality	High
Brandvold, 1990 ⁶¹ (NRS) 1982-1985 Lebanon, evac. to Israel Military Shrapnel: 72% Stones: 2.5% GSW: 16% Tangential, but indriven bone: 9%	N = 113 Started with 116, 3 dropped when charts did not reveal dural penetration Mean age: 21.6 y (range 2-52) GCS ≤10: 48% 75% (85) treated with surgery—conservative debridement	83 survived acute hospitalization 43 with data post hospitalization Retained fragments: 60.5% (26/43) Metal: 4 Bone: 9 Both: 13 No retained fragments on CT: 17 18/22 (86%) of patients with bone fragments had 1 >5 mm or more than 3 >2 mm in a 1 cm area	Follow-up: mean 5.9 y (range not provided) Infection With fragments: 0% (0/26) Without fragments: 5.9% (1/17) $P = .22$ No delayed abscess Seizure With fragments: 19.2% (5/26) Bone: 2 Both: 3 Without fragments: 29.4% (5/17) $P = .50$	High

TABLE 20. Continued.

Author, year (Study design) Years of treatment Country Civilian/Military MOI	Baseline characteristics	Fragments	Outcomes	Study risk of bias
Taha, 1991 ¹⁶⁵ (NRS) 1981-1988 Lebanon Military/Civilian: NR MOI: NR for all patients, only those with infection	N = 403 Characteristics: NR	63 (16%) postop retained bone fragments	Follow-up: mean 2.5 y (range 1 mo to 7 y) Infection With fragments: 20.6% (13/63) Without fragments: 1.8% (6/340) $P < .0001$ With fragments and no CSF fistula: 4% (2/50) With fragments and CSF fistula: 84.6% (11/13) With CSF fistula and no fragments: 21.1% (4/19) No CSF fistulas and no fragments: 0.6% (2/321)	High
Aarabi, 1989 ^{a,185} (NRS) 1981-1987 Iran Military GSW: 11% Shell fragment: 72% Could not be determined: 17%	N = 379 Male: 99.9% Mean age: 21 y (range NR) GCS: NR	310 with postop radiological studies With retained fragments: 53.5% (166/310) Metal: 112 Bone: 26 Both: 28 No fragments: 144	Follow-up of the 277 patients who survived to be discharged: mean 22 mo Infection Any fragments: 7.2% (12/166) Metal: 6 (5.4%) Bone: 3 (11.5%) Both: 3 (10.7%) No fragments: 2.7% (4/144) $P = .085$	High
Aarabi, 1990 ^{a,164} (NRS) 1981-1988 Iran Military Shell fragments: 72.1% GSW: 11.8% Not determined: 16.1%	N = 435 survived; Male: 99% Mean age: 21 y (range NR) Admission GCS GCS 13-15: 63% GCS 9-12: 13.1% GCS 6-8: 13.3% GCS 3-5: 10.6%	230 (56%) with bone or metal fragments retained of 414 with postop radiological studies 184 without retained fragments	Follow-up: mean 2.5 y (range 1mo to 7 y) Calculated from table Good outcome With retained fragments: 81.3% (187/230) Without retained fragments: 79.9% (147/184), $P = .87$ Poor outcome With retained fragments: 23.0% (53/230) Without retained fragments: 14.7% (27/184), $P = .054$ As reported in article With retained fragments: 187 (56.0%) of 334 with a good outcome With retained fragments: 53 (65%) of 80 patients with a poor outcome Not statistically significantly different, $P = .34$	High
Aarabi, 2000 ^{a,177} (NRS) 1980-1988 Iran Military Shell fragments: 71% Missiles: 10% Not determined: 19%	N = 489 Male: 99.5% Mean age: 21 y (range NR) Admission GCS GCS 13-15: 73.8% GCS 9-12: 13.9% GCS 6-8: 7.9% GCS 3-5: 4.2%	309 Postop Retained fragments Bone: 109 (22.2%) Metal: 200 (40.9%)	Follow-up mean: 39.4 mo (range 6-154) Seizure (univariate) Retained bone: 40.37%; Chi-square 2.901, $P = .088$ Retained metal: 34.00%; Chi-square 0.317, $P = .573$ In multivariate Retained bone: $P = .5527$ Retained metal not included in model Fragments were not associated with seizures	High

TABLE 20. Continued.

Author, year (Study design) Years of treatment Country Civilian/Military MOI	Baseline characteristics	Fragments	Outcomes	Study risk of bias
Amirjamshidi, 2003 ¹⁶⁹ (NRS) Iran-Iraq War ~1979 for 8 years (Iran-Iraq War) Iran Military/Civilian- battlefield areas Metal shrapnel: 98% Grenade fragments: 2%	N = 99 patients treated for low-velocity wounds without surgery and followed for up to 9 y Male: 100% Mean age: NR (range 13-55 y) GCS 13-14: 48% GCS 10-12: 41% GCS 8-10: 10% Indications for minimal debridement: patients with GCS $\geq$ 8, no rapid deterioration in consciousness, small entrance wound	All patients had entrance wounds and no exit wound Exact numbers of cases NR Figures 3 and 4 and text suggest most had metal and/ or bone Retained metal fragments 71 had 1 fragment ~9 had 2 fragments More than 1 patient had 3, 4, 5, or 6 (not legible from figure) Number of retained bone fragments ranged from 1 (12 cases) to >5 (16 cases)	Follow-up: mean 98 mo (range 90-124) Functional outcome Good (back to work): 91% (90) Poor (severe disability): 4% (4) Bad (dead due to severity of injury and meningitis): 5% (5) No brain abscess, epilepsy	High
Elzayat, 1986 ¹⁸⁴ (NRS) Iran-Iraq War: years NR Iraq Military GSW: 100% Bullets: 19% Shell fragments: 81%	N = 200 with missile injuries; 170 included, 8 excluded who died shortly after arriving and 22 who died within 1 wk of surgery Male: NR Mean age: NR (range 20-30 y) GCS: NR	31 retained metal fragments on postop x-ray 139 with no fragments Half of patients were given prophylactic anti-seizure medication	Seizure in the first week after injury With metal fragments: 3.2% (1/31) Without metal fragments: 2.9% (4/139) $P = .92$	High
1970s and before–10 studies				
Suddaby, 1987 ¹⁷⁰ (NRS) 1975-1985 Canada Civilian GSW .22 caliber: 100% Suicide attempts: 88%	N = 49 Male: 88% Mean age: 30.4 y (range 8-92) GCS 12-15: 20.4% GCS 8-11: 12.2% GCS $\leq$ 7: 65.4%	19 surviving patients All had retained metal fragments (61% mortality rate [30/49])	Outcome among survivors Follow-up period not specified Complication rate: 18% ^b Brain abscess: 1 CSF leaks: 5 Meningitis: 1 Hydrocephalus: 1 Late epilepsy: 1	High
Haddad, 1978 ¹⁷⁸ (NRS) 1975-1976 Lebanon Military/Civilian Shrapnel: 60% Bullet: 35% Data NR that totals to 100%	N = 219; 164 had surgery Male: 82% Age range: fetus to 70 y	14 (8.5%) retained bone of 164 who had surgery	Follow-up range: 3-15 mo No reoperations to remove fragments 0 brain abscess in 14 with retained bone No other negative effect reported	High

TABLE 20. Continued.

Author, year (Study design) Years of treatment Country Civilian/Military MOI	Baseline characteristics	Fragments	Outcomes	Study risk of bias
Hubschmann, 1979 ⁷³ (NRS) 1973-1975 United States Civilian GSW: 100%	N = 82 Male: NR Mean age: NR (range 14-67 y)	45 (55%) patients underwent surgery 13 (30%) had retained missile fragments	Records were reviewed up to 2 y after discharge No evidence of infection or ill effects in the 13 patients with retained fragments. No other outcomes reported related to fragments.	High
Lillard, 1978 ⁷⁵ (NRS) 1971-1975 United States Civilian GSW: 100%	N = 83 Male: 81% Mean age: 29.6 y (range 2-72)	57 (69%) retained missile fragments	No evidence of any complication or death related to missile fragments (no data provided) No indication that infection was a factor in mortality or morbidity 47 survivors (number with retained fragments NR) 6 (12.8%) post traumatic seizures, 4 had retained fragments Authors state there is no indication the retained fragments were related to seizure.	High
Carey, 1974 ⁶⁸ (NRS) 1968-1970 Vietnam Military GSW and fragments, but numbers NR	N = 103 91 survivors 31 with post debridement complications Characteristics: NR	16 (16%) with retained bone fragments 15 patients had 23 reoperations to remove bone fragments Mortality in patients without retained fragments: 13% (11/87)	Follow-up until death or discharge from service hospitals Results of reoperation to remove fragments Complications None: 11 Dysphasia: 1 Epidural abscess: 1 Hemorrhage, edema: 1 Hemorrhage, coma: 1 Death: 6.3% (1/16) Late brain abscesses With retained bone and reoperations: 0/16 Without retained bone: 2 Bone chips that were cultured were definitely positive for bacteria: 40% (4/10)	High
Meirowsky, 1982 ^{c,192} (NRS) 1967-1970 Vietnam Military GSW: 100% Bullets: 22.4% Fragments: 77.6%	N = 116 (10.2%) of 1133 with missile wounds reoperated for retained bone fragments Male: 100% Age: NR	N = 116 97 one reoperation 19 more than one Follow-up conducted 1976-1979 by reviewing records	Follow-up data included in records at time of review Results of reoperation to remove fragments Mortality: 10.3% (12/116) with secondary operations Due to initial injury: 5 Infections after initial operation: 5 Infections after secondary operations: 2 Without reoperation, fragment status NR: 6.2% (64/1017) Infection Prior to secondary surgery: 16 (13.8%) Following secondary surgery: 7 (6%)	High

TABLE 20. Continued.

Author, year (Study design) Years of treatment Country Civilian/Military MOI	Baseline characteristics	Fragments	Outcomes	Study risk of bias
Rish, 1981 ^{c,193} (NRS) 1967-1970 Vietnam Military GSW: 15.9% Fragment: 76.8% Other: 7.3%	N = 1221 Characteristics: NR	170 with retained bone fragments Follow-up conducted 1976-1980 by reviewing records	Follow-up range: 7 d to 9 y Brain abscess: 3.03% (37/1221) With retained bone: 6.4% (11/170) Without retained bone: 2.5% (26/1051) $P = .006$ 10 of 11 occurred during second and third week after injury Morality with brain abscess With bone fragments: 82% ^d (9/11) Without bone fragments: 42.3% (11/26) $P = .14$	High
Salazar, 1985 ^{c,194} (NRS) 1967-1970 Vietnam Military MOI: NR	N = 421 First 421 seen from registry for a phase II comprehensive follow-up Male: 100% Mean age at injury: 21 y	94 (22.3%) retained bone fragment 274 (65.1%) retained metal fragment	Follow-up mean: 5 y (range NR) Seizures Within 1 y of injury: 57% >5 y after injury: 18% With bone fragments: 63% (59/94) Without bone fragments: 50% (165/327), not statistically significant With metal: 59% (162/274) Without metal: 42% (62/147), $P \leq .05$	High
Raimondi, 1970 ¹⁵⁰ (NRS) 1964-1968 United States Civilian GSW: 100%	N = 150 Characteristics: NR	25 (17%) survived with retained missile fragments 14 had intracranial surgery 11 simple debridement, no surgery	Follow-up: mean 31 mo (range 20-56) Mortality: 0 Abscess: 0 Of 14 with retained fragments after surgery: 1 had seizures, 1 meningitis, 2 slight hemiparesis, 1 hemianopic Of 11 patients with retained fragments but no surgery: 1 mildly hemiparetic, 2 hemianopic No patients were institutionalized or required specialized nursing care; none died	High
Webster, 1946 ¹⁹⁷ (NRS) Unclear ~ 1944 Italy, then France U.S. military hospital Shell fragment or bullet: numbers NR	N = 206 Characteristics: NR	Number NR	33 brain abscesses With retained bone: 57.6% (19/33) With metal foreign bodies: 36.4% (12/33) With no retained fragments: 6% (2/33)	High

CI, confidence interval; CNS, central nervous system; CSF, cerebrospinal fluid; CT, computed tomography; GCS, Glasgow Coma Scale; GOS, Glasgow Outcome Scale; GSW, gunshot wound; IED, improvised explosive device; ISS, Injury Severity Scale; MOI, mechanism of injury; NR, not reported; NRS, non-randomized study; OR, odds ratio; U.S., United States.

^aPopulations overlap by some undetermined number in these three articles by Aarabi.

^bArticle says 16% in text; table suggests 9/49=18%.

^cMeirowsky, 1982; Rish, 1981; Salazar, 1985 are from the same registry of patients.

^dIn all cases, patients had other risk factors (e.g., facio-orbital-cranial and/or air sinus injury; coma; CSF fistula; multiple surgical procedures) in addition to retained bone.

included studies from this time period are about military experience or experience in war zones and did not involve U.S. forces.

Five studies of treatment provided from 1980 to 1999 included comparisons of data from patients with and without retained fragments and are included in the SOE assessment. Four studies compared rates of infection,^{61,70,165,185} three rates of seizures,^{61,177,184} and one the proportion of patients with good outcomes.¹⁶⁴ Three studies found relatively low rates of infection that were not significantly different for patients with and without retained fragments: 4% vs 7% in a study of 148 patients with bone or metal fragments treated in Turkey;⁷⁰ 0% vs 5.9% in a study of 43 patients treated with conservative debridement in Israel;⁶¹ and 7.2% vs 2.7% in a study of patients injured during the Iran-Iraq war and treated in Iran.¹⁸⁵ One study by Taha et al conducted in Lebanon reported a much higher and significantly different rate of infection for patients with retained bone fragments (20.6%) vs patients without retained bone fragments (1.8%); however further inquiry revealed that having a CSF fistula was an important driver of infection and only 4% of people with fragments and no CSF fistula developed infections, while 84.6% of patients with CSF fistula and bone fragments developed infections.¹⁶⁵ The three studies that compared seizure rates all reported that fragments were not associated with higher rates: a study by Brandvold et al in Israel treating military patients evacuated from the military hostilities with Lebanon that also reported infections, evaluated seizures and found a lower, but not significantly different rate for patients who survived hospitalization who had bone or metal and bone fragments vs those without retained fragments (19.2% vs 29.4%);⁶¹ univariable and multivariate analyses of data from the Iran-Iraq war cohort treated in Iraq by Elzayat et al concluded that fragments were not associated with seizures;¹⁸⁴ and a study of cases treated in an Iraqi hospital during the same conflict reported no difference in the rate of seizures in the first week after injury in patients with and without retained metal fragments.¹⁷⁷ Another analysis by Fathalla et al of Egypt evaluated patient outcomes, found that good outcomes were as likely in patients with retained bone and metal fragments as in patients without retained fragments (81.3% vs 79.9%).¹⁸⁷ The remaining six studies are included only in Table 20 as they did not provide data for patients with and without retained fragments. One study by Singh et al from the Indian military followed 60 patients, 40% with retained bone and 33% with retained metal on follow-up CT. In the 50 surviving patients none with or without fragments had any brain abscess and no other outcome reported by fragment status.¹⁶¹ A series by Cosar et al of 400 military patients treated in Turkey included 32.5% with bone and metal fragments remaining deep in the brain after surgery. The overall infection rate during long term follow-up (mean 2 years) was 5.5% and the authors stated that fragments did not seem to increase infection, but they did not provide the data for infections by fragment status.¹⁸² Another analysis by Erdogan et al of data from 374 military and civilian

patients treated in Turkey specified that 31.8% (119 of 374) of patients had retained deep bone or metal fragments after surgery and reported 18 infections, including five in cases with fragments and without CSF fistulas, but it is not clear if the other 13 patients with infections had retained fragments or not.¹⁹⁹ A study by Jankovic et al of 176 predominately military (86.4%) patients in Croatia did not provide the number of patients with retained fragments or the number with infections; but stated there was a statistically significant association between remaining bone fragments and infection, provided the p-value for a chi square, but added the caveat that all patients with infections and retained fragments also had at least two other risk factors for infection.¹⁸⁹ Another study by Tudor et al in Croatia of 176 injured military personnel confirmed that 41% of patients had retained fragments based on CT after surgery and 28 patients (15.9%) developed infections.^{195,196} The authors stated that infections were more common in the presence of fragments, but data were not provided in a way that allowed comparisons of patients with and without fragments. One additional study by Amirjamshidi et al followed 99 military patients or civilians in battlefield areas in Iran who were assessed and treated with minimal debridement. All the patients had entrance wounds and no exit wounds; all had some retained bone and metal fragments. The majority (91%) achieved good outcomes in long term follow-up and none of these patients developed brain abscesses or epilepsy.¹⁶⁹

Treatment before 1980

1 study for SOE in 2 articles was included (8 total studies in 10 articles^{68,73,75,150,170,178,192-194,197}).

Data were compiled in a registry from soldiers injured during the Vietnam War (1967 to 1970) who were initially treated in Vietnam and Japan and whose care continued when they returned to the United States. These data were analyzed and reported in several articles, two of which provide evidence for this question. These data contained mixed results for different outcome-fragment combinations. Rish et al. reported that 37 of 1121 patients developed brain abscesses and that the infection rate was significantly higher (6.4%) in the patients with retained bone fragments than in patients without (2.5%).¹⁹³ The same article reported that the mortality rate for patients with brain abscesses was 82% in patients with retained fragments vs 42.3% in patients without fragments. The authors added that all patients with abscess and retained fragments who died had other risk factors as well, but they did not report this information for the people without retained fragments, nor did they report the association between mortality and retained fragments in the 1084 patients who did not have a brain abscess.

Another analysis by Salazar et al of the same registry examined a subgroup of 421 patients who were the first to complete a comprehensive follow-up. The rate of seizures was significantly higher for patients with retained metal fragments (59% vs 42%), but not significantly different for patients with and without retained bone fragments.¹⁹⁴

The remaining eight articles are included in Table 20 as they did not provide comparisons or data that allowed comparisons of outcomes for patients with and without retained fragments.^{68,73,75,150,170,178,192,197}

Five of these studies provided information about small numbers of civilians; three about patients treated in the United States, one in Canada, and one in Lebanon that included civilians and military personnel. In a study by Hubschmann et al that examined the records of 45 patients who had surgery for a GSW to the head at a trauma center in the United States, out of 82 treated patients, 29.9% (N = 13) had retained missile/metal fragments but there was no evidence found of infection or other ill effects.⁷³ A second study by Lillard et al of GSW to the head in civilians in the United States found that 68.7% of patients (57 of 83) had retained missile/metal fragments and authors stated there was no evidence of any complication or death related to fragments.⁷⁵ The third study by Raimondi et al of 150 patients treated for GSW evaluated the 16.7% (25 of 150) who survived with retained missile fragments.⁷⁵ None of these patients developed brain abscesses; of the 14 patients who had surgery, one had seizures and one developed meningitis. One study by Suddaby et al of 49 patients with GSWs treated in Canada reported that all 19 surviving patients had retained metal fragments after surgery and their complications included one case each of brain abscess, meningitis, and late epilepsy.¹⁷⁰ A study by Haddad et al of 164 patients who had surgery, out of 219 civilians and military personnel treated in Lebanon, reported that 8.5% had retained bone fragments after surgery but that none of these patients developed brain abscesses during 15 months of follow-up.¹⁷⁸

Additional results in Table 20 from this period include three articles based on military experiences. Meriowsky et al¹⁹² uses the same patient registry from the Vietnam War that was used by Rish et al¹⁹³ and Salazar et al.¹⁹⁴ This analysis reported a different outcome, that 10.2% of patients had reoperations to remove retained fragments and described the outcomes of those surgeries. Mortality was 10.3% for patients with retained fragments who had another surgery vs 6.2% for those who did not have another surgery.¹⁹² Carey et al provided data on a different group of 103 patients from the Vietnam War and reported the results for 15 of the 16 patients with retained bone fragments who had one or more reoperations: one died (6.3%), but there was no brain abscess in this patient, and two abscesses in patients without retained bone fragments.⁶⁸ The final study by Webster et al evaluated 206 patients treated by a U.S. Military Hospital Unit in Europe at the end of World War II (~1944). While the number of patients with retained fragments was not reported, 33 patients developed brain abscesses and of these patients 57.6% had retained bone fragments, 36.4% had retained metal fragments, and 6% had no retained fragments. The overall number of patients with retained fragments was not reported.¹⁹⁷

Summary and Strength of Evidence

Table 19 summarizes the comparisons from 13 studies reported in 15 articles including data from 4326 patients.^{7,61,68,70,73,75,150,161,164,165,169,170,176-178,182,184-187,189,190,192-197}

The studies are all non-randomized, consisting of retrospective cohorts or case series that included data on patient outcomes for patients with and without retained fragments.

These studies provide low SOE that pTBI patients with retained fragments have similar rates of infection and other outcomes compared with patients without retained fragments. All but one of these studies was rated high risk of bias and the study limitations for this body of evidence are considered high due to concerns about selection bias, loss to follow-up, and lack of accounting for potential confounding in analyses. While the majority of the studies found that retained fragments did not increase poor outcomes, there are a minority of studies that report worse outcomes from different time periods, locations, and populations. These inconsistencies in the results create doubt and the need for more studies to either solidify the conclusion of similar outcomes or support another conclusion.

Discussion

This comprehensive review of the literature showed inconsistent data elements and outcome measures related to the retention of a foreign body after a pTBI, with a majority of the literature suggesting no change in outcome or risk of infection or seizure whether the retained objects are removed or not. When evaluating this type of literature, it must be acknowledged that each penetrating head injury is unique and with many elements that cannot be controlled; for example, the type of penetrating fragment (bullet vs a fragment of various material from a blast), contamination of the wound at the time of injury, the velocity of the fragment and hence the dissipation of kinetic energy to the surrounding tissues and its effect on outcome and seizures. Variation in prophylactic antibiotic administration is another variable. Furthermore, the mixing of military and civilian data needs to be interpreted with caution as this can introduce a wide variance in the type of weaponry utilized which can directly influence outcome. Despite these limitations, this is still an important question to answer and continue to study.

Some studies within the reviewed literature suggest that there is a higher risk of infection associated with retained bone fragments and a higher rate of seizure associated with retained metallic fragments.^{165,176,189,190,193,194} However, the overall SoE does not warrant treating retained fragments differently based on their composition.

Along with KQ 37, this recommendation is part of a continuum of care for the patient with a pTBI. During the initial surgery, there is a Level III recommendation for “Conservative debridement of devitalized brain, bone fragments, and foreign bodies including lesions directly visible or encountered during the removal of operative hematomas or during hemostasis should be performed.” This approach at the initial surgery sets up the increased possibility of retained fragments post-operatively. The next logical step is to evaluate if these retained fragments should be removed to improve outcome,

reduce the risk of infection, or reduce the risk of seizure. This is the impetus for the current question. Although the SOE is low, at this time it does not appear that the retention of foreign bodies alone significantly affects outcome, infection, or seizure risk.

The removal of intracranial fragments can involve iatrogenic trauma to the brain – neurosurgeons know that no study is required to demonstrate that. Surgical removal of foreign bodies would thus need to demonstrate a benefit to be justified. Such benefit was not noted in the literature we found. There are other caveats here that are important to consider. When foreign bodies are present within a site of intracranial infection it may be difficult or impossible to treat that infection without removal of the foreign body. In this situation the foreign body must be removed if possible. A more extensive effort to remove retained foreign bodies is also appropriate in the context of a heavily contaminated wound.

The topic of retained foreign bodies after pTBI raised the issue of two closely related topics. The first was the consideration of managing a visibly protruding foreign body resulting in a pTBI.²⁰⁰ The second was for the management of a migrating intracranial fragment.²⁰¹⁻²⁰³ A review of the literature on each topic found case reports and case series on these topics. However, the totality of the data did not rise to the level of evidence that would allow a recommendation to be made based on the literature.

The addition of a recommendation based on expert opinion regarding retained fragments that are protruding from the skull is also a very important for the management of pTBI. Lower velocity projectiles such as an arrow or a knife may result in an externally visible retained foreign body. There was uniform consensus within the guidelines subject matter expert working group on this matter. When a foreign body penetrates the brain and protrudes from skull – such as a knife or an arrow – it should be removed in a controlled environment, such as the operating room or perhaps an endovascular suite. Prior to removal, however, studies are needed to determine the anatomy and degree of brain injury as well as adjacent structures that need to be evaluated or monitored upon removal. Here potential vascular injury is particularly important to recognize and plan for.

The recommendation based on expert opinion to consider the removal of a migratory intracranial fragment also represents a practical, although less commonly encountered clinical scenario. There was uniform consensus within the guidelines subject matter expert working group that removal of symptomatic migratory fragments should be considered. Neuro-endoscopic approaches could be considered to remove intraventricular migratory fragments.²⁰¹

Expert Opinion

In most circumstances limited debridement of pTBI and removal only of easily accessible foreign bodies is appropriate. Heavily contaminated wounds might prompt more aggressive

removal. It is important to follow patients with retained fragments over time and to monitor for intracranial infection. Should intracranial infection occur then removal of the relevant foreign body is indicated provided that this is felt to be feasible and with acceptable risk. MRI safety is an important consideration in patients with intracranial metallic FBs. Removal of fragments in order to permit MRI safely can be considered. (See KQ7) A further, albeit uncommon indication for removal of a retained metallic fragment, is lead toxicity¹⁹¹ refractory to medical treatments.

With respect to protruding or embedded foreign bodies such as knives our group identified a number of key principles for patient care. Protruding foreign bodies should be stabilized to ensure they cannot move and further injure the brain. Initially patients should be imaged with relevant modalities to enable an understanding of the intracranial position and trajectory of the object. It is also important to identify whether a large vessel injury is likely to exist within the cranium. Angiography should be considered when there is involvement of the skull base or the region of the pterion. Risk of vascular injury mandates exposure to facilitate proximal vascular control and an ability to surgically access the site of the injury. Cervical exposure of the internal carotid artery may be necessary for proximal control in some circumstances. In many situations endovascular treatment can be considered. The ability to temporarily or permanently occlude a major vessel by endovascular means can be a critical intervention and means of proximal vascular control. Generally suitable controlled environments for foreign body removal include the operating room or the endovascular suite. In most cases wide surgical exposure is needed enabling access to known and unanticipated sites of injury. Extended skull base exposures may be required for FB penetration involving the orbits or skull base. Such foreign bodies should be removed by pulling them out opposite the trajectory they went in. Ideally these objects are not removed until needed exposure has been achieved and the plan for removal has been discussed with the operative team. Preparations may be needed for massive blood loss and perhaps for preservation of forensic data. A breadth of difficulties can be encountered during surgical removal of these objects and this can force the operative team to be thoughtful, adaptable and resourceful. The hospital must be aware that such cases can be demanding of human and non-human resources, and communication facilitating preparedness is key. We refer to the algorithms for vascular injury and skull base penetration accompanying these papers. (See Surgical Algorithms).

Future Directions

There are several areas within this question that future research can help strengthen the level of evidence behind these recommendations. Clearly documenting the type of fragment (bone vs metal) and the relationship to the outcome measure, whether it is infection, seizure, or general outcome,

provides an important distinction between types of retained fragments and may influence surgical decision making or post-operative management. Further attempts to reduce bias by reporting on all patients with a penetrating brain injury in a prospective fashion would clarify the risk and outcome associated with these injuries. And finally, identification of risk factors for fragments that may migrate and become

symptomatic may influence surgical decision making and follow-up care.

Prospective research on protruding or embedded objects is a challenge given the rarity and diversity of injuries encountered. Research comparing endovascular assistance with open vascular approaches would be beneficial. Here case reports sharing new and important lessons learned continue to be valuable.

VII-4 – Prevention of Cerebrospinal Fluid Leaks

B. Aarabi, J. Ecklund, K. Latham

Recommendations

CSF LEAKS

Level I

There is insufficient evidence to support a strong recommendation related to infection risk and treatment of CSF fistulae following pTBI.

Level II

CSF fistulae should be surgically repaired following pTBI to reduce the risk of infection and poor outcome.

DURAL REPAIR MATERIAL

Level I-IV

There is insufficient evidence to support an evidence-based recommendation for dural repair by an allograft or autograft to prevent CSF fistulas.

Level C – Expert Consensus (Delphi Voting)

In the absence of direct scientific evidence, EXPERT CONSENSUS concluded that:

- In the presence of a pTBI, it is recommended to prophylactically repair the violated dura directly or by application of an autograft (tensor fascia lata, pericranium, temporalis fascia) or allograft to prevent CSF leaks and prevent deep CNS infections and mortality. CSF drainage can be considered as an adjunctive measure. (93.3% consensus)

There is no evidence or expert opinion to support a distinct recommendation based on patient gender, age, wounding mechanism, or military vs civilian context.

Introduction

The human brain is immersed in CSF which is tightly sealed by dura and leptomeninges while supported by the cranial vault and scalp. As such there is no free communication of sub-arachnoid space with the skin surface, paranasal sinuses or mastoid air cells. pTBI, being an open wound, violates this secure environment.¹⁵³ Direct penetration of scalp and skull is followed by laceration of dura and pia-arachnoid resulting in CSF leakage and access of subarachnoid space by skin contaminants. Skull

base penetration of paranasal sinuses and mastoid air cells results in rhinorrhea and otorrhea with added risk of backward extension of nosocomial contaminants into the intracranial cavity.^{65,204} Experience from multiple conventional military engagements has indicated that violation of the ventricular systems and basal cisterns make victims of pTBI particularly prone to CSF leakage and deep CNS infections.¹⁶² Whereas CSF leaks in blunt TBI have a high probability of healing with conservative management or with CSF diversion, CSF fistulae

associated with pTBI are generally gaping and unlikely to resolve without surgical repair.

Prior Guideline Recommendations

Management recommendations in the previous edition of these guidelines were provided on this topic at the level of option.²⁰⁵ This was supported by 9 articles (seven military and two civilian GSWH). The recommendation stated that:

“Surgical correction is recommended for CSF leaks that do not close spontaneously, or are refractory to temporary CSF diversion. During the primary surgery, every effort should be made to close the dura and prevent CSF leak.”

Since 2001 8 articles (six civilians and two military) provided a higher level of evidence than in the first edition, leading to a moderate strength recommendation in this edition.

Scientific Foundation

We identified no comparative studies where some patients received planned water-tight dural closure and other patients received planned no dural closure or less-than-water-tight dural closure. We identified 16 non-randomized studies (N = 6452) that reported outcomes in patients where water-tight dural closure was attempted, though not always successfully (Table 21). Mean sample size was 403 (range 13 to 1732), average study mean age was 24.6 years (range 21 to 37.8 years) in studies that reported age (9 studies), average study proportion males was 94% in studies that reported proportion of males (11 studies). Eight studies were in a military population, six in a civilian population, and two in mixed military and civilian population. The vast majority of penetrating injuries involved GSW or shrapnel. Three studies were conducted in Vietnam and Turkey; two studies were conducted in the United States, Croatia, and Korea; one study each was conducted in Brazil, India, Iran, and Iraq. No specific harms of watertight closure of the dura were reported.

Four non-randomized studies (N = 2206) reported infection rates in the proportion of patients with CSF fistula compared with those without fistula.^{183,185,192,199}

1. In a military pTBI population (N = 379) from the Iran-Iraq War,¹⁸⁵ the authors reported watertight closure in all operative cases by the following means: primary closure (N = 49, 13%), tensor fascia lata (N = 288, 76%), and pericranium/temporalis fascia (N = 41, 11%). In all patients in this series the dura was closed with 4-0 nylon monofilament suture and plastic surgeon assistance was utilized for complex scalp wounds. CSF fistulas occurred in 33 patients (8.7%). Of those, the most common locations were from the scalp (N = 23), followed by orbit (N = 7), nose (N = 2), and ear (N = 1). Twelve of the 33 patients (36%) developed CNS infections compared with 1.7% (6/346) of patients without CSF fistula ($P < .001$). Of patients with CSF fistula and positive CSF culture (50%), all were secondary to gram negative infections with *Klebsiella pneumoniae*, *Enterobacter*, and/or *Pseudomonas aeruginosa*. The authors also noted that they were forced to perform daily lumbar puncture,

insert lumbar drainage catheters, or place shunts to prevent CSF fistulae in select cases and in some patients, reoperation that entailed re-suturing dural or scalp fistulas several times before CSF leaks ceased was required. However, no data were provided for these. Site of injury was not a contributing factor to rate of infection in this series. The major contributors to infection in this series were due to CSF fistula and gram-negative bacterial meningitis. There were no complications reported due to pericranium/tensor fascia lata/temporalis graft harvest and no complications attributed to watertight dural closure in this series. There were 32 total deaths in this series. Deaths due to infection occurred in seven patients (18 total infections, 38.8%). The mortality rate for gram negative bacterial infection was 71% (N = 5/7). The rate of gram-negative bacterial infection was higher in patients with CSF fistulae (54%) than those without fistulae (16.6%).

2. From the Vietnam War 1133 pTBI patients were studied.⁷⁶ The authors reported an incidence of CSF fistula of 8.9% (N = 101). Of these, 54 (53.4%) occurred at the vertex/wound site, 30 (29.7%) with rhinorrhea, and 23 (22.8%) with otorrhea. Two cases presented with rhinorrhea and a wound site fistula, while four cases presented with both otorrhea and a wound site fistula. There were 28 patients with presumptive trans-ventricular wounds who developed CSF fistulae. The infection rate of the entire cohort was 8.6% (97/1133). Of patients with and without CSF fistulae, the rates of infection were 49.5% (50/101) and 4.6% (47/1023), respectively. Of the patients with vertex/scalp CSF fistulae, 12 underwent initial attempted primary closure, 34 underwent grafted closure (graft type not described), two cases the closure type was unknown, and in six cases no closure of the dura was performed. Data for these patients were reported in aggregate. Of these patients (N = 54), 57.4% (N = 31) developed an infection. In the case of rhinorrhea 41.4% (12/30) developed an infection and for those with otorrhea 47.8% (11/23) developed infection. There were 11 patients in this series for which resolution of CSF leak was not achieved by surgery and they all died. The authors concluded that inadequate closure of the dura and scalp is a frequent cause of failure to prevent an infection. The mortality of patients with CSF fistulae was 22.8% (23/101) compared with 5.1% (53/1032) in patients without CSF fistulae. There were no adverse events reported secondary to graft harvest or watertight dural closure.
3. A cohort of 374 pTBI patients with missile head wounds were studied in Turkey. The authors reported infection rates associated with CSF fistulae in a mixed military/civilian cohort (N = 374) of patients with penetrating injuries in Turkey.¹⁹⁹ All patients in this series underwent surgical intervention, which consisted of debridement and watertight closure of the dura by the following means: primary (N = 59, 15.7%), pericranial/temporal fascia graft (N = 285, 76.2%), tensor fascia lata graft (N = 22, 5.9%), or cadaveric dural graft (N = 8, 2.1%). Nineteen patients developed CSF fistulae in this series (5.1%), of these, 13 developed CNS

TABLE 21. Evidentiary Base for Water-tight Closure of the Dura to Prevent CSF Leak

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Study risk of bias
Aarabi, 1989 ¹⁸⁵ (NRS) Iran-Iraq War, Iran Military GSW: 10.6% Shell fragment: 72% Unknown: 17.4% Penetrating: 61.5% Tangential: 25.6% Perforating: 7.4% Unknown: 5.5%	N = 379 Male: 99.9% (1/379 female) Mean age: 21 y (SD 6.1) Mean time since injury: 49 h (range 7-450) Site of injury Parietal: 146 Frontal: 123 Temporal and occipital: 53 Orbito-facial-cranial: 21 Other: 36	Surgical debridement: radical with watertight dural closure Primary dural closure was accomplished in 49 (13%), with tensor fascia lata in 288 (76%), pericranium/temporalis fascia in 42 (11%)	CSF fistulas: 33 (8.7%) Origin Scalp: 23 Orbit: 7 Nose: 2 Ear: 1 Patients with CNS infection With CSF fistulas: 36% (12/33) Without CSF leakage: 1.7% (6/346), $P < .001$ 50% (6) of patients with CSF leaks developed gram negative CNS infections (Klebsiella pneumonia, Enterobacter species, and Pseudomonas aeruginosa were highest frequency) Gram-negative infection: 54% with CSF fistula vs 16.6% without Total deaths: 31 Deaths due to infection: 38.8% (7/18) Mortality in gram-negative infection: 71% (5/7)	High
Meirowsky, 1981 ⁷⁶ (NRS) Vietnam Military Shell fragments: 75 Bullets: 26 Recorded as transventricular wound: 16 Surmised as transventricular wound: 12 Facio-orbitocranial wounds with CSF leak: 17 Missile crossed midline: 19 Perforating: 18	N = 1133 Male 100% Age: NR Developed CSF fistula: 101	Over 3 y patients with missile head wounds had surgical debridement, dural closure (primary or graft)	CSF fistula: 8.9% (101/1133) Wound site/scalp: 53.4% (54/101) Rhinorrhea: 29.7% (30/101) Otorrhea: 22.8% (23/101) Rhinorrhea and wound site infection: 2 Otorrhea and wound site fistula: 4 Transventricular wounds with fistula: 8 Infection: 8.6% (97/1133) With CSF fistula: 49.5% (50/101) Without CSF fistula: 4.6% (47/1032) Mortality with CSF fistula: 22.8% (23/101) Mortality without CSF fistula: 5.1% (53/1032) Wound site/scalp fistulas Primary closure: 12 Graft closure: 34 NR: 2 No attempt to close the dura: 6 Wound site/scalp fistulas developed an infection: 57.4% (31/54) Rhinorrhea developed an infection: 41.4% (12/30) Otorrhea developed an infection: 47.8% (11/23)	High

TABLE 21. Continued.

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Study risk of bias
Erdogan, 2002 ¹⁹⁹ (NRS) Turkey Military/Civilian GSW: 32.3% Shrapnel fragments: 67.7%	Male: 100% Mean age: 22 y (range 4-48)	Over a 7-y period 374 patients had surgical intervention and repair of dura Watertight dural closure was primary in 59 (15.7%) casualties; with pericranium/temporal fascia in 285 (76.2%); and with tensor fascia lata in 22 (5.9%) Cadaveric dural graft was used in 8 (2.1%) patients	CSF fistula: 5.1% (19/374) Developed an infection: 68.4% (13/19) Purulent ventriculitis: 5.3% (1/19) Cerebral abscess: 26.3% (5/19) Subdural empyema: 15.8% (3/19) Meningitis: 15.8% (3/19) Superficial infection: 5.3% (1/19) Infections without CSF fistula: 1.4% (5/355) Cerebral abscess: 80% (4/5) Superficial infection: 20% (1/5) Purulent ventriculitis, subdural empyema, and meningitis: 0	High
Gonul, 1999 ¹⁸³ (NRS) Turkey Military/Civilian Shrapnel: 65% GSW: 35%	Male: NR Mean age: 22 y (range 4-45)	Craniotomy, debridement, removal of superficial in-driven fragments, watertight dural closure Closure type Primary: 15.7% (45/288) Pericranium/temporal fascia: 76.4% (220/288) Tensor fascia lata: 5.9% (17/288) Cadaveric dural graft: 2.1% (6/288)	CSF fistula: 4.5% (13/288) Intracranial infection With fistula: 69.2% (9/13) Without fistula: 0.73% (2/275) With CSF fistula Purulent ventriculitis: 1 Cerebral abscess: 3 Subdural empyema: 2 Meningitis: 2 Superficial infection: 1 Without CSF fistula Purulent ventriculitis: 0 Cerebral abscess: 2 Subdural empyema: 0 Meningitis: 0 Superficial infection: 0	High
Aarabi, 1998 ¹⁵³ (NRS) Iran Military Shell fragments: 69% GSW: 9.4% Undefined projectiles: 21.6% Penetrating: 54.8% (528/964) Perforating: 7.5% (72/964) Tangential: 22.4% (216/964)	Male: 99.7% Mean age: 21 y GCS 13-15: 67% GCS 9-12: 12% GCS 6-8: 11% GCS 3-5: 7.7% GCS unknown: 2.7%	Over an 8-y period 414/964 had primary debridement in an academic center followed by critical care management until discharge to rehab center. Debridement was aimed at removing all the pulped brain followed by watertight closure of the dura by primary closure or application of a graft: Tensor fascia lata, pericranium or temporalis fascia.	Univariate analysis indicated an association of development of CSF fistulas and infection (53.13%, $\chi^2 = 187.75$, $P < .0001$) On multivariate analysis development of CSF fistula remained associated with development of infection (Wald $\chi^2 = 46.5260$, OR 11.931, $P = .0001$)	High

TABLE 21. Continued.

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Study risk of bias
Singh, 2003 ¹⁶¹ (NRS) India Military Shrapnel: 72% GSW: 20% IED: 8%	Male: 98% N = 60 (52 surgical) Mean age: 25 y (range 19-40) GCS 3-5: 13% GCS 5-8: 23% GCS 8-12: 50% GCS 13-15: 13% Site of injury Frontal: 18% Parietal: 33% Temporal: 17% Occipital: 7% Orbito-facio-cranio-cerebral: 25%	Craniotomy, debridement: 42 Craniectomy, debridement: 10 Watertight dural closure performed in all cases with pericranium or temporal fascia	Among 52 operated patients 0 instances of CSF leak/fistula and 0 instances of brain abscess/deep seated infection	High
Carey, 1974 ⁶⁸ (NRS) United States, Vietnam Military Fragments and GSW: 100%	Total population: N = 103; 91 survivors Characteristics: NR	Surgical debridement, implied watertight closure	CSF fistula: 2 1 incisional CSF leak 1 incisional CSF leak plus sterile meningitis Intraoperative discovery of failure of primary closure	High
Melada, 2002 ²⁰⁶ (NRS) Croatia, Balkan Wars Military Shrapnel: 90% GSW: 10%	N = 312 Male: 99.4% Mean age: NR (range 18-67 y)	Wound debridement, watertight dural closure	CSF fistula incidence: 14.4% (45/312) Wound site fistula: 4.8% (15/312) CSF Rhinorrhea: 7.4% (23/312) CSF Otorrhea: 2.2% (7/312) CSF fistulas Site of Injury: 33% (15/45) Rhinorrhea: 51% (23/45) Otorrhea: 15% (7/45) All patients with wound-site fistulas underwent surgery. 3 underwent reoperation for recurrent leak. Patch grafting: muscle, tensor fascia lata, or alloplastic material/lyophilized dura, fibrin glue Patients with CSF rhinorrhea: subfrontal approach (Trans- sphenoidal approach: N = 2) Incidence of postop meningitis: 13.3% (6/45) [only occurred in patients with CSF rhinorrhea]	High

TABLE 21. Continued.

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Study risk of bias
Vrankovic, 1992 ¹⁶⁶ (NRS) Croatia, Balkan Wars Civilian: 51.7% (N = 30) Military: 48.3% (N = 28)	Male: 87.1% Mean age: 30 y (range 14 to 80) No other demographics provided	Surgical debridement: 62 Watertight dural closures with graft: 45 (53 total procedures) Primary closures: 4 Grafts Group 1 (fascia, temporalis muscle): 2 Group 2 (lyodura): 6 Group 3 (periosteum): 22 Group 4 (tensor fascia lata): 15	Primary closures: mortality 50% (2/4), no evidence of intracranial infection Grafted closures Group 1 mortality: 50% (1) Group 2 mortality: 83.3% (5), CSF leak/meningitis: 1 Group 3 mortality: 41% (9) Living: 13 CSF leak/meningitis: 3 Encephalitis 1 Reoperations 3 Deaths with CSF leak/meningitis: 1 Group 4 mortality: 26.7% (4) Living: No CSF leaks Deaths with CSF leak/meningitis 2	High
Hammon, 1971 ¹⁷⁵ (NRS) United States, Vietnam Civilian: 32.4% (N = 561) Military: 67.6% (N = 1171) GSW: 10.7% Shrapnel: 87.2% Other: 2.0%	No demographics provided	Surgical debridement of missile head wounds Watertight dural closure with local grafts (muscle, fascia, galea)	Total operative mortality for U.S. military patients: 9.74% (114/1171) Direct cerebral mortality for U.S. military patients: 8.88% (104/1171) Total operative mortality for Vietnamese patients: 14.9% (84/561) Mortality of entire operative cohort: 11.23% (198/1732) Among patients with craniectomy/ debridement Postoperative CSF fistulas requiring reoperation/ further surgery: 0.63% (11) Postoperative meningitis: 0.63% (11)	High
Wallace, 1960 ²⁰⁷ (NRS) United States, Korean War Military Shrapnel: 50% Missiles: 29.6% Various objects: 6.5% Unknown: 15.9%	No demographics provided	Craniotomy/craniectomy, debridement, watertight closure with Fascia lata: 198 Temporal/occipital fascia: 186 Periosteum: 155 Gelfilm/fibrin film: 27 489 grafts inserted at primary craniectomy 64 grafts inserted at secondary craniectomy 37 instances grafts had to be reinserted or replaced in secondary operations	CSF fistula: 49 41 cases required secondary surgical closure 144 cases were secondarily explored Viable graft: 90 Viable graft with defect: 25 Non-viable graft: 20 Gelfilm in place: 4 Gelfilm displaced: 5 1 case of seizures thought secondary to cerebral herniation through dural defect	High

TABLE 21. Continued.

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Study risk of bias
Dolachee, 2019 ⁶³ (NRS) Iraq Civilian Shrapnel: 18% Bullets: 61% Others: 20%	N = 39 Male: 90% Mean age: NR GCS 13-15: 41% GCS 9-12: 43% GCS 5-8: 13% GCS unavailable: 3%	Craniotomy or craniectomy, watertight dural repair with patch graft Pericranium: 64.1% Tensor fascia lata: 35.9%	CSF leak incidence: 12.8% 40% poor outcome 60% good outcome Authors utilized GOS as measure of outcomes, however cut-off for good/ poor was not reported. There was no association with good or bad outcome by type of graft used (pericranium, TFL), $P = .7$	High
Ambrosi, 2012 ²⁰⁸ (NRS) Brazil Civilian GSW: 100%	Male: 93% Mean age: 26.9 y GCS admission: 11.5 (SD 3.7) GCS surgery: 10.8 (SD 3.7)	Surgical intervention including implied watertight closure of dura Duroplasty: 73% (81/105 available OR records)	Reoperation: 8.2% (9) Mortality: 24.5% (27) Developed CSF fistula: 13% (15/110) Survivors with CSF fistulas: 18% (15/83) Non-survivors with CS fistulas: 0% (0/27) $P = .0175$	High
Solmaz, 2009 ²⁰⁹ (NRS) Turkey Military Blast/shrapnel: 68% GSW: 32%	Male 99.3% Mean age: 23.2 y (range 4-54) GCS 3-8: 26.2% GCS 8-15: 73.7%	Dural closure, primary: 15.1% (67) Duroplasty Pericranium/temporalis fascia: 57% (252) Tensor fascia lata: 4.2% (19) Cadaveric dura graft: 2% (9)	GCS 8-15 mortality: 6.1% (20) GCS 3-8 mortality: 23.3% (27) CSF Fistula: 4.5% (20)	High
Kim, 2007 ²¹⁰ (NRS) Korea Civilian GSW: 100%	Male: 84.6% Mean age: 24.1 y (range 8-39) Mean GCS: 10.6 (range 4-15) GCS 13-15: 7 (53.8%) GCS 9-12: 2 (15.4%) GCS 6-8: 3 (23.1%) GCS <5: 1 (7.7%)	Watertight dural closure: 13	Mortality: 7.7% CSF leak/fistula: 2 (15.4%)	High
Sherman, 1980 ⁴¹ (NRS) United States Civilian GSW: 100%	N = 79 operative patients Male: 81% Mean age: 21 y (range 15 mo to 81 y)	Radical debridement with watertight closure	Mortality: 23% CSF fistula: 8 CSF rhinorrhea: 7 CSF otorrhea: 1 Meningitis: 2/8 Spontaneous resolution: 5/8 Reoperation: 2/8 1 patient died with persistent fistula	High
Aarabi, 2014 ²¹¹ (NRS) United States Civilian GSW: 100%	N = 786 Male: 84.1% Mean age: 37.8 y No demographics for small subgroup analyzed (N = 15)	Craniotomy/debridement, watertight dural closure: 15	CSF leak/rhinorrhea: 1 (6.7%) [required reoperation for dural repair] Subdural/epidural empyema: 1 (6.7%)	High

CNS, central nervous system; CSF, cerebrospinal fluid; GCS, Glasgow Coma Scale; GOS, Glasgow Outcome Scale; GSW, gunshot wound; IED, improvised explosive device; MOI, mechanism of injury; NR, not reported; NRS, nonrandomized study; TFL, tensor fascia lata.

infections (68.4%). There was one case of purulent ventriculitis (N = 1/19, 5.3%), five cerebral abscesses (N = 5/19, 26.3%), three subdural empyemas (N = 3/19, 15.8%), three with cases of meningitis (N = 3/19, 15.8%), and one superficial infection (N = 1/19, 5.3%). This is contrasted with an incidence of infection in the cohort without CSF fistulae (N = 5/355, 1.4%). In this group there were no instances of purulent ventriculitis, subdural empyema, or meningitis. There were four instances of cerebral abscess (80%, N = 4/5) and one superficial infection (20%, N = 1/5). There were no adverse events associated with watertight dural closure reported.

4. A mixed military/civilian pTBI cohort of 288 patients were reported from Turkey. The fourth study also reported infection rates in the setting of CSF fistulae in a mixed military/civilian cohort (N = 288) who underwent craniotomy, debridement, and watertight closure of the dura in Turkey.¹⁸³ Watertight dural closure was obtained by the following means: primary (15%, N = 45), pericranial/temporal fascia graft (76.4%, N = 220), tensor fascia lata (5.9%, N = 17), and cadaveric dural graft (2.1%, N = 6). The authors reported an incidence of CSF fistulae of 4.5% (N = 13). There were 11 intracranial infections in the total study cohort with a majority occurring in patients with CSF fistulae (69.2%, N = 9/13) compared with patients without CSF fistulae (0.73%, N = 2/275). No adverse events of watertight closure or grafting were reported by the authors.

A pooled analysis of these four pTBI studies found a greatly increased risk of infection in the presence of CSF fistulae compared with no fistulae (relative risk 30.18, 95% CI, 14.34 to 63.53, Figure).^{183,185,192,199} This analysis provides moderate strength evidence that infection risk is greater when patients have a CSF fistula.

5. An additional cohort pTBI study (N = 964) that also indicated a positive relationship between a CSF fistula and infection could not be added to the above analysis as raw data counts are not reported.¹⁵³ In this study, 54.8% had penetrating injuries (N = 528) and 7.5% had perforating injuries (N = 72) due to military conflict. Primary radical procedures, including watertight closure, were performed in 414 patients. Univariate analysis indicated an association of development of CSF fistula and infection (53.13%, $\chi^2 = 187.75$, $P < .0001$). On multivariable analysis development of CSF fistula remained associated with development of infection (Wald $\chi^2 = 46.5260$, OR 11.931, $P = .0001$). It should be noted that data for patients with watertight closure were reported in aggregate with patients for whom closure type was not available and variable treatments were performed for CSF fistulas including reoperation, lumbar punctures, and continuous CSF drainage.
6. Another pTBI study that could not be added to the above analysis because there were no patients with a CSF fistula was in a population of military patients (N = 60) in India.¹⁶¹ Of 60 patients who were admitted with penetrating cranial wounds, 52 underwent acute surgical intervention including six who had previously undergone limited surgical procedures at

forward operating bases. The authors reported that in all cases dural defects were closed with either a pericranial or temporal fascia graft to achieve a watertight closure. There were no CSF leaks in patients who underwent surgery and no patients developed brain abscesses. The authors attribute this to early surgical intervention (≤ 48 hours of injury) and the absence of CSF fistulae in this series. The average time to surgical intervention in this series was 36 hours post-injury (range 6 to 72 hours) and all patients were started on antibiotics within 6 hours of injury. There were no adverse events reported secondary to watertight closure of the dura.

The remaining 10 non-randomized studies reported other outcomes including rhinorrhea, otorrhea, reoperation, and overall mortality among others. These studies are further described below and in the table. Studies in a military population are presented first, followed by studies in a civilian population.

7. One study reported outcomes for a series of military patients with pTBI in the Vietnam War.⁶⁸ The study cohort was comprised of 103 patients with GSW to the head who underwent surgical intervention, however, complications were only reported for survivors (N = 91). The authors implied watertight dural closure was performed in all cases and noted an incidence of CSF leak of 2.1% (N = 2). In both cases, re-exploration identified an absent or misplaced dural suture at the primary closure site and determined this as the etiology of the leak.
8. A cohort of 312 pTBI's were studied from Croatia reported surgical debridement and watertight dural closure in all patients when deemed appropriate.²⁰⁶ The incidence of CSF fistula was 14.4% (45/312). The incidence of fistula for the entire cohort by site were: 4.8% (15/312) at wound site, CSF rhinorrhea 7.4% (23/312), and CSF otorrhea 2.2% (7/312). Of fistulae identified: 33% occurred at site of injury (15/45), 51% (23/45) were via the nose, and 15% (7/45) were via the ears. All patients with wound site fistulae underwent surgical intervention and three required subsequent reoperation for persistent leak. The authors utilized patch grafting with muscle, tensor fascia lata, or alloplastic material/lyophilized dura and fibrin glue. The incidence of postoperative meningitis was 13.3% in patients with CSF fistulae (6/45) and all instances occurred in patients with CSF rhinorrhea. It should be noted that it is unclear which patients underwent initial attempt at primary repair and which cases underwent a trial of spontaneous closure. It also should be noted that the cohort reported data in aggregate with 10 patients with closed head injuries.
9. A group of 62 military pTBI patients were reported from Croatia. Four patients had primary closure of the dura, 45 patients underwent watertight closure with grafts and 53 total procedures were performed in these patients.¹⁶⁶ The number of total procedures includes those with through and through/bilateral repair and eight patients who required reoperation. The authors separated the cohort into groups by graft type: fascia or temporalis muscle (Group 1), lyophilized dura (Group 2), periosteum

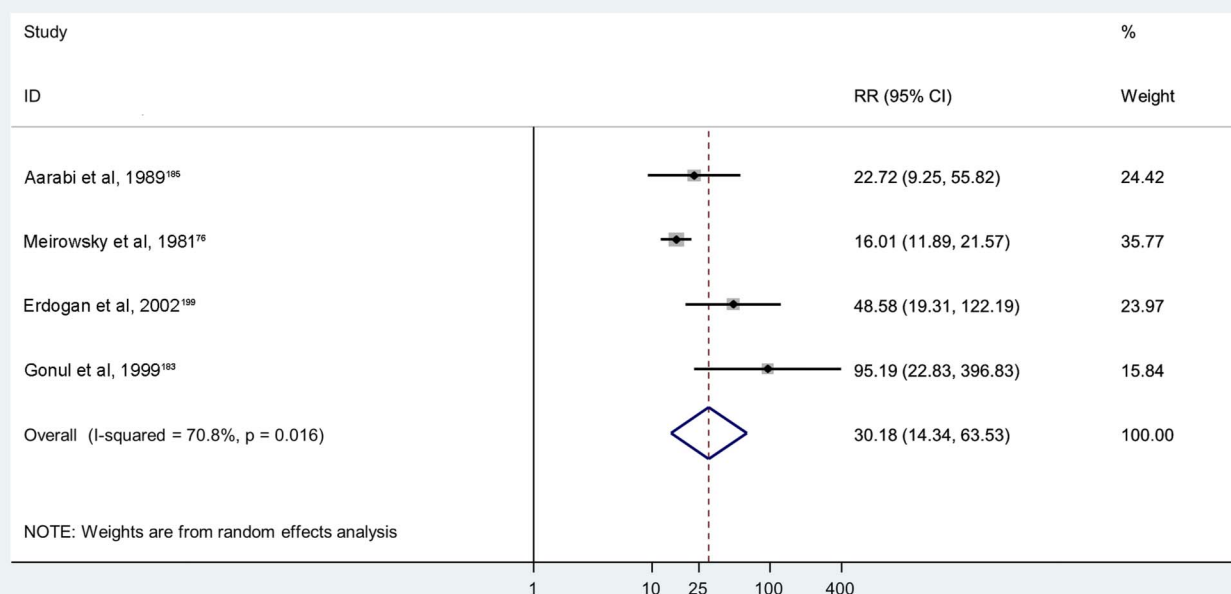


FIGURE. Pooled analysis of risk of infection in the presence of CSF fistula. CSF, cerebrospinal fluid; RR, relative risk.

(Group 3), tensor fascia lata (Group 4). Group 1 was comprised of only two patients and the mortality was 50%. Group 2 was comprised of six patients and mortality was 83.3% (N = 5/6), and one patient developed CSF leak and meningitis. There were no intracranial infections identified on autopsy of those who died. Group 3 was comprised of 22 patients of which nine died (41%). Among those who survived there were three patients who developed CSF leak and meningitis, one who developed encephalitis, and three who required reoperation where periosteum was replaced with tensor fascia lata grafts. Among the nine deaths in this group there was one CSF leak and one instance of meningitis. Group 4 was comprised of 15 patients, four of whom died (mortality 26.7%). Among those who survived there were no CSF fistulas. Among those who died (N = 4), there were two instances of CSF leak, wound dehiscence, and meningitis. There were no adverse events reported by the authors due to type of graft utilized for watertight closure.

10. One military pTBI cohort of 1171 patients were reported from Vietnam by Hammon et al. Outcomes of operative cases in the U.S. military and 561 cases in Vietnamese patients with pTBI in which watertight dural closure was achieved “in almost all cases” by dural grafting with muscle, fascia, or pericranium from the operative area.¹⁷⁵ If sterile graft material was not available in the immediate exposed area the authors extended a limb of the incision and obtained tissue from another cranial site. The mortality of the operative U.S. military cohort was 9.74% (114/1171). There were 104 deaths attributable to cerebral mortality (8.88%) in the U.S. military patients and 76 cerebral

deaths in the Vietnamese cohort (13.55%). Postoperative CSF fistula requiring reoperation or additional surgery occurred in 0.63% of cases (N = 11). Postoperative meningitis occurred in 0.63% of cases (N = 11). There were no adverse events reported by the authors due to watertight closure or graft harvest.

11. Wallace and Meirowsky reported 540 military pTBI patients from the Korean Campaign.²⁰⁷ There were 167 transventricular wounds in this study cohort. Dural grafts were utilized for closure and a total of 590 grafts were utilized in the surgical cohort. There were 489 grafts inserted during primary craniectomy, 64 grafts inserted at secondary craniectomy/craniotomy, and in 37 instances grafts required reinsertion or replacement during secondary operations. The following grafts were used: tensor fascia lata (N = 198), temporal/occipital fascia (N = 186), pericranium (N = 155), and gelfilm/fibrin film (N = 27). CSF fistulas occurred in 49 patients, 41 cases required secondary surgical closure of a dural defect. There were 144 cases of secondary surgical site exploration and graft viability was recorded: viable graft (N = 90), viable graft with visible defect (N = 25), non-viable graft (N = 20), and gelfilm failure/migration (N = 9). The authors did not report any adverse events secondary to dural graft harvest or watertight closure.
12. Thirty-nine civilian pTBI patients were reported from Iraq looking for association with type of dural patch graft (pericranium vs tensor fascia lata) and outcomes by the GOS.⁶³ All patients underwent craniotomy or craniectomy with watertight dural closure by pericranium (64.1%) or tensor fascia lata

- (35.9%) graft. The authors reported an incidence of CSF leak of 12.8% in the entire cohort. There was no association with type of graft used for dural closure ($P = .7$). Of the cohort of patients who developed CSF leak, 40% achieved a poor outcome and 60% achieved a good outcome. It should be noted that the authors utilized GOS for determination of quality of outcome, but no strict definition was provided. There were no reported complications secondary to graft harvest or watertight closure.
13. From Brazil a cohort of 110 civilian pTBI patients were reported to define the incidence of CSF fistulae following duroplasty and watertight dural closure.²⁰⁸ The authors noted that duroplasty was performed in 73% ($N = 81$) of patients in the cohort and indicated that watertight closure was attempted in all patients. The mortality of the cohort was 24.5% ($N = 27$). Reoperation occurred in 8.2% of cases ($N = 9$). Among 83 survivors a total of 15 patients developed CSF fistula (18%). No patients who expired developed CSF fistulae prior to death ($P = .0175$).
 14. One study from Turkey reported a single institution experience ($N = 442$) with civilian pTBI over a 16-year period.²⁰⁹ The authors reported that "in most cases" dura was closed primarily (15.1%, $N = 67$). In cases where the dura could not be primarily closed, the authors performed duroplasty with pericranium or temporalis fascia (57%, $N = 252$), tensor fascia lata (4.2%, $N = 19$), or cadaveric dura (2%, $N = 9$). The aggregate incidence of CSF fistula in this population was 4.5% ($N = 20$) and was not stratified by closure type. There were no comparison groups and definitive closure attempt was implied in all cases.
 15. Kim et al reported 13 patients with pTBI due to civilian GSW looking for CSF leaks following watertight dural closure.²¹⁰ The incidence of CSF leak was 15.4% ($N = 2$) and both cases resolved with CSF diversion without infection.
 16. Outcomes following civilian pTBI in the United States were studied by Sherman et al.⁴¹ The authors report operative outcomes for 79 patients who underwent operative intervention for GSW. In all cases dural closure was attempted. The authors reported a rate of CSF fistula of 10.1% for the entire study cohort. No leaks occurred at the surgical scalp wound or vertex. There were seven cases of CSF rhinorrhea and one case of CSF otorrhea. In these eight cases, five leaks resolved spontaneously and two required reoperation for definitive closure. One patient died with a persistent CSF fistula. The authors reported no adverse events from dural closure.
 17. In an epidemiologic cohort civilian pTBI study, Aarabi et al reported on outcomes for 192 patient who were admitted to nine trauma centers in Maryland over a two-year period.²¹¹ Of the study cohort 15 patients underwent craniotomy with watertight dural closure. Of these patients there was one patient with CSF leak (CSF rhinorrhea) that required reoperation and dural repair and one epidural/subdural empyema that required washout. No description was provided for primary or grafted dural closure and no adverse events were reported secondary to watertight closure. Demographics for this subgroup were unable to be elicited.
 18. From Balkan Campaign Tudor et al reported on their experience with CSF fistulae. In a military population with pTBI the investigators looked for an association of infection and reoperation with presence of a CSF fistula.¹⁹⁵ This study was not included as formal evidence nor included in the Table due to lack of surgical description or granularity with respect to closure or non-closure of the dura. However, this work is contained within the text due to the findings of: presence of CSF fistula was associated with development of infection. CSF fistula occurred in 11% of patients ($N = 21$). Of patients without CSF fistula, 12% developed infections. Of patients with CSF fistula, 47.6% developed infection ($\chi^2 = 15.33$, $P < .001$). The authors also reported higher rates of reoperation in patients with CSF fistulae (76%) compared with patients with deep seated infections (60%, $\chi^2 = 43.6$, $P = .00001$) and patients without infections (8.4%, $\chi^2 = 56.95$, $P = .00001$). It should be noted that no clear description of reparable or non-reparable (craniobasilar injuries) were given for this patient population. The authors defined watertight dural closure as "not allowing a CSF fistula to develop."
- Several other works were identified that support the above findings, but did not meet criteria for inclusion due to lack of granularity of injury patterns or procedures performed,¹⁸² or no clear description of dural closure were provided (watertight, primary-repair, onlay only, combination).^{87,212}
- One study was identified in a population of U.S. military patients that concluded that watertight closure, harvesting adjunct grafts (pericranium), or utilizing suturable grafts was time consuming and noted benefits were not apparent relative to the increased operative time in multiply injured patients.²¹³ However, no objective measures were provided supporting this claim. There were no harms reported secondary to watertight closure or associations with type of dural graft used.

Discussion

Cerebrospinal fluid leaks are the scourge of pTBI management and have to be taken seriously. The best evidence for this statement is not only the findings from the preceding literature review but also by considering the history of pTBI management.²¹⁴ Mortality/morbidity due to infection was appallingly high during the "Pre-Modern Era" of neurosurgical techniques in management of missile head wounds, which coincided with the end of the American Civil War in 1865.²¹⁴ The introduction of asepsis, antiseptics, and anesthesia during the "Modern Era, 1865-1918" combined with meticulous debridement of the pTBI tract and watertight closure of scalp by Cushing reduced infection rate to 35 percent.^{162,214,215} A simple comparison of Cushing's work with that of Whitaker who left the entrance wound of pTBI open indicates higher rate of mortality in the latter surgeon's surgical technique precipitated by deep CNS infections.^{162,215,216} It was Cushing's suggestion that penetration of the ventricular system was important in CSF leaks predisposing to meningitis and ventriculitis.^{162,215,217} The significance of CSF leaks and their relationship with deep CNS infections was taken very

seriously during the Second World War as expressed by Ascroft and Cairns.^{163,204,217-221} The relationship between CSF fistulas and orbitofaciocraniocerebral injuries, involvement of basal cisterns and cerebral ventricles was further confirmed during the Second World, Korean, Vietnam Wars, and Middle Eastern Conflicts.^{61,165,222,223} The fact that pTBI is the mother of all CSF leaks and the building block of deep CNS infections is clearly supported by Class II evidence collected from multiple conflicts starting from WWI^{162,215,216} to WWII,^{163,204,221} Korean Conflict,^{65,76,224} Vietnam War⁷⁶ and Middle East Campaigns,^{61,70,185,225} and our Consensus Delphi conference recommends repair of this pathologic entity by any means including primary repair, allo- or autograft. CSF diversion can be considered an adjunct in such repairs.

Expert Opinion

Harvey Cushing was first to recommend watertight closure of scalp in order to prevent CSF leaks especially if basal cisterns or the ventricular systems were violated.¹⁶² Subsequently it was learned that in the majority of cases with pTBI the hot projectile not only

will cut the dura, it will cause retraction of the latter with less chance to be repaired primarily.¹⁸⁵ During WWII, Korean, Vietnam, Middle East and Balkan conflicts we experienced the need for a fascial dural graft in order to prevent CSF leakage - especially in lacerations of basal dura, in order to prevent CNS infections.^{61,153,163,166,182,226,227} Based on this low level evidence, the Delphi Consensus decision was to recommend dural graft in the majority of patients with dural laceration in order to prevent CSF leaks and CNS infections.

Future Directions

Level II evidence supports a moderate strength recommendation that CSF fistulas predispose the victim of pTBI to deadly CNS infections and that they should thus be prevented. Future prospective observational studies should clarify if allografts are as effective as autografts (pericranium, temporalis fascia, tensor fascia lata) in preventing CSF fistulas and CNS infections, and what their relative risk for infection is.

VII-5 – Intraoperative Cultures

R. Kitagawa, B. Aarabi

Recommendations

Level I-IV

There is insufficient evidence to support an evidence-based recommendation regarding the utility of intraoperative cultures at an initial operation to guide antibiotic treatment.

Level C by Delphi Consensus

In the absence of direct scientific evidence, EXPERT CONSENSUS concluded that:

- Intra-operative cultures of the scalp, wound tract, or bone/metal fragments should not be routinely performed at the initial surgery to guide antibiotic prophylaxis. These cultures and subsequent treatments do not predict or prevent future cranial infections. (96.7% consensus)
- Intraoperative cultures are appropriate if intracranial infection is present at the time of surgery. (100% consensus)

No evidence or expert opinion supported distinct recommendations based on patient gender, age, wounding mechanism, or military vs civilian context.

Introduction

Infection is a major source of morbidity and mortality after pTBI as all pTBI wounds are inherently contaminated. The first pTBI guidelines reported rates for infection varying from 1 to 59% in their included series.²²⁸ When intracranial infection is present, it is the standard of care to obtain cultures from the infected tissue ideally prior to antibiotic initiation to guide future therapies.

The prophylactic use of antibiotics including the type and duration of therapy has been debated in pTBI. This topic is addressed in other sections of these guidelines, but previous authors have reported obtaining cultures of the soft tissue, debris, and wound tract to guide these antibiotic therapies or to predict the future infection pathogens.^{160,173,174} Opponents of this approach argue that these cultures do not predict the infective organism and modifying antibiotic therapy based on these cultures may select for other organisms not obtained in the limited sampled area.

Prior Guideline Recommendations

The prior guidelines reported studies of cultures of contaminated intraoperative surfaces.²²⁸ However, no recommendation was given regarding if cultures should routinely be performed at the time of index surgeries or if the results from such cultures could or should guide antibiotic therapies.

Scientific Foundation

No additional studies were identified after the publication of the prior pTBI guidelines²²⁸ indicating that the practice of

routine culturing of the debris at the time of index operation is less common nowadays. Per the inclusion criteria for this guideline project only one of the three prior studies was suitable to serve as evidence for this question (Table 22). Although we found studies where individuals had intraoperative cultures taken, we identified no study that compared obtaining intraoperative cultures vs not obtaining intraoperative cultures. We also identified no study that compared broad spectrum antibiotic therapy given initially to patients with pTBI vs antibiotic therapy tailored to culture results.

One study served as evidence for this topic; it was a study of 125 patients from the Iran-Iraq War (Aarabi et al.¹⁶⁰) classifying head wounds as penetrating (51.6%), perforating (7.4%), or tangential gutter type (22.4%). However, 18.6% could not be classified.¹⁶⁰ This study reported that out of 102 intraoperative brain cultures in 125 patients, 28% were positive and out of 95 intraoperative bone fragment cultures, 21% were positive.¹⁶⁰ Gram-positive organisms were grown more frequently from both brain cultures (59%) and bone cultures (76%) compared with gram-negative organisms.

The additional studies (Carey et al and Ecker et al) which were not formally included as evidence here demonstrated mostly gram-positive organisms but most deaths in the later study were from infective gram negative organisms, which may imply that the cultured organisms may not be the same bacteria that lead to overt infection.^{173,174}

No study reported harms related to obtaining a culture nor did studies report harms associated with antibiotic treatment. It is unknown if poorer outcomes would have resulted if cultures were

TABLE 22. Evidentiary Base for Intraoperative Cultures

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Risk of bias
Aarabi, 1987 ¹⁶⁰ (NRS) Iran Military Penetrating: 51.6% Perforating: 7.4% Tangential gutter type: 22.4% Could not be classified: 18.6%	N = 125 Male: 100% Mean age: 19.8 y	Intraoperative cultures from incurred wound, retained bone and metal fragments and brain tract	This study reported that out of 102 intraoperative brain cultures in 125 patients, 28% were positive and out of 95 intraoperative bone fragment cultures, 21% were positive. Gram-positive organisms were grown more frequently from both brain cultures (59%) and bone cultures (76%) compared with gram-negative organisms. Prolongation of time from injury to debridement did not have much effect on the rate of contamination or infection. While most of the contaminating organisms were gram positive, the majority of infective organisms were gram negative.	High

MOI, mechanism of injury; NRS, non randomized study.

not taken and tailored antibiotic therapy not provided resulting in insufficient evidence to determine the benefits and harms of obtaining intraoperative cultures.

Discussion

Two fundamental questions influence the decision to obtain cultures. Is there a relationship between contamination and subsequent CNS infection and can we prevent deep infections by knowing the contaminating organisms and prescribing antibiotics which target them? The question of antibiotic prophylaxis is addressed in other sections. However, the cultured organisms at the time of initial pTBI surgery do not necessarily correlate with the organisms present when intracranial infections develop,¹⁷³ and therefore tailoring antibiotics to these cultures may not prevent infection. If the information then does not alter patient management, routine cultures at the index operation are not recommended. Intraoperative cultures remain the standard of care during surgical debridement and cleansing of an active intracranial infection to guide further antibiotic treatments.

The lack of direct comparison between patients managed with and without intraoperative cultures limits the conclusions. Additionally, no study reported the patient outcomes including the infection rates or organisms based on tailoring the antibiotics to these intraoperative cultures.

Expert Opinion

While intraoperative cultures are safe to obtain, the information may not change clinical management or the patient outcome. To date, no study has found a correlation between the culture results and the organisms present at the time of infection nor has the choice of antibiotic based on these culture results led to decreased infection risk. Given this lack of data, we do not recommend routinely obtaining cultures of the soft tissue, debris, foreign bodies, and missile tract. Obtaining cultures during an active cranial infection remains the standard of care.

Future Directions

Future studies comparing the use of antibiotics tailored to intraoperative cultures against broad spectrum antibiotics or no antibiotics at all would be appropriate to definitively answer these questions. Obtaining cultures from scalp wound, brain tract and retained bone fragment may also be considered under specific circumstances. For example, prolonged delays in definitive surgical care as may be present in wartime conditions may increase the value of intraoperative cultures. Additionally, prolonged CSF fistulas that eventually require open surgical repair may be more likely to reveal an infective organism at time of intraoperative cultures. These scenarios may also be the subject of future research studies.

VII-6 – Management of Traumatic Pseudoaneurysms

R. S. Bell, R. A. Armonda, B. Aarabi

Recommendations

Level I-III

There is insufficient evidence to support a strong, moderate strength or weak recommendation for surgery or endovascular intervention to reduce the risk of traumatic intracranial arterial aneurysm (TICA) rupture and improve outcome.

Level IV

Endovascular treatment of TICA, which often require re-treatment, is recommended as a means of reducing the risk of aneurysmal rupture and the associated high rate of morbidity and mortality. There is, however, insufficient evidence to support superiority of endovascular aneurysm occlusion over open surgical parent vessel sacrifice despite a theoretical reduced risk of iatrogenic stroke.

Open surgery may be considered in the setting of TICA resulting from pTBI to reduce the chance of rupture and improve outcome.

Level C – Expert Consensus (Delphi Voting)

In the absence of direct scientific evidence, EXPERT CONSENSUS concluded that:

- A multi-disciplinary approach to vascular sequelae of pTBI (TICA, A-V fistula, vasospasm, etc.) for patients with traumatic vascular injury(ies) is preferred when feasible. (100% consensus)
- It is recommended that TICAs which increase in size be treated with either open or endovascular means because of a presumed elevated risk for rupture (87.5% consensus).
- It is recommended that larger TICAs should be more strongly considered for treatment because of a presumed elevated risk for rupture. There is insufficient evidence or expert consensus to recommend a size threshold, however. (80.5% consensus)
- It is recommended that TICAs treated endovascularly should be reassessed with cerebral angiography within 8 weeks of initial treatment because of a risk of treatment failure (i.e. aneurysm recurrence or re-growth) for which further therapeutic procedures may be necessary. (95% consensus)
- In certain circumstances it may be permissible for TICAs to undergo a short period of conservative management in hopes of achieving spontaneous regression. Close observation is required if such an approach is attempted. Reasons for observation may include the lack of available neuroendovascular expertise, or a perceived unfavorable risk:benefit ratio inherent to treatment (95% consensus).

No evidence or expert opinion supported distinct recommendations based on patient gender, age, wounding mechanism, or military vs civilian context.

Introduction

pTBI often injures the cerebral vasculature.^{96,99,101,104,105,108-114,123,229-234} In fact, the high frequency of complex neurovascular injuries might be considered a defining feature of pTBI and a key characteristic distinguishing pTBI from blunt TBI. Damage (including complete or partial transection) or irritation to the arterial wall can be associated with the formation of TICA.^{101,108} These “pseudo aneurysms” lack an aneurysmal wall and are contained only by clot in the subarachnoid space, distinguishing them from saccular or fusiform aneurysms. Moreover, TICAs are highly unstable and unpredictable, and are associated with delayed development, growth, rupture, and in some cases spontaneous

healing.^{99,101,109,111,123,230,234} Other cerebrovascular pathologies associated with pTBI include traumatic cerebral vasospasm, arterio-venous fistulas and complete occlusion of an arterial branch causing stroke.^{99,100,104,109} Historically there has been uncertainty as to when and how to screen for traumatic aneurysms, and if, in what circumstances and by what means they should be treated.^{99,101,105,109,110} Prior to the advent of specific endovascular techniques and technologies, open surgery following conventional angiography was the main treatment available.^{101,108,109,112} Open surgical treatment of TICAs almost always requires sacrifice of the parent artery and is technically challenging as the vessel typically bleeds profusely as efforts are made to expose

the lesion. This can, of course, cause a debilitating stroke if the artery supplies eloquent cortex.^{101,112} Endovascular treatments offer a less invasive approach to certain lesions, but may be hampered by the rapid need for surgical decompression prior to intervention, or, in certain circumstances, the need for systemic anti-platelet or anti-thrombotic medications.^{99,110,123,231} The possibility of preserving the parent vessel is a strong theoretical advantage of endovascular treatment of TICAs as compared with open surgery. Based on our current understanding of TICAs, we believe that they are as likely to hemorrhage as a ruptured, untreated saccular aneurysm with a similar rate of mortality.

Prior Guideline Recommendations

The prior pTBI guidelines addressed “Vascular Complications of Penetrating Brain Injury.”¹⁰³ Recommendations created in this edition were based on 8 articles which provided Class III evidence.^{101,108,109,112,117,118,233,235} Of these articles, 4 addressed the surgical management of traumatic aneurysms,^{101,108,109,112} two addressed the incidence of subarachnoid hemorrhage in pTBI,^{118,235} one addressed the incidence of traumatic arterio-venous injury following pTBI, and one addressed the incidence of SAH and vasospasm following pTBI.¹¹⁷ Based on the rigor and focus of the current guidelines along with the specific focus of the KQ asked, three of the prior included studies met criteria for inclusion in the current effort.^{101,108,112}

Three general levels of recommendations were utilized in the prior edition, and are related to the current edition as follows: “Standard” is now “Level I”; “Guideline” is now “Level II”; “Option” is “Level III and IV”. Of note, the “Option” designation in the prior guidelines edition admixed lower level direct evidence with expert consensus, but did not specifically distinguish the two. No Level I or Level II recommendations on this subject were provided in the prior edition. Level III/IV recommendations stated that surgical or endovascular management of TICAs or arterio-venous fistula was recommended. Direct evidence supporting the recommendation relating to endovascular intervention was lacking, however. Since 2001, significant advances have been witnessed in endovascular management of both non-traumatic and traumatic aneurysms.

Scientific Foundation

Background

Traumatic cerebrovascular injury is central to the management of pTBI. The incidence of TICAs resulting from pTBI in larger studies ranges from 3-40%.^{99,101,111,233} Contrasting with spontaneous saccular aneurysms that have a dome comprised of connective tissue (adventitia), TICAs lack such a dome. These traumatic “false” aneurysms are generally confined instead by organized blood clot within the subarachnoid space which is adjacent to the area of vessel damage.^{101,230} This results in an unpredictable natural history characterized by delayed formation and presentation, spontaneous healing, interval growth, and delayed rupture.^{99,101,109,123,230,234} TICA rupture has been

associated with significant morbidity and mortality. In one study, delayed rupture was associated with a nearly 50% mortality rate.⁹⁹

Physicians treating TICAs have had to balance the risk of rupture with the risks of treatment. Historically, TICAs were treated with open surgery, either at the time of initial presentation and surgical intervention, or in a delayed fashion after follow up imaging based diagnoses.^{101,109,112} This has typically involved significant risk of intraoperative rupture and the near ubiquitous need for parent vessel sacrifice which can lead to an iatrogenic stroke – sometimes of eloquent brain.^{101,109,112}

Technological advancements in endovascular materials, including detachable coils, aneurysm stents, and flow diverting devices, have made endovascular occlusion of TICAs a viable alternative. In contrast to the perceived impression that held that TICAs could not be coiled, experience and evidence has demonstrated that endovascular treatment is feasible.^{99,110,123,229-231,234,236-238}

Given the inherent complexities and divergent expert opinions on the topic, the management of TICAs is a pTBI subtopic which is particularly in need of evidence and consensus-based guidance which seek to identify and disseminate best care practices. Here we present evidence informing the open surgical and endovascular treatment of TICA supplemented with expert consensus statements.

B-Open surgical management of traumatic aneurysms

Seven non-randomized studies (6 case series, and 1 case report) were determined to be of sufficient quality to be included in the evidentiary base (Table 23). These studies provided evidence on the risk of TICA rupture following surgery compared with no surgery.^{99,101,108,111-113,229} All studies were rated high risk of bias due to study design. Injuries were due to high velocity missiles or stab wounds. To briefly summarize, a total of 1768 patients with penetrating head injury and vascular imaging were included in these studies. Within this population, a total of 129 TICAs were present in 110 patients (total incidence of traumatic aneurysms from pTBI 7.3%). A total of 65 patients received open surgery to address 74 aneurysms.

Bell et al evaluated 187 patients (162 penetrating) who received cerebral angiograms an average of 10 days after their primary injury.⁹⁹ A total of 31 TICAs were diagnosed in 24 patients in this study (total of 64 vascular injuries in 48 patients). Nine of 31 TICAs in 5/24 patients were treated with primary clip occlusion, and 3/31 TICAs in 3/24 patients were treated with a combination of coil occlusion and clip ligation. No ruptures were observed in patients treated with primary or secondary clip reconstruction. Eight TICAs in 8 patients were not treated, with rupture occurring in one of those patients resulting in death. Overall GOS was noted to be 3.1 in this study, without a specific outcome attributed to the TICA subgroup.

Haddad et al (N = 15) described findings associated with TICAs at presentation.¹¹² 14 of 15 patients in this study presented in the pre-CT era.¹⁰¹ Four patients presented with

subdural hematoma, all attributed by the authors to aneurysm rupture. Twelve patients presented with intracerebral hemorrhage, 11 attributed to aneurysm rupture by the authors. Of specific note, 5 patients suffered deterioration of clinical examination in a delayed fashion. One patient had a delayed headache and seizure, one a new hemiparesis, and three a deterioration of consciousness. While suspicious for delayed rupture, no specific conclusion can be made. Two of the five patients had what was described as a “good” outcome, one with “poor” outcome, and two with death. In all cases, surgical intervention (11 trapped and excised, 1 coagulated, 1 treatment completed but not specified) appeared in this study to occur after hemorrhage findings associated with the aneurysm. Outcomes in this study were attributed to the condition of the patient at presentation, without association specifically to the traumatic aneurysm. However, 2/13 surgical patients died. There were no reported aneurysm ruptures after treatment.

Aarabi evaluated 255 patients with penetrating brain injury who received cerebral angiography an average of ~17 days after injury during the Iran-Iraq War.¹⁰⁸ Eight of 255 patients presented with traumatic aneurysms. Two of 8 ruptured prior to treatment. 7 of 8 aneurysms were treated with surgery and clip exclusion of the aneurysm. Of those treated surgically, 2 patients died, and 5 recovered with varying degrees of outcome (confusing, as the study published what looks like the MRS outcome by score, but referred to it as the GCO or Glasgow Coma Outcome). There were no reported ruptures after surgical treatment. The patient not treated had a favorable long-term recovery at 47 weeks. These patients were also included in a larger series of 964 patients, with a total of 22 TICAs. Fourteen of these aneurysms were discovered by cerebral angiogram and 8 were discovered following rupture. Average follow-up was 71 days. All but 5 of the patients underwent surgical treatment of their TICA. Of those managed conservatively the GOS was scored as 4 or 5 (good recovery or moderate disability) in 3 patients and one died. In the surgical group GOS was scored as 4 or 5 (good recovery or moderate disability) in 12 patients and four died. Because of the overlap in included patients between these two studies we have only included the latter, larger manuscript as evidence supporting this KQ.

Kieck et al evaluated the incidence of vascular injury in 109 patients with cranial stab wounds with 79/109 receiving cerebral angiograms.¹¹³ A total of 11 TICAs were noted in 11 patients. Six of 11 patients received surgery described as “clip, trap, or excise”, without specific attribution of type of surgery to a specific patient. The paper reports good outcomes in all six of these patients, however it does note a delayed hemorrhage in a patient receiving a prior craniotomy and aneurysm clip at day 98 from a delayed rupture from a second aneurysm confirmed at autopsy (0 or 16% rupture risk after surgery). In this case, 1/6 patients is suspicious for delayed rupture after initial treatment. A total of 5/11 aneurysms were not treated, with aneurysm rupture and death occurring in 4/5 patients (80%).

Du Trevou et al evaluated the incidence of vascular injury in 250 patients stabbed in the head, with 181 patients receiving cerebral angiography.¹¹¹ A total of 21 patients harboring 24 TICAs were noted in this population. Of those patients, 16 patients received “surgery”, however the type of surgery was not specifically specified. Of the 5 patients not receiving surgery, 2 patients refused with outcomes not recorded, 2 patients aneurysms resolved on follow up angiogram, and 1 patient died. Of note, no patients who were treated surgically suffered a re-hemorrhage.

Mansour et al evaluated 128 patients with penetrating brain injury, and included the 72 patients who received a CTA within 72 hours.²²⁹ A total of 37 arterial injuries were noted in 26 patients, with 11 TICAs noted in 8 patients. Of those patients, only one patient received surgery, 3 patients received coil occlusion, and 4 patients were observed. Outcomes in the observed population were noted to be unfavorable, with no reference to delayed hemorrhage in either the treated or untreated groups.

Other studies reported the quality of overall outcomes (e.g., good, fair, poor, unfavorable, died, did well, surgery successful) with surgery vs NS or reported GOS score after surgery or at discharge (Table 23). Patients tended to do better with surgery compared with NS. However, individuals who did not have surgery may have been more gravely injured (likely not to survive anyway) or have smaller aneurysms (where watchful waiting may be an acceptable treatment) than individuals who underwent surgical clipping or other surgery.

Nathoo et al evaluated the outcomes in 597 patients with transcranial stab wounds, specifically focusing on 17 with trans-brainstem penetrating injury.¹¹⁴ Within this population, 1 patient was diagnosed with a delayed basilar bifurcation aneurysm. This patient received craniotomy and aneurysm clipping, but ultimately died. Autopsy revealed that the aneurysm was “well clipped”, and did not mention delayed hemorrhage. A ruptured posterior communicating artery aneurysm was discovered at autopsy in a second patient. This patient, by report did receive a cerebral angiogram prior to death which was negative. It is not clear from this study whether or not the rupture was the cause of death. However, the aneurysm was untreated, with a 100% incidence of rupture.

Overall, these studies provide very low level evidence that surgery in the setting of TICA may reduce the risk of rupture and may lead to more favorable outcomes than NS.

B-Endovascular Management of Traumatic Aneurysms

A total of 9 studies were determined to be of sufficient quality for inclusion in the evidentiary base. Bell et al evaluated outcomes in patients with pTBI and TICAs treated with coil occlusion (N = 12), and one additional treated with stent buttress coil occlusion.⁹⁹ Most injuries were blast-related (67%), with GSW (25%) and knife wound (8%) the other mechanisms of injury. The anterior cerebral artery was the vessel most commonly affected (60% of patients) followed by the middle cerebral artery (25% of patients). In general, those TICAs noted to increase in size or that

TABLE 23. Evidentiary Base for Open Surgery Versus No Surgery for TICA

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Risk of bias
Bell, 2010 ⁹⁹ (NRS) Iraq Military Blast: 60% GSW: 25% Knife: 8%	Total population: 187 Average time to angio: 10 d Total patients w TICA: 24 Total # TICA: 31 Male: 99% Mean age: 26 y Admission GCS: 8.4 ISS: 24	Total surgery: 8 Primary surgery: 5; 9 TICA clip Revision surgery: 2 had endovascular coil retreated with a clip and 1 had a clip retreated with a coil No surgery: 8 Note: 1 had 1 TICA (ACA) clipped and 1 TICA (MMA) not treated	Untreated: 12.5% (1/8) rupture and death, 75% (6/8) resolved, 12.5% (1/8) stable Surgery: no stratified outcomes by surgery No ruptures after treatment in in this group. Overall GOS at discharge: 3.1, not stratified by TICAs	High
Haddad, 1991 ¹¹² (NRS) Lebanon Military: 47% Civilian: 53% Shrapnel: 93% Bullet: 7%	Total population: 15 Number TICAs: 19 Male: 100% Age military: 26 y (range 18-35) Age civilian: 19 y (range 6-57) Associated findings: SDH-4 ICH-12 all prior to surgery	Surgery: 13 Trapped/excised: 11 Coagulated: 1 Not mentioned: 1 Aneurysms treated: 17/19 No surgery: 2 TICA not treated: 2/19 Note: Text indicates that 14 patients had surgery; Table 5 indicates that 13 patients had surgery	Rupture (all occurred prior to treatment): 5 suspicious delayed rupture (pre-CT, clinical deterioration) Good outcome: 40% (2/5) Poor outcome or died: 60% (3/5) Outcome after trapping and excision Good: 45% (5/11) Fair: 18% (2/11) Poor: 9% (1/11) Died: 18% (3/11) Outcome after unspecified surgery: Poor: 100% (1/1) Outcome after coagulation: Died: 100% (1/1) Outcome after no operation Fair: 50% (1/2) Poor: 50% (1/2)	High
Aarabi, 1995 ¹⁰¹ (NRS) Iran Military Shell fragments: 19 Bullet: 1	Total population: 964 Patients with TICA: 18 2 add'l patients with pTBI outside of this population added Total patients: 21 Total TICAs: 22 Mean age: 20 y Arteries MCA: 10 ACA: 6 ICA: 6	Surgery consisted of trap, excision, clip (no comment on parent artery preservation), and Arutinov procedure Trap/excised: 14 TICA in 13 patients Clip: 2 TICA in 2 patients AR: 1 TICA in 1 patient No treatment: 5	Aneurysms discovered By cerebral angiogram: 14 Following rupture: 8 Follow-up mean: 71 d Deaths: 5 (GOS is reversed in this paper) Surgical patients: 80% (4/5) Observation patients: 20% (1/5) Observation GOS 4 or 5: 60% (3/5) GOS 1: 20% (1/5) Unknown GOS: 20% (1/5) Surgical GOS 4 or 5: 75% (12/16) GOS 1: 25% (4/16)	High
Kieck, 1984 ¹¹³ (NRS) South Africa Civilian Stabbing: 100%	Total population: 109 Total angio: 79 Total TICA: 11 Male: NR Age: NR Aneurysms Cranial: 8 Orbital: 3	Cranial and orbital aneurysms Surgery: 6 (surgery described as "clip, trap, or excise". Specific number of each not specified) No surgery: 5	Outcomes Surgery: all 6 did "well" Hemorrhage or rupture: 0/6 *Note: 1/6 patients suffered a delayed rupture from a separate, untreated aneurysm and died No surgery: 4 died of delayed SAH; 1 lost to follow-up Hemorrhage without treatment: 80% *0 or 1 hemorrhage after first treatment	High

TABLE 23. Continued.

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Risk of bias
Du Trevou, 1992 ¹¹¹ (NRS) South Africa Civilian Stabbing: 100%	Total population: 250 Total angio: 181 Total patients w TICA: 21 Total TICAs: 24 Male: NR Age: NR Underwent angiography: >7 d after surgery	Angiograms <7 d: 30 With TICA: 15; 14 surgery, 1 resolved Angiograms >7: 51 With TICA: 6; 2 surgery, 2 refused, 1 rupture, 1 resolved Surgery: 16, type not specified No surgery: 5	Outcomes in patients with aneurysms Surgery: "successfully operated on" with "good recovery": 16, ≥16 aneurysms No surgery: 2 refused surgery, no outcomes reported Died from brain damage: 1 Traumatic aneurysm resolved: 2 No hemorrhages reported after treatment Article does not specify surgical outcomes based on aneurysms, only patients	High
Mansour, 2021 ²²⁹ (NRS) United States Civilian GSW: 100%	Total population: 128 Total CTA: 72 Arterial injuries: 37 in 26 patients TICA: 11 in 8 patients Occlusion: 7 Transections: 8 Dissections: 6 Intimal injuries: 4 Male: 80% Mean age: 28 y GCS: 4T, 3T, 5T, 5T, 3T (individual GCS scores)	Surgery: 1 TICA: 1 (GCS 5T) Endo coil: 3 TICA: 3 (GCS 8T, 15, 3T) Observation: 4 TICA: 7 (GCS 4T, 3T, 5T, 3T)	Surgical: "unfavorable", (GOSE 3) Endo: 2 favorable (GOSE 4 and 6), one unfavorable (death) Observation: "Unfavorable": all 4 patients, discharge details NR	High
Nathoo, 2000 ¹¹⁴ (Case report) South Africa Civilian Stabbing: 100%	597 cranial stab wounds 17 patients with brainstem penetration 15/17 received DSA 1/17 with basilar TICA 1/17 post mortem ruptured TICA Male: 100% (1/1) Age: 28 y GCS: 9 Admitted 3 wks after assault	Ventriculostomy, craniotomy for clipping of basilar bifurcation aneurysm	Deaths: 76% (13/17) Surgical: 1 (GOS 1), autopsy confirmed no evidence of re-rupture 1/17 patients with ruptured, untreated TICA at autopsy	High

ACA, anterior cerebral artery; GCO, Glasgow Coma Outcome; GCS, Glasgow Coma Scale; GOS, Glasgow Outcome Scale; GOSE, Glasgow Outcome Scale-Extended; GSW, gunshot wound; ISS, Injury Severity Score; MMA, middle meningeal artery; MOI, mechanism of injury; NR, not reported; NRS, non-randomized study; SAH, subarachnoid hemorrhage; TICA, traumatic intracranial aneurysm.

were treated in this study were larger than those that were not treated. Following initial TICA treatment, 4/12 (33.3%) patients experienced aneurysm recurrence and required re-treatment with coil or stent-coil (3/5) or clip (2/5). There were no aneurysm ruptures that occurred following coil occlusion in this study. This compares with one recurrence/retreatment (20%) in the five pTBI patients with TICA treated with a clip, and one rupture (12.5%) in the eight pTBI patients whose TICA was not treated. However, the size/severity/location of the TICA was likely a confounding factor in the specific treatment or lack of treatment provided (Table 24).

In another non-randomized study (N = 2) from a Level 1 trauma center in Jerusalem, Cohen et al evaluated two patients with pTBI and TICAs treated with endovascular coils.¹¹⁰ One

patient (17 years) suffered a missile wound in a bus bombing and following treatment had a GOS score of 5; the other patient (5 years) was stabbed with an umbrella (transorbital-transcavernous) with a post-treatment GOS of 4.

In a third non-randomized study (N = 2), Hemphill et al reported one adult patient with a nail gun injury and TICA that was treated with endovascular coils and recovered without infarction (callosomarginal territory).²³⁰ The other adult patient in this study experienced a TICA due to a gunshot wound to the head. Follow-up angiography at 2 months indicated an enlargement of the TICA, which was then treated with detachable coils, sparing the parent artery.

Another study (Mansour et al) reported that three patients with pTBI were treated with endovascular embolization for TICAs but

TABLE 24. Evidentiary Base for Endovascular Management of TICA

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Risk of bias
Bell, 2010 ⁹⁹ (NRS) Iraq Military Blast: 60% GSW: 25% Knife: 8%	Total population: 187 Male: 99% Mean age: 26 y Admission GCS: 8.4 ISS: 24 Average time to angio: 10 d Total patients w TICA: 24 Total #TICA: 31	pTBI patients with TICA treated with coil: 12 Surgery: 5, 9 TICA clip No surgery: 8 Note: 1 patient had 1 TICA (ACA) clipped and 1 TICA (MMA) not treated 2 patients had endovascular coil re-treated with a clip and 1 patient had a clip retreated with a coil	Initial Treatment TICA patients treated initially with coil: 12 Rupture: 0% Parent artery preservation: 50% Recurrence: 27% Re-treatment: 36% (with coil or clip) All TICA pTBI patients treated initially with clip: 5 Rupture: 0 Recurrence: 20% Re-treatment: 20% All untreated pTBI patients with TICA: 8 Rupture: 12.5% Resolved or stable: 87.5% Average size ruptured TICA: 8.3 mm Average size not ruptured TICA: 3.2 mm Average time to rupture: 15 d (range 4-32 d)	High
Cohen, 2008 ¹¹⁰ (NRS) Israel Civilian Blast: 50% Umbrella: 50%	Total population: 25 Total TICAs: 10 Male: 0% (2 patients both female) Age: 17 and 5 y GCS: 7 and 13	10 pTBI patients with TICA treated 2 coil or stent coil 8 PAO with NBCA	Coil results 17-year-old (blast): GOS score 5 5-year-old (umbrella): GOS score 4 Noted complete occlusion	High
Hemphill, 1999 ²³⁰ (NRS) United States Civilian Nail gun: 50% GSW: 50%	Total population: 4 Total with pTBI: 2 Male: 50% (2 patients, 1 male, 1 female) Age: 39 and 33 y	2 pTBI patients with TICA treated with coil	39-year-old (nail gun): recovered without infarction (callosomarginal territory) 33-year-old (GSW): angiography at 2 mo showed worsening TICA treated with detachable coils sparing parent artery	High
Aljuboori, 2020 ²³¹ (Case report) United States Civilian GSW	Male Age: 19 y	1 pTBI patient with TICA treated with coil	Treated with coil embolization, recurrence at 2 wks, treated with a Pipeline Flex embolization device; patient remained neurologically intact, follow-up angiography at 6 mo showed resolution	High
Hachemi, 2007 ²³⁷ (Case report) France Civilian GSW	Female Age: 10 y	1 pTBI patient with TICA treated with coil	Aneurysm presented with rupture post injury day 7 prior to treatment. Good neurological recovery at 6 mo	High
Darsaut, 2007 ²³⁶ (Case report) Canada Civilian Knife	Male Age: 32 y GCS: 3	1 pTBI patient with TICA treated with coil	Coil embolization was followed by knife removal which led to "contrast extravasation from the coiled vessel stump", so additional coiling was deployed and extravasation stopped; in ICU patient died after removal of life support (patient had elevated intracranial pressure: 70 mmHg)	High

TABLE 24. Continued.

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Risk of bias
Sirko, 2018 ²³⁸ (Case report) Ukraine Military Shrapnel	Male Age: NR GCS: 11	1 pTBI patient with TICA treated with coil (Patient had comorbid injuries requiring thoracotomy and removal of foreign body from heart)	Middle cerebral artery bleeding was treated with clipping, bipolar coagulation, and surgery At 3 mo TICA was discovered and treated with detachable microcoils without further deterioration	High
Feng, 2018 ²³⁴ (Case report) China Civilian Bamboo branch	Female Age: 62 y Stable vitals but fixed right pupil (transorbital penetration)	1 pTBI patient with TICA treated with coil	Foreign body was surgically removed; 3 wks after discharge the patient returned with swelling, pain, and bleeding from nose and mouth CTA showed TICA of right ICA treated with coiling, patient followed up for 12 wks and recovered except for loss of vision in right eye	High
Yoon, 2022 ¹²³ (Case report) United States Civilian GSW	Gender: NR Age: NR	1 pTBI patient with TICA treated with coil	Stable pseudoaneurysm on admission but expanded 27 d after admission treated with stenting and coiling; long-term outcomes NR	High
Mansour, 2021 ²²⁹ (Case report) United States Civilian GSW: 100%	Total patients: 128 with pTBI Total CTA: 72 patients 37 arterial injuries in 26 patients (11TICA, 7 occlusion, 8 transections, 6 dissections, 4 intimal injuries) 8 patients, 11 TICAs 1F, 7M Male: 87.5% Mean age: 28 y GCS: 4T, 3T, 5T, 5T, 3T (individual GCS scores)	Surgery: 1 patient, 1 TICA (GCS 5T) Endo coil: 3 patients, 3 TICA (GCS8T, 15, 3T) Observation: 4 patients, 7 TICA (GCS 4T, 3T, 5T, 3T)	Surgical: "unfavorable", (GOSE 3) Endo: 2 favorable (GOSE 4 and 5), 1 unfavorable (death) Observation "Unfavorable": all 4 patients, discharge details not reported	High

CTA, computed tomography angiography; GCS, Glasgow Coma Scale Score; GOS, Glasgow Outcomes Scale Score; GSW, gunshot wound; ISS, Injury Severity Scale; MOI, mechanism of injury; NBCA, N-butyl-2-cyanoacrylate; NR, not reported; NRS, non-randomized study; PAO, parent artery occlusion; pTBI, penetrating traumatic brain injury; TICA, traumatic intracranial aneurysms.

did not mention the use of coils.²²⁹ One patient had a GOS-E of 6 at discharge, one with a GOS-E 4 at discharge, and one patient died in the hospital. There is no mention of aneurysm re-rupture in this study.

Other reports of treatment of TICA in pTBI with endovascular coiling were limited to case reports. Results were mixed.^{123,231,234,236-238}

These studies provide very low level evidence that coil embolization of TICA in the setting of pTBI may reduce the risk of further bleeding outcomes or need for retreatment but do not provide evidence for endovascular coiling compared with other treatments in the absence of potential confounding factors.

Discussion

As has been previously discussed, pTBI is a highly lethal wounding mechanism that is very difficult to study with prospective, randomized

trials. With this in mind, the body of literature in general, and on this subject in particular, remains largely retrospective, observational, or case report in nature (Class III or IV), and therefore does not support Level I or II recommendations. That said, it is the lethal and unpredictable nature of pTBI in general, and TICAs in specific, that support the nature of the above recommendations.

At the time of the creation of the prior pTBI guidelines in 2001, open surgical management of TICAs (when feasible) was the primary means of treatment.^{101,108,112} This was in part secondary to the early and somewhat rudimentary nature of the endovascular technologies available at that time as well as a concern that coils would not be contained by the TICA clot. Technologies, including the advent of aneurysm stents and flow diverters, have advanced considerably.

The purpose of treatment of TICAs is not to reverse the primary injury, but to help reduce the risk of additional brain

injury, often catastrophic, from aneurysm rupture. Open surgical techniques remain a viable approach but can involve substantial hemorrhage (especially if the TICA is large and proximal) as well as the morbidity of stroke in the distribution of the parent artery if sacrifice is necessary. From an algorithmic perspective, this approach may be preferred at the time of initial surgical intervention for superficial and active arterial bleeding. However, endovascular occlusion in the acute setting is a viable alternative that may (1) reduce the risk, at the time of open surgical decompression, of catastrophic hemorrhage from large, skull base arterial injury, (2) reduce the need for return to the operating room for clip reconstruction of an aneurysm in an injured and inflamed cortical environment, (3) identify, with the necessary pre-treatment gold standard cerebral angiogram, arterial injury (TICA, arteriovenous fistula, etc.) not visualized with CTA, (4) allow for treatment of arteriovenous fistula sub-optimally visualized on non-invasive imaging, and (5) provide a means of preserving the parent artery at the time of initial treatment (see Traumatic Vascular Injury algorithm).

Included Evidentiary Support for Open Surgical Management of TICA's

The Level IV recommendation supporting consideration for open surgical management of traumatic intracranial aneurysms is based on a total of 110 patients who harbored 120 TICAs in the studies referenced.^{99,101,108,111-114,229} Within this population, a total of 58 patients received surgery (described as “clip”, “trap and excision”, “coagulation”, or “unspecified”) as the first operation to treat a total of at least 67 TICAs. Another two patients received a surgical clip after initial coil occlusion, and one received coil occlusion of a previously clipped aneurysm. Outcomes in this group were described as GOS 1 or “death” in 9 (16.2%), GOS 2-3 or “poor” in 4 (5.9%), GOS 4-5 or “good” or “fair” in 45 (66.2%), and not specified in 8 (11.8%). There were no reported aneurysm re-ruptures after initial or secondary treatment in this group. In comparison, another 30 patients harboring 34 aneurysms were observed or received no treatment. Within this group, outcomes were described as death in 8 (26.7%), poor or unfavorable in 5 (16.7%), TICA resolved or outcome good in 13 (43.3%), and lost to follow up in 4 (13.3%). Concerning mortality, in 6/8 deaths, definitive rupture was noted as causal (20%).

Concerning TICAs, and while the study risk of bias is considered high given the study designs, there appears to be a uniform effect with respect to protection from aneurysm rupture following treatment with open surgery. This treatment effect was present at each outcome measure, but could not be verified by meta-analysis given the small population and variable reporting measures. It should be noted that surgical management in the referenced studies was described in a number of ways, and almost always included parent artery occlusion with coagulation or aneurysm clip, often with resection of the traumatic aneurysm. There is no mention of parent artery preservation in any of the studies referenced. Neurologic outcomes, when included, are almost always attributed to the degree of underlying brain injury at presentation in those

treated. With this in mind, it should be remembered that open surgery carries a risk of stroke with parent vessel sacrifice. This may not be a concern if the artery supplies already injured brain. It is a particular concern if the vessel supplies uninjured, eloquent brain.

Included Evidentiary Support for Endovascular Management of TICAs

The Level IV recommendation supporting endovascular occlusion of intracranial traumatic aneurysms in pTBI to reduce delayed hemorrhage is based on the reported literature experience of 33 endovascularly treated aneurysms, with 25 treated with coil occlusion, (one with stent-coil), one coil re-treated with flow diversion, and 8 treated with parent artery sacrifice.^{99,110,123,229-231,234,236-238} The rate of re-rupture following initial treatment was 1/25 (4%). In this one case, the aneurysm was diagnosed at the time of patient presentation with a protruding foreign body (knife), the aneurysm was coiled with the microcatheter left in place, and continued bleeding after the knife was removed and was immediately treated. Overall, while counterintuitive to coil a false aneurysm or blood clot, the data support this option as a means of preventing aneurysm rupture and preserving the parent artery. One study specifically noted a rate of parent artery preservation as high as 50%.⁹⁹ While this offers an advantage over surgery, the aneurysm recurrence rate is relatively high, necessitating early post intervention follow up angiography (preferably within approximately 4-8 weeks). Aneurysm re-treatment may be necessary should recurrence be noted. In these cases, technology that includes the use of one of the many flow diverters currently available may be a viable option, as was demonstrated in the case report by Aljuboori et al.²³¹ Flow diversion as a primary means of treatment may also be considered, depending on the location of injury and the need to preserve the parent artery (i.e. internal carotid, proximal middle cerebral artery/PCA/anterior cerebral artery). As flow diversion mandates the extended use of dual antiplatelet therapy (3 or more months), the timing of this intervention must take into account the need for additional open surgical intervention.

Limitations

It should be noted that there remain relatively few published cases or studies of the open surgical and endovascular management of penetrating traumatic cerebrovascular injury. The level IV recommendation reflects this reality.

Expert Opinion

Traumatic aneurysms

It is our opinion that one of the most important aspects of these updated pTBI guidelines are those related to TICA. Even amongst recognized TBI experts there have been diverse opinions on screening for TICA and their need for treatment. This likely relates in large part to the fact that even for most neurotrauma experts these lesions are encountered infrequently. Our panelists represent many of the world's highest experts with the most experience with pTBI and TICA. The resounding opinion of our

experts is that in most circumstances an aggressive effort to detect TICA is needed and that they should almost always be treated urgently when identified. Our experts recounted numerous disastrous outcomes from re-hemorrhage in cases not managed aggressively. While there may still be a role in select circumstances for observing these lesions in hopes they will regress, our panelists felt that such an approach should only be rarely attempted. Small aneurysms where treatment risks infarcting eloquent brain may be such a circumstance. If an initial conservative approach is attempted, frequent re-imaging is needed and treatment should be initiated if the lesion grows or does not regress.

Another key aspect of these 2nd edition guidelines is ensuring practitioners are aware of evidence and experience related to coiling or other endovascular management strategies for pseudoaneurysms. The historic belief that pseudoaneurysms cannot be coiled is clearly incorrect. It is important that the feasibility and potential superiority of endovascular treatment is widely disseminated.

That said, while the available evidence supports screening for traumatic aneurysms (preferably with DSA) and treating them, it does not at this time support evidence-based recommendations concerning the timing of initial diagnostic assessment and treatment of pTBI related traumatic aneurysms, whether observation or non-treatment of some traumatic aneurysms is warranted and the conditions where this might apply, the size threshold for mandatory treatment, and the frequency of follow up diagnostic imaging in the setting of observed or treated traumatic aneurysms. With this in mind, a Delphi model was used to develop consensus statements through dedicated, in-person surveys of the multi-disciplinary subject matter expert team during a 5-day guidelines consensus conference. Aneurysm treatment, timing of follow up evaluation for treated aneurysms (7-21 days, see Key Questions 2-4), and conditions where observation may be warranted were addressed. While the diagnosis of pTBI associated vasospasm was addressed with evidence-based recommendations, endovascular treatment was not addressed in this guideline.

We are aware of diverse management strategies for TICAs including some who currently favor conservative management of these lesions. It was, however, the strong opinion of our expert group that a failure to diagnose and treat these lesions can have catastrophic consequences. Our expert panel advocates, and the evidence supports, aggressively screening for and treating TICAs. These lesions require complex judgment individualized to specific patients and circumstances, however. Clinicians caring for pTBI patients must have both a high index of suspicion in pTBI, and a low threshold for treatment. In short, all traumatic aneurysms should be considered for treatment, and consensus was achieved amongst our panelists that large aneurysms and those noted to increase in size must be treated with particular urgency (80.5% and 87.5% consensus respectively). A consensus recommendation for minimum size threshold for aneurysm treatment was not obtained. One study⁹⁹ (Bell et al) identified the average size of aneurysms treated (4.72 mm), observed (2.21 mm), and ruptured (8.3 mm). While smaller aneurysms have been noted to heal on interval imaging, they have also been noted to grow, rupture, and result in

death. It is with this in mind that the consensus recommendation that observation can be considered under certain specific conditions was made (95% Consensus). In this setting, early follow up cerebral angiography (within 4-8 weeks) should be considered.

It should be noted that aneurysm recurrence in the setting of endovascular occlusion of traumatic aneurysms was reported as high as 27%.⁹⁹ This is a significant limitation of this type of intervention, and requires early follow up (4-8 weeks) cerebral angiography as noted above (95% consensus). Secondly, it is also acknowledged that the full scope of endovascular treatment modalities, including aneurysm stents and flow diverters, may be considered too high risk in the acute setting secondary to the need for dual anti-platelet therapies with these interventions. These approaches may be best considered with delayed or recurrent traumatic aneurysm presentation.²³¹

The addition of a recommendation to consider a multi-disciplinary approach to TICAs arises from the understanding that the treatment of cerebrovascular pathology of any kind requires consideration of open and endovascular surgical strategies. This recommendation also reflects the fact that endovascular techniques have advanced considerably over the past 22 years, making management of these highly complex and unstable conditions safer. *There was uniform consensus within the guidelines subject matter expert working group on this matter.*

Given that endovascular coil occlusion of TICAs has proven feasible and efficacious and with the ability to preserve the parent artery, it is our view that endovascular treatment is now preferred over open surgery when feasible. Endovascular surgery is likely safer with less risk of blood loss and the probability of avoiding a stroke in the distribution of the parent artery. Repeat endovascular treatment is often needed, however. Endovascular treatment is not universally available, however, particularly in austere environments. There are also TICAs that cannot be treated or optimally treated with endovascular therapy. For this reason open surgery remains an important means of treating TICAs as indeed the alternative is a high risk of mortality.

Traumatic vasospasm and AV-fistula

The available evidence did not support the creation of specific evidence-based recommendations concerning the treatment of traumatic vasospasm. Studies included in the 1st edition guidelines addressed the incidence and outcomes of patients with vasospasm following pTBI, but these studies did not meet inclusion criteria for the current guidelines.^{117,118} An additional study that did not meet inclusion criteria (Armonda et al) evaluated the outcomes in patients with traumatic vasospasm during wartime.¹⁰⁰ While this study demonstrated worse outcomes in patients with traumatic vasospasm, endovascular treatment modalities did not improve outcomes. It is our opinion that screening for vasospasm following pTBI should be considered, and if diagnosed, critical care and perhaps endovascular interventions also considered.

Concerning traumatic arteriovenous fistula, these entities should be diagnosed and treated in a manner similar to TICAs. CTA is not an effective method of diagnosing dynamic pathologies, further supporting the recommendation for DSA following

pTBI. The presence of an AV fistula in pTBI usually signifies a significant arterial injury that will require treatment.

Future Directions

Our understanding of how TICA characteristics like size and location influence risk of rupture and the risk:benefit of different treatment options is advancing, but these remain very important topics for further research and elucidation. Much remains insufficiently understood about TICA natural history. We acknowledge that if neurosurgeons adhere to our recommendations and treat pseudoaneurysm aggressively, it will impede our ability to understand their natural history. In our opinion it would now be unethical to randomize patients to treatment vs no treatment or

to open surgical vs endovascular treatment. Additional study of the characteristics associated with coiled traumatic aneurysm re-treatment, and techniques for doing so is needed. Additionally, a further characterization of the risks and benefits of different endovascular and open surgical therapies would be beneficial. High quality prospective studies which assess outcomes based on different aneurysm characteristics and treatments would be highly valuable contributions to the literature. Specifically, studies addressing the incidence of iatrogenic stroke and re-hemorrhage in populations treated with vessel-sparing vs parent artery occlusion strategies are needed. As well, the optimal timing of diagnosis and treatment, and characteristics associated with aneurysm healing, would be beneficial.

VII-7 – Management of Penetrating Venous Sinus Injuries

R. S. Bell, R. A. Armonda, B. Aarabi

Recommendations

Level I-III

There is insufficient evidence to support a strong, moderate strength or weak recommendation for operative repair of venous sinus injuries for the purposes of improving survivability and sinus patency.

Level IV

Sinus injuries should be repaired by open surgery when exsanguination or death from herniation would be more likely to occur in the absence of intervention to improve survivability.

No evidence or expert opinion supported distinct recommendations based on patient gender, age, wounding mechanism, or military vs civilian context.

Introduction

Venous sinus injuries fall within the spectrum of traumatic cerebrovascular injury suffered from foreign body penetration.^{41,106,175,178,207,229,239-245} Initial consequences of injury include rapid exsanguination, brain swelling and venous infarction if ligated, as well as a risk of air embolism. Delayed consequences include sinus thrombosis that can result in additional venous infarction events. Though surgical repair of these lesions can be extremely challenging, it is a neurosurgical truism that venous sinus injuries must be repaired to prevent the above consequences. The purpose of this KQ was to determine whether or not there is evidence supporting benefits or harms of surgical or endovascular management strategies in the specific setting of pTBI.

Prior Guideline Recommendations

The prior head injury guidelines did not address this specific topic directly.¹⁶

Scientific Foundation

Three studies met inclusion criteria for formal inclusion as evidence for this topic (Table 25). There was one large retrospective nonrandomized study identified in a primarily military population by Kapp et al with pTBI and dural venous sinus injuries in the Vietnam War that assessed management of venous sinus injuries and reported mortality outcomes.²⁴² The authors reported outcomes for two distinct groups, those with injuries from 1968 to 1970 (N = 78), and those with injuries from 1971 to 1972 (N = 16). Ninety-three cases were managed operatively at the 24th Evacuation Hospital in Vietnam and one case was managed in Memphis, Tennessee. The authors report an operative repair protocol of: 1-Insertion of a large bore IV into a large vein to facilitate rapid blood transfusion; 2-A venous graft was harvested if deemed possible that a graft would be necessary for sinus repair; 3-Sinus bleeding was controlled by inflation of balloon catheters within the sinus; 4-An internal shunt was used to

prevent venous sinus stasis rather than temporary sinus occlusion; 5-Non-essential sinuses were ligated if ligation was technically easier than repair; 6-Essential sinuses were repaired primarily if possible or with vein graft (reversed saphenous vein segments) if there was extensive injury. The authors reported no demographics for either study cohort. For the 1968 to 1970 cohort, there were 22 anterior superior sagittal sinus (SSS) injuries, 35 posterior SSS injuries, and 21 transverse sinus (TS) injuries. The mortality rates for anterior SSS, posterior SSS, and TS injuries were 5% (N = 1/22), 43% (N = 15/35), and 24% (N = 5/21), respectively. The overall mortality for this cohort was 27% (N = 21). For the 1971 to 1972 cohort the mortality rates were as follows: anterior SSS (0%, N = 0/5), posterior SSS (0%, N = 0/8), TS (33%, N = 1/3). The overall mortality for this cohort was 6%. The anterior SSS was ligated in 27 cases from both cohorts. The mortality for this group was 4% (N = 1/27). There were five patients who underwent primary sinus repair of the posterior SSS or TS and the mortality rate was 0%. There were six patients who underwent vein grafting for repair of the posterior SSS or TS and the mortality rate was 16.7% (N = 1/6). The death in this group occurred in a patient with a TS injury. The authors advocate that if primary repair could be accomplished with less than 50% luminal narrowing, this should be done. Sinus repair by primary means remained patent without thrombosis in 100% of cases (N = 5/5). Sinus repair by venous grafting remained patent in 83.3% of cases (N = 5/6). There was one sinus thrombosis that occurred in a patient with a TS injury and venous grafting. The authors conclude that sinus repair can be accomplished with reduced blood loss and improved brain swelling by these means and that the greatest benefit of sinus reconstruction is in patients with injury involving the posterior SSS. However, there was no mention in this study of prevention or occurrence of venous infarction in patients with venous sinus injury.

Abdallah et al outlined surgical management of a traumatic SSS tangential injury that occurred in the Syrian Civil War.²³⁹ The authors report a case of a 33 year-old male injured by shrapnel with resultant midsagittal penetrating injury with deep-seated bone fragments within the right parietal lobe and interhemispheric subdural hematomas. Intraoperatively the authors noted an approximately 4 cm dural laceration at the junction of the middle and posterior third of the SSS. Immediate control of bleeding was obtained with manual pressure followed by insertion of two 16F Foley catheters with balloon inflation, both proximally and distally within the venous sinus. Once vascular control was obtained, the sinus was repaired with synthetic polytetrafluoroethylene vascular graft sutured in place with 6-0 polypropylene suture. Post-procedurally the patient was extubated and their GCS score was 11. The authors initiated deep vein thrombosis prophylaxis 48 hours postoperatively for a total of 2 days and subsequently was prescribed a 3-month course of 100 mg oral aspirin daily. The patient ultimately improved and was discharged on postoperative day 5. At time of discharge his GCS had improved to 15 from 5 at admission. Long-term follow-up beyond 3 months was not available. The authors report no adverse events

from repair of the sinus injury with vascular graft and the patient did not develop venous infarction.

An additional case report by Pricola et al. outlined surgical management and venous sinus repair in a patient with a gunshot wound and retained fragment within the torcula.²⁴³ The authors report a case of a 21 year-old male with an occipital gunshot wound and an initial GCS of 10. Non-contrasted CT of the head demonstrated midline occipital comminuted fracture with a retained bullet fragment within the torcula, along with small bilateral occipital epidural hematomas, and hyperdensity of the straight sinus and posterior aspect of the SSS concerning for thrombosis. CT venogram demonstrated thrombosis of the SSS, straight sinus, and poor opacification of the bilateral transverse and sigmoid sinuses suggestive of thrombosis. The patient was taken for emergent occipital and suboccipital decompression, which demonstrated a 1.5 cm laceration of the torcula. The authors removed all foreign and bony fragments and performed a combination primary repair (4-0 nylon) and patch graft (dura-matrix, 4-0 surgilon suture) of the venous sinus defect. Continuous doppler monitoring was utilized and did detect venous air emboli throughout the repair. A Duragen onlay and cranioplasty were then performed. Postoperative CT angiogram demonstrated patency of the SSS, straight sinus, vein of Galen, Basal Veins of Rosenthal, and internal cerebral veins. A small nonocclusive thrombus was still present in the right TS. The patient was discharged home on postoperative day 3 with a complete neurologic recovery.

Several additional studies (not meeting inclusion criteria) were identified that reported outcomes for patients with dural venous sinus injuries although none directly addressed the KQ and results were typically reported in aggregate for patients with concomitant arterial injuries.^{41,106,175,178,207,229,240,241,244-246} Additionally, the bulk of these cases were managed without direct surgical or endovascular intervention. There were no studies identified which reported incidence or outcomes relative to venous infarction and sinus injuries.

One study by Pylypenko et al from Ukraine evaluated surgical management in 21 patients with dural venous sinus injury sustained in battle.²⁴⁶ Overall, 17 patients had direct repair of the sinus if one or two sinus walls were involved, and 4 patients required dural venous sinus ligation. Outcomes were not consistently reported in this manuscript, however the majority of patients achieved a 12 month GOS of 4 or better.

One study by Hammon et al reported active exsanguination from venous sinus injury as an indication for immediate neurosurgical intervention.¹⁷⁵ The authors reported that if identified, major venous sinus injury bleeding was controlled by over-sewing a free muscle graft to maintain sinus patency and if transection had occurred, the sinus was ligated. The study cohort included 1732 patients with pTBI during the Vietnam War who underwent operative intervention. The authors reported five deaths from venous sinus exsanguination and did not report incidence of venous infarction or granular results applicable to sinus repair.

One case series by Khan et al was identified which included three cases of surgically managed venous sinus injury.²⁴⁵ In one

TABLE 25. Evidentiary Base for Management of Penetrating Venous Sinus Injuries

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Study risk of bias
Kapp, 1977 ²⁴² (NRS) Vietnam, United States Military/Civilian pTBI (unspecified)	N = 94 Injuries Anterior SSS: 27 Posterior SSS: 43 Transverse sinus: 24	Operative repair of venous sinus injury Primary: 5 Venous grafting: 6 Anterior SSS ligation 27	Overall mortality by injury site Cohort 1 (1968-1970, 78) Anterior SSS: 5% (1/22) Posterior SSS: 43% (15/35) Transverse sinus: 24% (5/21) Cohort 2 (1971-1972, 16) Anterior SSS: 0% (0/5) Posterior SSS: 0% (0/8) Transverse sinus: 33% (1/3) Mortality by repair type Primary repairs: 0% (0) Venous grafting: 0% (0) Anterior SSS ligation: 4% (1/27) Sinus patency Primary repairs: 100% (5/5) Venous grafting: 83.3% (5/6) The lone sinus thrombosis occurred in a patient with venous grafting	High
Abdallah, 2022 ²³⁹ (Case report) Syria Civilian Shrapnel	Male Age: 33 y Time from injury to surgery: 2.5 h 4 cm dural laceration (SSS)	Surgical debridement, repair of SSS Synthetic polytetrafluoroethylene vascular graft patch, sutured with 6-0 polypropylene Early VTE thromboprophylaxis (48 h postop) Oral aspirin (100 mg daily, 3 mo)	Successful repair of sinus injury No venous infarction Discharged on postoperative day 5	High
Pricola, 2011 ²⁴³ (Case report) United States Civilian GSW	Male Age: 21 y Admission GCS: 10	Occipital/suboccipital craniectomy for removal of bullet Repair of sinus defect (torcula) – Combination primary and patch graft (Duramatrix)	Restoration of proximal and distal sinus flow/patency Preservation of neurologic function	High

GCS, Glasgow Coma Scale; GSW, gunshot wound; MOI, mechanism of injury; SSS, superior sagittal sinus; VTE, venous thromboembolism.

case a small SSS injury was directly repaired with suture (case 9). In a second case a SSS laceration was repaired with periosteal graft (case 11). In a third case a torn “lateral” sinus was ligated (case 17). Results of these cases were reported in aggregate with those of other cases and no conclusions can be drawn.

These studies provide insufficient evidence to determine the benefits and harms of surgical management of venous sinus injuries *to prevent venous infarction*. They do, however, provide very low strength evidence that operative repair of venous sinus injuries is feasible and may improve survivability (assuming exsanguination would be more likely to occur in the absence of surgery) and sinus patency.

Discussion

Amongst the many goals of surgical intervention in the setting of pTBI, addressing hemorrhage ranks among the highest. As with all literature in this area, high quality, prospective randomized

studies in the management of penetrating sinus injury are not possible. The literature experience outlined above provides a useful guide in this area.^{41,106,175,178,207,229,239-245} Control of hemorrhage from sinus injuries is of paramount importance should it exist. This can be accomplished by direct or augmented repair, interposition of a graft, sinus ligation, or a combination of these strategies. Sinus ligation, if in the anterior SSS or non-dominant TS, may be prudent and necessary. Care should be taken to preserve the middle and posterior thirds of the SSS when possible, with ligation as a last resort. Usage of multiple materials for repair (venous grafts, muscle, pericranium, dural inversion, synthetic materials) with sinus shunting are useful techniques in this area. While there is a successful case report of synthetic repair with a graft, long term follow up and ultimate outcome were not reported.²³⁹ The need for anti-coagulation/anti-platelet administration with this approach should be considered in the larger

context of the global penetrating injury. It should be noted that, while there are numerous literature descriptions of the management of cerebral venous sinus thrombosis, a complication of traumatic sinus injury, by endovascular means, there are few reports of applications of these techniques in the setting of pTBI.²⁴⁷ Endovascular treatment has the potential to control blood loss if the expertise is available, if time permits (i.e. emergent cranial decompression can wait), or if achieved in a combined operating room with a multi-disciplinary team.

Expert Opinion

Many patients with penetrating cerebral venous injuries will die before they can be helped. Those who survive to hospital likely have characteristics that make them potentially salvageable. In some circumstances when there is not external hemorrhage these lesions can be managed non-operatively. In some circumstances endovascular treatment can be employed in conjunction with open surgery to help reduce blood loss. Open surgery for these lesions is extremely high risk and technically challenging. The entire operative team must be aware of and prepared for the risks of substantial blood loss, air embolism and perioperative arrest. These can be desperate surgeries. Vascular neurosurgical expertise is very helpful when available. Good patient outcomes can be

achieved in many of these patients, however, through a combination of luck and technical prowess.

Future Directions

In general, endovascular management of penetrating venous sinus injuries is not well described in the literature. There are no published case reports or described techniques (to our knowledge) advocating for endovascular intervention to preserve the venous sinus. It may be possible to help control active exsanguination with endovascular balloon assistance, but this would require combined endovascular operating rooms and acute multi-disciplinary management. Description of the rapid employment of this approach in practice would be beneficial. Current nitinol stent systems are, in general, designed for arterial deployment, are challenging to navigate in the cerebral venous sinus system, and require a period of dual antiplatelet therapy after deployment. Covered stent systems share the same characteristics with the added negative of covering and occluding draining cortical veins. Additional research and development of specific cerebral venous sinus stent systems that do not require dual antiplatelet therapy may provide some benefit in this and other areas. Here rigorously reported case reports and case series can make important contributions to the sparse literature.

VII-8 – Timing of Cranioplasty

K. Latham, R. S. Bell, B. Aarabi

Recommendations

Level I-III

There is insufficient evidence to support a strong, moderate strength or weak recommendation related to benefits and harms of early vs delayed cranioplasty.

Level IV

Cranioplasty, irrespective of its timing, is indicated in order to optimize outcome following pTBI.

Level C – Expert Consensus (Delphi Voting)

In the absence of direct scientific evidence, EXPERT CONSENSUS concluded that:

- Cranioplasty can be performed as soon as medically and surgically feasible. (88.5 % consensus)

No evidence or expert opinion supported distinct recommendations based on patient gender, age, wounding mechanism, or military vs civilian context.

Introduction

Penetrating traumatic brain injuries often result in skull defects due to surgical decompression or bone loss resulting from the injury itself. Cranioplasty is an important part of patient recovery and rehabilitation after pTBI. Cranioplasty, the surgical repair of cranial defects, is essential for restoring the brain's protective barrier and promoting neurological recovery.²⁴⁸ Cranioplasty contributes to the restoration of ICP, cerebral blood flow, and cerebrospinal fluid dynamics, aiding in the normalization of brain function.²⁴⁹ Improved neurological outcomes and reduced complications, such as seizures and infection, have been observed post-cranioplasty.²⁵⁰ In general, cranioplasty plays a pivotal role in enhancing patients' quality of life, addressing the psychosocial impact of skull defects.²⁵¹⁻²⁵³ Size of defects for decompressive craniectomy have varied over the decades and in more recent times decompressive craniectomy sizes are larger than in the past (130-150 cm²).²⁵⁴ Timing of cranioplasty is typically called ultra-early (<30 days), early (30-90 days), typical >30 days - <12 months, and delayed or late (>1 year).²⁵⁵

Timing of cranioplasty and choice of materials are controversial. Some studies support the benefits of early cranioplasty and some demonstrate increased risks with early cranioplasty.²⁵⁶⁻²⁶⁷ The patient's overall medical condition and stabilization of pTBI-related complications influence the optimal timing for cranioplasty. Stability in ICP, resolution of infections, and control of seizures are crucial considerations.²⁶⁸ Timing may be influenced by the extent of neurological recovery, ensuring that the brain is adequately healed before cranioplasty to minimize complications. Material selection is influenced by factors such as biocompatibility, availability, and the surgeon's preference.²⁶⁹ There is a

paucity of data specific to timing of cranioplasty after pTBI and timing of cranioplasty in pTBI may differ from timing of cranioplasty in other patients who have acquired skull defects. Since the time of the prior guidelines twenty years ago¹⁶ there have been significant advances in care for critically injured patients with pTBI, antibiotic coverage, microsurgery, and patient specific synthetic cranioplasty implants.

Prior Guideline Recommendations

In the 2001 guideline the existing literature at the time was not sufficient to support an evidence-based recommendation for timing of cranioplasty.¹⁶

Scientific Foundation

Four articles met inclusion criteria and all of them were determined to have high bias (Table 26). Therefore no evidence based recommendations are presented at this time for timing of cranioplasty after penetrating brain injury. The Rish²⁷⁰ study is the only study that met inclusion criteria in both the previous guidelines twenty years ago and this review. The Rish²⁷⁰ and Stephens²⁷¹ studies specifically address war related pTBI injuries and cranioplasty. Matthew²⁷² and Javadi²⁷³ specifically study cranioplasty in the pediatric population with Mathew's paper describing outcomes for pediatric patients injured in a war zone. Javadi presents data on pediatric patients with pTBI in Iran. There are studies that present data on pTBI injuries in adult civilian populations, however they did not meet inclusion criteria as the population was mixed with non-pTBI cranioplasty patients. The recommendations presented regarding cranioplasty after pTBI are expert opinion.

TABLE 26. Evidentiary Base for Timing of Cranioplasty

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Study risk of bias
Stephens, 2010 ²⁷¹ (NRS) United States Military Explosive blast injury: 67% GSW: 28% MVA: 2.8% Helicopter crash: 0.9% Falling: 0.9% Stabbing: 0.9%	N = 108 Penetrating TBI: 93 Closed TBI: 15 Male: 99% Mean age: 26 y Initial Presentation Mean GCS: 7.5 Mean ISS: 33 Peri-injury factors: CSF leak, infection raw data not available	Mean time injury to cranioplasty: 190 d (SD 91, range 7-546) Cranioplasties: 117 Material PMMA: 89 (82%) Titanium mesh: 19 (18%)	Death: 1 (0.9%), epidural hematoma Prosthesis removal: 12 (11%) Extra axial hematomas: 3 Infections: 9 (41% of those having complications) Mean GOS 1- 2 y post injury: 4.0 (SD 0.93) Total complications: 29 (24%) Infection: 13 (12%) Seizure: 8 (7.4%), 3 new onset Extra axial hematoma: 8 (7.4%) 12 required removal or implant (11%); 3 for extraxial hematoma and 9 for infection Characteristics associated with infectious complications Skull base injury: 7 (54%) Orbitofacial fracture: 5 (39%) Sinus injury: 4 (31%) Preexisting fluid collection: 1 (7.7%) CSF leakage: 1 (7.7%) Infection rate 0-90 d: 1 (7.7%) 90-180 d: 4 (31%) 180-270 d: 4 (31%) 270-360 d: 1 (7.7%) >360 d: 3 (23%) No assoc between risk to revise or reverse cranioplasty and injury type, CSF leak, CNS infection, cranioplasty material (PMMA vs woven Ti) No significant difference in complications or need to revise or reverse when time to cranioplasty was stratified by 90-day intervals Infection rate for 90-270 d approached significance ($P = .061$) No factors were found to be associated with cranioplasty failure or GOS score	Moderate

TABLE 26. Continued.

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Study risk of bias
Rish, 1979 ²⁷⁰ (NRS) United States Military (patients) Mixed (hospitals) Missile fragments: 76.4% GSW: 16.3% MVA: 4.1% Other: 3.2% (all pTBI)	N = 1030 with pTBI Mean age at injury: 21.3 y Location: # defect/# treated with cranioplasty/ % Frontal: 376/280/74.5% Parietal: 325/206/63.4% Temp: 166/57/34.3% Occip: 103/41/39.8% # repair/# cranioplasty/% Due to size >20 cm ² : 482/317/65.8% Due to size 11-20 cm ² : 218/112/51.4% Due to size 1-10 cm ² : 132/31/23.5%	Cranioplasties performed at multiple facilities including military, VA, and private civilian hospitals; numbers NR Cranioplasties: 491 Material Acrylic: 341 Metal: 71 Plastic: 12 Autogenous Bone: 20 Unlisted: 47	Time from injury to cranioplasty 1-6 mo: 89, 7, complications (7.9%) 7-12 mo: 187, 10, complications (5.3%) 12-18 mo: 132, 6, complications (4.5%) >18 mo: 83, 4, complications (4.8%) 10 cases after 12 mo 4 minor complications 1 bone plate dislodged with trauma; 1 bone infected and resorbed 4 infections with removal Complications from initial surgery 1-12 mo: 51, 10, complications (20%) If infection was the initial complication then 1-12 mo (56%) 13-24 mo: 52, 2, complications (4%) 18 initial complications and 0% if >12 mo Death: 1 (0.2%) related to cranioplasty performed 3 mo after initial injury. Patient developed CSF rhinorrhea or died due to chronic meningitis.	High
Mathew, 2013 ²⁷² (NRS) Afghanistan Civilian (patients) Military (trauma center) Blast: 13 (83%) GSW: 3 (17%) Penetrating: 12 Perforating: 1 Tangential: 2 Cranial facial Degloving: 1	Patients with DC, intended cranioplasty: 6/16 (37.5%) Demographics for 6 Male: 67% Mean age: 9 y (range 6-12) Penetrating: 5 Perforating: 1	Completed cranioplasties: 5/6 (83.3%) Bone was stored in a left anterior abdominal wall subcutaneous pocket	Time to cranioplasty after discharge, 4 as planned 8 wks: 1 10 wks: 2 5 wks: 1 Initial complication CSF leak for 1 No initial infection, seizure 1 earlier than planned: 4 wks All wounds were healed and reopening presented no technical difficulty Discharge within 1 wk: 5 fully conscious with no focal neurological deficits and no further follow-up 1 patient did not return for follow-up and cranioplasty. Outcome for this patient is unknown.	High
Javadi, 2021 ²⁷³ (NRS) Iran Civilian Blast injury due to land mine: 100%	N = 3 Ages: 7, 8, and 9 y GCS on admission: 4 GCS 5 d post DC: 7 GCS 2 wks post DC: 9 GCS 1-mo post DC: 14	Cranioplasty performed at 3 mo	1-y No major motor deficits Excellent school performance 1 case of contralateral dominance and handedness	High

CSF, cerebrospinal fluid; DC, decompressive craniectomy; GOS, Glasgow Outcome Scale; GSC, Glasgow Coma Scale; GSW, gunshot wound; ISS, Injury Severity Scale; MVA, motor vehicle accident; PMMA, polymethylmethacrylate; pTBI, penetrating brain injury; SD, standard deviation; TBI, traumatic brain injury; Ti, titanium; VA, Veterans Administration.

Rish and Stephens report outcomes of cranioplasties received by U.S. soldiers who sustained penetrating brain injuries in overseas actions.²⁴⁸ The repairs were conducted in the United States and the studies had medium to large sample sizes. The potential utility of the evidence these studies provide is lessened because the authors provided no or very limited information on the characteristics of patients who received cranioplasties at different times and any differences in the patients are not incorporated into the analyses. This makes it difficult to attribute differences in outcomes to the timing of the cranioplasty.

Stephens²⁷¹ provides a retrospective review of cranioplasties performed at two U.S. military hospitals between April 2002 and October 2008. Data were collected on soldiers injured and initially treated in Iraq or Afghanistan and included 117 cranioplasties on 108 patients.²⁴⁹ Ninety-three of these patients had penetrating brain injuries, mostly from blasts. The patients were young, with a mean age of 26 years and only one was female. The time from injury to cranioplasty ranged from 7 to 546 days with a mean of 190 days. There was one death (0.9%) and 12 patients of the 29 patients who experienced complications required reoperation to remove the prosthesis. The mean Glasgow Outcome Score was 4.0 at 1 to 2 years post injury, but details on the follow-up period and the distribution of scores were not provided. As improvement often continues over longer periods, this may not be the definitive finding. Time to cranioplasty was stratified by 90-day intervals and the authors report they found no difference in complications or the need for reoperation across the time intervals (data was not provided in the article). Injury type, pre-cranioplasty CSF leak, pre-cranioplasty CNS infection, cranioplasty material, time to cranioplasty had no statistically significance on need to revise or reverse cranioplasty (though the raw data was not provided).

The Rish²⁷⁰ study is based on a registry created by military surgeons in Vietnam of 1,030 cases of penetrating brain injury among soldiers treated from 1967 to 1970 and their records were reviewed by the National Research Council from 1976 to 1979 to obtain follow-up information.²⁴⁸ They identified 491 cranioplasties conducted at military, Veterans Administration, and private civilian hospitals to repair these injuries. When cranioplasties were sorted by the time from initial operation, the rate of complications decreased as the time from injury increased and leveled out at under 5% after 12 months. When only cases with complications after the initial surgery are examined, the complication rate for cranioplasties done in the 2nd year after the original surgery was lower (4%) than the rate for patients with cranioplasties in the 1st year (20%). The Rish²⁷⁰ study was discussed in the previous guidelines and although there were no recommendations on timing many surgeons of the time considered delayed cranioplasty after one year, especially in the face of contamination. Although not voted on through the Delphi process the experts identified that the management of pTBI has changed significantly since the Vietnam era so the applicability of the Rish²⁷⁰ study to modern pTBI care was in question. The management of penetrating brain injury, size of cranioplasty,

medical management of traumatic brain injury and antibiotic options have changed significantly since the Vietnam War decreasing the validity of these results for today's pTBI patient population.

Mathew²⁷² and Javadi²⁷³ provide information about the timing of cranioplasty in pediatric patients, limited by design and low numbers of patients. We included these since studies of pediatric patients with penetrating brain injury are limited. Both involve children injured in war zones. One study reported on all cases of children treated at the Multinational Medical Unit at Kandahar Airfield in Afghanistan by the only neurosurgeon in the region.²⁵⁰ During three periods totaling 237 days between September 2008 and April 2010 in which the unit could take local cases, 16 children under 15 years old treated for penetrating brain injuries were included and followed. In six cases the bone flap was left out and the patient discharged, with instructions about when to return for cranioplasty, based on both expectations of healing and operational availability. Four returned as scheduled 5, 8, and 10 weeks later, one patient returned early at 4 weeks and one patient did not return. All five of the cranioplasties were completed without difficulties and the patients were discharged with no focal neurological deficits.

Javadi²⁷³ presents a prospective series of patients who underwent decompressive craniectomies to treat penetrating blast injuries in children treated in a 2-year period in Iran near the border with Iraq (dates and hospital location not reported).²⁵¹ All three of the children who survived had cranioplasties 3 months later and all had good outcomes at 1 year with no major motor deficits and reports of excellent school performance.

These four studies that meet inclusion criteria provide very low strength evidence that the timing of cranioplasty is associated with outcomes. This is based on the inconsistent findings and study risk of bias due to a lack of reporting and adjustment for patient characteristics by early and late cranioplasty that may have influenced findings. Specific difference in management based on age, gender or military status were not supported by the evidence.

Discussion

Penetrating brain injury is a lethal mechanism of injury that is very difficult to study with prospective, randomized trials. The literature remains largely retrospective or observational in nature with many mere case reports (Class III or IV). The literature therefore does not support Level I or II recommendations. Timing of cranioplasty remains controversial. Conclusions in the literature are varied.²⁵⁶⁻²⁶⁸ While some studies reported a reduced rate of complications when cranioplasty is performed at late post-injury time points, other studies found good outcomes when cranioplasty was performed early. In the absence of guiding evidence, it is important that clinicians exercise good judgement with respect to the timing of cranioplasty. Cranioplasty is a crucial surgical intervention in the comprehensive rehabilitation of patients with traumatic brain injuries. The timing and type of reconstruction are influenced by a myriad of factors, necessitating a multidisciplinary approach to optimize patient outcomes.²⁷³ The

literature reviewed did not provide robust evidence-based variables that could help us to determine optimal timing of cranioplasty. Also of note, we considered whether patients with complications following the index surgery should undergo a delayed cranioplasty with the goal of reducing the risk of infection. In Delphi voting 52% of our panelists supported delayed surgery in this context but this did not meet our 80% threshold reflecting some but not strong support for the idea.

In the discussion leading up to the vote the expert panel acknowledged the complexity involved in determining the appropriate timing of cranioplasty. The experts discussed factors that may influence timing including complete wound healing, resolution of brain swelling, presence or absence of hydrocephalus, history of CSF leak, history of infection or active sources of infection, infection risk, and findings of syndrome of the trephined. The consensus is that cranioplasty should be done as early as feasible per our Delphi vote. A definition for feasibility or further defining criteria to proceed with cranioplasty were not further clarified by our group despite extensive debate and discussion. (see Table 2)

Timing of cranioplasty may be influenced by the management and rehabilitation for other injuries and surgical planning is often best performed with a team approach in a holistic manner considering various medical and surgical needs of the patient. Patients may benefit from additional procedures to prepare for cranioplasty especially in the case of soft tissue deficiencies, CSF leak or persistent communications with air sinuses. Indeed, efforts to reduce the risk of infection and removal of the cranioplasty after placement is key and central to the decision of when it is best to perform a cranioplasty. Each patient may have unique mechanisms of injury, complications, rehabilitation needs and family support requirements that also can influence timing. Here decision-making must thus be tailored to the individual patient. Given the complexity of presentations of pTBI and the lack of evidence to base recommendations on, timing of cranioplasty recommendations are limited to consensus that cranioplasty should be performed as soon as medically and surgically feasible.

There was some evidence that pediatric patients may benefit from early cranioplasty^{273,274} however, the consensus opinion of our group was that this finding was not robust enough to generate an evidence-based or consensus recommendation. Pediatric patients may benefit from use of autologous bone in early or ultra-early cranioplasty when possible, although the evidence was not robust enough to generate an evidence based recommendation. The two studies that met inclusion criteria described autologous cranioplasty.

Expert Opinion

The timing of cranioplasty is generally a more complex issue following pTBI than blunt TBI. Issues of soft tissue injury and wound contamination make decision making in pTBI more challenging. Multidisciplinary care is an important care strategy in care of all trauma patients and remains the case for patients who have sustained pTBI. Members of the team focused on associated

soft tissue and facial injuries may be essential team members to help in optimizing the soft tissue healing and determining the timing of cranioplasty. The timing of cranioplasty is best individualized based on our current understanding. The brain must be sunken and the wound should be well-healed without erythema or scabbing. Every effort should be made to ensure that risk of the implant becoming infected is minimized. In the setting of poly-trauma coordination with the trauma team to ensure the patient is free from infection at other sources is also important to consider when planning cranioplasty. While there has been a view that delaying cranioplasty may allow the body additional time to clear microbes from the surgical site, the literature has not provided consistent support for this notion. Importantly, our recommendation to perform cranioplasty “as soon as feasible” (Table 2) does not reflect a desire to rush the procedure. Instead, it reflects that benefits of cranioplasty are desirable as soon as they can be achieved safely with low surgical risk. There is some evidence that performing a cranioplasty can lead to neurological improvement perhaps as a result of the brain returning to its more normal shape. This combined with the restoration of protection of the brain as well as a desire to advance the patient’s care with reasonable expediency have us favoring cranioplasty as early as possible. Surgeons should not hesitate to delay a cranioplasty if they feel it could improve the odds the procedure will be durably successful (Table 3).

It is generally considered that hydrocephalus cannot be diagnosed before a cranioplasty is performed. If possible, consideration of a shunt is delayed until after the cranioplasty. Lumbar puncture can often be performed safely to enable cranioplasty if ventricles are enlarged preventing a cranioplasty. An external ventricular drain is another option. In some cases with progressive ventricular enlargement shunting prior to a cranioplasty can be required.

A multidisciplinary approach is often helpful with cranial reconstruction. Plastic surgery techniques like additional scalp dissection or subcutaneous slits can help to achieve soft tissue closure that would not be otherwise possible. The scalp flap contracts with each surgery at the site so many patients troubled by recurrent surgical site infections may require scalp expanders or microsurgical flaps prior to another attempt at cranioplasty.²⁶⁸ Plastic surgery involvement with complex skull defects and especially those involving the orbit or face can also be helpful and important.²⁶⁸

Future Directions

Unlike other aspects of pTBI, cranioplasty is highly amenable to rigorous academic study. High quality prospective studies which assess cranioplasty outcomes, timing and materials based on different patient characteristics and treatments would be highly valuable contributions to the literature. Study comparing the incidence of postoperative complications including infection, based on the timing of cranioplasty and materials selected would be very helpful in patients with pTBI. Demographics and patient characteristics (such as previous infection, CSF leak, scalp healing problems, neurologic status) would be helpful to discern if there

are outcome differences based on patient specific variables. The medical factors and surgical variables required to move forward with cranioplasty are not agreed upon and should also be an area for future research. If enough data could be assembled, it is possible that a prediction model could be developed to assist neurosurgeons with decision-making. Our understanding of the ideal timing to perform a cranioplasty in the setting of pTBI

remains to be determined. Future research should focus on refining guidelines for cranioplasty and exploring emerging technologies to further improve the efficacy of this essential procedure. Additionally, future studies should look beyond infection and other complication rates and include benefits and comprehensive neurorehabilitation outcome data, including speed of recovery and neurological status after cranioplasty.

VII-9 – Multidisciplinary Surgical Approach

R. Kitagawa and B. Aarabi

Recommendations

Level I-IV

There is insufficient evidence to support an evidence-based recommendations for a multidisciplinary team surgical approach in patients with facio-orbito-cranio-cerebral injuries.

Level C – Expert Consensus (Delphi Voting)

In the absence of direct scientific evidence, EXPERT CONSENSUS concluded that:

- When accessible, a multidisciplinary teamwork approach to surgical management of pTBI involving face, orbits and frontal skull base is recommended. (100% consensus)
- If a multidisciplinary approach to surgical management of pTBI involving face, orbits and skull base is not immediately feasible, life-saving damage control surgical procedures followed by transfer to a center with available multidisciplinary teams is appropriate when able. (100% consensus)

There is no evidence or expert opinion consensus to support a distinct recommendation based on patient gender, age, wounding mechanism, or military vs civilian context.

Introduction

pTBI involving the face, orbits and cranium²⁷⁵⁻²⁷⁷ is a devastating phenomenon that requires capable surgeons to repair the disfigurement of the face, cranium and orbits while simultaneously preventing cerebrospinal fluid (CSF) leakage through the air sinuses. Often these injuries involve facial and orbital repairs outside of traditional neurosurgical training, and therefore plastic, oromaxillofacial and ophthalmological surgeons are also needed.

These injuries may involve the face and orbits alone, but when pTBI is present, the neurosurgeon has a vital role in the reconstruction of the anterior skull base and prevention/treatment of CSF leakage through the air sinuses. The mechanism may involve low velocity injury penetration such as present with the knife,²⁷⁸ blast injuries as are seen frequently in military conflict,^{76,185,271} or civilian injuries.²⁷⁸ One common civilian injury is submental or transoral, self-inflicted gun shot wounds.^{275,276} As the trajectory involves the face, eyes, and brain, a multidisciplinary approach is essential.

Prior Guideline Recommendations

The prior pTBI guidelines did not endeavor to address this topic.¹⁶

Scientific Foundation

We identified no studies that compared a multidisciplinary with a single-disciplinary approach to pTBI surgery or management. However, we identified several noncomparative studies that reported using a multidisciplinary team.²⁷⁵⁻²⁷⁷ As there were no comparative studies, all recommendations we provide are based on expert consensus.

One retrospective database by Stephens et al²⁷¹ reviewed 108 injuries from Operation Iraqi Freedom and Operation Enduring Freedom (Afghanistan) who underwent a decompressive craniectomy and subsequent cranioplasty.²⁷¹ Ninety-three (86%) had a penetrating injury primarily due to an explosive blast. Repairing the soft tissue and skull base required a multidisciplinary team consisting of neurosurgery, reconstructive plastic,

oral-maxillofacial, and ophthalmologic surgery that was individualized for each patient. One patient died (0.93%). Other complications included infection (12%), seizure (7.4%), and extra-axial hematoma (7.4%).

A study by Elegbede et al²⁷⁵ of 69 patients with a self-inflicted gunshot wound to the face (submental [57%], intraoral [22%] and temporal [12%]) reported multispecialty surgical management including facial reconstructive surgery (57%), ophthalmology (14%), and neurosurgery (26%). Additionally, 33% required a tracheostomy and 38% required a gastrostomy. Twenty-eight (41%) had a GCS score greater than 8 at baseline. Eighteen patients died (26%). However, only 41% of the patients (N = 28) sustained a pTBI.

Another combat study by Weichel et al²⁷⁷ of 152 casualties from Operations Iraqi Freedom and Enduring Freedom experienced 207 globe/oculoplastic injuries and were treated by ophthalmology, as well as other medical and surgical specialties. However, only 14% had pTBI. Mortality and vision loss were not reported in this study.

One study by Kim et al²⁷⁸ of 82 patients with craniofacial impalement injury by a metallic object used a multidisciplinary team (otolaryngologists, neurosurgeons, ophthalmologists, plastic surgeons, and anesthesiologists) for the removal of the foreign body under general anesthesia at two craniomaxillofacial trauma centers. Items of impalement in the eight patients included a saw wheel, knife, metal plate, and iron bar. Complications in these eight patients included one brain abscess, chronic pain, pseudoaneurysm, and hypertrophic scarring.

One study of 11 patients by Kriet et al²⁷⁶ with self-inflicted submental and transoral GSW and brain injuries were treated by neurosurgery, ophthalmology, and otolaryngology. Ophthalmological and craniomaxillofacial injuries were addressed following frontal craniotomy. One person received only supportive care and died. Complications for the other 10 patients included: cerebrospinal fluid leak, delayed frontal lobe infarction, scalp wound dehiscence, and extradural abscess.

We found evidence that a multidisciplinary team is sometimes available and employed. However, we found no evidence to determine whether care from a multidisciplinary team results in superior or inferior outcomes when compared with care from a single-disciplinary team. However, consensus among experts with experience with these patterns of injury recommend a multidisciplinary approach when available or transfer to a center with these capabilities after medical stabilization and damage control surgery if needed.

Discussion

Self-inflicted GSW and blast injuries can frequently involve submental, intraoral and trans-temporal regions, causing injury to the face, orbits, air sinuses and frontal skull base. These injuries may occur in civilian or conflict environments and may be low velocity pTBI, GSW, or blast injuries.^{271,275,276,278} Blast injuries especially may involve multiple fragments penetrating the skull

base secondary to the location of the exploding device. These injuries are extremely complex but are also survivable.^{271,275,276}

Therefore, whether received in casualty clearing stations near the front-line or in a civilian hospital, every-effort should be made to bring together multispecialty surgeons in order to simultaneously repair the sub-frontal dura defect, air sinuses, orbital roofs and facial soft-tissue structures.

If immediate, simultaneous repair is not possible, damage control surgical and medical interventions are appropriate followed by timely definitive surgical repair with a multispecialty team to avoid increased risk for infection. Often, transfer to another facility may be necessary after stabilization in both conflicts and civilian environments.

The multidisciplinary nature of these conditions extends beyond the surgical repair. As the trajectory of penetrating object can involve the SSS, anterior cerebral arteries, and potentially the basal cisterns, involvement of neurovascular and endovascular experts is often required as well. However, vascular injuries in pTBI are addressed in other aspects of these guidelines. Rehabilitation specialists are also required as well to achieve best outcomes. Rehabilitation not only helps to build muscle and adaptive strategies, it stimulates brain plasticity as well as other types of neural repair.

Following review of the literature, no studies were found that compared a multidisciplinary with an isolated neurosurgical approach to pTBI of the face and orbits. As facial and orbital/eye repair is outside of the traditional training of most neurosurgeons, effective surgical treatment of these injuries is only possible through multidisciplinary teams. Although multiple individual operations are possible from each service, this approach carries the risk of multiple anesthetic administrations, increased risk of infection from additional operations, and potential disruption of previous surgical repair. For example, access to the orbit and forehead after cranialization of the frontal sinus could potentially de-vascularize the pericranial graft and threaten the CSF leak repair.

Expert Opinion

In modern medicine, multidisciplinary care is essential to achieving best outcomes. pTBI patients can be extremely complex requiring the expertise of multiple medical and surgical disciplines. Therefore, a multidisciplinary teamwork approach to surgical management of pTBI involving face, orbits and frontal skull base is recommended. If these teams are not available, transfer to an appropriate facility with these services after medical and surgical stabilization is also recommended. Even the neurosurgical care may require the involvement of multiple neurosurgeon subspecialists such as those with advanced trauma, vascular, skull base and spine training.

Future Directions

While the benefits of multidisciplinary care are obvious, evidence supporting this premise would be a valuable addition to the literature. However, the impact of delays from presentation to

definitive repair would certainly benefit from further study. This delay involves both transfer of the patient to facilities with all services available as well as finding operating room and surgeon availabilities as these cases can be long in duration. Increased wait

times likely increase the risk of infection as CSF leakage is often present and the environment involves the nonsterile sinus mucosa. Therefore, further research on how time to definitive operative repair influences outcome is needed.

VIII – INTENSIVE CARE EVIDENCE-BASED RECOMMENDATIONS AND EXPERT CONSENSUS STATEMENTS

Section Leads: Halinder S. Mangat and Jamshid Ghajar

VIII-1 – Coagulopathy and Viscoelastic Testing

D. M. Stein, B. Dengler

Recommendations

Level I-IV

There is insufficient evidence to support an evidence-based recommendation for routine use of viscoelastic testing (VET) or routine reversal of coagulopathy in patients with penetrating traumatic brain injury (pTBI).

Level C – Expert Consensus (Delphi Voting)

In the absence of direct scientific evidence, EXPERT CONSENSUS concluded that:

- VET may be used to guide the correction of coagulopathy. (88% consensus)
- In patients with pTBI, coagulopathy should be corrected to minimize the risk of worsening of intracranial hemorrhage. (100% consensus)

No evidence or expert opinion supported distinct recommendations based on patient gender, age, wounding mechanism, or military vs civilian context.

Introduction

Coagulopathy in traumatic brain injury is a well-recognized and common phenomenon with scientific literature demonstrating that TBI-induced coagulopathy follows a distinct pathological pathway.²⁷⁹ TBI-induced coagulopathy is associated with worse outcomes in both blunt and penetrating TBI and in both military and civilian populations,^{48,280-284} and has been reported in as many 45-64% of patients with pTBI.^{48,282,284,285} Though various theories have been advanced as to the cause of this phenomenon such as the release of thromboplastin from injured brain tissue, TBI-induced coagulopathy remains poorly understood. A variety of independent risk factors for the development of coagulopathy have been described and include penetrating mechanism,²⁸⁶ low Glasgow Coma Scale (GCS) score,^{48,284,287} effacement of cisterns/cerebral edema,^{48,284} transfusion requirement⁴⁸ and subarachnoid hemorrhage.²⁸⁴ Given the known morbidity of coagulopathy in patients with TBI from a variety of mechanisms, an attempt to reverse coagulopathy with plasma, prothrombin complex concentrates, vitamin K, or other agents is widely considered standard of care.

Traditional evaluation of coagulopathy has relied on platelet count, the international normalized ratio, partial thromboplastin time and prothrombin time. There is a large body of data that has described the coagulopathy associated with TBI based on these

“conventional clotting assays.”^{284,285,287-289} There is an increasing body of evidence that VET via thromboelastography (TEG) and rotational thromboelastometry may be more accurate for detecting and characterizing coagulopathy in patients with trauma.²⁹⁰⁻²⁹²

Prior Guideline Recommendations

The previous pTBI guidelines did not endeavor to provide any recommendations for the use of VET or the reversal of coagulopathy.

Scientific Foundation

Use of VET

No studies were identified that met criteria for inclusion in the guidelines evidence tables. Routine VET has been widely utilized in mixed populations of patients with both blunt and penetrating TBI to define and detect coagulopathy.^{282,286,293-296} However, few studies have specifically examined the issue of use of VET to define coagulopathy in patients with pTBI (Table 27). We identified one study, Folkerson, et al, that examined determination of coagulopathy by use of rapid TEG (rTEG).²⁸² These authors defined coagulopathy as activated clotting time greater than 128 seconds, K-Time greater than 2.5 minutes, angle less than 56 degrees, maximum amplitude less than 55 mm, and LY-

TABLE 27. Evidentiary Base for Correction of Coagulopathy

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Study risk of bias
Aiyagari, 2005 ²⁹⁷ (NRS) United States Civilian GSW	Male: 100% Mean age: 26.33 y GCS Patient 1: "2T" Patient 2: "2T" Patient 3: 6	Administration of Recombinant activated Factor VII: 3	Mortality: 100% Hemorrhage cessation: 100%	High

GCS, Glasgow Coma Scale; MOI, mechanism of injury; NRS, non-randomized study.

30 greater than 3.0%, or platelet count 150 000/ μ L or less. There were no outcomes or associations reported from rTEG use.²⁷⁹ Ninety-nine patients had pTBI. Coagulopathy was associated with early mortality (adjusted odds ratio 3.99, 95% CI, 1.37 to 11.72) after controlling for age, gender, Glasgow Coma Scale score, blood pressure, and base excess in this study.²⁷⁹ Another study compared blunt to pTBI patients, and pTBI were found to be more coagulopathic as compared to those with blunt mechanisms of injury by a variety of TEG parameters.²⁸⁶

Benefits and harms of correction of coagulopathy

The data on correction of coagulopathy in patients with pTBI as measured by VET is extremely limited. One small case series was identified and included for completeness, (N = 3) that examined rates of hemorrhage cessation with reversal of coagulopathy with recombinant activated Factor VII in addition to standard reversal agents that specifically looked at patients with penetrating TBI. The authors reported a 100% rate of hemorrhage cessation in this series of three patients, however all progressed to brain death and two underwent organ donation. Hematologic parameters were reported before and after administration of recombinant activated Factor VII.²⁹⁷ Additional products, however, were given prior to treatment with recombinant activated Factor VII (e.g., fresh frozen plasma, cryoprecipitate, platelets, red blood cells). This study provides very low strength of evidence that cessation of refractory hemorrhage may be achieved with the use of recombinant activated Factor VII, although clinical outcomes were uniformly poor.

We found one study not meeting inclusion criteria (n = 89) that looked at the reversal of coagulopathy as measured by CCAs in patients with pTBI.⁴⁸ In this study, mortality rates were significantly higher in coagulopathic patients (73% vs 25%; $P < .001$), but for the small percentage of patients coagulopathic on admission (n = 40) who were alive at 24 hours (n = 25), normalization of the coagulation profile was not associated with statistically significant survival advantage (75% vs 38%; $P = .29$).

The risks of coagulopathy reversal are limited and consist of allergic reactions, transfusion reactions, and a slight increased risk

of thromboembolic complications, depending on the agent used. These therapies are typically well tolerated and considered standard of care for reversal of coagulopathy in a variety of patient populations.

Discussion

Use of VET and reversal of coagulopathy

The data that informs VET and reversal of coagulopathy in pTBI is limited. However, upon extrapolation of data from mixed populations of brain injury, a likely supportive role for VET in the management of the patient with pTBI exists. VET's ability to detect different defects in the coagulation profile such as fibrinogen deficiency, platelet dysfunction, and hyperfibrinolysis make it an attractive tool for more precise resuscitation and reversal of coagulopathy. Whether or not physicians should reverse coagulopathy in patients with pTBI cannot be guided exclusively by data at this time, but rather must be considered from related populations of blunt TBI or mixed mechanisms wherein worse outcomes occur in coagulopathic patients. Correction of coagulopathy is also considered standard of care prior to neurosurgical intervention and to minimize the risk of progression of injury. The therapies used to reverse coagulopathy are typically well tolerated and pose little inherent additional risk to critically ill patients.

Expert Opinion

With few exceptions, reversal of coagulopathy - whether iatrogenic or metabolic - is appropriate for pTBI patients and is considered a standard of care. Neurosurgeons typically require correction of deranged coagulation profiles before it is considered safe to proceed with neurological surgery. Given that complex vascular injuries are a defining characteristic of pTBI, intra-operative hemorrhage is already a substantial concern when operating on pTBI patients and the additional challenge inherent to coagulopathy is undesirable in this context. Although it is unclear whether reversal of coagulopathy following pTBI results in improved outcomes, there is little downside to the use of typical

agents other than their expense and resource allocation issues. Some of our panelists shared the opinion that the results of VET testing do not always align with the patient's clinical phenotype however – patients who clinically manifest coagulopathy can have relatively normal VET parameters and vice versa.

Future Directions

The management of coagulopathy in patients with pTBI remains a challenging area of clinical practice, underpinned by limited direct evidence and a reliance on extrapolations from broader traumatic brain injury (TBI) populations. Given the emerging role of VET in detecting and characterizing coagulopathy, prospective studies focusing on pTBI populations are important. Research should aim to compare the efficacy of VET with traditional coagulation assays in predicting hemorrhagic complications, need for surgical interventions, and patient outcomes. Studies should identify specific VET parameters that are most predictive of adverse outcomes in pTBI and evaluate the cost-effectiveness of implementing VET in routine clinical practice for pTBI management. There is also a need for RCTs that compare different coagulopathy correction strategies (including plasma, prothrombin complex concentrates, vitamin K, and other agents) in terms of efficacy, safety, and impact on clinical outcomes and explore the timing and thresholds for intervention to

optimize patient outcomes. Understanding the underlying mechanisms of coagulopathy in pTBI could lead to the development of novel therapeutic targets. The exploration of biomarkers that could predict the development of coagulopathy or response to treatment should also be explored.

Studies that examine the trajectory of recovery and identify factors associated with better functional outcomes and quality of life as well as those which develop and validate prognostic models would guide better clinical decision-making. Given the heterogeneity of the pTBI population, comparative effectiveness research also has promise for assessing the effectiveness of VET and coagulopathy correction strategies across different patient subgroups defined by age, gender, mechanism of injury, and other relevant factors. It can also explore differences in management strategies and outcomes between military and civilian populations, the impact of pre-existing comorbidities and concurrent injuries on the management and outcomes of coagulopathy in pTBI. Addressing these research priorities requires a multidisciplinary approach, leveraging advances in technology, biomarker discovery, and therapeutic interventions. Ultimately, the goal of future research is to develop more robust evidence-based guidelines that can be tailored to individual patient characteristics, improving outcomes for those affected by pTBI and coagulopathy.

VIII-2 – Intracranial Pressure and Cerebral Perfusion Pressure

J. Ghajar, G. W. J. Hawryluk, H. S. Mangat, A. Valadka

Recommendations

Level I-II

There is insufficient evidence to support a strong or moderate strength recommendation related to intracranial pressure (ICP) or cerebral perfusion pressure.

Level III

Pediatric and adult severe pTBI patients should be managed using ICP monitoring to reduce mortality, though it is associated with longer duration of intensive care.

Level IV

ICP should be maintained below 22 mmHg in pediatric and adult severe pTBI patients to reduce mortality and improve 6-month neurological outcomes.

Level C – Expert Consensus (Delphi Voting)

In the absence of direct scientific evidence, EXPERT CONSENSUS concluded that:

- Cerebral perfusion pressure (CPP) should be managed as per recommendations provided in the 4th edition adult coma guidelines²⁸ and the 3rd edition pediatric guidelines for non-penetrating TBI²⁹⁸ (92% consensus):

Adult: “The recommended target cerebral perfusion pressure (CPP) value for survival and favorable outcomes is between 60 and 70 mmHg. Whether 60 or 70 mmHg is the minimum optimal CPP threshold is unclear and may depend upon the patient’s autoregulatory status.”²⁸

Pediatric: “Age dependent thresholds should be used for pediatric patients with a minimum CPP of 40-50 mm Hg, with infants at the lower end and adolescents at the higher end.”²⁹⁸

- ICP monitoring can facilitate the detection of an expanding intracranial mass lesion following pTBI. (100% consensus)

No evidence or expert opinion supported distinct recommendations based on patient gender, wounding mechanism, or military vs civilian context.

Introduction

Intracranial pressure can be a source of secondary insult following TBI. As ICP elevation can reduce cerebral perfusion (CPP = MAP-ICP), concomitant measurement of CPP can help to ensure adequate perfusion of the injured brain. Treatment thresholds for ICP and CPP have been identified and an effort is made to optimize these values during the critical care management of severe TBI patients. It is uncertain if the critical values for ICP and CPP are the same in pTBI as they are in blunt TBI.^{28,298} Given the higher preponderance of vascular injuries in pTBI it is possible that distinct values could be indicated.

Over the 4 iterations of the Brain Trauma Foundation adult coma guidelines for severe TBI, the ICP threshold has evolved from 25 to 20 to 22 mm Hg.²⁸ A randomized controlled trial demonstrated harm when CPP values >70 mmHg are targeted in severe TBI.²⁹⁹ This has also led to a recommended CPP range of 60-70 mm Hg.²⁸ The importance of cerebral autoregulation has been demonstrated in recent years²⁰ and it is important for clinicians to be able to diagnose when pressure autoregulation is intact and when it is dysfunctional.

Patients who have preserved autoregulation can tolerate a wider range of CPP compared to those with impaired autoregulation. Such patients may benefit from higher CPP values as these are associated with a reduction in ICP.^{300,301} Conversely, pressure passive patients with dysfunctional pressure autoregulation benefit from lower CPP values as these lower values reduce ICP in such patients. Different techniques for assessing autoregulation have been established including transcranial doppler, ICP waveform, cerebral oximetry and others.³⁰² ‘Optimal CPP’ - or CPP_{opt} - has been defined as the CPP at which the pressure reactivity index is most negative suggesting optimized autoregulatory processes, and is being further investigated by the CoGItATE trial.^{22,303} Management targeting CPP_{opt} is currently supported by limited evidence, however.

Prior Guideline Recommendations

The prior penetrating head injury guidelines (2001) make an ‘optional’ recommendation (Level III/IV) that “early ICP monitoring is

recommended when the clinician is unable to assess the neurological exam accurately,^{16,304} the need to evacuate a mass lesion is unclear; or imaging studies suggest elevated ICP.”³⁰⁴

Furthermore, they stated that in the absence of studies specific to penetrating TBI, recommendations from contemporary guidelines for the overall management of severe TBI be used. Of the 6 studies included in the first edition of the guidelines, none met inclusion criteria for informing these new recommendations.

Scientific Foundation

A. Intracranial pressure monitoring

The data on benefits and harms of ICP monitoring in pTBI is sparse (Table 28). We identified one non-randomized study from the National Trauma Data Bank (2017 to 2019) in adults (N = 466, mean age 32 years) with primarily gunshot wounds to the head.³⁰⁵ This study used propensity-score matching to compare outcomes in patients who underwent ICP monitoring with patients who did not receive ICP monitoring, and found a lower mortality rate with ICP monitoring (30.9% vs 40.8%, odds ratio [OR] 0.65; 95% CI, 0.44 to 0.95), but twice the length of intensive care unit (ICU) stay with ICP monitoring (median 15 days vs 7 days, $P < .001$).

We also identified one non-randomized study of pediatric patients (aged 0 to 18 years) from the National Trauma Data Bank (2014 to 2017) that examined the association of clinical and treatment variables on outcomes in a population of pediatric patients with cranial gunshot wounds (N = 209).³⁰⁶ ICP monitor placement occurred in 25.8% of the study population (N = 54). Regression analyses were performed with covariates: age, presence of shock, ICP monitor placement, craniotomy, sex, ethnicity, and insurance status to determine impact on mortality. The authors report a lower risk of mortality associated with ICP monitor placement (OR 0.267; 95% CI, 0.082 to 0.864). This association was not present on subgroup analysis in patients presenting with GCS scores of 9 to 15 (OR 0.65; 95% CI, 0.038 to 11.054). Discharge disposition was also examined, and the authors reported that no association was present between ICP monitor placement and discharge disposition for the entire group (OR 0.707; 95% CI, 0.196 to 2.551) or on subgroup analysis for patients with a GCS of 9 to 15 (OR 0.596; 95% CI, 0.089 to 3.998).³⁰⁶

Additionally, one non-randomized study in an adult population (aged 18 to 90 years) that aimed to determine the rate and risk factors for central nervous system (CNS) infection after pTBI and to examine the impact of antibiotic prophylaxis on those outcomes.^{188,307} The authors reported an association of ICP monitor placement with development of CNS infection. Twenty nine percent of patients (N = 223/763) in the study underwent ICP monitor placement after pTBI. The authors reported an increased proportion of infections in the ICP monitor group compared with those without a monitor placed (N = 540, 12% vs 4%, $P < .0001$). On multivariable analysis ICP monitor placement was associated with an infection OR of 2.27 (95% CI, 1.18

to 4.4, $P = .01$). However, infections were determined clinically and supported by CSF cultures, only available with ventricular CSF ICP monitors, and wound swabs when available, which occurred in 74% of reported cases.

These studies provide low-strength evidence that ICP monitoring is associated with lower mortality in adults and pediatric populations, increased length of stay; and no difference in discharge disposition compared with no ICP monitoring in patients suffering penetrating TBI. These studies provide very low strength evidence that ICP monitor placement compared with no monitor placement is associated with increased risk of cerebral infection/ventriculitis though we believe that recent advent of antibiotic catheter impregnation reduces this risk substantially in modern neurosurgical practice.

B. Intracranial pressure thresholds

In blunt TBI blood pressure, ICP and cerebral perfusion pressure (CPP) thresholds are established and central to patient care. Indeed, compliance with these thresholds has been associated with improved outcomes.²⁸ It is unclear if those same thresholds should be applied in pTBI or if different values are appropriate. No studies were identified that examined systolic, diastolic, or mean blood pressure thresholds for either ICP or CPP directed treatment strategies in pTBI.

For ICP/CPP management thresholds, one small non-randomized study in pediatric patients (aged 8 months to 15 years) with gunshot wounds to the head (N = 33) reported that ICP monitoring was performed in 18 patients with a threshold of 20 mmHg used in treatment⁴² (Table 29). Of the 18 children who received ICP monitoring, eight died with ICP greater than 40 mmHg and one patient died of pneumonia with ICP less than 30 mmHg. Of the nine survivors, ICP was less than 20 mmHg for all readings in three patients, two patients had an ICP less than 30 mmHg with treatment and four patients had ICP measurements greater than 40 mmHg despite treatment. At 6 months, two of the four patients with ICP measures greater than 40 mmHg had severe disability and two had moderate disability.

Kelly et al report a non-randomized study in adult patients (N = 26 had ICP monitoring, mean age 38 years) with gunshot wounds to the head reported that ICP less than 20 mmHg was maintained with hyperosmolar therapy.¹³⁹ Median maximum ICP in those who survived to discharge was 22 mmHg and was 33 mmHg in those who did not survive to discharge. Median maximum ICP in those with a good functional outcome was 22 mmHg and was 26 mmHg in those with a poor functional outcome.

Other Studies Not Included

One non-randomized study in mostly adults (N = 119, aged 12 to 73 years) reported patients with gunshot wounds to the head received vasopressors and fluids to keep CPP greater than 60 mmHg, with an ICP target less than 20 mmHg, managed with CSF drainage, sedation, mannitol, and hyperventilation.¹³¹ Individuals who presented with an *initial* ICP of 21 mmHg or more

TABLE 28. Evidentiary Base for ICP Monitoring in Penetrating Traumatic Brain Injury

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Study risk of bias
Mansour, 2023 ^{a,305} (NRS) United States Civilian GSW: 93.6% Low-velocity mechanisms: 6.4%	Male: 85% Mean age: 32 y ISS median: 25.0 GCS 3: 60.1% GCS 4: 6.7% GCS 5: 4.5% GCS 6: 10.3% GCS 7: 10.9% GCS 8: 7.5%	ICP monitor placement: 50% (233, propensity-score matched) No ICP monitor placement: 50% (233, propensity-score matched)	Mortality rate with use of ICP monitor vs no monitor: 30.9% vs 40.8%, OR 0.65; 95% CI 0.44-0.95 ICU days with ICP monitor vs without monitor: 15 vs 7 d, $P < .001$ Discharge disposition was not associated with ICP monitoring	Moderate
Lannon, 2022 ³⁰⁶ (NRS) United States Civilian GSW: 100%	Male: 86% Mean age: NR (range 0-18 y) GCS 3: 48% GCS 4-8: 21% GCS 9-12: 11% GCS 13-15: 20%	ICP monitor placement: 25.8% (54/209) No ICP monitor placement: 74.2% (155/209)	Risk of mortality with the use of ICP monitors vs no monitor: OR 0.267; 95% CI 0.082-0.864 Mortality benefit was not present in subgroup analysis for patients GCS 9-15 ICP monitor use not associated with discharge disposition: OR 0.707; 95% CI 0.196-2.551	Moderate
Harmon, 2019 ¹⁸⁸ (NRS) United States Civilian GSW: 90% Knife: 6% Nail gun/hammer/ arrow: 4%	Male: 85% Mean age: 35 (range 18-90 y) CNS infection vs no CNS infection ISS 0-8: 2% vs 3% ISS 9-15: 10% vs 13% ISS 16-24: 39% vs 29% ISS ≥ 25 : 45% vs 53%	ICP monitor placement: 29% (223/763) No ICP monitor placement: 71% (540/763)	ICP monitor placement CNS infection: 27 (12%) No CNS infection: 196 (88%) No ICP monitor placement CNS infection: 24 (4%) No CNS infection: 516 (96%) $P < .0001$ Risk of infection with ICP monitor placement vs no monitor: OR 2.27; 95% CI 1.18-4.4, $P = .01$	Moderate

CNS, central nervous system; GCS, Glasgow Coma Scale; GSW, gunshot wound; ICP, intracranial pressure; ISS, Injury Severity Score; NR, not reported; NRS, non-randomized study.

^aThe results section of the study publication states that there was no difference in "favorable discharge disposition" between ICP and no ICP monitoring and refers to Table 2 in the text of the study publication. However, the same data in Table 2 of the study publication is listed under "unfavorable outcome." Because of this discrepancy, we do not report data for discharge disposition for this study.

were more likely to die than those who did not (50% [11/22] vs 24% [10/41]), although the results were not statistically significant (OR 2.56; 95% CI, 0.85 to 7.68). However, ICP and CPP pressure readings during the course of treatment or at death were not provided.

Other studies reported that ICP was associated with favorable or unfavorable outcomes or not associated with outcomes, but did not report ICP or CPP management thresholds,^{87,130,235,241,308,309} while other studies reported thresholds used, but did not report outcomes by ICP or CPP,^{18,117,211,244,273,310-313} and 1 study reporting both had only 4 survivors in a case series of 11 comatose children suffering gunshot wounds to the head.³⁸

These studies provide very low strength of evidence that successful management of ICP to maintain a threshold of 20-22 mmHg or lower is associated with better outcomes (mortality, function) than if ICP thresholds are not targeted. However, as detailed in the discussion below, for pragmatic reasons and to avoid confusion amongst practitioners, the ICP threshold has

been chosen to be consistent with the 4th edition severe TBI threshold of <22 mm Hg.²⁸

Discussion

While ICP monitoring as well as ICP-directed management is supported and practiced extensively in blunt severe TBI, the data specific to pTBI remains sparse. In fact, the included 2 studies were published in the past 5 years.

The enduring discussion and study of ICP following all forms of TBI reflects the presumed importance of ICP despite the fact that there remains paucity of high-quality evidence that conclusively show a relationship between ICP-directed treatment and improved outcomes. Ultimately, in spite of only Level III recommendations supporting ICP monitoring in the management of adult and pediatric severe TBI,^{28,298} there has been widespread adoption of ICP directed treatment with up to 90% of neurotraumatologists in European Level I trauma centers using ICP monitoring in severe TBI patients.³¹⁴

TABLE 29. Evidentiary Base for ICP Thresholds in Penetrating Traumatic Brain Injury

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Study risk of bias
Miner, 1990 ⁴² (NRS) United States Civilian GSW: 100%	Total population: 33 Male: 70% Age range: 8 mo to 15 y Suicide attempt: 33% GCS >8: 15% GCS 6-8: 21% GCS 3-5: 64%	ICP threshold <20 mm Hg: 18 Treated with sedatives, muscle relaxants, hyperventilation, osmotic diuretics, and barbiturate coma	Mortality: 50% 8 patients died with ICPs >40 mm Hg; 1 died of pneumonia with ICP <30 mm Hg 8 survived: 3 had all ICPs <20 mm Hg, 2 had ICPs <30 mm Hg with treatment; 4 had ICPs >40 mm Hg despite treatment At 6 mo: 2 surviving patients with ICP >40 mm Hg had severe disabilities and 2 had moderate disabilities	High
Kelly, 2021 ¹³⁹ (NRS) United States Civilian GSW: 100%	Total population: 297 Male: 85% Mean age: 38 y White: 73% GCS >8: 19% GCS 5-8: 4% GCS 3-4: 76%	ICP threshold <20 mm Hg: 26 Treated with hyperosmolar therapy of 3% saline	Median max ICP in survivors (N = 15): 22 mm Hg (IQR 16-34 mm Hg) Median max ICP in those who died (N = 11): 33 mm Hg (IQR, 21-95 mm Hg), <i>P</i> = .082 Median max ICP in those with good functional outcome: 22 mm Hg (IQR 13-27 mm Hg) Median max ICP in those with poor functional outcome: 26 mm Hg (IQR 18-37 mm Hg), <i>P</i> = .240	Moderate

CPP, cerebral perfusion pressure; GCS, Glasgow Coma Scale; GSW, gunshot wound; ICP, intracranial pressure; IQR, interquartile range; NRS, non-randomized study.

When ICP exceeds the focal and regional arteriolar critical closing pressure, nutrients cannot flow to the brain and there is therefore no question that ICP elevation can be harmful and is more than a mere marker of disease severity. However, the benefits of treating raised ICP remain insufficiently informed. The precise ICP threshold which should be employed also remains uncertain. The adult severe TBI guidelines have recommended 25 mmHg, 20-25 mmHg, 20 mmHg and now 22 mmHg over the course of its four editions, depending on newer studies.²⁸ It is also unclear if there may be a basis for individualizing the treatment threshold.³¹⁵ Recent studies raise the possibility that this harm may begin below 20 mmHg and cumulative ICP dose may be a more critical determinant of outcomes.^{316,317}

It must be remembered that ICP is a very information-dense measurement. It can be used to derive CPP and to determine autoregulatory status which is increasingly viewed as playing an important role in neurocritical care. Analysis of the ICP waveform is also believed to inform compliance/compensatory reserve. Evidence suggests that ICP be monitored and treated through the course of pTBI management, even if a decompressive craniectomy is performed as ICP can be elevated despite a DC having been performed. And of course ICP monitoring can detect an expanding intracranial mass lesion requiring surgical evacuation.

However, a key question at hand is whether there is sufficient evidence to recommend a distinct ICP treatment threshold for pTBI as compared with the over-arching recommendation provided by the 4th edition guidelines.²⁸ The value of 20-22 mmHg

identified in the two pTBI studies taken as evidence here does not provide clear evidence that that either specific value is more meaningful in pTBI. Kelly et al¹³⁹ demonstrated that in a large sample (*n* = 297) of GSW victims treated for ICP lowering, the median maximum ICP amongst survivors was 22 mmHg. Therefore, in view of the authors, selecting a more uniform ICP threshold of 22 mmHg is useful and consistent with the recommendations in the 4th edition of the severe TBI management guidelines,²⁸ which provides pragmatic consistency in treatment of all TBI patients, and equally importantly minimizes confusion for practitioners.

Expert Opinion

With no available data on CPP management in pTBI, the expert panel opined to seek consensus on whether 4th edition guidelines²⁸ may be used for thresholds that would encompass pTBI in addition to blunt severe TBI. High-level consensus was reached on adopting such a measure, viz. CPP thresholds be 60-70 mmHg for adults, and 40-50 mm Hg for children,²⁹⁸ with infants being closer to the lower limit and adolescents to the upper limit.

Future Directions

The role of ICP monitoring and the treatment threshold that should be used remains a matter of ongoing investigation across the breadth of TBI. As studies aim to refine the role of ICP monitoring and the specific treatment threshold that should be

utilized – as well as whether there is a basis for individualizing the threshold – there should be an effort to determine whether patients with pTBI should be subject to distinct treatment. Randomized controlled trials have proven feasible for examining ICP monitoring, providing hope that future high-quality studies will improve upon what we have learned to date. Indeed, as in closed TBI, data for treatment of pTBI patients comes largely from retrospective cohort studies so far, which limits the quality of

evidence currently available. Compliance with ICP monitoring remains heterogenous across the United States. Comparative effectiveness research which associates variations in practice with outcome thus also holds promise for improving our understanding of ICP monitoring, ICP-CPP thresholds, and the role of cerebral autoregulation in pTBI compared to closed TBI, and whether autoregulation determined CPP (CPP_{opt}) achieves improved outcomes in pTBI.

VIII-3 – Seizure Prophylaxis

J. Benjamin, G. Grant, A. Hoffer, A. Lumba-Brown, H. S. Mangat, G. Rosenthal

Recommendations

Level I-IV

There is insufficient evidence to support an evidence-based recommendation related to the benefits and harms of seizure prophylaxis in the critical care setting.

Level C – Expert Consensus (Delphi Voting)

In the absence of direct scientific evidence, EXPERT CONSENSUS concluded that:

- Anti-seizure prophylaxis is indicated for 7 days or longer in patients with pTBI to reduce the risk of post-traumatic seizures. (96.7% consensus)
- No specific anti-epileptic drug can be recommended as being superior for the prevention of early post-traumatic seizures. (100% consensus)

No evidence or expert opinion supported distinct recommendations based on patient gender, wounding mechanism, or military vs civilian context.

Introduction

The association between seizures and pTBI has been described since antiquity and subsequently reported in the medical literature associated with most major military conflicts. While understood to be more prevalent than in blunt TBI, the rate of seizures after pTBI is, however, difficult to elucidate given the vast heterogeneity of the study populations. Indeed, the risk of readmission for seizure is nearly 3 times higher in pTBI patients than blunt TBI patients.³¹⁸

Post-traumatic seizures following pTBI are relatively common, though the exact incidence is unknown. The extent and location of injury, presence, and type of retained material, and follow up time are often not fully described or disparate between studied populations, creating difficulty when trying to make any comparative deductions. Transcranial bihemispheric or intraventricular injury increases the risk of seizures considerably.²¹⁰ Much more is known about post-traumatic seizures in blunt TBI. Seizures following blunt severe TBI, focal or generalized, occur in up to 20% of patients.³¹⁹ They cause increased sympathetic drive, increased cerebral blood flow and can precipitate an increase in ICP – or even herniation – as well as metabolic crises leading to

secondary injury.³²⁰ Notably, prophylaxis against early seizures does not impact development of post-traumatic epilepsy.³²¹ which occurs in 1.06% of combat veterans.³²¹ Other risk factors in pTBI are dural penetration with metal and bone fragments, multiple cranial surgeries, multiple subcortical contusions, subdural hematoma, midline shift greater than 5 mm, and GCS score.³²²

Prior Guideline Recommendations

The prior penetrating head injury guidelines addressed ‘Anti-seizure Prophylaxis for Penetrating Brain Injury.’³²³ Recommendations created in this edition were based on 9 articles with 4 defined as Class I and 5 defined as Class III. No Level I or Level II recommendations on this subject were provided. Level III/IV recommendations stated antiseizure medication in the first week following pTBI was recommended, and subsequent prophylaxis could not be recommended. Direct evidence supporting this recommendation was lacking, however. None of the Class I studies met inclusion criteria for the updated pTBI guidelines because most of the patients studied had blunt TBI, while a small number had pTBI. Moreover, results were not presented based on TBI type.

Amongst these studies, some explored onset of early seizures (<7 days), late seizures (>7 days) and post-traumatic epilepsy as a syndrome. This temporal distinction established the convention for classification of early and late seizures.³²⁴ Most studies showed little benefit of prophylactic anti-epileptics in reducing rates of post-traumatic epilepsy, while carbamazepine³²⁵ and phenytoin³²⁴ reduced risk of seizures in the first week in the mixed TBI cohort. Since it is not possible to extricate data on pTBI patients from these publications, none of them were included for the specific evidence-base for pTBI.

In the last iteration of the guidelines for management of severe blunt TBI, a Level IIA recommendation was made for the use of phenytoin to decrease the incidence of early post-traumatic seizures when the overall benefit is felt to outweigh the risks of this treatment.²⁸ It must be borne in mind that administering phenytoin in the ICU to critically ill patients can have side effects. With enteral administration, feeding needs to be paused for 1 hour prior and 2 hours after administration for optimal absorption, and blood levels need to be checked to ensure high therapeutic levels and to avoid toxicity or underdosing. Severe allergic reactions can be seen including rare incidence of toxic epidermal necrolysis. Phenytoin is metabolized by cytochrome P450 and interacts with a long list of medications, which can alter drug levels unpredictably. Lastly, when administered intravenously, cardiac, and hemodynamic risks exist. It is acknowledged that levetiracetam is now commonly used as seizure prophylaxis however literature support for this practice is lacking despite an apparent favorable side-effect profile and neuroprotective properties.^{326,327} Throughout this document, we have made efforts to identify evidence specific to pTBI management.

Scientific Foundation

Early vs late posttraumatic seizures

While there is consensus that a posttraumatic seizure occurring in the first week after injury is considered “early” and subsequent episodes are “late” seizures, this is largely based on non-penetrating TBI literature.³²⁴ Of the 13 articles used to support this update, early seizures were defined by two studies as occurring within the first week and the remaining 11 failed to stratify events by timing of occurrence during hospital stay.

Prophylactic use of anticonvulsants

No studies met criteria for formal inclusion as evidence for this topic. We identified no studies that compared seizure prophylaxis with no seizure prophylaxis or a different seizure prophylaxis in patients with pTBI.

We identified 11 noncomparative studies (N = 1227) that reported the rate of seizures after seizure prophylaxis.^{54,121,165,169,186,195,328-332} Sample sizes ranged from 21 to 520, with most studies having fewer than 100 patients. Six studies were in civilians,^{54,121,186,329-331} while the other five were in military or war-affected populations. Seizure prophylaxis was mainly phenytoin (or diphenylhydantoin) 300 to 500 mg/day for adults and

4 to 7 mg/kg/day in children, when it was reported. One study administered levetiracetam³²⁸ and one study reported administering barbiturates (drug not specified) for seizure prophylaxis,¹⁹⁵ while three studies did not report the type of seizure prophylaxis used.^{54,330,332}

Four studies (N = 207) reported no deaths occurred,^{121,165,329,332} one study (N = 99) reported 5% of patients died within 10 and 15 days of injury,¹⁶⁹ one study (N = 36) reported that five patients died but it was unclear the proportion of patients that died with penetrating injuries,³²⁸ four studies (N = 709) reported between 13% and 23% of patients died within 0 to 3 months,^{54,186,330,331} and one study (N = 176) did not report deaths.¹⁹⁵

Four studies (N = 354) reported that no seizures occurred with diphenylhydantoin or barbiturates given prophylactically,^{165,169,195,329} while other studies reported low rates of seizures (6 studies [N = 795] reported 5% to 14% of patients developed a seizure after prophylaxis,^{121,186,328,330-332} 1 study [N = 78] reported a 28% posttraumatic seizure rate⁵⁴). Three of the studies indicated seizure prophylaxis was continued from the ED,^{54,165,169} while one study initiated seizure prophylaxis in the emergency room only in ventilated individuals.³³⁰ Three studies reported initiating seizure prophylaxis in the ICU,^{121,186,332} while the remaining four were unclear when the medications were initiated.^{195,328,329,331}

Only one small study from Petridis et al included 27 patients with gunshot wounds to the head reported not giving seizure prophylaxis; one patient had symptomatic convulsions after cranial reconstructive surgery, which occurred 6 months after the initial injury, with no seizures experienced in the remaining patients.⁸⁷ The majority of patients had a Glasgow Coma Scale score of 3 to 8 (70%), and the overall mortality was 47%. The authors conclude from this small study that only patients with retained fragments and evidence of epileptiform activity on EEG should receive anticonvulsants.

Atwood et al (N = 36) administered levetiracetam for seizure prophylaxis in Iraq and Afghanistan war veterans, reported two patients with pTBI (5.5%) had a posttraumatic seizure.³²⁸ Both patients suffered a transcranial bihemispheric gunshot wound, whereas most patients who did not have a seizure suffered a blast injury. Both patients who had a posttraumatic seizure eventually died. Although this study did include patients who did not receive seizure prophylaxis, these patients were cleared by neurosurgery for no prophylaxis or had isolated subarachnoid hemorrhage and likely did not have a penetrating injury.

Safety of anticonvulsants

Cosar et al provided a large study (N = 400) which reported harms after prophylactic phenytoin which was administered using an 11 mg/kg intravenous (IV) and a 13 mg/kg intramuscular (IM) parenteral loading dose, and oral maintenance dose (therapeutic blood concentrations of 10-20 mcg/mL) and were followed for 12 to 36 months after surgery.¹⁸² A skin reaction occurred in 11% of patients between 5 and 70 days after surgery, and of those, two patients developed exfoliative dermatitis.

Discussion

The benefit of anticonvulsant medications in the early post injury period with pTBI patients is widely accepted though the risks of antiepileptic drugs must be considered. However, given the risks inherent to phenytoin use in intensive care many now administer levetiracetam given its availability, low cost and improved side-effect profile. However, encephalopathy in geriatric patients and those with renal impairment must still be reason to deliberate.

The evidence presented in the previous guidelines has received further support from subsequently published literature. While this consisted entirely of case studies, the data continue to substantiate administering anticonvulsants to pTBI patients in the first seven days post injury. No new evidence was reviewed to recommend anticonvulsants after one week. In addition, only one study utilized levetiracetam for most patients and had a low incidence of early post-injury seizures; therefore, while there isn't evidence to favor utilizing one medication over another, there is evidence underlying the use of levetiracetam as initial seizure prophylaxis.

Expert Opinion

pTBI patients are at high risk of seizures and at higher risk than patients with blunt TBI. Seizures can precipitate intracranial hypertension or its worsening and cerebral herniation events. Seizure prophylaxis is well established in severe TBI care and is likely even more important in pTBI patients. Injuries to the frontal and temporal lobes are likely more epileptogenic than injuries to other brain regions.

Although phenytoin has traditionally been administered as prophylaxis for TBI patients and has the most evidentiary support, levetiracetam has emerged as the preferred agent in modern practice. Though supportive literature is deficient, levetiracetam seems to be both efficacious and safe – perhaps safer than phenytoin which is associated with risk of very serious complications such as drug interactions, hemodynamic instability and rarely toxic epidermal necrolysis. Interestingly, Operation Brain Trauma Therapy which systematically studied promising pre-clinical

neuroprotective agents, found that levetiracetam was the most promising pharmaceutical studied though relevant human studies are awaited.³²⁷

Our group did not reach consensus related to the duration of anticonvulsant therapy in pTBI nor criteria for the cessation of prophylaxis. The notion of obtaining a neurology consultation and potentially EEG testing prior to cessation of seizure prophylaxis was discussed but did not receive consensus support from the group.

Future Directions

Further high-quality studies are required pertaining to the use of anti-seizure prophylaxis based on injury mechanism and neurological injury, as well as duration of use and procedures for seizure prophylaxis in pTBI patients. Such studies could be readily conducted in environments treating a high volume of pTBI patients. Studies comparing different agents are desirable as well as those exploring differences in best care between blunt and penetrating TBI patients. Some pTBI patients are likely higher risk for seizures such as those with frontal or temporal lobe injuries, bihemispheric or intraventricular injury. It is possible that ideal treatment protocols for such patients may differ from other pTBI or TBI patients. Given that seizure prophylaxis is an entrenched aspect of TBI care there may be ethical challenges inherent to some investigations. Notwithstanding this, with the access to continuous video electroencephalograms with computer tomography and MRI compatible electrodes, another option that may be explored is to use antiseizure treatment when certain electrographic markers of cortical irritability are seen, or actual non-convulsive seizures.

Though clinical trials are needed, comparative effectiveness studies may also be undertaken with propensity matching between cohorts who are routinely prescribed antiseizure medications and those who are not. For this and several other topics in this guideline, the establishment of a penetrating TBI research consortium is essential.

VIII-4 – Antibiotic Prophylaxis

J. Benjamin, B. Dengler, A. Hoffer, H. S. Mangat, G. Rosenthal, D. W. Wright

Recommendations

Level I-II

There is insufficient evidence to support a strong or moderate strength recommendation regarding antibiotic prophylaxis in pTBI.

Level III

Prophylactic antibiotics in patients with pTBI can be considered.

Level IV

No specific antibiotic regimen or duration of treatment has demonstrated superiority for infection prophylaxis in pTBI patients as compared with others.

Level C – Expert Consensus (Delphi Voting)

In the absence of direct scientific evidence, EXPERT CONSENSUS concluded that:

- It is reasonable to treat pTBI patients who have violation of the dura or who are undergoing invasive procedures with prophylactic antibiotics (87.5% consensus).
- It is reasonable to treat patients with pTBI related to blasts, air sinus penetration, retained bone fragments, grossly contaminated objects with prophylactic antibiotics as these are at higher risk of infections (95.8% consensus).
- In pTBI patients at higher risk of intracranial infections it is reasonable to administer broad-spectrum antibiotic prophylaxis (95.8% consensus) including anaerobic coverage (81.8% consensus) for duration of up to 5 days (91% consensus).
- In patients who are NOT at higher risk of intracranial infections it is reasonable to administer antibiotic prophylaxis (87.5% consensus) for duration of up to 3 days (100% consensus).
- When prophylactic antibiotics are administered, they should be administered as soon as possible after injury (100% consensus).

No evidence or expert opinion supported distinct antibiotic recommendations based on patient gender, wounding mechanism, or military vs civilian context.

Introduction

Intracranial infection following pTBI is not uncommon and carries significant morbidity.²¹⁶ There is still a scarcity of data regarding the utility of prophylactic antibiotics for preventing subsequent intracranial infections and informing the optimal timing for the initial administration of these antibiotics. Historically, infection rates were high, and therefore led to routine prophylactic use of antibiotics in such patients, with the belief that antibiotics were ‘essential’ to prevent intracranial infections. However, with improving surgical debridement techniques, rates of infection have been decreasing overall since earlier studies from the World Wars. Moreover, bacteria isolated from pTBI-related infections are different from those obtained when surveillance wound swabs are performed at the time of an initial surgery. In line with this, an expanding body of evidence and experience has begun to question this belief, offering insights into which patients

may face a higher risk and challenging the universal application of prophylactic antibiotics.

The risk of post-pTBI intracranial infection can range from 7% in civilian populations to as high as 25% in military populations.^{188,190} Additionally, complicating the overall infection rate in these patients is a large number who go on to have invasive surgical procedures which can also lead to increased infection rates, making it unclear whether or not prophylactic antibiotics help prevent infections.⁶² There have been no randomized controlled trials evaluating the use of prophylactic antibiotics and the best time for initiation.

Physicians treating pTBI have routinely given prophylactic antibiotics aiming to prevent the increased morbidity and mortality associated with intracranial infections. Historically, this represented broad spectrum of coverage against gram positive, gram negative, and anaerobic bacteria. This has often involved

giving cefazolin 2 gm IV every six to eight hours with the addition of metronidazole and cefepime if there is clear contamination.³³³ Additionally, the time course of the antibiotics and when to start them has been incredibly variable throughout the literature ranging from one to five days. Additionally, multiple studies have evaluated the risk factors for intracranial infection after pTBI and found that continued CSF leak and operative procedures were placing patients at the highest risk of infection.^{62,188} With rising rates of antimicrobial resistance (AMR) within communities globally, it is also important to be good stewards in the use of antibiotic prophylaxis.

Prior Guideline Recommendations

In the prior edition of the guidelines (2001), an 'optional' recommendation (equivalent to a current Level III/IV) was made supporting the prophylactic use of antibiotics in patients with pTBI.²²⁸ Recommendations created in this first edition were based on 14 articles defined as Class III. Level III/IV recommendations stated that *the use of prophylactic broad-spectrum antibiotics is recommended for patients with penetrating brain injury.*

Data supporting this recommendation noted increased rates of infection in pTBI patients with associated CSF leak, air sinus penetration, or retained bone fragments. Use of prophylactic antibiotics for patients with pTBI was an option based on the decrease in infection rate after the onset of routine antibiotic use for these injuries and extrapolation from data on clean, elective neurosurgical cases. In the literature examined for these recommendations (1966-2000), routine use of prophylactic antibiotics and absence of direct comparative studies led to comparison of these data with data from World War I wherein routine infection rate in pTBI patients was 58.5%.²¹⁶ However, in comparison since, the risk of cranial infections has been found to be significantly lower, thought to be due to less contaminated wounds, decreased time to medical care and improved intensity of care. In addition, since all the studies included use of antibiotics and thus did not provide direct evidence in the prior guidelines, they were not included in this edition.

Scientific Foundation

There is scant evidence of benefit from routine use of prophylactic antibiotics in patients with pTBI. We identified no clinical trials that evaluate the use of prophylactic antibiotics, antibiotic regimen, or duration of antibiotics in this setting. The studies that were included are in civilian populations and are summarized below in Table 30. Seven studies are described for use of prophylactic antibiotics, while one study describes duration of use.

The largest study included (Harmon et al) was a retrospective review of 11 years (2006 to 2016) of records from 17 trauma centers in the United States that identified 763 adult patients with penetrating brain injuries, including 62% (N = 475) who were treated with antibiotics within 24 hours of admission.¹⁸⁸ The overall rate of CNS infections was 7% and this was not statistically

significantly different for patients who did or did not receive antibiotics. Another large study of 192 non missile penetrating head injuries treated in one medical center in South Africa published by Harrington et al focused on categorizing management and complications of these injuries and how they differed from gunshot wounds.³³⁴ The authors reported that 33% of the patients received no antibiotics, 52% received antibiotics in less than 24 hours from the time of injury, and 15% received antibiotics more than 24 hours after injury. The rate of infections was significantly lower among patients who received antibiotics at any time compared with those who did not (8% vs 26%, $P = .002$) in both univariate and adjusted models. However, the characteristics of the patients who did and did not receive antibiotics and the variables used in the adjusted model were not reported, as this was not the focus of the study.

Three studies were limited to patients with gunshot wounds. Johnson et al included 75 patients over 16 years old treated in a single U.S. civilian hospital for gunshot wounds to the head, surviving over 48 hours and compared them based on antibiotic regimens: no antibiotics, a single agent, or multiple antibiotics.⁶² In cases from 6 years (2012 to 2018), there were only a total of 8 (10.7%) intracranial infections documented over 1 week to 3 years from injury. There were more infections in patients who received the multiple antibiotics in unadjusted analyses, but in the adjusted analysis, neither the antibiotic group (single antibiotic or multiple antibiotics) nor duration of antibiotic prophylaxis were statistically significant. There were also 13 nosocomial infections reported in this study, but these were also not different across the antibiotic groups and were not associated with later intracranial infections. A study in Colombia followed 160 adult patients with gunshot wounds to the head who did or did not receive prophylactic antibiotics at the discretion of the treating neurosurgeon.¹⁹⁰ A higher proportion of the patients who received antibiotics (33.9%) developed infections than those who did not (19.8%), but this difference was not statistically significant, and receipt of antibiotics was not included in multivariate analysis of risk factors for infection.

Another study by Doherty et al examined patients treated for gunshot wounds to the head in a single trauma center in the United States. It identified 59 patients who survived more than 48 hours.³³⁵ Thirty-eight (64%) were given systemic antibiotics within 36 hours of admission; 26 as preparation for a surgical procedure and 12 without surgery. Twenty-nine percent of these patients developed infections (N = 11), while none of the patients who did not receive antibiotics developed infections.

Two further studies examined routine use of prophylactic antibiotics. Meister et al¹⁹⁸ included 106 military personnel or dependents with pTBI or an open skull fracture while deployed in Iraq or Afghanistan between 2009-2014 and who were treated in US hospitals. Of these only 2 did not receive early (<48 hours from injury) prophylactic antibiotics. Infection rates were 11.3% with a total of 12 infections, all of which occurred amongst those receiving antibiotics. Harrington et al³³⁴ provide data from cranial stab wounds found predominantly in young males with a variety

TABLE 30. Evidentiary Base for Antibiotic Prophylaxis in pTBI

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention (prophylactic antibiotics)	Results	Study risk of bias
Duration of prophylactic antibiotics				
Harmon, 2019 ¹⁸⁸ (NRS) United States 17 trauma centers Civilian GSW: 90% Knife: 6% Nail gun/hammer/arrow: 4%	N = 763 survived >48 h Male: 85% Mean age: 35 y (range 18-90) White: 45% Black: 42% Hispanic: 5% Asian: 1% Other: 7% Mean ISS: 24 (range 1-75) Retained foreign body: 63% Dural penetration Diffuse: 60% Local: 40%	Prophylactic antibiotics: 62% (475) within 24 h of admission Duration of antibiotics None: 36% <24 h: 14% 24-72 h: 21% 3-7 d: 19% >7 d: 10%	CNS infections Total: 7% (51) Antibiotics vs none: 7% vs 6%, $P = .50$ Total mortality: 71% (541/763) CNS infection Died: 8% Survived: 92% No CNS infection Died: 75% Survived: 25% $P = .006$ Timing of infection diagnosis 1-4 d: 4 (8%) 5-10 d: 11 (21%) >10 d: 32 (63%) Unknown: 4 (8%)	Moderate
Johnson, 2021 ⁶² (NRS) United States Civilian GSW: 100%	N = 75 survived >48 h Males: 84% Median age: 30 y (IQR 20-45) White: 48% Black: 48% Other, not specified: 4% Median GCS: 10 (IQR 6-15) Median ISS: 25 (IQR 13-30) CSF leak: 8% Surgery: 41.3% Tangential injuries: 32%	Prophylactic antibiotics None: 13 (18%) Single: 28 (37%) Multiple: 34 (45%) 5-day median duration Most common 69% cephalosporins 43% vancomycin Initial median (IQR) GCS None: 15 (13-15) Single: 10.5 (6.8-15) Multiple: 8 (6-13.8) Surgical intervention None: 7.7% Single: 28.6% Multiple: 64.7%	Intracranial infections: 8 None vs single vs multi Unadjusted: 1 vs 1 vs 6, $P = .019$ Antibiotic duration, $P = .42$ Survival at 6-mo: 53.8% (7) vs 67.9% (19) vs 44.1% (15), $P = .422$ Multivariable logistic regression (included demographics, GCS, ISS, injury characteristics, comorbidities) Antibiotic group and duration: NS Infection associated with CSF leak and diabetes 75% gram positive Nosocomial infections (13): 1 vs 6 vs 6, $P = .556$ Agent used $P = .8$, duration $P = .18$ Nosocomial not related to later intracranial infection, $P = .621$	Moderate
Jimenez, 2013 ¹⁹⁰ (NRS) Colombia Civilian GSW: 100%	N = 160 Male: 91% Mean age: 29 y (range 15-61) Rural: 26% GCS ≥ 9 : 66% GCS ≤ 8 : 34%	Prophylactic antibiotics: 36.8% (59) No antibiotics: 63.2% (101) Based on decision of treating neurosurgeon; all surgery patients Ceftriaxone: 36% Cephadrine: 19% Ampicillin/sulbactam: 19% Mean follow-up: 39 mo (range 3-92)	Intracranial infections: 25% (40) With antibiotics vs without: 33.9% (20/59) vs 19.8% (20/101), NS (not included in multivariate analysis) Good (GOS 4-5): 59% vs 54% Bad (GOS 1-3): 41% vs 46% 3 variables significantly associated with infection 1. Presence of fragments post-surgery on CT 2. Projectile trajectory through natural orifices 3. Hospital stay >4.5 d 95% of infections emerged within 30 d	Moderate

TABLE 30. Continued.

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention (prophylactic antibiotics)	Results	Study risk of bias
Doherty, 2004 ³³⁵ (NRS) United States Civilian GSW: 100%	N = 59 survived >48 h Male: 86% Mean age: 29 y (range 2-76) GCS 3-5: 10% GCS 6-8: 12% GCS 9-12: 17% GCS 13-15: 61% Local irrigation, debridement: 40 (68%) Craniotomy, local debridement: 11 (19%) Craniotomy, extensive debridement: 4 (7%) Craniotomy, hematoma evacuation: 4 (7%)	Prophylactic antibiotics within 36 h of admission: 38 Related to a surgical procedure: 26 (44%) Without surgery: 12 (20%) Any antibiotics: 53 (90%) 10 additional >36 h after admission Topical only: 5 Cefazolin was most common (numbers not reported)	0 infections in 11 patients with no antibiotics Infections in 38 patients with prophylactic antibiotics CNS: 3 IVC: 2 Initial wound: 1 Type NR: 5 8 infections in the 10 patients who received later antibiotics IVC infections: 4 Prophylactic antibiotics: 2 None: 2 Injuries to air sinuses (risk factor for infections): 7 Required Camino catheter monitors: 2 Both treated with antibiotic 2-7 d (unclear if both prophylaxis and treatment) Tracheobronchitis: 1 Died intraabdominal abscess and sepsis: 1	High
Meister, 2023 ¹⁹⁸ (NRS) Injured in Iraq and Afghanistan; treated in U.S. hospitals Military GSW: 37.7% Blast: 56.6% Other: 5.7%	N = 106 Male: 100% Median age: 25 y ISS 16-25 (severe): 4.7% ≥26 (critical): 95.3% Retained fragments: 73.6%	Early antibiotics (within 48 h post-trauma): 104 Did not receive antibiotic: 2	CNS infections: 11.3% (12/106) Meningitis/ventriculitis: 10 Brain abscesses: 3 Epidural infections: 3 Encephalitis: 2 Infections in Patients given antibiotics 11.5% (12/104) Patients not given antibiotics: 0% (0/2)	High
Harrington, 2020 ³³⁴ (NRS) South Africa Civilian Assault: stab wounds Knife: 81% Screwdriver: 9% Nail gun: 0.5% Garden fork: 0.5% Barbeque fork: 0.5% Unknown: 8%	N = 192 Male: 96% Mean age: 26.2 y (range 18- 58) GCS 15: 37% GCS 12-14: 34% GCS 9-11: 14% GCS 7-8: 8% GCS 4-6: 6% GCS 3: 1% Weapon in situ Yes: 18% No: 82%	Prophylactic antibiotics None: 33% (64) <24 h: 52% (99) >24 h: 15% (29) Time from injury to antibiotic administration, as presented in article	Total infections: 14% (27) Antibiotics vs none Univariate: 8% vs 26%, $P = .002$ Adjusted (variables included not specified): OR 0.3 (95% CI 0.1-0.8), $P = .02$ Types of infections Abscess: 41% Meningitis: 30% Empyema: 15% Wound infection: 7% Abscess/empyema: 4% Ventriculitis 4%	High

TABLE 30. Continued.

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention (prophylactic antibiotics)	Results	Study risk of bias
Extracranial infections				
Marut, 2020 ³³⁶ (NRS) United States Civilian GSW: 94% Stab wound: 6%	N = 33 Male: 82% Mean age: 32 y White: 85% Black: 15% Severity: NR Retained metal fragments: 70%	Received ≥1 dose: 24 Did not receive antibiotic: 9 Median time to administration: 52.8 min (IQR 18-120) Median duration: 24 h (IQR 7-84) Cephalosporin First generation: 58% Second generation: 4% Third generation: 38% Other beta-lactams: 17% No beta-lactams: 8%	Infections CNS: 0 Skin: 0 Soft tissue: 0 Pneumonia: 12% (4) Mortality: 33% Neither mortality nor infection (pneumonia) reported by whether the patient received an antibiotic or not.	High
Duration of prophylactic antibiotics				
Etheridge, 2017 ³³⁷ (NRS) United States Civilian GSW: 100%	N = 22 Male: 95% Mean age: 28.3 y (range 18 to NR) Mean GCS: 10.15 Mean ISS: 18.98 Urgent operation: 77.3% Managed medically: 22.7%	Short-term ≤48 h: mean 1.2 d (9) Extended >48 h: mean 6.3 d (13)	Short-term vs extended CNS infections: 0 vs 30.8% (4), $P = .066$ 1 meningitis, 1 intracranial abscess, and 2 suspected meningitis 30-day all-cause mortality: 11.1% (1) vs 7.7% (1), $P = .784$ No multidrug resistant infections	Moderate

CI, confidence interval; CNS, central nervous system; CSF, cerebrospinal fluid; CT, computed tomography; GCS, Glasgow Coma Scale; GOS, Glasgow Outcome Scale; GSW, gunshot wound; IQR, interquartile range; ISS, Injury Severity Score; IVC, intravascular catheter; MOI, mechanism of injury; NR, not reported; NRS, non-randomized study; NS, not significant; OR, odds ratio; US, United States.

of weapons ranging from knives (81%), screwdrivers (9%) to garden forks etc. with 18% having retained weapon. No antibiotics were administered to 33% (64), in less than 24 hours in 52% (99) and later than 24 hours in 15% (29). Intracranial infections were seen in 8% of those who received antibiotics at any time and 26% in those who did not receive any antibiotics, with an adjusted odds ratio of 0.3 (95% CI 0.1-0.8) in favor of antibiotics. This study included a majority of penetrating injuries from knives which tend to occur infrequently in clinical practice and may differ from other penetrating injuries due to contamination of knives.

In regard to extracranial infections, a non-randomized study by Marut et al reviewed charts of patients with penetrating brain injuries treated at a single Level 1 trauma center in Northeast Ohio (U.S.) from December 1, 2015 through July 31, 2018.³³⁶ Patients were included if they were over 16 years old and were not transferred to a pediatric institution or transferred from another facility 24 hours after presentation. The primary objective was to determine what proportion of patients received prophylactic

antibiotics to inform quality improvement. Thirty-three patients were included and 24 (73%) received antibiotics with a median time to administration of 52.8 minutes from admission and a median duration of 24 hours. There were no nervous system, skin, or soft tissue infections during the hospital admission, but four patients (12%) were treated for pneumonia. Thirty-three percent of the patients died. Neither the pneumonia cases nor deaths are reported by whether the patient received an antibiotic or not.

Etheridge et al provided the one study on the duration of antibiotics that was identified, and used a registry from one trauma center to identify a small sample (N = 22) of adult patients with penetrating gunshot wounds to the head who received short-term prophylactic antibiotics, for 48 hours or less (N = 9) or extended treatment for over 48 hours (N = 11).³³⁷ In follow-up that lasted for a mean of 15 months, no infections occurred in the patients with short-term treatment and four patients (30.8%) developed infections in the extended treatment group. One patient in each group died within 30-days of any cause and neither infection nor mortality were statistically significantly different,

however, the study was not sufficiently powered to detect a difference in infection rates.

Studies not Included in Evidence Synthesis

Below are several case series that did not meet criteria for inclusion in evidentiary tables but are described:

Jankovic (1997) and Hecimovic (2000) and Tudor (2005) report case series from the Croatian War (1991 to 1994).^{189,195,212} In all three, the authors state all patients were given prophylactic antibiotics as part of initial emergency treatment, according to policy, but few additional details are provided and no information is given on patients who did not receive antibiotics. One study (N = 138) reviewed the cases of Croatian soldiers treated for penetrating intracranial injury that focused on the role of computer tomography in diagnosis and treatment.¹⁹⁵ In the 138 soldiers given prophylactic antibiotics, nine (6.5%) developed infections, including eight with meningitis/cerebritis and one abscess; four of whom died. In another study (N = 88) of patients treated for missile brain wounds at a university hospital, 15 (17%) developed infections: meningitis alone (4 patients), abscess alone (3 patients), cerebritis alone (1 patient), meningitis plus abscess (4 patients), and one patient each developed meningitis plus subdural empyema, meningitis plus abscess plus osteomyelitis, and meningitis plus abscess plus epidural empyema.¹⁹⁵ Eight of the 15 patients died (53.3% of those who developed infections) and two additional patients had poor outcomes (Glasgow Outcomes Scale score of 3). In 176 patients treated for penetrating craniocerebral injuries at a different university hospital where all were given routine antibiotic therapy on admission, 28 patients (15.9%) developed infections; 13 were superficial and 15 (8.52%) were CNS infections (meningitis, meningoencephalitis or ventriculitis).²¹² Reoperations were required for 60% of the patients with CNS infections.

The two additional case series were from the Iran-Iraq war. One study (N = 125) compared patients treated from April 1983 to November 1984 based on whether there was operative exploration, then if primary debridement was definitive or if a secondary exploration was needed.¹⁶⁰ All patients were started on antibiotics at the casualty clearing station, seven developed infections; six meningitis, one a brain abscess, and one a brain abscess and meningitis. Mortality for patients with infections was 23% (2 of 7). None of the patients with positive early cultures of the wound, bone, or brain developed infections. In a study of patients at the same hospital from February 1981 to August 1987, 397 patients with dural penetrating missile head wounds were followed after primary debridement and closure who had antibiotics started at the frontline and continued for 10 days after surgery.¹⁸⁵ Eighteen patients developed infections; 16 patients developed meningitis, one patient an abscess, and one patient developed both meningitis and an abscess. Twelve of these 18 patients had cerebrospinal fluid fistulas. Seven (38.8%) of the patients with infections died, one was lost to follow-up, and two had minimal, six moderate, and two with severe disability at follow-up (23.7 ± 11 months).

One case series reported 32 missile injuries to the brain were treated between 1981 and 1988 during the Lebanese conflict.¹⁶⁵ Patients were selected who were neurologically stable with a Glasgow Comas Scale score greater than 10, examined within 6 hours of the time of injury, with an entry wound less than 2 cm, no exit wound, missile tract that did not cross the proximal sylvian fissure, no epidural or subdural hematoma, and no intracerebral hematoma that enlarged or measured more than 4 cm. Patients were given 1 g of methicillin on arrival and continued for 14 days. Their wound was debrided and closed in the ED without drainage. One patient (3.1%) developed a brain abscess indicated by a seizure and left hemiparesis 20 days after injury. The abscess was excised, treatment included three weeks of cefotaxime and the patient recovered.

In another case series (N = 82) of patients with penetrating gunshot wounds treated at an urban U.S. hospital from 1973 to 1975, all patients received antibiotics (oxacillin 2 g, ampicillin 2 gm) with resuscitative measures on admission.⁷³ Thirty-seven patients did not undergo an operation, of whom 34 died, and three patients with more minor injuries recovered. The 45 patients treated with surgery were the subject of infection surveillance: two developed meningitis and none had brain abscesses. Two patients had scalp infections and 13 patients with retained fragments had no infections during the 3.5-year follow-up period.

Together these studies provide low strength of evidence that routine prophylactic antibiotic administration following pTBI makes no significant difference in infection rates compared with no antibiotics.

Discussion

The use of prophylactic antibiotics has long been thought to potentially be beneficial after pTBI in order to prevent intracranial infections due to dural penetration, even though there has been lack of evidence to support this. Furthermore, studies have shown that early bacteriological swab isolates do not correlate with bacteria causing subsequent intracranial infections. Despite the significant morbidity and mortality associated with pTBI and the consequent infections, current evidence is insufficient to provide a strong recommendation for the routine use of prophylactic antibiotics.

In the above studies there was little evidence to support the routine use of antibiotics following pTBI. However, the landscape of pTBI has also changed significantly, from highly contaminated wounds in WWI to shrapnel injury in warfare. Meanwhile, civilian epidemiology of pTBI varies by regions; in US the commonest cause of pTBI being gunshot wounds which have a lower incidence of infections, compared to farm or other handheld metal objects in other countries. While intracranial infections can be fatal, AMR also poses an important problem. This was witnessed in the COVID pandemic which saw an associated jump in incidence of AMR due to routine use of antibiotics to treat viral pneumonias.

The available evidence limited the recommendations that could be generated for penetrating brain injuries. Delphi consensus was

thus used to bridge available evidence with the need to make clinical decisions.

All studies that have attempted to look at rates of infection and use of prophylactic antibiotics in pTBI were retrospective. The heterogeneity of injuries, the process of decision-making for the administration of antibiotics, and which antibiotics were selected for use are all significant sources of bias in these studies. Whether the patients who received prophylactic antibiotics were actually at high risk of infections remains undetermined. For example, pTBI from blast injuries as opposed to gunshot injuries are at high risk of contamination, retained fragments, and resulting infection. This additional selection bias must also be taken into account when considering the results of these studies, as they limit the external validity of some findings. Of note, in the main supportive study, there was a significant delay in presentation for many patients. Furthermore, no study described complication rates specifically associated with antibiotic use. While some patients with pTBI may have other systemic injuries that could predispose to toxicity of antibiotics, there is no reason to assume that the head injury itself would do so.

Expert Opinion

Prophylactic antibiotics are a complex issue in neurotrauma. While pre-procedural antibiotics are now a standard of care for surgical procedures, there is concern that they do not reduce the rate of infection in patients with CSF leaks nor do they reduce the risk of ventriculitis in patients with external ventricular drains in situ. There is concern with these latter indications that they may lead to infections with antibiotic resistant bacteria and that they could provoke *clostridium difficile* diarrhea/pseudomembranous colitis. Post-insult antibiotic prophylaxis was recommended for patients with pTBI in the first pTBI guidelines making such an application of prophylactic antibiotics after an event unique within neurotrauma.²²⁸ Here we have revisited this recommendation.

On balance with one study suggesting some benefit¹⁹⁸ of prophylactic antibiotics for pTBI, the expert panel decided that a consensus would be helpful in addressing risk-stratification of patients for the use of prophylactic antibiotics. High risk patients

were considered by expert consensus to be those with violation of dura, patients who are undergoing invasive procedures, air sinus penetration or retained contaminated objects/fragments. The consensus concluded that it is reasonable to utilize prophylactic antibiotics in high-risk patients with the goal of reducing the risk of infection. Along the same lines, consensus on prophylactic antibiotic use was obtained on TBI-related blast injuries where air sinus penetration occurs, or there are retained bone fragments of penetration from grossly contaminated objects.

To make a comprehensive consensus recommendation, we also reviewed type of antibiotics to be used, and when they were used. The consensus was that if prophylactic antibiotics were to be used, the choice should be in favor of broad-spectrum antibiotics including anaerobic coverage and for a duration of up to 5 days in high-risk patients and up to 3 days in low-risk patients. Finally, consensus was clear on when prophylactic antibiotics were utilized, they should be administered as soon as possible.

Future Directions

In the face of critically rising AMR, and the balance of immediate benefit to patient but delayed societal harm, further research into the routine prophylactic antibiotic use in pTBI patients is required. It would be easy to conduct relevant studies in centers treating a high volume of pTBI; this guideline suggests that it would not be unethical to withhold prophylactic antibiotics for such investigations. Key elements are classification of contamination in civilian and combat settings, which constitute different phenotypical injuries, and subsequent risk-stratification for the development of intracranial infections following pTBI. This can also be performed by large registries and observational studies, for which data may already exist in national databases.

Randomized controlled trials provide very valuable information. Given that the incidence of civilian pTBI from firearms is rising it may, however, be more efficient to perform these studies by cohort or comparative effectiveness methods. Specific areas of research required remain the utility of prophylaxis vs early treatment, the type of antibiotics i.e broad-spectrum vs narrow spectrum, the timing and importantly duration of prophylaxis.

VIII-5 – Venous Thromboembolism Prophylaxis

O. Harris, A. Hoffer, H. S. Mangat

Recommendations

Level I-III

There is insufficient evidence to make a strong, moderate strength, or weak recommendation related to the benefits and harms of venous thromboembolism (VTE) prophylaxis.

Level IV

Early initiation of pharmacological VTE prophylaxis within 48 hours of injury may be considered in adult patients with penetrating TBI who have not suffered an increase in incident hemorrhage volume without increasing the risk of consequent intracranial hemorrhage, emergent reoperation, or death. There is, however, insufficient evidence of efficacy and insufficient evidence to make recommendations about the choice of pharmacologic agent, time to initiation, dosage, and duration for VTE prophylaxis.

Level C – Expert Consensus (Delphi Voting)

In the absence of direct scientific evidence, EXPERT CONSENSUS concluded that:

- Mechanical VTE prophylaxis should be considered for all adult patients with pTBI. (100% consensus)
- VTE chemoprophylaxis may be considered for all adult patients with pTBI 24 - 48 hours after cranial surgery and/or stable hemorrhage on CT scan. (96.7% consensus)

No evidence or expert opinion supported distinct recommendations based on patient gender, wounding mechanism, or military vs civilian context, or for pediatric age groups.

Introduction

The optimal type and timing of VTE prophylaxis is insufficiently understood across the breadth of TBI. It is a particularly deficient and underexplored area of critical care for pTBI patients. pTBI patients may be at higher risk of both VTE and hemorrhagic complications given the extent of brain tissue and vascular injury which these patients experience. Traumatic injury is well known to activate tissue factor and induce coagulopathy, whereas confinement in ICU limits mobility increases risk of deep venous thrombosis and VTE. Moreover, TBI severity increases risk of venous thrombosis, and presence of extracranial injuries further adds significantly to this risk.^{338,339} Defense forces must often transport patients long distances in acutely injured conditions, likely predisposing to unique VTE risks distinct from those faced by civilian patients.

Accurate diagnosis of DVT and VTE is also complex. If routine screening or high suspicion is not present, diagnosis of asymptomatic venous thrombosis may be missed. In the CRASH2 trial of 13,273 patients, tranexamic acid did not increase risk of symptomatic DVT or VTE and overall rates were low (0.9%) though patients were not routinely screened.^{340,341}

Prior Guideline Recommendations

The prior edition of the pTBI guidelines (2001) did not endeavor to review or report on this topic.¹⁶

Scientific Foundation

The data on VTE prophylaxis in pTBI is sparse. We identified one small retrospective study (N = 67) of army blast victims published by Meyer et al that compared early VTE chemoprophylaxis in military patients injured in Afghanistan with no prophylaxis¹⁰⁶ (Table 31). The authors defined early prophylaxis as within 48 hours post-injury and the majority of patients received 30 mg of enoxaparin (91%) twice daily. Early prophylaxis was associated with a 5% absolute risk reduction in DVT/PE though this difference was not statistically significant. In this study early prophylaxis was not associated with either an increased incidence of hemorrhage expansion or change in the rate of VTE. There was also no association with increased rates of emergent reoperation or 30-day mortality. This study provides very low strength evidence that early deep vein thrombosis (DVT) prophylaxis results in little change in likelihood of VTE incidence, while 30-day mortality, likelihood of intracranial hemorrhage, and likelihood of emergent reoperation were not increased. This cohort was 100% male and military which limits generalizability. Additionally, the study was underpowered to demonstrate a difference between early prophylaxis and no prophylaxis for these outcomes and a larger study may have different findings.

Discussion

As demonstrated above, data on VTE prophylaxis specific to pTBI is severely lacking. Only one study met inclusion criteria as

TABLE 31. Evidentiary Base for Venous Thromboembolism Prophylaxis

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Study risk of bias
Meyer 2017 ¹⁰⁶ (NRS) Afghanistan Military GSW: 22% Blast: 78%	Male: 100% Mean age: 25 y (range 19-38) GCS: 10.3 vs 8.3 ISS: 24.8 vs 27.7 AIS: 3.8 vs 4.1	DVT prophylaxis: 32, 91% received enoxaparin 30 mg twice daily; 7% received UFH 5000 U thrice daily; time to first dose 24.5 h and 17.7 h, respectively No DVT prophylaxis: 35	30-day mortality: 3% vs 9%, aRR ^a 1.50, 95% CI 0.07-34.0 DVT or PE: 12% vs 17%, aRR ^a 0.88, 95% CI 0.20-3.93 Worse ICH: 16% vs 29%, aRR ^a 0.56, 95% CI 0.17-1.85 Incident-worsened ICH: 16% vs 17%, aRR ^a 0.76, 95% CI 0.21-2.79 Non-elective reoperation: 3% vs 9%, aRR ^a 0.72, 95% CI 0.06-8.71	High

AIS, Abbreviated Injury Scale; aRR, adjusted relative risk; DVT, deep vein thrombosis; GCS, Glasgow Coma Scale; GSW, gunshot wound; ICH, intracranial hemorrhage; ISS, Injury Severity Score; NRS, non-randomized study; PE, pulmonary embolism; U, units; UFH, unfractionated heparin.

^aAdjusted for GCS, ISS, AIS.

detailed above. As a retrospective study, it is biased; it is unknown whether the patients who received VTE prophylaxis were deemed low risk for intracranial hemorrhagic complications. The sample size is small and underpowered. Furthermore, the study includes only male patients. Use of oral contraceptives is associated with increased thrombotic events, and it is quite possible the risk-benefit profile for females is quite different than men.

Given the paucity of evidence informing VTE prophylaxis in pTBI, it is necessary to consider data from the study of blunt TBI patients. Post-hoc analysis of data from the Erythropoietin in TBI (EPO-TBI) study³³⁹ which excluded pTBI patients demonstrated a risk of deep venous thrombosis (DVT) of 16.9% and pulmonary embolism risk of 4%, with a median time to diagnosis of 6 days. 91% of these patients received mechanical prophylaxis on day 1, 97% by day 3, and 98% by day 7. 5% of patients had received chemoprophylaxis for VTE by day 1, 30% by day 3, and 57% by day 7. As per study protocol they all underwent twice weekly lower limb ultrasound screening for DVT. Of note, in this study development of VTE was not associated with increased mortality. However, it must be noted that this protocol of surveillance nor chemoprophylaxis is not routine in clinical practice.

Pediatric patients with TBI are also at risk of VTE. The BTF's pediatric TBI guidelines do not provide recommendations related to DVT prophylaxis;²⁹⁸ the decision to prescribe VTE prophylaxis in pediatric patients is more controversial than in adults. In a pediatric general trauma population of 753 children, DVT rates were 8.9% and PE rates of 0% while 0% developed DVT on chemoprophylaxis.³⁴² TBI was a risk factor for VTE in this study. Treatment of diagnosed venous thrombosis was not associated with improved VTE outcomes, however. We did not find any evidence informing VTE prophylaxis in pediatric pTBI patients.

In comparison, the BTF's parent adult coma guidelines make a level 3 recommendation that "Low molecular weight heparin (LMWH) or low-dose unfractionated heparin may be used in combination with mechanical prophylaxis. However, there is an increased risk for expansion of intracranial hemorrhage".²⁸ However, compared to blunt TBI, pTBI is known to be associated with greater incidence of coagulopathy, and more prevalent neurovascular injuries. While this recommendation is inherently applicable to pTBI as written, is uncertain whether practitioners should consider modifying their practice in light of the unique risk profile of pTBI patients.

Expert Opinion

VTE are a significant source of morbidity and mortality in TBI patients. This pathology is particularly sinister as it often occurs just as a patient is beginning to show clinical improvement. Over the last decade there has been a shift to increasingly aggressive prophylaxis with earlier initiation of pharmacoprophylaxis. We feel that before initiating pharmacoprophylaxis repeat CT head imaging demonstrating stability of intracranial hemorrhage is advisable when resources allow. Neurosurgeons are increasingly comfortable initiating pharmacoprophylaxis 24-48 hours after surgery and some report doing so within 24 hours. Many neurosurgeons prefer unfractionated heparin for DVT prophylaxis because of perceived lower risk for hemorrhagic complications than LMWH as well as the ease of instantaneous reversal with protamine if hemorrhagic complications are encountered.

Physical methods of DVT prophylaxis are safe and effective and should be liberally employed. Nothing in medicine is truly benign, however – beware of common peroneal nerve injuries from excessive pressure on the fibular head when this method is used. There are few contraindications to the use of anti-embolic

stockings but such examples of contraindications could include associated limb injury, thrombosis, infection, etc.

Future Directions

VTE prophylaxis is relevant to every blunt TBI and pTBI patient and should be facile to study. Prospective randomized or comparative effectiveness studies should be easy to complete, though a multi-center approach would likely be necessary to have adequate sample size and power for such an investigation in pTBI patients. These studies would likely be low-cost to perform and could achieve very high impact given the paucity of

evidence currently available to guide decision making. While hemorrhagic complications are easily detected in most instances, VTE can be occult so there would need to be careful decision-making related to the aggressiveness with which VTE will be sought and diagnosed. Key questions to be answered are the optimal agent and the optimal timing for prophylaxis. It is important to understand if optimal care of pTBI patients differs from patients with blunt TBI and whether all pTBI patients should be managed uniformly. Given the rising rates of pTBI as a public health problem, such a prospective study is not only feasible but essential.

VIII-6 – Timing of Organ Donation

O. Harris, H. S. Mangat, D. M. Stein

Recommendations

Level I-IV

There is insufficient evidence to support an evidence-based recommendation on the timing of organ donation.

Level C – Expert Consensus (Delphi Voting)

In the absence of direct scientific evidence, EXPERT CONSENSUS concluded that:

- After declaration of death by neurologic criteria following pTBI, organ donation should proceed as soon as organ function has been optimized to maximize organ function in recipients. (93.3% consensus)

No evidence or expert opinion supported distinct recommendations based on patient gender, wounding mechanism, or military vs civilian context.

Introduction

A nihilistic approach to pTBI is highly discouraged. However given the severity of brain injury that is often inherent to pTBI, many pTBI victims will progress to death by neurological criteria. Thus end of life care is an important topic in pTBI care.

The Uniform Determination of Death Act was approved by the American Medical Association in 1980 and the American Bar Association in 1981.³⁴³ It defines death as either the irreversible cessation of all brain functions including the brain stem, or the irreversible cessation of circulatory and respiratory functions. Though the law has been adopted in all states, medical standards used to determine neurologic brain death vary slightly amongst jurisdictions and institutions.

Every effort should be made to aggressively treat patients per best practice guidelines until a judgement is made by an experienced provider that such treatment is, in fact, futile or the patient has lost all neurological function. When death by neurological criteria occurs, it must be remembered that this tragedy affords the opportunity to fulfill prior stated wishes for organ donation

amongst many critically ill patients, to save other lives. Organ donations from heart-beating and non-heart beating donors serve a multitude of transplant recipients with acute or chronic organ failures. For optimal success, transitions of care from aggressive care to end of life care must be smooth, streamlined and carefully organized, coupled with providing support to the patients' near and dear ones.

Prior Guideline Recommendations

The previous guidelines do not provide any recommendations for timing of organ donation following pTBI and there was no attempt to address this topic.¹⁶

Scientific Foundation

We found no studies that specifically addressed this question in patients with penetrating TBI which could be formally included as evidence. However, there were a few studies that attempt to address the issue of timing of organ donation following declaration of brain death in the broader TBI population that included

some pTBI patients (Table 32). We decided it was appropriate to include these manuscripts as formal evidence for this question given the absence of alternatives. Two non-randomized studies mentioned the timing of organ donation, interventions to stabilize patients for better outcomes of organ donation or greater number of organs donated prior to death by neurologic criteria caused by a head injury.^{344,345}

Kogan et al published a non-randomized study of 173 patients in Israel receiving heart transplants over a 20-year period (1997 to 2017). Some of the brain dead donors succumbed to TBI.³⁴⁴ The study reported 10-year survival of recipients was similar between short and long time interval groups based on the median time from injury to brain death, from brain death to aortic cross-clamp in donors, and time from donor aortic cross-clamp to unclamping in the recipient. The study reported no differences in the rate of 10-year survival and no major adverse events when the time from injury to declaration of brain death was less than 97 hours or 97 hours and longer. For these groups, the study also reported no differences in in-hospital mortality or the mean total rejection score of recipients. In addition, the study reported there were no differences in the rate of survival without rejection in any of the groups but did not report the specific data. This study does suggest that delaying donation until the patient is hemodynamically stable may not worsen recipient outcomes.

Resnick et al investigated nearly 300 brain dead donors in a retrospective analysis of the Gift of Life database, which serves parts of Pennsylvania, New Jersey, and all of Delaware. The donors were identified between 2011 and 2015 and all were reported to have progressed to brain death following a head trauma.³⁴⁵ Twenty-eight per cent had a penetrating injury. The aim of the study was to determine if organ procurement should be delayed allowing for more donor management goals to be met. Based on the stated national goal for organ donation to be 3.75 organs transplanted per donor, the study compared characteristics of donors who donated more than four organs with those who donated four or less organs. For the donor management goals, four of the seven goals showed no differences between groups in the percent who met that goal. The study reported significantly shorter mean time, for those who donated more than four organs, from admission to declaration of brain death and between admission and organ procurement with those who donated four or less organs, however there was no difference in the time between declaration of brain death and organ procurement. This study suggests that a shorter time from admission to brain death and from admission to organ procurement is associated with a greater number of organs donated, but numbers of organs donated was not associated with time from brain death to organ procurement.

In a report of three cases of gunshot wounds to the head published by Aiyagari et al,²⁹⁷ two male patients ages 27 and 33 years old with Glasgow Coma Scale scores of “2T” and active bleeding were managed to allow organ donation.²⁹⁷ Two of the patients progressed to brain death despite aggressive efforts to correct coagulopathy. One donated his left kidney, pancreas, heart, and liver while the other donated his left and right kidneys,

heart, and liver. After 8-10 months of follow-up recipients of the organs were doing well, with the exception of one patient who died due to noncompliance with medication.

We judged the body of evidence insufficient to generate even very low strength evidence-based recommendations. We do acknowledge, however, that these studies provide some evidence that a shorter time (mean 35 hours vs 53 hours) from brain trauma to brain death is associated with more organs donated but a shorter time (median <97 hours vs >97 hours) is not associated with recipient mortality or organ rejection. There was no difference in number of organs donated and recipient outcomes based on time from brain injury to organ procurement, however. We also note that one study provided evidence that more organs are transplanted when independent donor goals of cardiac ejection fraction greater than 45% and PaO₂:FiO₂ greater than 300 are met which suggests that waiting for organ procurement until the patient is hemodynamically stable may be preferred. In these studies lack of adjustment for differences in baseline donor characteristics between patients who donated more than four organs and those who donated fewer organs may have introduced bias.

Discussion

As there is no data to guide the timing of organ donation following declaration of death by neurological criteria specific to patients with penetrating TBI, extrapolation from other donor populations implies that proactive organ donor management should be attempted and that longer times from declaration of death to donation do not necessarily result in adverse outcomes for recipients. The recommendations within this document are limited to expert opinion but are consistent with other published guidelines.³⁴⁶⁻³⁴⁸ The main impetus to wait to proceed with organ donation following declaration of death by neurological criteria is to allow for the physiological derangement that occurs following brain death to be mitigated by organ donor management. Organ donation following donation after cardiac death from termination of futile care is somewhat different as there are set ischemic times following onset of terminal hypotension and / or hypoxia.

There are a number of physiological derangements that occur following progression to death by neurologic criteria as a result of loss of central regulatory mechanisms. This results in significant alterations in hemodynamics, endocrine function, and temperature.^{349,350} Frequent complications of brain death include, but are not limited to hypotension, hypothermia, diabetes insipidus, coagulopathy, hyperglycemia, arrhythmias, and respiratory failure.^{346,349} In order to optimize recipient outcomes, the process of organ donor management is recommended whereby specific goals for organ function are attempted.^{351,352} There are also several variations in donor management goals, which may be based on organ procurement organization or medical institution policy.^{352,353}

Examples of donor management goals are³⁵³:

- Mean arterial pressure, mm Hg: 60-110
- Central venous pressure, mm Hg: 4-12

TABLE 32. Evidentiary Base for Timing of Organ Donation^a

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Study risk of bias
Kogan, 2019 ³⁴⁴ (NRS) Israel Civilian MOI: NR	N = 173: heart transplant recipients from donors with penetrating and closed head injuries or definable intracranial bleed that progressed rapidly to brain death Male: 72% Mean age: 32.5 y	Short BIT ^a (<97 h): 87 Long BIT ^a (≥97 h): 86 Short BDI ^b (<12 h): NR Long BDI ^b (≥12 h): NR Short and long allograft ischemia time ^c based on overall median, but exact time NR Short and long total injury time ^d based on overall median, but exact time NR	Short BIT vs long BIT, recipient outcomes In-hospital mortality: 8.4% vs 14.3%, $P = .33$ 10-y survival: 58% vs 78%, $P = .102$; HR 1.12 (95% CI 0.80-1.44) 10-y survival and free of major adverse events: 43.2% vs 51.8%, HR 1.17 (95% CI 0.78-1.15) Mean total rejection score (SD): 0.45 (0.38) vs 0.39 (0.36), $P = .46$ 10-y survival in recipients (sample sizes for these groups NR) Short BDI vs long BDI: 56% vs 69%, $P = .172$ Short allograft ischemia time vs long allograft ischemia time: 70% vs 75%, $P = .607$ Short total injury time vs long total injury time: 65% vs 74%, $P = .213$ Survival free of rejection similar for all time intervals, data not reported	Low
Resnick, 2017 ³⁴⁵ (NRS) United States Civilian MOI: NR	N = 297 brain dead secondary to head trauma Male: 79.1% Mean age: 36.0 y Penetrating: 27.9%	Donated >4 organs: 123 Donated ≤4 organs: 174	Donated >4 organs vs ≤4 Donor management goals met ≤1 vasopressor used: 84.6% vs 75.9%, $P = .08$ MAP >60 mm Hg: 89.4% vs 88.5%, $P = .85$ Ejection fraction >45%: 91.1% vs 65.5%, $P < .001^e$ Sodium <155 mEq/L: 87.0% vs 91.4%, $P = .25$ Glucose <150 mg/dL: 25.2% vs 26.4%, $P = .89$ Average urine output (0.05-3 mL/kg/h): 53.7% vs 66.7%, $P = .03$ PaO ₂ :FiO ₂ ratio >300: 79.7% vs 36.2%, $P < .001$ Comorbidities >4 organs vs ≤4 organs Diabetes: 1.6% vs 7.5%, $P = .03$ Hypertension: 6.5% vs 22%, $P < .001$ Distribution of transplanted organs Heart (N = 194 recipients): 56.7% vs 43.3%, $P < .001$ Lung (N = 193 recipients): 91.7% vs 8.3%, $P < .001$ Liver (N = 271 recipients): 43.9% vs 56.0%, $P = .006$ Pancreas (N = 69 recipients): 91.3% vs 8.7%, $P < .001$ Kidneys (N = 518 recipients): 47.1% vs 52.8%, $P < .001$ Mean (SD) time interval (h) From admission to declaration of brain death: 34.98 (44.20) vs 52.79 (72.68), $P = .02$ From declaration of brain death to procurement: 31.63 (9.62) vs 29.39 (11.65), $P = .08$ From admission to procurement: 66.62 (45.12) vs 82.18 (73.30), $P = .04$	Moderate

TABLE 32. Continued.

Author, year (Study design) Country Civilian/Military MOI	Baseline characteristics	Intervention	Results	Study risk of bias
Aiyagari, 2005 ²⁹⁷ (Case reports) United States Civilian GSW: 100%	N = 2 patients with active bleeding Male: 100% Age: 27 and 33 y GCS: "2T" (for both)	Patient 1: infused 4.8 mg of FVIIa (90 µg/kg) and 1 unit of cryoprecipitate Patient 2: 6 mg (90 µg/kg) of FVIIa were infused	Both patients immediately responded to therapy (15 and 30 min after) and bleeding stopped. Both patients later met neurologic criteria for death and donated four organs each. After 8 and 10 mo of follow-up organ recipients were doing well, with the exception of a heart transplant recipient who died secondary to noncompliance with medication.	High

BDI, brain death interval; BIT, brain injury time; FVIIa, activated factor VII; GSW, gunshot wound; MAP, mean arterial pressure; NR, not reported; NRS, non-randomized study; pTBI, penetrating traumatic brain injury; SD, standard deviation.

^aNote that distinct from the other key questions which were focused on pTBI patients, the studies presented in table reflect studies of all TBI patients in whom some pTBI patients were studied. No studies specifically pertaining to pTBI patients were found.

^bInterval from brain death declaration to application of an aortic cross-clamp during the donor heart procurement.

^cTime from donor aortic cross-clamp to aortic unclamping in the recipient.

^dTime from initial incident to aortic unclamping in the recipient.

^e $p < 0.001$ is our calculations; the p-value reported by study authors is 0.52, indicating that either the data provided or the p-value for the comparison is incorrect.

- Ejection fraction, %: ≥ 50
- Low-dose vasopressors (dopamine at 10 µg/kg/min or less, neosynephrine at 60 µg/min or less, and norepinephrine at 10 µg/min or less) No. of agents: ≤ 1
- Arterial blood gas, pH: 7.3-7.5
- PaO₂:FIO₂ ratio: ≥ 300
- Serum sodium, mEq/L: ≤ 155
- Urine output, mL/kg/h over 4 hours: ≥ 0.5
- Glucose, mg/dL: ≤ 150

Optimization of the organ donor following declaration of death by neurologic criteria in a patient with TBI can take time however and the optimal timing of organ donation and procurement is unknown.

Expert Opinion

The expert panelists were reluctant to opine on issues pertaining to brain death and organ donation fearing that it could promote a nihilistic approach to pTBI patients. Indeed, these patients are often subject to the incorrect view that pTBI is synonymous with medical futility. The experts note that many pTBI patients can achieve acceptable outcomes if given the chance. Aggressive care is perhaps the single most important factor in pTBI patient outcomes. In military neurosurgeons' experience, better outcomes are achieved compared to civilian patients despite treating injuries from higher velocity firearms. pTBI patients should not simply be viewed as a potential source of organs for donation. The prime duty of medical personnel is to give the pTBI patient the best chance for an optimal outcome.

Despite this, we do recognize that there is a cohort of pTBI patients that are, in fact, nonsurvivable. Recognition of these individuals as an important source of viable organs for donation, particularly as it pertains to an individual's end-of-life care, should be acknowledged by clinicians providing care for these patients. It is important to maintain somatic life and organ support for individuals after a determination of medical futility or non-survivability until such time as donation has been declined or the patient has been ruled out as an acceptable donor by the local organ procurement organization.

The key message of this chapter is that donor organs have the best chance of positively impacting their recipients if organs are implanted early after donor physiology is optimized.

Future Directions

Optimization of donor recipient outcomes should be the goal once declaration of death or termination of care occurs in the pTBI patient, and subsequently (or concurrently) the decision is made to proceed with organ donation. There is a large body of literature that addresses newer and novel techniques to improve organ function and maximize recipient outcomes, such as continual renal replacement therapy and direct personal resuscitation. Further research aiming to optimize organ recovery and transplant recipient outcomes should be pursued. Although it is unlikely that donor patients with pTBI would be optimally treated with a unique and distinct protocol, investigators should be open to such a possibility.

VIII-7 – Rehabilitation

G. W. J. Hawryluk, H. S. Mangat, D. Pannell, R. Puffer

Recommendations

Level I-IV

There is insufficient evidence to support an evidence-based recommendation related to rehabilitation for pTBI.

Level C – Expert Consensus (Delphi Voting)

In the absence of direct scientific evidence, EXPERT CONSENSUS concluded that:

- Rehabilitation should be initiated for patients with neurologic deficits after pTBI if the rehabilitation treatment does not interfere with necessary medical interventions. (100% consensus)
- We cannot recommend any specific type, duration, or timing of initiation of rehabilitation services in pTBI. (100% consensus)

No evidence or expert opinion supported distinct recommendations based on patient gender, wounding mechanism, or military vs civilian context.

Introduction

pTBI often results in significant mortality and morbidity, the latter related to disability amongst survivors. While many surviving patients are offered rehabilitation services, little is known about the benefits and/or harms associated with initiation of these services at various time points after injury.

Multidisciplinary rehabilitation services play an important role in the continuum of care after pTBI. Rehabilitation services are often multidisciplinary, including physical, occupational and speech therapy. These services help to provide not only coping strategies for patients with functional deficits, but also may play a role in functional recovery by enlisting and augmenting neuroplasticity for improvement and recovery over the long term.

Prior Guideline Recommendations

The prior penetrating brain injury guidelines (2001) did not review or inform the benefits or harm of rehabilitation, or when rehabilitation should be initiated.¹⁶

Scientific Foundation

We identified no studies that compared rehabilitation vs no rehabilitation in the same patient population (e.g., with a randomized trial) or a similar population (e.g., a cohort study that matched patients based on such factors as mechanism of injury and severity of injury) to determine the benefits and harms of rehabilitation vs no rehabilitation. Thus no study qualified based on inclusion and exclusion criteria. However, indirect evidence related to rehabilitation is demonstrated in the studies described below, though they did not include comparator groups who did not undergo rehabilitation.

Studies not included

Zafonte and colleagues³⁵⁴ demonstrated improvement with rehabilitation across all domains of civilian victims of gunshot

wounds to the head, between admission and discharge, with a mean stay of 38.5 days in 33 of 442 patients: 86% were male with a mean age of 28 years, disability rating scale improved from 13.7 to 6.2, functional improvement measure (FIM) on cognitive domain improved from 16.4 to 24.2, FIM-motor from 41.1 to 71.6, total FIM from 57.4 to 95.8, and the Los Ranchos cognitive functioning scale from 4.9 to 6.6. The authors state that rehabilitation is justified if patients “are proven to have favorable outcomes.” However, 51.8% of patients had severe injuries and 41.5% mild and it may be that the severely injured succumbed and those with mild injuries underwent rehabilitation. A study by Hotz et al³⁵⁵ replicated the short-term benefits demonstrated with rehabilitation. Zafonte et al also reported continued functional improvements at 1 year in pTBI patients able to undergo rehabilitation.³⁵⁶ Two further studies from army blast injuries, where rehabilitation was implied but not specified, reported improved GOS scores from 6 to 24 months post-injury.^{7,13}

These studies do not provide evidence that rehabilitation compared to no rehabilitation provides distinct benefits or harms in pTBI patients. However, they do support that some patients admitted to a rehabilitation program or facility following pTBI improve in function. There is no evidence to say that these patients would or would not have similarly improved without rehabilitation.

Discussion

There are no research articles that address the specific question of benefits/harms or type and timing of rehabilitation in the setting of pTBI. Several studies report outcomes and discharge disposition for patients, including discharge to rehab, however these studies are not designed to answer the question of benefits or harms of rehabilitation initiation. While many patients discharged to rehab demonstrated improved outcomes over time, it is

impossible to determine whether or not these same patients would have also improved and to what degree they may have improved without rehabilitation services. It is strongly believed, however, that the initiation of rehabilitation services is beneficial for functional recovery after pTBI. There is no evidence to suggest harm from initiation of rehabilitation services during the acute treatment phase or the recovery phase.

The National Academies of Science, Engineering and Medicine published a monograph titled ‘Traumatic Brain Injury: Roadmap for Accelerating Progress’ in which the topic of rehabilitation was addressed in TBI as a whole (not specific to pTBI).³⁵⁷ This document provides a useful resource.

Expert Opinion

As an extension of the above, rehabilitation is assumed to augment the functional recovery of patients who sustain a pTBI. In addition to building strength, improving balance, and promoting adaptive strategies, rehabilitation may stimulate plasticity and other repair processes. Although rehabilitation is a standard of care, quality of rehabilitation is known to vary and access to it can be problematic for a variety of reasons. The expert consensus states that acute rehabilitation be started as soon as possible, once the patient is medically stable, though evidence does not currently inform what type of rehabilitation or a component thereof is likely to provide the most benefit.

Future Directions

Most patients who survive a pTBI will require rehabilitation. Those who survive to initiate rehabilitation are predicted to have good functional outcomes. Future investigations including randomized and non-randomized studies of rehabilitation strategies should be performed although there may be need for multi-center collaboration to achieve needed patient enrollment. Different rehabilitation modalities also require study. It would of course be unethical to withhold rehabilitation in relevant studies given indirect evidence from blunt TBI. Additional studies focusing on timing of rehabilitation service initiation, as well as comparative outcome studies for patients who did and did not receive rehabilitation services due to barriers, would be beneficial to assist in answering this question. In the absence of these studies, decisions on timing of rehabilitation service initiation should fall to local standards of practice.

Funding

Our project “The Development of Best Practice Penetrating TBI Guidelines for Military and Civilian Patients” was funded by The U.S. Army Medical Research and Development Command (Award Number: W81XWH21C0102) with contract support from The Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc. (Contract No. 1039446). The systematic review was completed by the Pacific Northwest Evidence-based Practice Center at Oregon Health & Science University with funding through a subcontract with Stanford University (subaward number 62889663-193508).

REFERENCES

- Shackelford SA, Del Junco DJ, Reade MC, et al. Association of time to craniectomy with survival in patients with severe combat-related brain injury. *Neurosurg Focus*. 2018;45(6):e2.
- Deng H, Yue JK, Winkler EA, Dhall SS, Manley GT, Tarapore PE. Adult firearm-related traumatic brain injury in United States Trauma Centers. *J Neurotrauma*. 2019;36(2):322-337.
- Deng H, Yue JK, Winkler EA, Dhall SS, Manley GT, Tarapore PE. Pediatric firearm-related traumatic brain injury in United States trauma centers. *J Neurosurg Pediatr*. 2019;24(5):498-508.
- Kessely YC, Ndortolnan A, Toudjingar FG, et al. Craniocerebral gunshot injuries in Chad: a study of 44 cases. *World Neurosurg*. 2022;163:e458-e463.
- Lilford RD, Hossain I, Dahlberg M, et al. Increased incidence and mortality of civilian penetrating traumatic brain injury in Sweden: a Single-Center Registry-Based Study. *World Neurosurg*. 2024;182:e493-e505.
- Benjamin ER, Demetriades D, Owattanapanich N, et al. Therapeutic interventions and outcomes in civilian and military isolated gunshot wounds to the head: a Department of Defense Trauma Registry and ACS TQIP-matched study. *Ann Surg*. 2023;278(1):e131-e136.
- Larkin MB, Graves EKM, Boulter JH, et al. Two-year mortality and functional outcomes in combat-related penetrating brain injury: battlefield through rehabilitation. *Neurosurg Focus*. 2018;45(6):e4.
- Bell RS, Vo AH, Neal CJ, et al. Military traumatic brain and spinal column injury: a 5-year study of the impact blast and other military grade weaponry on the central nervous system. *J Trauma*. 2009;66(4 Suppl):S104-S111.
- Bell RS, Mossop CM, Dirks MS, et al. Early decompressive craniectomy for severe penetrating and closed head injury during wartime. *Neurosurg Focus*. 2010;28(5):e1.
- DuBose JJ, Barmparas G, Inaba K, et al. Isolated severe traumatic brain injuries sustained during combat operations: demographics, mortality outcomes, and lessons to be learned from contrasts to civilian counterparts. *J Trauma*. 2011;70(1):11-18; discussion 16-18.
- Ecker RD, Mulligan LP, Dirks M, et al. Outcomes of 33 patients from the wars in Iraq and Afghanistan undergoing bilateral or bicompartamental craniectomy. *J Neurosurg*. 2011;115(1):124-129.
- Rosenfeld JV, McFarlane AC, Bragge P, Armonda RA, Grimes JB, Ling GS. Blast-related traumatic brain injury. *Lancet Neurol*. 2013;12(9):882-893.
- Weisbrod AB, Rodriguez C, Bell R, et al. Long-term outcomes of combat casualties sustaining penetrating traumatic brain injury. *J Trauma Acute Care Surg*. 2012;73(6):1525-1530.
- Bell RS, Ecker RD, Severson MA, 3rd, Wanebo JE, Crandall B, Armonda RA. The evolution of the treatment of traumatic cerebrovascular injury during wartime. *Neurosurg Focus*. 2010;28(5):e5.
- Breeze J, Bowley DM, Harrison SE, et al. Survival after traumatic brain injury improves with deployment of neurosurgeons: a comparison of US and UK military treatment facilities during the Iraq and Afghanistan conflicts. *J Neurol Neurosurg Psychiatry*. 2020;91(4):359-365.
- Aarabi B, Alden TD, Chesnut R, Downs J, Ecklund J, Eisenberg H. Part 1. Guidelines for the management of penetrating brain injury. Introduction and methodology. *J Trauma*. 2001;51(2 Suppl):S3-S6.
- Geddes AE, Burlew CC, Wagenaar AE, et al. Expanded screening criteria for blunt cerebrovascular injury: a bigger impact than anticipated. *Am J Surg*. 2016;212(6):1167-1174.
- Muehlschlegel S, Ayturk D, Ahlawat A, et al. Predicting survival after acute civilian penetrating brain injuries: the SPIN score. *Neurology*. 2016;87(21):2244-2253.
- Okonkwo DO, Shutter LA, Moore C, et al. Brain oxygen optimization in severe traumatic brain injury phase-II: a phase II randomized trial. *Crit Care Med*. 2017;45(11):1907-1914.
- Hawryluk GWJ, Aguilera S, Buki A, et al. A management algorithm for patients with intracranial pressure monitoring: the Seattle International Severe Traumatic Brain Injury Consensus Conference (SIBICC). *Intensive Care Med*. 2019;45(12):1783-1794.
- Czosnyka M, Czosnyka Z, Smielewski P. Pressure reactivity index: journey through the past 20 years. *Acta Neurochir (Wien)*. 2017;159(11):2063-2065.
- Tas J, Beqiri E, van Kaam RC, et al. Targeting autoregulation-guided cerebral perfusion pressure after traumatic brain injury (COGiTATE): a feasibility randomized controlled clinical trial. *J Neurotrauma*. 2021;38(20):2790-2800.

23. Mathur R, Cheng L, Lim J, et al. Evolving concepts in intracranial pressure monitoring - from traditional monitoring to precision medicine. *Neurotherapeutics*. 2025;22(1):e00507.
24. Bullock R, Chesnut RM, Clifton G, et al. Guidelines for the management of severe head injury. Brain Trauma Foundation. *Eur J Emerg Med*. 1996;3(2):109-127.
25. Hawryluk GWJ, Ghajar J. Evolution and impact of the brain trauma foundation guidelines. *Neurosurgery*. 2021;89(6):1148-1156.
26. Gerber LM, Chiu YL, Carney N, Härtl R, Ghajar J. Marked reduction in mortality in patients with severe traumatic brain injury. *J Neurosurg*. 2013;119(6):1583-1590.
27. Hawryluk GWJ, Selph S, Lumba-Brown A, et al. Rationale and methods for updated guidelines for the management of penetrating traumatic brain injury. *Neurotrauma Rep*. 2022;3(1):240-247.
28. Carney N, Totten AM, O'Reilly C, et al. Guidelines for the management of severe traumatic brain injury, fourth edition. *Neurosurgery*. 2017;80(1):6-15.
29. Chesnut R, Aguilera S, Buki A, et al. A management algorithm for adult patients with both brain oxygen and intracranial pressure monitoring: the Seattle International Severe Traumatic Brain Injury Consensus Conference (SIBICC). *Intensive Care Med*. 2020;46(5):919-929.
30. Critical pathway for the treatment of established intracranial hypertension. Brain Trauma Foundation. *J Neurotrauma*. 1996;13(11):719-720.
31. The Brain Trauma Foundation. The American Association of Neurological Surgeons. The Joint Section on Neurotrauma and Critical Care. Critical pathway for the treatment of established intracranial hypertension. *J Neurotrauma*. 2000;17(6-7):537-538.
32. Brain Trauma Foundation; American Association of Neurological Surgeons; Congress of Neurological Surgeons. Guidelines for the management of severe traumatic brain injury. *J Neurotrauma*. 2007;24(Suppl 1):S1-S106.
33. Alden TD, Maas AIR, Narayan RK, et al. Part 2. Prognosis in penetrating brain injury. *J Trauma*. 2001;51(2 Suppl):S44-S86.
34. Sanders WR, Barber JK, Temkin NR, et al. Recovery potential in patients who died after withdrawal of life-sustaining treatment: a TRACK-TBI propensity score analysis. *J Neurotrauma*. 2024;41(19-20):2336-2348.
35. Agency for Healthcare Research and Quality (US). *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*. Agency for Healthcare Research and Quality (US); 2023.
36. Lulla A, Lumba-Brown A, Totten AM, et al. Prehospital guidelines for the management of traumatic brain injury - 3rd Edition. *Prehosp Emerg Care*. 2023;27(5):507-538.
37. Kaufman HH, Makela ME, Lee KF, Haid RW Jr., Gildenberg PL. Gunshot wounds to the head: a perspective. *Neurosurgery*. 1986;18(6):689-695.
38. Sarnaik AP, Kopec J, Moylan P, Alvarez D, Canady A. Role of aggressive intracranial pressure control in management of pediatric craniocerebral gunshot wounds with unfavorable features. *J Trauma*. 1989;29(10):1434-1437.
39. Byrnes DP, Crockard HA, Gordon DS, Gleadhill CA. Penetrating craniocerebral missile injuries in the civil disturbances in Northern Ireland. *Br J Surg*. 1974;61(3):169-176.
40. Grahm TW, Williams FC, Jr., Harrington T, Spetzler RF. Civilian gunshot wounds to the head: a prospective study. *Neurosurgery*. 1990;27(5):696-700; discussion 700.
41. Sherman WD, Apuzzo ML, Heiden JS, Petersons VT, Weiss MH. Gunshot wounds to the brain—a civilian experience. *West J Med*. 1980;132(2):99-105.
42. Miner ME, Ewing-Cobbs L, Kopaniky DR, Cabrera J, Kaufmann P. The results of treatment of gunshot wounds to the brain in children. *Neurosurgery*. 1990;26(1):20-25; discussion 24-25.
43. Kaufman HH, Levy ML, Stone JL, et al. Patients with Glasgow Coma Scale scores 3, 4, 5 after gunshot wounds to the brain. *Neurosurg Clin N Am*. 1995;6(4):701-714.
44. Makoshi Z, Alkherayf F, Da Silva V, Lesiuk H. Nail gun injuries to the head with minimal neurological consequences: a case series. *J Med Case Rep*. 2016;10:58.
45. Demetriades D, Chahwan S, Gomez H, Falabella A, Velmahos G, Yamashita D. Initial evaluation and management of gunshot wounds to the face. *J Trauma*. 1998;45(1):39-41.
46. Haller I, Lederer W, Glodny B, Wiedermann FJ. Severe craniofacial trauma after multiple pistol shots. *Open Med (Wars)*. 2019;14(1):629-632.
47. Nicolaisen N, Ahmed A, Hancock T, Ogren R. Field airway management of a construction worker with an impaling rebar injury to the neck and brain. *Prehosp Emerg Care*. 2012;16(4):548-552.
48. Mansour A, Loggini A, Goldenberg FD, et al. Coagulopathy as a Surrogate of Severity of Injury in Penetrating Brain Injury. *J Neurotrauma*. 2021;38(13):1821-1826.
49. Can C, Bolatkale M, Sarhan A, Savran Y, Acara AC, Bulut M. The effect of brain tomography findings on mortality in sniper shot head injuries. *J R Army Med Corps*. 2017;163(3):211-214.
50. Wani AA, Ramzan AU, Dar TI, et al. Management dilemma in penetrating head injuries in comatose patients: scenario in underdeveloped countries. *Surg Neurol Int*. 2012;3:89.
51. Glapa M, Zorio M, Snyckers FD, et al. Gunshot wounds to the head in civilian practice. *Am Surg*. 2009;75(3):223-226.
52. Kong VY, Weale RD, Sartorius B, Bruce JL, Laing GL, Clarke DL. Routine cervical spine immobilisation is unnecessary in patients with isolated cerebral gunshot wounds: a South African experience. *Emerg Med Australas*. 2018;30(6):773-776.
53. Joseph B, Aziz H, Pandit V, et al. Improving survival rates after civilian gunshot wounds to the brain. *J Am Coll Surg*. 2014;218(1):58-65.
54. Ahmed S, Baishya B, Hussain Z, Hazarika R, Saikia A, Singh B. Paradigm shift in management strategies of craniocerebral missile injuries improving survival rates and functional outcome score. *Indian J Neurotr*. 2015;12(01):053-061.
55. McNickle AG, Chestovich PJ, Fraser DR. Cervical spine injury is rare in self-inflicted craniofacial gunshot wounds: an institutional review and comparison to the US National Trauma Data Bank (NTDB). *Prehosp Disaster Med*. 2020;35(5):524-527.
56. Ospina-Delgado D, Mosquera Salas LM, Enríquez-Marulanda A, Hernández-Morales J, Pacheco R, Lobato-Polo J. Characterization of 95 patients with traumatic brain injury due to gunshot wounds at a referral center in Cali, Colombia. *Neurocirugia (Astur: Engl Ed)*. 2018;29(5):217-224.
57. Bolatkale M, Acara AC. The intracranial number of foreign bodies as a predictor of mortality after penetrating brain injury. *Am J Emerg Med*. 2019;37(3):433-438.
58. İcer M, Zengin Y, Dursun R, et al. Factors affecting dural penetration and prognosis in patients admitted to emergency department with cranial gunshot wound. *Eur J Trauma Emerg Surg*. 2017;43(5):611-615.
59. Kim KA, Wang MY, McNatt SA, et al. Vector analysis correlating bullet trajectory to outcome after civilian through-and-through gunshot wound to the head: using imaging cues to predict fatal outcome. *Neurosurgery*. 2005;57(4):737-747; discussion 737-747.
60. Stone JL, Lichtor T, Fitzgerald LF, Barrett JA, Reyes HM. Demographics of civilian cranial gunshot wounds: devastation related to escalating semiautomatic usage. *J Trauma*. 1995;38(6):851-854.
61. Brandvold B, Levi L, Feinsod M, George ED. Penetrating craniocerebral injuries in the Israeli involvement in the Lebanese conflict, 1982-1985. Analysis of a less aggressive surgical approach. *J Neurosurg*. 1990;72(1):15-21.
62. Johnson MD, Carroll C, Cass D, Andaluz N, et al. Single-center experience with antibiotic prophylaxis and infectious complications in civilian cranial gunshot wounds. *Neurosurgery Open*. 2021;2(1):okaa013.
63. Dolachee AA, Lafta GA, Mohammed AN, Al-Zubaidi AK. Factors affecting the outcome in surgically treated civilian penetrating head injury: case series. *Int J Res Pharm Sci*. 2019;10(3):2120-2126.
64. Ameen AA. The management of acute craniocerebral injuries caused by missiles: analysis of 110 consecutive penetrating wounds of the brain from Basrah. *Injury*. 1984;16(2):88-90.
65. Arendall RE, Meirowsky AM. Air sinus wounds: an analysis of 163 consecutive cases incurred in the Korean War, 1950-1952. *Neurosurgery*. 1983;13(4):377-380.
66. Benzel EC, Day WT, Kesterson L, et al. Civilian craniocerebral gunshot wounds. *Neurosurgery*. 1991;29(1):67-72; discussion 71-72.
67. Carey ME, Young HF, Mathis JL. The neurosurgical treatment of craniocerebral missile wounds in Vietnam. *Surg Gynecol Obstet*. 1972;135(3):386-389.
68. Carey ME, Young HF, Rish BL, Mathis JL. Follow-up study of 103 American soldiers who sustained a brain wound in Vietnam. *J Neurosurg*. 1974;41(5):542-549.
69. Chaudhri KA, Choudhury AR, al Moutaery KR, Cybulski GR. Penetrating craniocerebral shrapnel injuries during "Operation Desert Storm": early results of a conservative surgical treatment. *Acta Neurochir (Wien)*. 1994;126(2-4):120-123.
70. Gönül E, Baysefer A, Kahraman S, et al. Causes of infections and management results in penetrating craniocerebral injuries. *Neurosurg Rev*. 1997;20(3):177-181.
71. Gordon DS. Surgery of violence. V. Missile wounds of the head and spine. *Br Med J*. 1975;1(5958):614-616.

72. Helling TS, McNabney WK, Whittaker CK, Schultz CC, Watkins M. The role of early surgical intervention in civilian gunshot wounds to the head. *J Trauma*. 1992;32(3):398-400.
73. Hubschmann O, Shapiro K, Baden M, Shulman K. Craniocerebral gunshot injuries in civilian practice—prognostic criteria and surgical management: experience with 82 cases. *J Trauma*. 1979;19(1):6-12.
74. Levi L, Borovich B, Guilburd JN, et al. Wartime neurosurgical experience in Lebanon, 1982-85. I: penetrating craniocerebral injuries. *Isr J Med Sci*. 1990; 26(10):548-554.
75. Lillard PL. Five years experience with penetrating craniocerebral gunshot wounds. *Surg Neurol*. 1978;9(2):79-83.
76. Meirowsky AM, Caveness WF, Dillon JD, et al. Cerebrospinal fluid fistulas complicating missile wounds of the brain. *J Neurosurg*. 1981;54(1):44-48.
77. Nagib MG, Rockswold GL, Sherman RS, Lagaard MW. Civilian gunshot wounds to the brain: prognosis and management. *Neurosurgery*. 1986;18(5):533-537.
78. Rish BL, Dillon JD, Weiss GH. Mortality following penetrating craniocerebral injuries. An analysis of the deaths in the Vietnam Head Injury Registry population. *J Neurosurg*. 1983;59(5):775-780.
79. Smith AS, Hurst GC, Duerk JL, Diaz PJ. MR of ballistic materials: imaging artifacts and potential hazards. *AJNR Am J Neuroradiol*. 1991;12(3):567-572.
80. Teitelbaum GP, Yee CA, Van Horn DD, Kim HS, Colletti PM. Metallic ballistic fragments: MR imaging safety and artifacts. *Radiology*. 1990;175(3):855-859.
81. Oliver C, Kabala J. Air gun pellet injuries: the safety of MR imaging. *Clin Radiol*. 1997;52(4):299-300.
82. Exadaktylos AK, Stettbacher A, Bautz PC, Terries J. The value of protocol-driven CT scanning in stab wounds to the head. *Am J Emerg Med*. 2002;20(4):295-297.
83. Demetriades D, Kuncir E, Murray J, Velmahos GC, Rhee P, Chan L. Mortality prediction of head Abbreviated Injury Score and Glasgow Coma Scale: analysis of 7,764 head injuries. *J Am Coll Surg*. 2004;199(2):216-222.
84. Demetriades D, Kuncir E, Velmahos GC, Rhee P, Alo K, Chan LS. Outcome and prognostic factors in head injuries with an admission Glasgow Coma Scale score of 3. *Arch Surg*. 2004;139(10):1066-1068.
85. Hofbauer M, Kdolsky R, Figl M, et al. Predictive factors influencing the outcome after gunshot injuries to the head—a retrospective cohort study. *J Trauma*. 2010; 69(4):770-775.
86. Peek-Asa C, McArthur D, Hovda D, Kraus J. Early predictors of mortality in penetrating compared with closed brain injury. *Brain Inj*. 2001;15(9):801-810.
87. Petridis AK, Doukas A, Barth H, Mehdorn M. Outcome of craniocerebral gunshot injuries in the civilian population. Prognostic factors and treatment options. *Cent Eur Neurosurg*. 2011;72(1):5-14.
88. Leake D. Transorbital intracranial penetrating injury: evaluation of associated vascular injury with CTA and conventional angiography. *Emerg Radiol*. 2012; 19(5):377.
89. Monterey M, Kerr K, Dannenbaum M, Chen PR, Blackburn S. Open surgery for extraction of an embolized pellet in the middle cerebral artery from a shotgun injury. *Oper Neurosurg*. 2019;17(3):e119-e123.
90. Babl FE, Lyttle MD, Bressan S, et al. Penetrating head injuries in children presenting to the emergency department in Australia and New Zealand: a PREDICT prospective study. *J Paediatr Child Health*. 2018;54(8):861-865.
91. Bakay L. The value of CT scan in gunshot injuries of the brain. *Acta Neurochir (Wien)*. 1984;71(3-4):189-204.
92. Besenski N, Jadro-Santel D, Jelavić-Koić F, et al. CT analysis of missile head injury. *Neuroradiology*. 1995;37(3):207-211.
93. Chibbaro S, Tacconi L. Orbito-cranial injuries caused by penetrating non-missile foreign bodies. Experience with eighteen patients. *Acta Neurochir (Wien)*. 2006; 148(9):937-942; discussion 941-942.
94. Cooper PR, Maravilla K, Cone J. Computerized tomographic scan and gunshot wounds of the head: indications and radiographic findings. *Neurosurgery*. 1979; 4(5):373-380.
95. Kalousek M, Hat J, Krolo I, Marotti M, Lupret V, Smiljanic D. Computed tomography analysis of head and spinal cord injuries inflicted by missiles and explosives. *J Neuroimag*. 1993;3(3):178-183.
96. Pabuscu Y, Bulakbasi N, Kocaoglu M, Ustünsöz B, Tayfun C. A different approach to missile induced head injuries. *Comput Med Imaging Graph*. 2003;27(5): 397-409.
97. Rappaport ZH, Sahar A, Shaked I, Findler G, Tadmor R. Computerized tomography in combat-related craniocerebral penetrating missile injuries. *Isr J Med Sci*. 1984;20(8):668-671.
98. Wagner AK, Sasser HC, Hammond FM, Wiercisiewski D, Alexander J. Intentional traumatic brain injury: epidemiology, risk factors, and associations with injury severity and mortality. *J Trauma*. 2000;49(3):404-410.
99. Bell RS, Vo AH, Roberts R, Wanebo J, Armonda RA. Wartime traumatic aneurysms: acute presentation, diagnosis, and multimodal treatment of 64 craniocervical arterial injuries. *Neurosurgery*. 2010;66(1):66-79; discussion 79.
100. Armonda RA, Bell RS, Vo AH, et al. Wartime traumatic cerebral vasospasm: recent review of combat casualties. *Neurosurgery*. 2006;59(6):1215-1225; discussion 1225.
101. Aarabi B. Management of traumatic aneurysms caused by high-velocity missile head wounds. *Neurosurg Clin N Am*. 1995;6(4):775-797.
102. Neuroimaging in the management of penetrating brain injury. *J Trauma*. 2001; 51(Supplement):S7-S11.
103. Vascular complications of penetrating brain injury. *J Trauma*. 2001;51(Supplement):S26-S28.
104. Ares WJ, Jankowitz BT, Tonetti DA, Gross BA, Grandhi R. A comparison of digital subtraction angiography and computed tomography angiography for the diagnosis of penetrating cerebrovascular injury. *Neurosurg Focus*. 2019;47(5):e16.
105. Bodanapally UK, Shanmuganathan K, Boscak AR, et al. Vascular complications of penetrating brain injury: comparison of helical CT angiography and conventional angiography. *J Neurosurg*. 2014;121(5):1275-1283.
106. Meyer RM, Larkin MB, Szulifta NS, et al. Early venous thromboembolism chemoprophylaxis in combat-related penetrating brain injury. *J Neurosurg*. 2017; 126(4):1047-1055.
107. Meyer RM, Grandhi R, Lim DH, et al. A comparison of computed tomography angiography and digital subtraction angiography for the diagnosis of penetrating cerebrovascular injury: a prospective multicenter study. *J Neurosurg*. 2024;141(2): 306-309.
108. Aarabi B. Traumatic aneurysms of brain due to high velocity missile head wounds. *Neurosurgery*. 1988;22(6 Pt 1):1056-1063.
109. Amirjamshidi A, Rahmat H, Abbassioun K. Traumatic aneurysms and arteriovenous fistulas of intracranial vessels associated with penetrating head injuries occurring during war: principles and pitfalls in diagnosis and management. A survey of 31 cases and review of the literature. *J Neurosurg*. 1996;84(5):769-780.
110. Cohen JE, Gomori JM, Segal R, et al. Results of endovascular treatment of traumatic intracranial aneurysms. *Neurosurgery*. 2008;63(3):476-486; discussion 485-486.
111. du Trevoir MD, van Dellen JR. Penetrating stab wounds to the brain: the timing of angiography in patients presenting with the weapon already removed. *Neurosurgery*. 1992;31(5):905-911; discussion 911-912.
112. Haddad FS, Haddad GF, Taha J. Traumatic intracranial aneurysms caused by missiles: their presentation and management. *Neurosurgery*. 1991;28(1):1-7.
113. Kieck CF, de Villiers JC. Vascular lesions due to transcranial stab wounds. *J Neurosurg*. 1984;60(1):42-46.
114. Nathoo N, Boodhoo H, Nadvi SS, Naidoo SR, Gouws E. Transcranial brainstem stab injuries: a retrospective analysis of 17 patients. *Neurosurgery*. 2000;47(5): 1117-1123; discussion 1123.
115. Catapano JS, Hutchens DM, Cadigan MS, Srinivasan VM, Albuquerque FC, Bristol RE. Pediatric intracranial arterial injuries by penetrating gunshot wounds: an institutional experience. *Childs Nerv Syst*. 2021;37(4):1279-1283.
116. Diaz-Daza O, Arraiza FJ, Barkley JM, Whigham CJ. Endovascular therapy of traumatic vascular lesions of the head and neck. *Cardiovasc Intervent Radiol*. 2003; 26(3):213-221.
117. Kordestani RK, Counelis GJ, McBride DQ, Martin NA. Cerebral arterial spasm after penetrating craniocerebral gunshot wounds: transcranial Doppler and cerebral blood flow findings. *Neurosurgery*. 1997;41(2):351-360; discussion 359-360.
118. Levy ML, Rezaei A, Masri LS, et al. The significance of subarachnoid hemorrhage after penetrating craniocerebral injury: correlations with angiography and outcome in a civilian population. *Neurosurgery*. 1993;32(4):532-540.
119. Rahimzadeh A, Abtahi H, Daylami MS, Tabatabaei MA, Haddadian K. Traumatic cerebral aneurysms caused by shell fragments. Report of four cases and review of the literature. *Acta Neurochir (Wien)*. 1987;84(3-4):93-98.
120. Dawoud FM, Feldman MJ, Yengo-Kahn AM, et al. Traumatic cerebrovascular injuries associated with gunshot wounds to the head: a single-institution ten-year experience. *World Neurosurg*. 2021;146:e1031-e1044.
121. Ozkan U, Kemaloglu S, Ozates M, Aydin MD. Analysis of 107 civilian craniocerebral gunshot wounds. *Neurosurg Rev*. 2002;25(4):231-236.

122. Rostomily RC, Newell DW, Grady MS, Wallace S, Nicholls S, Winn HR. Gunshot wounds of the internal carotid artery at the skull base: management with vein bypass grafts and a review of the literature. *J Trauma*. 1997;42(1):123-132.
123. Yoon J, Gebran S, Elegbede A, et al. Blunt cerebrovascular injury-like injury observed in patients with craniofacial self-inflicted gunshot wounds. *J Craniofac Surg*. 2022;33(4):1046-1050.
124. Özkan Arat Y, Arat A, Aydın K. Cerebrovascular complications of transorbital penetrating intracranial injuries. *Ulus Trauma Acil Cerrahi Derg*. 2015;21(4):271-278.
125. Sweeney JM, Lebovitz JJ, Eller JL, Coppens JR, Bucholz RD, Abdulrauf SI. Management of nonmissile penetrating brain injuries: a description of three cases and review of the literature. *Skull Base Rep*. 2011;1(1):39-46.
126. Siccardi D, Cavaliere R, Pau A, Lubinu F, Turtas S, Viale GL. Penetrating craniocerebral missile injuries in civilians: a retrospective analysis of 314 cases. *Surg Neurol*. 1991;35(6):455-460.
127. Barbosa GdS, Gaspar JdO, Nogueira LdS, Vieira RdCA, Lima KP, Sousa RMCd. Performance of the modified rapid emergency medicine score in patients with and without traumatic brain injury. *J Neurosci Nurs*. 2022;54(3):130-135.
128. Mikati AG, Flahive J, Khan MW, et al. Multicenter validation of the survival after acute civilian penetrating brain injuries (SPIN) score. *Neurosurgery*. 2019;85(5):e872-e879.
129. Kong VY, Oosthuizen GV, Sartorius B, et al. Validation of the Baragwanath mortality prediction score for cerebral gunshot wounds: the Pietermaritzburg experience. *Eur J Trauma Emerg Surg*. 2018;44(4):615-620.
130. DeCuyper M, Muhlauer MS, Boop FA, Klimo P Jr. Pediatric intracranial gunshot wounds: the Memphis experience. *J Neurosurg Pediatr*. 2016;17(5):595-601.
131. Gressot LV, Chamoun RB, Patel AJ, et al. Predictors of outcome in civilians with gunshot wounds to the head upon presentation. *J Neurosurg*. 2014;121(3):645-652.
132. Turina D, Sustić A, Tićac Z, et al. War head injury score: an outcome prediction model in War casualties with acute penetrating head injury. *Mil Med*. 2001;166(4):331-334.
133. Mukerji S, Darwin S, Suchdev K, et al. Persistent coagulopathy after gunshot traumatic brain injury: the importance of INR and the SPIN score. *Eur J Trauma Emerg Surg*. 2022;48(6):4813-4822.
134. Yengo-Kahn AM, Patel PD, Kelly PD, et al. The value of simplicity: externally validating the Baylor cranial gunshot wound prognosis score. *J Neurosurg*. 2021;135(5):1560-1568.
135. Kong VY, Odendaal J, Sartorius B, et al. Developing a simplified clinical prediction score for mortality in patients with cerebral gunshot wounds: the Maritzburg Score. *Ann R Coll Surg Engl*. 2018;100(2):97-100.
136. Stoffel M, Hüser N, Kayser K, Kriner M, Degiannis E, Doll D. Cerebral gunshot wounds: a score based on three clinical parameters to predict the risk of early mortality. *ANZ J Surg*. 2009;79(11):789-793.
137. Lindfors M, Lindblad C, Nelson DW, et al. Prognostic performance of computerized tomography scoring systems in civilian penetrating traumatic brain injury: an observational study. *Acta Neurochir (Wien)*. 2019;161(12):2467-2478.
138. Johnson MD, Stolz U, Carroll CP, et al. An independent, external validation and component analysis of the Surviving Penetrating Injury to the Brain score for civilian cranial gunshot injuries. *J Neurosurg*. 2022;137(6):1839-1846.
139. Kelly PD, Patel PD, Yengo-Kahn AM, et al. Incorporating conditional survival into prognostication for gunshot wounds to the head. *J Neurosurg*. 2021;135(5):1550-1559.
140. Mandrekar JN. Receiver operating characteristic curve in diagnostic test assessment. *J Thorac Oncol*. 2010;5(9):1315-1316.
141. Hemphill JC, 3rd, White DB. Clinical nihilism in neuroemergencies. *Emerg Med Clin North Am*. 2009;27(1):27-37. vii-viii.
142. Sarigul B, Bell RS, Chesnut R, et al. Prognostication and goals of care decisions in severe traumatic brain injury: a survey of The Seattle International Severe Traumatic Brain Injury Consensus Conference Working Group. *J Neurotrauma*. 2023;40(15-16):1707-1717.
143. Hawryluk GWJ. Editorial. Prognostication in traumatic brain injury: now what? *J Neurosurg*. 2024;141(2):412-416.
144. Gascho D, Tappero C, Zoelch N, et al. Synergy of CT and MRI in detecting trajectories of lodged bullets in decedents and potential hazards concerning the heating and movement of bullets during MRI. *Forensic Sci Med Pathol*. 2020;16(1):20-31.
145. Rosenfeld JV, Bell RS, Armonda R. Current concepts in penetrating and blast injury to the central nervous system. *World J Surg*. 2015;39(6):1352-1362.
146. Moore JM, Thomas PA, Gruen RL, Chan P, Rosenfeld JV. Simultaneous multisystem surgery: an important capability for the civilian trauma hospital. *Clin Neurol Neurosurg*. 2016;148:13-16. Erratum in: *Clin Neurol Neurosurg*. 2016;151:145.
147. Moore JM, Thomas PA, Gruen RL, Chan P, Rosenfeld JV. Corrigendum to "Simultaneous multisystem surgery: an important capability for the civilian trauma hospital" [Clin. Neurol. Neurosurg. 148 (2016) 13-16]. *Clin Neurol Neurosurg*. 2016;151:145. Erratum for: *Clin Neurol Neurosurg*. 2016;148:13-16.
148. Surgical management of penetrating brain injury. *J Trauma*. 2001;51(Supplement):S16-S25.
149. Clark WC, Muhlauer MS, Watridge CB, Ray MW. Analysis of 76 civilian craniocerebral gunshot wounds. *J Neurosurg*. 1986;65(1):9-14.
150. Raimondi AJ, Samuelson GH. Craniocerebral gunshot wounds in civilian practice. *J Neurosurg*. 1970;32(6):647-653.
151. Wei LF, Wang SS, Jing JJ, et al. Surgical therapy for craniocerebral firearm injury. *Turk Neurosurg*. 2013;23(4):491-497.
152. Sertbaş İ, Karatay M. The effect of the delay between injury and surgery on mortality, morbidity, and complications in craniocervical gunshot wounding. *Trauma*. 2020;22(3):193-200.
153. Aarabi B, Taghipour M, Alibai E, Kamgarpour A. Central nervous system infections after military missile head wounds. *Neurosurgery*. 1998;42(3):500-509; discussion 507-509.
154. Bullock MR, Chesnut R, Ghajar J, et al. Surgical management of acute subdural hematomas. *Neurosurgery*. 2006;58(3 Suppl):S16-S24; discussion Si-iv.
155. Bullock MR, Chesnut R, Ghajar J, et al. Surgical management of acute epidural hematomas. *Neurosurgery*. 2006;58(3 Suppl):S7-S15; discussion Si-iv.
156. Seelig JM, Becker DP, Miller JD, Greenberg RP, Ward JD, Choi SC. Traumatic acute subdural hematoma: major mortality reduction in comatose patients treated within four hours. *N Engl J Med*. 1981;304(25):1511-1518.
157. Lin DJ, Lam FC, Siracuse JJ, Thomas A, Kasper EM. Time is brain" the Gifford factor - or: why do some civilian gunshot wounds to the head do unexpectedly well? A case series with outcomes analysis and a management guide. *Surg Neurol Int*. 2012;3:98.
158. Gurney JM, Tadolock MD, Dengler BA, et al. Committee on Surgical Combat Casualty Care position statement: neurosurgical capability for the optimal management of traumatic brain injury during deployed operations. *J Trauma Acute Care Surg*. 2023;95(2S Suppl 1):S7-S12.
159. Liebenberg WA, Demetriades AK, Hanks M, Hardwidge C, Hartzenberg BH. Penetrating civilian craniocerebral gunshot wounds: a protocol of delayed surgery. *Neurosurgery*. 2005;57(2):293-299; discussion 293-299.
160. Aarabi B. Comparative study of bacteriological contamination between primary and secondary exploration of missile head wounds. *Neurosurgery*. 1987;20(4):610-616.
161. Singh P, Misra GS, Singh A, Murthy M. Missile injuries of brain - an experience in northern sector. *Med J Armed Forces India*. 2003;59(4):290-297.
162. Cushing H. A study of a series of wounds involving the brain and its enveloping structures. *J Br Surg*. 1917;5(20):558-684.
163. Ascroft P. Treatment of head wounds due to missiles. Analysis of 500 cases. *Lancet*. 1943;242(6260):211-218.
164. Aarabi B. Surgical outcome in 435 patients who sustained missile head wounds during the Iran-Iraq War. *Neurosurgery*. 1990;27(5):692-695; discussion 695.
165. Taha JM, Saba MI, Brown JA. Missile injuries to the brain treated by simple wound closure: results of a protocol during the Lebanese conflict. *Neurosurgery*. 1991;29(3):380-384; discussion 384.
166. Vranković D, Hećimović I, Splavski B, Dmitrović B. Management of missile wounds of the cerebral dura mater: experience with 69 cases. *Neurochirurgia (Stuttg)*. 1992;35(5):150-155.
167. Krueger EM, Benveniste RJ, Lu VM, et al. Simple wound closure compared with surgery for civilian cranial gunshot wounds. *J Neurosurg*. 2023;138(2):437-445.
168. Kadhim AHK, Neamah MJ, Nema IS. Cranial falling bullet injuries, a series of 30 cases in Iraq. *Br J Neurosurg*. 2020;34(2):135-141.
169. Amirjamshidi A, Abbassioun K, Rahmat H. Minimal debridement or simple wound closure as the only surgical treatment in war victims with low-velocity penetrating head injuries. Indications and management protocol based upon more than 8 years follow-up of 99 cases from Iran-Iraq conflict. *Surg Neurol*. 2003;60(2):105-111; discussion 110-111.

170. Suddaby L, Weir B, Forsyth C. The management of .22 caliber gunshot wounds of the brain: a review of 49 cases. *Can J Neurol Sci.* 1987;14(3):268-272.
171. Whiting TL, Will D. Achieving humane outcomes in killing livestock by free bullet I: penetrating brain injury. *Can Vet J.* 2019;60(5):524-531.
172. Carey ME, Sarna GS, Farrell JB, Happel LT. Experimental missile wound to the brain. *J Neurosurg.* 1989;71(5 Pt 1):754-764.
173. Ecker AD. A bacteriologic study of penetrating wounds of the brain, from the surgical point of view. *J Neurosurg.* 1946;3(1):1-6.
174. Carey ME, Young H, Mathis JL, Forsythe J. A bacteriological study of craniocerebral missile wounds from Vietnam. *J Neurosurg.* 1971;34(2 Pt 1):145-154.
175. Hammon WM. Analysis of 2187 consecutive penetrating wounds of the brain from Vietnam. *J Neurosurg.* 1971;34(2 Pt 1):127-131.
176. Pilipenko G, Sirko A, Dzyak L, Miziakina E. Results of brain injury primary surgical treatment in a complex care for patients with combat-related penetrating craniocerebral gunshot wound at a specialized medical facility. *Georgian Med News.* 2020;301:13-20.
177. Aarabi B, Taghipour M, Haghnegahdar A, Farokhi M, Mobley L. Prognostic factors in the occurrence of posttraumatic epilepsy after penetrating head injury suffered during military service. *Neurosurg Focus.* 2000;8(1):e1.
178. Haddad FS. Wilder Penfield Lecture: nature and management of penetrating head injuries during the Civil War in Lebanon. *Can J Surg.* 1978;21(3):233-240.
179. Strojnik T. A review of civilian gunshot wounds to the head in northeast Slovenia: 1992 to 2002. *Wien Klin Wochenschr.* 2004;116(Suppl 2):19-23.
180. Martins RS, Siqueira MG, Santos MT, Zanon-Collange N, Moraes OJ. Prognostic factors and treatment of penetrating gunshot wounds to the head. *Surg Neurol.* 2003;60(2):98-104; discussion 104.
181. Jamous MA. Outcome of craniocerebral penetrating injuries: experience from the syrian war. *J Neurol Surg A Cent Eur Neurosurg.* 2019;80(5):345-352.
182. Coşar A, Gönül E, Kurt E, Gönül M, Taşar M, Yetişer S. Craniocerebral gunshot wounds: results of less aggressive surgery and complications. *Minim Invasive Neurosurg.* 2005;48(2):113-118.
183. Gonul E, Erdogan E, Izci Y, Baysefer A, Seber N. Craniocerebral gunshot wounds: analysis of 288 cases, a clinical review. *Turkish Neurosurgery.* 1999;9(1-2):1-7.
184. Elzayat S. G., AA A. Incidence of post-traumatic epilepsy. *J Neurol Orth Med S.* 1986;7(1):69-70.
185. Aarabi B. Causes of infections in penetrating head wounds in the Iran-Iraq War. *Neurosurgery.* 1989;25(6):923-926.
186. Darwazeh R, Darwazeh M, Sbeih I, Yan Y, Wang J, Sun X. Traumatic brain injury caused by missile wounds in the north of Palestine: a single institution's experience with 520 consecutive civilian patients. *World Neurosurg.* 2018;116:e329-e339.
187. Fathalla H, Ashry A, El-Fiki A. Managing military penetrating brain injuries in the war zone: lessons learned. *Neurosurg Focus.* 2018;45(6):e6.
188. Harmon LA, Haase DJ, Kufera JA, et al. Infection after penetrating brain injury—An Eastern Association for the Surgery of Trauma multicenter study oral presentation at the 32nd annual meeting of the Eastern Association for the Surgery of Trauma, January 15-19, 2019, in Austin, Texas. *J Trauma Acute Care Surg.* 2019; 87(1):61-67.
189. Janković S, Bradarić N, Busić Z, Dujčić Z, Anđelinović S, Primorac D. Early intracranial infections after brain missile injuries—the role of computer tomography in diagnosis and treatment. *Acta Med Croatica.* 1997;51(4-5):233-237.
190. Jimenez CM, Polo J, España JA. Risk factors for intracranial infection secondary to penetrating craniocerebral gunshot wounds in civilian practice. *World Neurosurg.* 2013;79:749-755.
191. Kershner EK, Tobarran N, Chambers A, Wills BK, Cumpston KL. Retained bullets and lead toxicity: a systematic review. *Clin Toxicol (Phila).* 2022;60(10): 1176-1186.
192. Meierowsky AM. Secondary removal of retained bone fragments in missile wounds of the brain. *J Neurosurg.* 1982;57(5):617-621.
193. Rish BL, Caveness WF, Dillon JD, Kistler JP, Mohr JP, Weiss GH. Analysis of brain abscess after penetrating craniocerebral injuries in Vietnam. *Neurosurgery.* 1981;9(5):535-541.
194. Salazar AM, Jabbari B, Vance SC, Grafman J, Amin D, Dillon JD. Epilepsy after penetrating head injury. I. Clinical correlates: a report of the Vietnam Head Injury Study. *Neurology.* 1985;35(10):1406-1414.
195. Tudor M, Tudor L, Tudor KI. Complications of missile craniocerebral injuries during the Croatian Homeland War. *Mil Med.* 2005;170(5):422-426.
196. Tudor M. Prediction of outcome in patients with missile craniocerebral injuries during the Croatian War. *Mil Med.* 1998;163(7):486-489.
197. Webster JE, Schneider RC, Lofstrom JE. Observations on early type of brain abscess following penetrating wounds of the brain. *J Neurosurg.* 1946;3(1):7-14.
198. Meister MR, Boulter JH, Yabes JM, et al. Epidemiology of cranial infections in battlefield-related penetrating and open cranial injuries. *J Trauma Acute Care Surg.* 2023;95(2S Suppl 1):S72-S78.
199. Erdogan E, Seber N. Craniocerebral gunshot wounds. *Neurosurgery Quarterly.* 2002;12(1):1-18.
200. Caldicott DG, Pearce A, Price R, Croser D, Brophy B. Not just another 'head lac'. low-velocity, penetrating intra-cranial injuries: a case report and review of the literature. *Injury.* 2004;35(10):1044-1054.
201. Duddleston PJ, Gendreau JL, Little KA, Andrews A, Thompson WD. Navigation-guided neuroendoscopic removal of an intracranial migratory pellet from the thalamus of a 4-year-old girl. *J Neurosurg Pediatr.* 2020;26(4):445-448.
202. Materij J, Ahmed AK, Kalluri AL, Ammar A, Cohen AR. Prophylactic removal of a migratory missile from the cerebral ventricles: case report. *Childs Nerv Syst.* 2024; 40(4):1307-1310.
203. Rapp LG, Arce CA, McKenzie R, Darmody WR, Guyot DR, Michael DB. Incidence of intracranial bullet fragment migration. *Neurol Res.* 1999;21(5): 475-480.
204. Cairns H. Injuries of the frontal and ethmoidal sinuses with special reference to cerebrospinal rhinorrhea and aerocoeles. *J Laryngol Otol.* 1937;52(9): 589-623.
205. Management of cerebrospinal fluid leaks. *J Trauma.* 2001;51(2 Suppl):S29-S33.
206. Melada A, Marcikić M, Mrak G, Stimac D, Šcap M. Cerebrospinal fluid fistula as a consequence of war head injury. *Mil Med.* 2002;167(8):666-670.
207. Wallace PB, Meierowsky AM. The repair of dural defects by graft. An analysis of 540 penetrating wounds of the brain incurred in the Korean War. *Ann Surg.* 1960; 151(2):174-180.
208. Ambrosi PB, Valenca MM, Azevedo-Filho H. Prognostic factors in civilian gunshot wounds to the head: a series of 110 surgical patients and brief literature review. *Neurosurg Rev.* 2012;35(3):429-436; discussion 435-436.
209. Solmaz I, Kural C, Temiz C, et al. Traumatic brain injury due to gunshot wounds: a single institution's experience with 442 consecutive patients. *Turk Neurosurg.* 2009;19(3):216-223.
210. Kim TW, Lee JK, Moon KS, et al. Penetrating gunshot injuries to the brain. *J Trauma.* 2007;62(6):1446-1451.
211. Aarabi B, Tofighi B, Kufera JA, et al. Predictors of outcome in civilian gunshot wounds to the head. *J Neurosurg.* 2014;120(5):1138-1146.
212. Hećimović I, Dmitrović B, Kurbel S, Blagus G, Vranes J, Rukovanjski M. Intracranial infection after missile brain wound: 15 war cases. *Zentralbl Neurochir.* 2000;61(2):95-102.
213. Ragel BT, Klimo P, Jr., Martin JE, Teff RJ, Bakken HE, Armonda RA. Wartime decompressive craniectomy: technique and lessons learned. *Neurosurg Focus.* 2010;28(5):e2.
214. Thorell W, Aarabi B. History of neurosurgical techniques in head injury. *Neurosurg Clin N Am.* 2001;12(1):11-22. vii.
215. Cushing H. *From a Surgeon's Journal 1915-1918.* Little, Brown & Co; 1936.
216. Whitaker R. Gunshot wounds of the cranium: with special reference to those of the brain. *J Br Surg.* 1915;3(12):708-735.
217. Carey ME. Cushing and the treatment of brain wounds during World War I. *J Neurosurg.* 2011;114(6):1495-1501.
218. Cairns H. Head injuries in war, with especial reference to gunshot wounds, including a report on the late results in some of Harvey Cushing's cases of 1917. *War Med.* 1942;2(5):772-785.
219. Cairns H. Gunshot head wounds in the acute stage. *Br Med J.* 1944;1(4331): 33-37.
220. Cairns H. Neurosurgery in the British Army, 1939-1945. *Br J Surg.* 1947; 55(Suppl 1):9-26.
221. Cairns H, Calvert CA, et al. Complications of head wounds, with especial reference to infection. *Br J Surg.* 1947;55(Suppl 1):198-243.
222. Calvert CA. Orbito-facio-cranial gunshot wounds. *Br J Surg.* 1947;55(Suppl 1): 119-141.
223. Discussion on injuries of the frontal and ethmoidal sinuses. *Proc R Soc Med.* 1942; 35(12):805-810.
224. Meierowsky AM. Penetrating craniocerebral trauma: observations in Korean war. *J Am Med Assoc.* 1954;154(8):666-669.
225. Erdogan E, Izci Y, Gonul E, Timurkaynak E. Ventricular injury following cranial gunshot wounds: clinical study. *Mil Med.* 2004;169(9):691-695.

226. Carey ME. The treatment of wartime brain wounds: traditional versus minimal debulking. *Surg Neurol*. 2003;60(2):112-119.
227. Gonul E, Erdogan E, Tasar M, et al. Penetrating orbitocranial gunshot injuries. *Surg Neurol*. 2005;63(1):24-30; discussion 31.
228. Aarabi B, Alden TD, Maas AIR, et al. Antibiotic prophylaxis for penetrating brain injury. *J Trauma*. 2001;51(Supplement):S34-S40.
229. Mansour A, Loggini A, El Ammar F, et al. Cerebrovascular complications in early survivors of civilian penetrating brain injury. *Neurocrit Care*. 2021;34(3):918-926.
230. Hemphill JC, Gress DR, Halbach VV, Halbach VV. Endovascular therapy of traumatic injuries of the intracranial cerebral arteries. *Crit Care Clin*. 1999;15(4):811-829.
231. Aljuboori Z, Meyer K, Ding D, James R. Endovascular treatment of a traumatic middle cerebral artery pseudoaneurysm with the pipeline flex embolization device. *World Neurosurg*. 2020;133:201-204.
232. Bodanapally UK, Saksobhavit N, Shanmuganathan K, Aarabi B, Roy AK. Arterial injuries after penetrating brain injury in civilians: risk factors on admission head computed tomography. *J Neurosurg*. 2015;122(1):219-226.
233. Jinkins JR, Dadsetan MR, Sener RN, Desai S, Williams RG. Value of acute-phase angiography in the detection of vascular injuries caused by gunshot wounds to the head: analysis of 12 cases. *AJR Am J Roentgenol*. 1992;159(2):365-368.
234. Feng L, He X, Chen J, Ni S, Jiang B, Hua JM. Complications in transorbital penetrating injury by bamboo branch: a case report. *Medicine (Baltimore)*. 2018;97(19):e0706.
235. Aldrich EF, Eisenberg HM, Saydjari C, et al. Predictors of mortality in severely head-injured patients with civilian gunshot wounds: a report from the NIH Traumatic Coma Data Bank. *Surg Neurol*. 1992;38(6):418-423.
236. Darsaut TE, Ashforth RA, Chow MM, Findlay JM. Endovascular management of an embedded intracranial knife. *Can J Neurol Sci*. 2007;34(4):460-463.
237. Hachemi M, Jourdan C, Di Roio C, et al. Delayed rupture of traumatic aneurysm after civilian craniocerebral gunshot injury in children. *Childs Nerv Syst*. 2007;23(3):283-287.
238. Sirko A, Kyrpa I, Lazorishinets V, et al. Successful surgical treatment of a patient with combined gunshot shrapnel injuries in the heart and brain complicated by middle cerebral artery pseudoaneurysm. *Trauma Case Rep*. 2018;18:17-23.
239. Abdallah OI, Clark D, Essibayi MA. Surgical reconstruction of a traumatic superior sagittal sinus injury using synthetic vascular graft in a resource-limited civilian field hospital during the Syrian civil war. *World Neurosurg*. 2022;159:126-129.
240. Alexopoulos G, Quadri N, Khan M, et al. Ballistic lobar trajectory outcomes in civilian firearm penetrating brain injury. *J Neurosurg*. 2020;135(2):574-583.
241. Beattie G, Cohan CM, Smith EA, Lee SI, Riordan M. A comparison of clinical characteristics, radiographic findings, and outcomes of bihemispheric versus unihemispheric gunshot wounds to the head. *Am J Emerg Med*. 2022;60:78-82.
242. Kapp JP, Gielchinsky I, Deardourff SL. Operative techniques for management of lesions involving the dural venous sinuses. *Surg Neurol*. 1977;7(6):339-342.
243. Pricola KL, Zou H, Chang SD. Successful repair of a gunshot wound to the head with retained bullet in the torcular herophili. *World Neurosurg*. 2011;76:362.e1-362.e4.
244. Sirko A, Pilipenko G, Romanukha D, Skrypnik A. Mortality and functional outcome predictors in combat-related penetrating brain injury treatment in a specialty civilian medical facility. *Mil Med*. 2020;185(5-6):e774-e780.
245. Khan AA, Rahman ML, Ali MI, Ziauddin M, Murshiduzzaman NM. Penetrating craniocerebral trauma report of 20 cases. *Bangladesh J Neurosci*. 1994;10(1):1-8.
246. Pylypenko HS, Sirko AH, Botikov VV. Surgical Management of battle gunshot injuries to the dural venous sinuses, combined with brain injury: an analysis of observations. *Zaporozhye Med J*. 2020;22(1):54-59.
247. Anush Rangarajan S, Ramachandran D, Mishra T, et al. Endovascular treatment for cerebral venous sinus thrombosis: comparison among different endovascular procedures. *Ann Indian Acad Neurol*. 2024;27(2):140-145.
248. Alkhaibary A, Alharbi A, Alnefaie N, Oqalaa Almubarak A, Aloraidi A, Khairy S. Cranioplasty: a comprehensive review of the history, materials, surgical aspects, and complications. *World Neurosurg*. 2020;139:445-452.
249. Ozoner B. Cranioplasty following severe traumatic brain injury: role in neuro-recovery. *Curr Neurol Neurosci Rep*. 2021;21(11):62.
250. Malcolm JG, Rindler RS, Chu JK, et al. Early cranioplasty is associated with greater neurological improvement: a systematic review and meta-analysis. *Neurosurgery*. 2018;82(3):278-288.
251. Mustafa MA, Richardson GE, Gillespie CS, et al. Health-related quality of life following cranioplasty - a systematic review. *Br J Neurosurg*. 2023;39(1):12-22.
252. Zaramo TZ, Zelko I, Ragland D, et al. Can we do better at measuring patient-reported outcomes after cranioplasty? A systematic review. *Neurosurg Rev*. 2023;46(1):109.
253. von Steinbuechel N, Covic A, Polinder S, et al. Assessment of health-related quality of life after TBI: comparison of a disease-specific (QOLIBRI) with a generic (SF-36) instrument. *Behav Neurol*. 2016;2016(1):7928014.
254. Janatpour ZC, Szuffita NS, Spinelli J, Coughlin DJ, Rosenfeld JV, Bell RS. Inadequate decompressive craniectomy following a wartime traumatic brain injury - an illustrative case of why size matters. *Mil Med*. 2019;184(11-12):929-933.
255. Sethi A, Chee K, Kaakani A, Beauchamp K, Kang J. Ultra-early cranioplasty versus conventional cranioplasty: a retrospective cohort study at an academic level 1 trauma center. *Neurotrauma Rep*. 2022;3(1):286-291.
256. Piedra MP, Ragel BT, Dogan A, Coppa ND, Delashaw JB. Timing of cranioplasty after decompressive craniectomy for ischemic or hemorrhagic stroke. *J Neurosurg*. 2013;118(1):109-114.
257. Archavlis E, Carvi Y, Nieves M. The impact of timing of cranioplasty in patients with large cranial defects after decompressive hemicraniectomy. *Acta Neurochir (Wien)*. 2012;154(6):1055-1062.
258. Bender A, Heulin S, Röhrer S, et al. Early cranioplasty may improve outcome in neurological patients with decompressive craniectomy. *Brain Inj*. 2013;27(9):1073-1079.
259. Wachter D, Reineke K, Behm T, Rohde V. Cranioplasty after decompressive hemicraniectomy: underestimated surgery-associated complications? *Clin Neurol Neurosurg*. 2013;115(8):1293-1297.
260. Li A, Azad TD, Veeravagu A, et al. Cranioplasty complications and costs: a national population-level analysis using the marketscan longitudinal database. *World Neurosurg*. 2017;102:209-220.
261. Chibbaro S, Di Rocco F, Mirone G, et al. Decompressive craniectomy and early cranioplasty for the management of severe head injury: a prospective multicenter study on 147 patients. *World Neurosurg*. 2011;75:558-562.
262. Cheng YK, Weng HH, Yang JT, Lee MH, Wang TC, Chang CN. Factors affecting graft infection after cranioplasty. *J Clin Neurosci*. 2008;15(10):1115-1119.
263. Patir R, Mahapatra AK, Banerji AK. Risk factors in postoperative neurosurgical infection. A prospective study. *Acta Neurochir (Wien)*. 1992;119(1-4):80-84.
264. Chen R, Ye G, Zheng Y, et al. Optimal timing of cranioplasty and predictors of overall complications after cranioplasty: the impact of brain collapse. *Neurosurgery*. 2023;93(1):84-94.
265. Chang V, Hartzfeld P, Langlois M, Mahmood A, Seyfried D. Outcomes of cranial repair after craniectomy. *J Neurosurg*. 2010;112(5):1120-1124.
266. Thavarajah D, De Lacy P, Hussien A, Sugar A. The minimum time for cranioplasty insertion from craniectomy is six months to reduce risk of infection—a case series of 82 patients. *Br J Neurosurg*. 2012;26(1):78-80.
267. Kumar AR, Tantawi D, Armonda R, Valerio I. Advanced cranial reconstruction using intracranial free flaps and cranial bone grafts: an algorithmic approach developed from the modern battlefield. *Plast Reconstr Surg*. 2012;130(5):1101-1109.
268. Mundinger GS, Latham K, Friedrich J, et al. Management of the repeatedly failed cranioplasty following large postdecompressive craniectomy: establishing the efficacy of staged free latissimus Dorsi transfer/tissue expansion/custom polyetheretherketone implant reconstruction. *J Craniofac Surg*. 2016;27(8):1971-1977.
269. Henry J, Amoo M, Taylor J, O'Brien DP. Complications of cranioplasty in relation to material: systematic review, network meta-analysis and meta-regression. *Neurosurgery*. 2021;89(3):383-394.
270. Rish BL, Dillon JD, Meirowsky AM, et al. Cranioplasty: a review of 1030 cases of penetrating head injury. *Neurosurgery*. 1979;4(5):381-385.
271. Stephens FL, Mossop CM, Bell RS, et al. Cranioplasty complications following wartime decompressive craniectomy. *Neurosurg Focus*. 2010;28(5):e3.
272. Mathew P, Gibbons AJ, Christie M, Eisenburg MF. Operative treatment of paediatric penetrating head injuries in southern Afghanistan. *Br J Neurosurg*. 2013;27(4):489-496.
273. Javadi SAH, Balu P, Naderi Behdani F, Orandi AH, Ahmadipour E, Pestei K. Long-term outcome following decompressive craniectomy in pediatric penetrating blast brain injury: a prospective study. *Arch Neurosci*. 2021;8(4):e117264.

274. Mee H, Anwar F, Timofeev I, et al. Cranioplasty: a multidisciplinary approach. *Front Surg*. 2022;9:864385.
275. Elegbede A, Wasicek PJ, Mermulla S, et al. Survival following self-inflicted gunshot to the face. *Plast Reconstr Surg*. 2019;144(2):415-422.
276. Kriet JD, Stanley RB Jr, Grady MS. Self-inflicted submental and transoral gunshot wounds that produce nonfatal brain injuries: management and prognosis. *J Neurosurg*. 2005;102(6):1029-1032.
277. Weichel ED, Colyer MH, Bautista C, Bower KS, French LM. Traumatic brain injury associated with combat ocular trauma. *J Head Trauma Rehabil*. 2009;24(1):41-50.
278. Kim SW, Youn SK, Kim JT, Cho SH, Kim YH, Hwang KT. Management of an unusual craniofacial impalement injury by a metallic foreign body. *J Craniofac Surg*. 2012;23(2):e140-e146.
279. Zhang J, Zhang F, Dong JF. Coagulopathy induced by traumatic brain injury: systemic manifestation of a localized injury. *Blood*. 2018;131(18):2001-2006.
280. Harhangi BS, Kompanje EJ, Leebeek FW, Maas AI. Coagulation disorders after traumatic brain injury. *Acta Neurochir (Wien)*. 2008;150(2):165-175; discussion 175.
281. Wafaisade A, Lefering R, Tjardes T, et al. Acute coagulopathy in isolated blunt traumatic brain injury. *Neurocrit Care*. 2010;12(2):211-219.
282. Folkerson LE, Sloan D, Davis E, et al. Coagulopathy as a predictor of mortality after penetrating traumatic brain injury. *Am J Emerg Med*. 2018;36(1):38-42.
283. Cap AP, Spinella PC. Severity of head injury is associated with increased risk of coagulopathy in combat casualties. *J Trauma*. 2011;71(1 Suppl):S78-S81.
284. Talving P, Benfield R, Hadjizacharia P, Inaba K, Chan LS, Demetriades D. Coagulopathy in severe traumatic brain injury: a prospective study. *J Trauma*. 2009;66(1):55-62; discussion 61-62.
285. Lustenberger T, Talving P, Kobayashi L, et al. Time course of coagulopathy in isolated severe traumatic brain injury. *Injury*. 2010;41(9):924-928.
286. Martin G, Shah D, Elson N, et al. Relationship of coagulopathy and platelet dysfunction to transfusion needs after traumatic brain injury. *Neurocrit Care*. 2018;28(3):330-337.
287. Böhm JK, Güting H, Thorn S, et al. Global characterisation of coagulopathy in isolated traumatic brain injury (iTBI): a CENTER-TBI analysis. *Neurocrit Care*. 2021;35(1):184-196.
288. Bordes J, Joubert C, Esnault P, et al. Coagulopathy and transfusion requirements in war related penetrating traumatic brain injury. A single centre study in a French role 3 medical treatment facility in Afghanistan. *Injury*. 2017;48(5):1047-1053.
289. Mathur R, Suarez JI. Coagulopathy in isolated traumatic brain injury: myth or reality. *Neurocrit Care*. 2023;38(2):429-438.
290. Holcomb JB, Minei KM, Scerbo ML, et al. Admission rapid thrombelastography can replace conventional coagulation tests in the emergency department: experience with 1974 consecutive trauma patients. *Ann Surg*. 2012;256(3):476-486.
291. Da Luz LT, Nascimento B, Shankarakutty AK, Rizoli S, Adhikari NK. Effect of thromboelastography (TEG®) and rotational thromboelastometry (ROTEM®) on diagnosis of coagulopathy, transfusion guidance and mortality in trauma: descriptive systematic review. *Crit Care*. 2014;18(5):518.
292. Veigas PV, Callum J, Rizoli S, Nascimento B, da Luz LT. A systematic review on the rotational thromboelastometry (ROTEM®) values for the diagnosis of coagulopathy, prediction and guidance of blood transfusion and prediction of mortality in trauma patients. *Scand J Trauma Resusc Emerg Med*. 2016;24(1):114.
293. Cucher D, Harmon L, Myer B, et al. Critical traumatic brain injury is associated with worse coagulopathy. *J Trauma Acute Care Surg*. 2021;91(2):331-335.
294. Webb AJ, Brown CS, Naylor RM, Rabinstein AA, Mara KC, Nei AM. Thromboelastography is a marker for clinically significant progressive hemorrhagic injury in severe traumatic brain injury. *Neurocrit Care*. 2021;35(3):738-746.
295. Schöchl H, Solomon C, Traintinger S, et al. Thromboelastometric (ROTEM) findings in patients suffering from isolated severe traumatic brain injury. *J Neurotrauma*. 2011;28(10):2033-2041.
296. Samuels JM, Moore EE, Silliman CC, et al. Severe traumatic brain injury is associated with a unique coagulopathy phenotype. *J Trauma Acute Care Surg*. 2019;86(4):686-693.
297. Aiyagari V, Menendez JA, Diringner MN. Treatment of severe coagulopathy after gunshot injury to the head using recombinant activated factor VII. *J Crit Care*. 2005;20(2):176-179.
298. Kochanek PM, Tasker RC, Carney N, et al. Guidelines for the management of pediatric severe traumatic brain injury, third edition: update of the brain trauma foundation guidelines. *Pediatr Crit Care Med*. 2019;20(3S Suppl 1):S1-S82.
299. Robertson CS, Valadka AB, Hannay HJ, et al. Prevention of secondary ischemic insults after severe head injury. *Crit Care Med*. 1999;27(10):2086-2095.
300. Czosnyka M, Smielewski P, Kirkpatrick P, Menon DK, Pickard JD. Monitoring of cerebral autoregulation in head-injured patients. *Stroke*. 1996;27(10):1829-1834.
301. Czosnyka M, Smielewski P, Piechnik S, Steiner LA, Pickard JD. Cerebral autoregulation following head injury. *J Neurosurg*. 2001;95(5):756-763.
302. Vu EL, Brown CH, Brady KM, Hogue CW. Monitoring of cerebral blood flow autoregulation: physiologic basis, measurement, and clinical implications. *Br J Anaesth*. 2024;132(6):1260-1273.
303. Beqiri E, Smielewski P, Robba C, et al. Feasibility of individualised severe traumatic brain injury management using an automated assessment of optimal cerebral perfusion pressure: the COGiTATE phase II study protocol. *BMJ Open*. 2019;9(9):e030727.
304. Intracranial pressure monitoring in the management of penetrating brain injury. *J Trauma*. 2001;51(Supplement):S12-S15.
305. Mansour A, Rowell S, Powl P, Horowitz P, Goldenberg FD, Lazaridis C. Comparative effectiveness of intracranial pressure monitoring vs no monitoring in severe penetrating brain injury management. *JAMA Netw Open*. 2023;6(3):e231077.
306. Lannon MM, Duda T, Martyniuk A, Engels PT, Sharma SV. Pediatric craniocerebral gunshot injuries: a National Trauma Database study. *J Trauma Acute Care Surg*. 2022;92(2):428-435.
307. Infection after penetrating brain injury—An Eastern Association for the Surgery of Trauma multicenter study oral presentation at the 32nd annual meeting of the Eastern Association for the Surgery of Trauma, January 15-19, 2019, in Austin, Texas: Erratum. *J Trauma Acute Care Surg*. 2019;87(3):744.
308. Bandt SK, Greenberg JK, Yarbrough CK, Schechtman KB, Limbrick DD, Leonard JR. Management of pediatric intracranial gunshot wounds: predictors of favorable clinical outcome and a new proposed treatment paradigm. *J Neurosurg Pediatr*. 2012;10(6):511-517.
309. Lane PL, Skoretz TG, Doig G, Girotti MJ. Intracranial pressure monitoring and outcomes after traumatic brain injury. *Can J Surg*. 2000;43(6):442-448.
310. Levy ML, Masri LS, Levy KM, et al. Penetrating craniocerebral injury resultant from gunshot wounds: gang-related injury in children and adolescents. *Neurosurgery*. 1993;33(6):1018-1025; discussion 1024-1025.
311. Frösen J, Frisk O, Raj R, Hernesniemi J, Tukiainen E, Barner-Rasmussen I. Outcome and rational management of civilian gunshot injuries to the brain: retrospective analysis of patients treated at the Helsinki University Hospital from 2000 to 2012. *Acta Neurochir (Wien)*. 2019;161(7):1285-1295.
312. Ewing-Cobbs L, Thompson NM, Miner ME, Fletcher JM. Gunshot wounds to the brain in children and adolescents: age and neurobehavioral development. *Neurosurgery*. 1994;35(2):225-233; discussion 233.
313. Rashid BA, Wani MA, Kirmani AR, et al. Comparative outcome of non-metallic and metallic craniocerebral missile injuries. *Curr Neurobiol*. 2010;1(2):151-160.
314. Cnossen MC, Huijben JA, van der Jagt M, et al. Variation in monitoring and treatment policies for intracranial hypertension in traumatic brain injury: a survey in 66 neurotrauma centers participating in the CENTER-TBI study. *Crit Care*. 2017;21(1):233.
315. Lazaridis C, DeSantis SM, Smielewski P, et al. Patient-specific thresholds of intracranial pressure in severe traumatic brain injury. *J Neurosurg*. 2014;120(4):893-900.
316. Güiza F, Depreitere B, Piper I, et al. Visualizing the pressure and time burden of intracranial hypertension in adult and paediatric traumatic brain injury. *Intensive Care Med*. 2015;41(6):1067-1076.
317. Hawryluk GWJ, Nielson JL, Huie JR, et al. Analysis of normal high-frequency intracranial pressure values and treatment threshold in neurocritical care patients: insights into normal values and a potential treatment threshold. *JAMA Neurol*. 2020;77(9):1150-1158.
318. Walker WC, Ketchum JS, 3rd, Marwitz JH, Kolakowsky-Hayner SA, McClish DK, Bushnik T. Global outcome and late seizures after penetrating versus closed traumatic brain injury: a NIDRR TBI model systems study. *J Head Trauma Rehabil*. 2015;30(4):231-240.
319. Vespa PM, Nuwer MR, Nenov V, et al. Increased incidence and impact of non-convulsive and convulsive seizures after traumatic brain injury as detected by continuous electroencephalographic monitoring. *J Neurosurg*. 1999;91(5):750-760.
320. Vespa PM, Miller C, McArthur D, et al. Nonconvulsive electrographic seizures after traumatic brain injury result in a delayed, prolonged increase in intracranial pressure and metabolic crisis. *Crit Care Med*. 2007;35(12):2830-2836.

321. Pugh MJ, Orman JA, Jaramillo CA, et al. The prevalence of epilepsy and association with traumatic brain injury in veterans of the Afghanistan and Iraq wars. *J Head Trauma Rehabil.* 2015;30(1):29-37.
322. Englander J, Bushnik T, Duong TT, et al. Analyzing risk factors for late post-traumatic seizures: a prospective, multicenter investigation. *Arch Phys Med Rehabil.* 2003;84(3):365-373.
323. Aarabi B, Alden TD, Maas AIR, et al. Antiseizure prophylaxis for penetrating brain injury. *J Trauma.* 2001;51(Supplement):S41-S43.
324. Temkin NR, Dikmen SS, Wilensky AJ, Keihm J, Chabal S, Winn HR. A randomized, double-blind study of phenytoin for the prevention of post-traumatic seizures. *N Engl J Med.* 1990;323(8):497-502.
325. Glötzner FL, Haubitz I, Miltner F, Kapp G, Pflughaupt KW. [Seizure prevention using carbamazepine following severe brain injuries]. *Neurochirurgia (Stuttg).* 1983;26(3):66-79.
326. Lafrenaye A, Mondello S, Povlishock J, et al. Operation brain trauma therapy: an exploratory study of levetiracetam treatment following mild traumatic brain injury in the micro pig. *Front Neurol.* 2020;11:586958.
327. Browning M, Shear DA, Bramlett HM, et al. Levetiracetam treatment in traumatic brain injury: operation brain trauma therapy. *J Neurotrauma.* 2016;33(6):581-594.
328. Atwood R, Walker P, Walper D, Elster E, Bradley M. Use of levetiracetam for post-traumatic seizure prophylaxis in combat-related traumatic brain injury. *Mil Med.* 2023;188(11-12):e3570-e3574.
329. Döşoğlu M, Orakdöğen M, Somay H, Ateş O, Ziyal I. Civilian gunshot wounds to the head. *Neurochirurgie.* 1999;45(3):201-207.
330. Khan MB, Kumar R, Irfan FB, Irfan AB, Bari ME. Civilian craniocerebral gunshot injuries in a developing country: presentation, injury characteristics, prognostic indicators, and complications. *World Neurosurg.* 2014;82:14-19.
331. Malav RA, Chandra A, Singh S, et al. Outcome of penetrating brain injury in civilian practice. *Indian J. Neurotr.* 2015;12(02):122-127.
332. Splavski B, Vranković D, Sarić G, et al. Early surgery and other indicators influencing the outcome of war missile skull base injuries. *Surg Neurol.* 1998;50(3):194-199.
333. McCafferty R, Neal C, Marshall S, Pamplin J, Bell R, Rivet D. Neurosurgery and severe head injury (CPG ID:30). *Joint Trauma System Clinical Practice Guideline*; 2017.
334. Harrington BM, Gretsichel A, Lombard C, Lonsner RR, Vlok AJ. Complications, outcomes, and management strategies of non-missile penetrating head injuries. *J Neurosurg.* 2021;134(5):1658-1666.
335. Doherty PF, Rabinowitz RP. Gunshot wounds to the head: the role of antibiotics. *Infect Med.* 2004;21(6):297-300.
336. Marut D, Shammassian B, McKenzie C, Adamski J, Traeger J. Evaluation of prophylactic antibiotics in penetrating brain injuries at an academic level 1 trauma center. *Clin Neurol Neurosurg.* 2020;193:105777.
337. Etheridge JC, Vignali JD, Collins JN. Duration of antibiotic prophylaxis in patients with gunshot wounds to the head. *Am Surg.* 2017;83(8):e271-273.
338. Chen D, Luo J, Zhang C, et al. Venous thrombus embolism in polytrauma: special attention to patients with traumatic brain injury. *J Clin Med.* 2023;12(5):1716.
339. Skrifvars MB, Bailey M, Presneill J, et al. Venous thromboembolic events in critically ill traumatic brain injury patients. *Intensive Care Med.* 2017;43(3):419-428.
340. CRASH-3 Trial Collaborators. Effects of tranexamic acid on death, disability, vascular occlusive events and other morbidities in patients with acute traumatic brain injury (CRASH-3): a randomised, placebo-controlled trial. *Lancet.* 2019;394(10210):1713-1723.
341. Roberts I, Perel P, Prieto-Merino D, et al. Effect of tranexamic acid on mortality in patients with traumatic bleeding: prespecified analysis of data from randomised controlled trial. *BMJ.* 2012;345:e5839.
342. Leeper CM, Vissa M, Cooper JD, Malec LM, Gaines BA. Venous thromboembolism in pediatric trauma patients: ten-year experience and long-term follow-up in a tertiary care center. *Pediatr Blood Cancer.* 2017;64(8):e26415.
343. Keely GC, McGill Gorsuch A, McCabe JM, et al. Uniform determination of Death Act. *Conn Med.* 1982;46(5):259-260.
344. Kogan A, Ram E, Nachum E, Kassif Y, Lavee J, Peled Y. Does duration of donor brain injury impact heart transplantation outcomes? *Clin Transplant.* 2019;33(8):e13660.
345. Resnick S, Seamon MJ, Holena D, Pascual J, Reilly PM, Martin ND. Early declaration of death by neurologic criteria results in greater organ donor potential. *J Surg Res.* 2017;218:29-34.
346. Anwar A, Lee JM. Medical management of brain-dead organ donors. *Acute Crit Care.* 2019;34(1):14-29.
347. Ball IM, Hornby L, Rochwerf B, et al. Management of the neurologically deceased organ donor: a Canadian clinical practice guideline. *CMAJ.* 2020;192(14):e361-e369.
348. Greer DM, Kirschen MP, Lewis A, et al. Pediatric and adult brain death/death by neurologic criteria consensus guideline. *Neurology.* 2023;101(24):1112-1132.
349. Essien EO, Fioretti K, Scalea TM, Stein DM. Physiologic features of brain death. *Am Surg.* 2017;83(8):850-854.
350. Essien EO, Parimi N, Gutwald-Miller J, Nutter T, Scalea TM, Stein DM. Organ dysfunction and failure following brain death do not preclude successful donation. *World J Surg.* 2017;41(11):2933-2939.
351. Wood KE, Becker BN, McCartney JG, D'Alessandro AM, Coursin DB. Care of the potential organ donor. *N Engl J Med.* 2004;351(26):2730-2739.
352. Kotloff RM, Blosser S, Fulda GJ, et al. Management of the potential organ donor in the ICU: Society of Critical Care Medicine/American College of Chest Physicians/Association of Organ Procurement Organizations Consensus Statement. *Crit Care Med.* 2015;43(6):1291-1325.
353. Patel MS, Zatarain J, De La Cruz S, et al. The impact of meeting donor management goals on the number of organs transplanted per expanded criteria donor: a prospective study from the UNOS Region 5 Donor Management Goals Workgroup. *JAMA Surg.* 2014;149(9):969-975.
354. Zafonte RD, Wood DL, Harrison-Felix CL, Valena NV, Black K. Penetrating head injury: a prospective study of outcomes. *Neurol Res.* 2001;23(2-3):219-226.
355. Hotz GA, Stewart KJ, Petrin D, et al. Neurobehavioural outcomes of penetrating and tangential gunshot wounds to the head. *Brain Inj.* 2000;14(7):649-657.
356. Zafonte RD, Mann NR, Millis SR, Wood DL, Lee CY, Black KL. Functional outcome after violence related traumatic brain injury. *Brain Inj.* 1997;11(6):403-407.
357. National Academies of Sciences, Engineering, and Medicine; Health and Medicine Division; Board on Health Care Services; Board on Health Sciences Policy; Committee on Accelerating Progress in Traumatic Brain Injury Research and Care. *Traumatic Brain Injury: A Roadmap for Accelerating Progress*. Matney C, Bowman K, Berwick D, eds. National Academies Press (US); 2022.

Supplemental digital content is available for this article at neurosurgery-online.com.

Supplemental Digital Content 1. Appendix A. Methods, Key Questions Used for Searching, Search Strategies, Risk of Bias (Quality) Assessment of Individual Studies, Data Analysis and Synthesis, Grading the Strength of the Body of Evidence. **Appendix B.** Literature Flow Diagram. **Appendix C.** Included Studies List. **Appendix D.** Excluded Studies List. **Appendix H.** Appendix References.

Supplemental Digital Content 2. Appendix E. Evidence.

Supplemental Digital Content 3. Appendix F. Risk of Bias Assessment.

Supplemental Digital Content 4. Appendix G. Details on Strength of Evidence.

Supplemental Digital Content 5. Systematic Review.

Supplemental Digital Content 6. Pre-Conference Delphi Consensus Voting Results. Online Survey 1.

Supplemental Digital Content 7. Pre-Conference Delphi Consensus Voting Results. Online Survey 2.

Supplemental Digital Content 8. Pre-Conference Delphi Consensus Voting Results. Online Survey 3.

Supplemental Digital Content 9. Pre-Conference Delphi Consensus Voting Results. Online Survey 4.

Supplemental Digital Content 10. Pre-Conference Delphi Consensus Voting Results. Online Survey 5.

Supplemental Digital Content 11. In-Person Consensus Voting Results. Prognosis in pTBI Voting Results.

Supplemental Digital Content 12. In-Person Consensus Voting Results. In-Person Meeting Delphi Voting Results.

Supplemental Digital Content 13. Post-Consensus Voting Results. Online Survey 6.

Supplemental Digital Content 14. Post-Consensus Voting Results. Online Survey 7.
