

The American Venous Forum clinical practice guideline on the care of patients with upper extremity deep venous thrombosis



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ABSTRACT

The American Venous Forum has formulated evidence-based clinical practice guidelines to provide recommendations on the care of patients with upper extremity deep venous thrombosis. All recommendations follow a systematic review of workup and therapy options for patients with upper extremity deep venous thrombosis. Potential limitations of these guidelines are due to the lack of evidence on some specific subareas, such as risk stratification and long-term outcomes. (J Vasc Surg Venous Lymphat Disord 2026;14:102461.)

Keywords: Deep vein thrombosis; Upper extremity; Endovenous; Venous thrombectomy; Guidelines

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Disclaimer: The American Venous Forum (AVF) develops evidenced-based clinical practice guidelines as a resource to assist medical providers in the treatment of venous disease. The guideline recommendations contained herein are based on a recent review of available body of evidence. However, it must be noted that their applicability needs to reflect the limitations of those data, as they are subject to reassessment and revision when new knowledge emerges. Given these limitations, clinical practice guidelines are not intended to represent a statement of the standard of care, nor do they substitute for clinician judgment, nor supplant patient preference or

shared decision-making. The AVF recognizes that departure from guidelines may be warranted when, in the reasonable judgment of the treating clinician, such course of action is indicated by the clinical presentation of the patient, limitations of available resources, new advances in knowledge or technology, or patient preference. The reader must rely solely on their own judgment to determine what practices and procedures, whether included in this practice guideline or not, are appropriate for them, their patient, their institution, or their practice.

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INTRODUCTION AND RATIONALE

Upper extremity deep venous thrombosis (UEDVT) is defined as a venous thrombosis occurring in the deep veins of upper extremities, which include the innominate, internal jugular, subclavian, axillary, brachial, ulnar, and radial veins ([Fig 1](#)). UEDVT accounts for 5% to 10% of all cases of DVT.¹ Anatomical distribution of UEDVT is depicted in [Table I](#). Owing to the low prevalence of UEDVT management strategies have been derived from insights on treatment of lower extremity DVT (LEDVT). However, significant differences between the two exist in terms of pathophysiology, comorbid conditions, outcomes, and complications. The prevalence and incidence of UEDVT is shown in [Table II](#).

The pathophysiology and implications of UEDVT warrant unique guidelines and not an extension of those for LEDVT because there are differences between the two pathologies and etiologies. This has become due to the rising use of central venous catheters (CVCs), pacemakers, and implantable defibrillators. In addition, the greater awareness of thrombophilia and hypercoagulable states has resulted in increased diagnostic

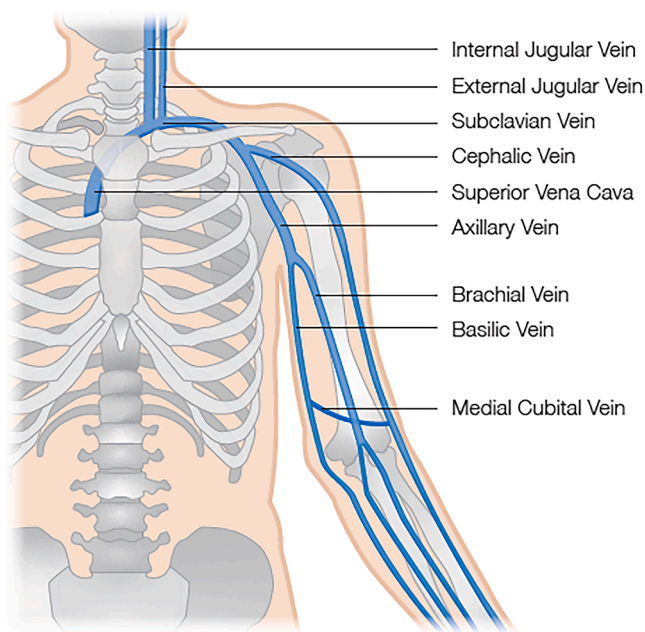


Fig 1. Upper extremity venous anatomy relevant to upper extremity deep venous thrombosis (UEDVT). Illustration of the major deep and superficial veins of the upper extremity, including the brachial, axillary, subclavian, internal jugular, and innominate veins, which together define the anatomic distribution of upper extremity deep venous thrombosis (UEDVT).

evaluation, which has increased the incidence of UEDVT over the past decades.

Unlike LEDVT, UEDVT presents unique challenges in diagnosis, management, and prevention owing to its distinct anatomical and physiological characteristics. UEDVT can also lead to serious complications, including recurrent thromboembolism, pulmonary embolism (PE), and post-thrombotic syndrome (PTS).³⁰ These complications significantly affect patient morbidity, quality of life, and health care resource utilization. Despite its clinical significance, the management of UEDVT remains under-represented in the literature compared with LEDVT.³¹ Variations in clinical practice, a lack of consensus on diagnostic criteria, and inconsistent use of anticoagulation therapy highlight the need for clear, evidence-based guidelines. Although the outcomes of UEDVT are outside the scope of this document, Table III summarizes the literature regarding UEDVT clinical outcomes.

The aim of these guidelines is to provide a comprehensive framework for the diagnosis, management, and prevention of UEDVT, thereby improving patient outcomes and standardizing care across health care settings. This document addresses key aspects of UEDVT management, including etiology, risk stratification, clinical presentation, diagnostic modalities, and therapeutic approaches. Special considerations are given to higher risk individuals, such as patients with catheter-associated

Table I. Anatomical distribution of upper extremity deep venous thrombosis (UEDVT)

Author, year	Patient population	No. of patients	% Distribution of UEDVT
Cires-Drouet et al, 2022 ²	First 1000 consecutive patients with UEDVT	1000 patients with UEDVT confirmed	Internal jugular 51.4% Subclavian 16.2% Axillary 15.6% Brachial 10.0% Innominate (brachiocephalic) 6.9%
Rokosh et al, 2020 ³	All consecutive inpatients diagnosed with acute VTE	35 UEDVTs	22.9% central (IJV, SCV) 27.6% Isolated arm (axillary/brachial) 47.6% Mixed
Beiswenger et al, 2020 ⁴	All patients who underwent venous UE DUS of the upper extremity	172 patients with UEDVT; 74.1% inpatients	17.6% IJV only 7.2% SCV only 12.1% AxV only 21.4% multiple central veins 14.7% BV only 25.7% both peripheral and central veins
Lazo-Langer et al, 2015 ⁵	All adult patients with a DUS confirming symptomatic UEDVT	141 UEDVTs (75 NCA-UEDVTs, 66 CA-UEDVTs)	1.4% SVC 21.3% IJV 68.8% SCV 10.6% innominate vein 51.8% AxV
Schleyer et al, 2014 ⁶	Symptomatic adult inpatients diagnosed with UEDVT	50 patients with 76 UEDVTs	37% IJV 16% SCV 30% AxV 25% BV
Lee et al, 2012 ⁷	Patients who underwent UEDVT investigation with DUS	94 patients with acute UEDVT (73% inpatients)	45% IJV 62% SCV 26% innominate vein 45% AxV 29% BV

AxV, Axillary vein; BV, brachial vein; DUS, duplex ultrasound; IJV, internal jugular vein; PICC, peripherally inserted central catheter; SCV, subclavian vein; VTE, venous thromboembolism; UE, upper extremity.

Table II. Prevalence and incidence of upper extremity deep venous thrombosis (UEDVT)

Author, year	Patient population	Prevalence of UEDVT	Incidence of UEDVT	Region
Population and registry studies				
Cires-Drouet et al, 2022 ²	63,045 patients admitted to the hospital 3695 upper extremity venous DUS	1000 (1.6%) of all admissions had UEDVT	N/R	University of Maryland (Maryland, USA)
Rokosh et al, 2020 ³	4495 screened 96 with VTE	35 (36.5%) of all VTEs were UEDVT	0.78%/7-month period (of those screened)	NYU Langone inpatients (New York, USA)
Beiswenger et al, 2020 ⁴	911 Screened for UEDVT	182 (20.0%) of patients screened had UEDVT	20%/1-year period	UHCMC (Cleveland, USA)
Yamashita et al, 2019 ⁸	19,634 Screened 2498 with acute DVT	74 (3.0%) of all acute DVTs were UEDVT	0.38%/4 years 7 months (of those screened)	COMMAND-VTE registry population (Japan)
Agno et al, 2019 ⁹	10,685 with acute VTE	438 (4.1%) UEDVT	N/R	GARFIELD-VTE registry (International)
Beitland et al, 2019 ¹⁰	70 Medical and surgical ICU patients on dalteparin prophylaxis	9 (12.9%) CA-UEDVT 2 (2.9%) NCA-UEDVT	N/R	Oslo University Hospital (Oslo, Norway)
Delluc et al, 2019 ¹¹	502 with acute DVT	48 (9.6%) CA-UEDVT 24 (4.8%) NCA-UEDVT	9.8/100,000 inhabitants	EPIGETBO data (Western France)
Menaker et al, 2017 ¹²	51,049 that underwent port placement	926 (1.81%) CA-UEDVT	N/R	Healthcare Cost and Utilization Project's Florida State Ambulatory Surgery and Services Database (Florida, USA)
Cote et al, 2017 ¹³	37,366 with acute DVT	1334 (3.6%) NCA-UEDVT 938 (2.5%) CA-UEDVT	N/R	RIETE registry (International)
Chopra et al, 2017 ¹⁴	23,010 with PICC	475 (2.1%) CA-UEDVT	2.1%/2 years and 6 months	MHMS consortium (Michigan, USA)
Underhill et al, 2017 ¹⁵	10,907 medical or surgical ICU patients	96/6027 (1.59%) CA-UEDVT in the medical ICU 97/4880 (1.99%) CA-UEDVT in the surgical ICU	1.8%/5 years	University of Michigan Health System (Michigan, USA)
Spirk et al, 2016 ¹⁶	493 patients with cancer-associated VTE 1569 VTE patients without cancer	79 (16%) UEDVT (cancer) 110 (7%) UEDVT (no cancer)	N/R	SWIVTER Swiss Venous ThromboEmbolic Registry (Switzerland)
Greene et al, 2015 ¹⁷	76,242 Total inpatients 3780 patients with PICC 876 total VTEs	124 (0.2%) NCA-UEDVT 84 (2.2%) CA-UEDVT 208/876 (23.7%) of all VTEs	0.32/10,000 patient-days (total) 0.20/10,000 patient-days (no) 2.75/10,000 patient-days	Multicentric (Michigan, USA)
Chung et al, 2015 ¹⁸	11,019 underwent DUS 213 screened for UEDVT	34 (14.4%) UEDVT 34/822 (7.6%) of all acute DVTs	0.31%/13 years (of patients undergoing DUS)	Radiology Information System of the Hong Kong Hospital Authority (Hong Kong, China)

Table II. Continued.

Author, year	Patient population	Prevalence of UEDVT	Incidence of UEDVT	Region
Winters et al, 2015 ¹⁹	299 patients with hospital-acquired VTEs in medical inpatients	91 (30.4%) UEDVT	1.4/1000 admissions (total) 0.2/1000 admissions (no CVC) 8.1/1000 admissions (PICC) 4.7/1000 admissions (CVC)	Medical Inpatient and Thrombosis (MITH) study, University of Vermont (Vermont, USA)
Sartori et al, 2015 ²⁰	242 screened for UEDVT	24 (10%) UEDVT 35 (14.6%) UESVT	N/A (Not consecutive patients)	Orsola-Malpighi University Hospital (Bologna, Italy)
Lamontagne et al, 2014 ²¹	3746 medical-surgical ICU patients	137 (3.7%) UEDVT 70 (1.9%) CA-UEDVT	N/R	PROTECT trial data (Canada, Australia, Brazil, Saudi Arabia, New Zealand)
Liem et al, 2012 ²²	831 UE DUS performed	154 (18.5%) UEDVTs 57 (6.9%) CA-UEDVTs (PICC)	N/R	Oregon Health and Science University (Oregon, USA)
Gbaguidi et al, 2011 ²³	1948 patients with DVT	64 (3.29%) UEDVT	N/R	Rouen University Hospital (Rouen Cedex, France)
Jones et al, 2010 ²⁴	1761 screened for UEDVT	253 (14.4%) UEDVT 101 (5.7%) CA-UEDVT	N/R (4 years 6 months)	Oregon Health and Sciences University (Oregon, USA)
Isma et al, 2010 ²⁵	1203 with VTE	63 (5%) UEDVT	3.6/100,000 (UEDVT)	MATS Population study (Malmö, Sweden)
Spencer et al, 2006 ²⁶	483 with acute DVT	26 (5.4%) NCA-UEDVT 43 (8.9%) CA-UEDVT	16/100,000 (UEDVT)	Worcester VTE Population Study (Worcester, Massachusetts, USA)
Ong et al, 2006 ²⁷	317 patients screened for UEDVT	76 (24.0%) CA-UEDVT (PICC) 13 (4.1%) CA-UEDVT (CVC) 26 (8.2%) NCA-UEDVT	N/R	Princess Alexandra Hospital (Queensland, Australia)
Joffe et al, 2004 ²⁸	5388 patients with acute DVT	324 (6.0%) CA-UEDVT 268 (5.0%) NCA-UEDVT	N/R (cross-sectional)	US DVT registry database (multicentric)
Lindblad et al, 1988 ²⁹	296 patients screened for UEDVT	73 (24.7%) vTOS-associated UEDVT 47 (15.9%) secondary UEDVT 120 UEDVTs (2.1% of all DVTs).	2/100,000 vTOS-associated UEDVT 1/100,000 secondary UEDVT	Malmo General Hospital (Malmo, Sweden) 1971-1986

CA-UEDVT, Catheter-associated upper extremity deep venous thrombosis; CVC, central venous catheter; DUS, duplex ultrasound; DVT, deep venous thrombosis; ICU, intensive care unit; NCA-UEDVT, noncatheter-associated upper extremity deep venous thrombosis; N/R, not reported; PICC, peripherally inserted central catheter; UE, upper extremity; UEDVT, upper extremity deep venous thrombosis; UESVT, upper extremity superficial vein thrombosis; VTE, venous thromboembolism; vTOS, venous thoracic outlet syndrome.

Table III. Upper extremity deep venous thrombosis (UEDVT) clinical outcomes

Author, year	Type of study	Patient population	No. of patients	Outcomes
Cires-Drouet et al, 2022 ²	Single-institution retrospective study	First 1000 consecutive UEDVTs diagnosed (63,045 total patients admitted during this period)	1000 confirmed UEDVTs	In-hospital mortality: 12.1% 90-day PE: 4.8% UEDVT recurrence within 90-days: 6.1% Major bleeding events after initiation of therapy: 21.4% (1% fatal) Concomitant LEDVT: 0.6% Treated with anticoagulation: 84.4%
Beiswenger et al, 2020 ⁴	Single-institution retrospective study	All patients who underwent UE venous DUS	911 patients (182 with confirmed UEDVT)	Treated with anticoagulation: 30-day mortality: 12.2% 30-day PE: 8.6% 30-day stroke: 0.7% 6-month mortality: 24.5% Not treated with anticoagulation: 30-day mortality: 30.2% 30-day PE: 2.3% 30-day stroke: 4.7% 6-month mortality: 37.2%
Rokosh et al, 2020 ³	Single-institution retrospective cohort study	All consecutive inpatients with acute VTE	622 patients who underwent venous DU 35 with confirmed exclusive UEDVT 7 with confirmed concomitant UEDVT and LEDVT	In-hospital mortality: 28.5% Concomitant PE: 8.6% Concomitant LEDVT: 16.7%
Thiyagarajah et al, 2019 ³²	Systematic review	Systematic review of patients with UEDVT	3550 with confirmed UEDVT	Recurrence of UEDVT: 7.5% PTS: 19.4% Major bleeding (after anticoagulation alone): 5.0% Major bleeding (after thrombolysis and/or surgery): 3.8%
Yamashita et al, 2019 ³	Multicenter retrospective registry study	Patients with acute, symptomatic VTE (COMMAND VTE Registry)	3027 consecutive patients (74 UEDVTs)	3-year VTE recurrence: 9.8% 3-year major bleeding: 1.4% 3-year all-cause death: 41.6% Concomitant PE at diagnosis: 14%
Agno et al, 2019 ⁹	Multicenter retrospective registry study	Patients with acute VTE (GARFIELD-VTE Registry)	438 confirmed UEDVTs	VTE recurrence rate: 4.0/100 person-years VTE recurrence rate at 1 year: 3.5% Major bleeding rate: 1.3/100 person-years Major bleeding rate at 1 year: 1.2% All-cause mortality: 9.7/100 person-years All-cause mortality at 1 year: 8.6%
Newton et al, 2017 ³³	Multicenter prospective international registry study	Patients with symptomatic, isolated, proximal NCA-UEDVT (RIETE Registry)	1100 confirmed NCA-UEDVT	Recurrent VTE at 1 year: 5.4% PE at 1 year: 1.2% (0.3% fatal) Bleeding event at 1 year: 4.5% Major bleeding at 1 year: 1.7% (0.5% fatal) Overall patient survival at 1 year: 85%

Table III. Continued.

Author, year	Type of study	Patient population	No. of patients	Outcomes
Cote et al, 2017 ¹³	Multicenter prospective international registry study	Patients with unprovoked NCA-UEDVT (vTOS-associated UEDVT), provoked NCA-UEDVT and CA-UEDVT (Secondary UEDVT) (RIETE Registry)	672 unprovoked NCA-UEDVT 662 provoked NCA-UEDVT 938 CA-UEDVT	Unprovoked NCA-UEDVT Recurrent DVT: 4.90/100 patient-years Recurrent PE: 0.24/100 patient-years Fatal PE: 0.24/100 patient-years Major bleeding: 1.43/100 patient-years Death: 2.37/100 patient-years Provoked NCA-UEDVT Recurrent DVT: 2.81/100 patient-years Recurrent PE: 2.5/100 patient-years Fatal PE: 1.8/100 patient-years Major bleeding: 6.59/100 patient-years Death: 35.3/100 patient-years CA-UEDVT Recurrent DVT: 3.36/100 patient-years Recurrent PE: 3.82/100 patient-years Fatal PE: 0.94/100 patient-years Major bleeding: 7.14/100 patient-years Death: 24.5/100 patient-years
Bleker et al, 2016 ³⁴	Systematic review	Systematic review of patients with UEDVT	4580 confirmed UEDVTs	Recurrent VTE: 5.1% in prospective studies 9.8% in retrospective studies Bleeding during anticoagulant therapy: 3.1% in prospective studies 6.7% in retrospective studies All-cause mortality at 1 year: 19% in prospective studies 32% in retrospective studies
Bleker et al, 2016 ³⁴	Multicentric international prospective study (ARMOUR study)	Patients with confirmed UEDVT	104 UEDVTs (102 complete follow-up information)	Median follow-up 3.5 years Recurrent VTE: 9% All-cause mortality: 26% Mild PTS: 28% Moderate PTS: 8% Bleeding event during anticoagulant therapy: 11% (major bleeding 5%)
Lazo-Langer et al, 2015 ⁵	Multicentric prospective cohort study	Patients with confirmed, symptomatic UEDVT	141 UEDVTs 75 NCA-UEDVTs 66 CA-UEDVTs	2-year cumulative incidence: VTE recurrence: 3.5% Major bleeding: 2.8% All-cause mortality: 22%
Lee et al, 2012 ⁷	Retrospective single-center cohort study	All consecutive patients undergoing upper extremity venous DUS scanning	94 confirmed UEDVTs	Concomitant LEDVT: 16% Concomitant PE: 9% 1-month all-cause mortality: 6.4%
Flinterman et al, 2008 ³⁵	Multicentric population-based case-control study	Patients with first-episode UEDVT from the Multiple Environmental and Genetic Assessment of Risk Factors for Venous Thrombosis (MEGA) study	224 confirmed first-episode UEDVTs	Recurrent venous thrombosis at 2 years: 8% (95% CI, 4%-12%) 1-year mortality: 11.2%

(Continued on next page)

Table III. Continued.

Author, year	Type of study	Patient population	No. of patients	Outcomes
Spencer et al, 2007 ³⁶	Multicentric population-based cohort study.	Patients with confirmed UEDVT or LEDVT in the geographic region of Worcester, MA, in 1999 (Worcester Venous Thromboembolism study).	69 confirmed UEDVTs 414 confirmed LEDVTs	UEDVT outcomes: 30-day recurrent VTE: 8.7% 30-day recurrent PE: 1.5% 30-day major bleeding: 11.6% 30-day mortality: 4.4% 6-month recurrent VTE: 15.9% 6-month recurrent PE: 1.5% 6-month major bleeding: 13% 6-month mortality: 4.4% 1-year recurrent VTE: 14.5% 1-year recurrent PE: 1.5% 1-year major bleeding: 13.3% 1-year mortality: 20.3% LEDVT outcomes: 30-day recurrent VTE: 4.6% 30-day recurrent PE: 1.2% 30-day major bleeding: 7.5% 30-day mortality: 5.8% 6-month recurrent VTE: 9.4% 6-month recurrent PE: 2.2% 6-month major bleeding: 9.9% 6-month mortality: 5.8% 1-year recurrent VTE: 11.4% 1-year recurrent PE: 2.9% 1-year major bleeding: 10.9% 1-year mortality: 14.7%

CA-UEDVT, Catheter-associated upper extremity deep venous thrombosis; CI, confidence interval; DUS, duplex ultrasound; ICU, intensive care unit; LEDVT, lower extremity deep venous thrombosis; NCA-UEDVT, noncatheter-associated upper extremity deep venous thrombosis; PE, pulmonary embolism; PICC, peripherally inserted central catheter; PTS, post-thrombotic syndrome; UE, upper extremity; UEDVT, upper extremity deep venous thrombosis; VTE, venous thromboembolism; VTOS, venous thoracic outlet syndrome.

thrombosis, cancer-associated thrombosis, and thrombophilia. The AVF has developed the following guidelines as a tool for the practicing physician who treats patients with UEDVT to simplify and standardize the treatment and terminology for UEDVT in clinical scenarios, as well as to provide background on the most important information relevant to this clinical entity. This guideline seeks to fill the gaps in current practice and support clinicians in making informed decisions, ultimately contributing to safer and more effective patient care for those at risk of or diagnosed with UEDVT.

METHODS

The following guidelines are an initiative of The AVF's guidelines committee and were prepared in accordance with the modified GRADE framework and guideline methodology endorsed by the Society for Vascular Surgery.³⁷ A diverse panel was convened, including experts in deep venous disease within the AVF guidelines and research committees. The panel identified key clinical questions related to UEDVT, focusing on diagnosis, treatment, and prevention. These questions were formulated using the PICO format (Population, Intervention, Comparator, Outcome) to ensure clarity and relevance. A systematic review of the literature to gather evidence addressing the PICO questions was performed.

Evidence was gathered without restrictions related to study design pertaining to UEDVT. Risk of bias was

assessed for methodological quality using standardized tools. The panel addressed consistency and precision considering agreement among data published on the direction and magnitude of outcomes while gauging reliability of outcome measurements and their estimates.

For each recommendation, the Grade (I or II) is based on the perceived risk/benefit ratio of an intervention or process. The words "We recommend" are used for Grade I (strong) statements and the words "We suggest" are used for Grade II (weak) statements. Grade I recommendations are those in which the benefits clearly outweigh the risks or that the risk is minimal and is justified by the potential existing benefits. Grade II recommendations are those in which the distinction is less clear, and the risks and benefits are more closely balanced; therefore, other individual, institutional, and clinical factors must be considered, as well as conducting a comprehensive discussion with the patient regarding risks, potential benefits, and alternative therapies. This framework was used to gauge the quality of published evidence and to rank the strength of recommendations.

The Level of Evidence of evidence is described as A, B, or C in accordance with the GRADE system.³⁸ Statements with a Level of Evidence of evidence A are unlikely to change, either owing to the high Level of Evidence already available, or because this has been established as the standard of care and new research is exceedingly unlikely to change this. Statements with

a Level of Evidence of B might change, depending on what new research may show, given that the available evidence is of a lower quality or has risk of bias. Statements with a Level of Evidence of C are very likely to change once more definitive research has been conducted in an appropriate manner to address these questions.

The statements contained within these guidelines have been prepared after a supportive systematic review was performed in partnership with the University of Maryland. After the systematic review had been performed and the evidence synthesized and interpreted, the statements were drafted. These were then presented to the guidelines committee for several rounds of review, until consensus was achieved. The statements that the committee had agreed upon were then sent for external review and returned with suggestions for improvement which have been incorporated into the final version. Owing to the relative paucity of high-quality data regarding UEDVT, many of the statements here have been influenced by the current standard of care that is accepted for LEDVT. When these differ, this is explicitly mentioned within the text. Additionally, the recommendations have been divided based on etiology of the UEDVT, given that the committee understands that the underlying pathophysiology is markedly different when comparing the three main groups of UEDVT discussed in this document. The recommendations for diagnosis, treatment, and prophylaxis therefore reflect these differences. The risk factors, clinical presentation, anatomical distribution, and the outcomes also differ significantly among these groups. Each section is then divided based on these groups and dedicated to describing their unique characteristics and management.

Recommendations were developed based on the balance of benefits and harms, patient values, and resource availability. Extensive AVF panel group discussions using consensus-building techniques with formal voting were carried out. Disagreements were documented and addressed through further evidence review or expert consultation. Draft guidelines underwent peer review by external experts and stakeholders. Feedback was incorporated to ensure accuracy, clarity, and applicability.

SUMMARY OF RECOMMENDATIONS

Guideline 1: Gradeification of UEDVT

Guideline 1.1: Gradeification system for UEDVT. We suggest the use of a Gradeification based on etiology instead of an anatomic system to standardize the reporting and treatment of UEDVT. [BEST PRACTICE]

Guideline 1.2: Gradeification system based on etiology. We suggest Gradeifying UEDVT into venous thoracic outlet syndrome (vTOS)-associated UEDVT,

cancer-related UEDVT, and noncancer UEDVT. [GRADE - 2; LEVEL OF EVIDENCE OF EVIDENCE - B]

Guideline 2: Epidemiology and risk factors

Guideline 2.1: vTOS-associated UEDVT. vTOS-associated UEDVT is more common in patients who are younger, have fewer comorbid conditions, and are outpatients. [GRADE - 1; LEVEL OF EVIDENCE OF EVIDENCE - B]

Guideline 2.2: Secondary catheter-associated UEDVT or noncatheter-associated UEDVT. Secondary catheter-associated (CA) UEDVT or noncatheter-associated (NCA) UEDVT is more common in inpatient populations, who are older, and have more comorbid conditions. [GRADE - 1; LEVEL OF EVIDENCE OF EVIDENCE - B]

Guideline 2.3: Risk factors for UEDVT. Some common risk factors of UEDVT are costoclavicular compression, the presence of an intravenous device, active malignancy, and surgery or trauma of the upper extremity. [GRADE - 1; LEVEL OF EVIDENCE OF EVIDENCE - B]

Guideline 3: Risk prediction models and laboratorial markers

Guideline 3.1: Clinical probability tool and scoring system for UEDVT diagnosis. We suggest that the clinical probability of UEDVT using either the Constans or Extended Constans score should be preferred over the modified Wells score, and it should guide subsequent investigation. [GRADE - 2; LEVEL OF EVIDENCE OF EVIDENCE - B]

Guideline 3.2: Clinical probability of UEDVT. For patients unlikely to have UEDVT based on clinical probability scores, we suggest that further testing with D-dimer should not be performed unless all other potential causes of acute upper extremity edema have been excluded. [GRADE - 2; LEVEL OF EVIDENCE OF EVIDENCE - B]

Guideline 3.3: D-dimer for patients with UEDVT and cancer. We suggest that D-dimer testing should NOT be used to rule out CA-UEDVT. [GRADE - 2; LEVEL OF EVIDENCE OF EVIDENCE - B]

Guideline 3.4: D-dimer for patients with noncancer-associated UEDVT. We recommend that D-dimer testing with a cutoff value of 500 µg/L may be used as a cost-effective initial test for ruling out NCA-UEDVT in patients with low pretest probability. [GRADE - 1; LEVEL OF EVIDENCE OF EVIDENCE - B]

Guideline 4: Diagnosis and workup

Guideline 4.1: Duplex ultrasound for UEDVT. For patients with clinically suspected UEDVT, we recommend that an upper extremity duplex ultrasound (DUS) should be the first diagnostic imaging examination. [GRADE - 1; LEVEL OF EVIDENCE OF EVIDENCE - B]

Guideline 4.2: DUS for UEDVT in central veins. If proximal UEDVT involving central veins is suspected, we recommend considering that upper extremity DUS in this case may have low sensitivity and specificity [GRADE - 1; LEVEL OF EVIDENCE OF EVIDENCE - B]

Guideline 4.3: Screening for UEDVT in patients with indwelling catheters and cancer with DUS. We recommend that screening for CA-UEDVT in patients with long-term indwelling catheters be based on institutional policies starting with DUS, but should not be routinely performed in asymptomatic patients. [GRADE - 1; LEVEL OF EVIDENCE OF EVIDENCE - B]

Guideline 4.4: Additional imaging tests after negative DUS. If the initial upper extremity DUS is negative, but clinical suspicion remains high, we recommend additional investigation with either magnetic resonance venography (MRV) or computed tomography venography (CTV) to avoid delaying treatment. [GRADE - 1; LEVEL OF EVIDENCE OF EVIDENCE - B]

Guideline 4.5: MR as a second testing modality for UEDVT. Owing to lack of current evidence regarding CTV, we suggest that MRV should be the preferred advanced imaging modality when available for diagnosing UEDVT. [GRADE - 2; LEVEL OF EVIDENCE OF EVIDENCE - B]

Guideline 4.6: Catheter-based venography for the diagnosis of UEDVT. If noninvasive studies remain inconclusive and the index of suspicion remains high, we suggest that venography may be considered as the next step to diagnose and treat UEDVT in one setting when the patient is a candidate for endovascular thrombus removal after a comprehensive discussion of risks and benefits. [GRADE - 2; LEVEL OF EVIDENCE OF EVIDENCE - B]

Guideline 4.7: Catheter-based venography for the diagnosis of UEDVT. We recommend that catheter-based venography may be considered to reevaluate the degree of stenosis or compression of the upper extremity veins after thrombus removal if symptoms persist and with intention to treat. [GRADE - 1; LEVEL OF EVIDENCE OF EVIDENCE - B]

Guideline 4.8: Intravascular ultrasound for the diagnosis and therapy guidance for UEDVT. We recommend considering that intravascular ultrasound (IVUS) outperforms venography in evaluating the degree of stenosis and should be used, when possible, to guide treatment and rule out residual stenosis during endovascular interventions for UEDVT. [GRADE - 1; LEVEL OF EVIDENCE OF EVIDENCE - B]

Guideline 5: Prophylaxis

Guideline 5.1: Intermittent mechanical compression devices for prophylaxis of UEDVT. We recommend against mechanical devices with intermittent compression as a sole prophylaxis maneuver for the prevention of UEDVT. [GRADE - 1; LEVEL OF EVIDENCE OF EVIDENCE - A]

Guideline 5.2: Pharmacomechanical prophylaxis for VTOS-associated UEDVT. We recommend against the use of pharmacomechanical prophylaxis when VTOS-associated UEDVT has been confirmed. [GRADE - 1; LEVEL OF EVIDENCE OF EVIDENCE - B]

Guideline 5.3: Intermittent mechanical compression devices for patients with CA-UEDVT. We recommend avoiding mechanical prophylaxis with intermittent compression devices for CA-UEDVT. [GRADE - 1; LEVEL OF EVIDENCE OF EVIDENCE - B]

Guidelines 5.4: Routine chemical prophylaxis for patients with CA-UEDVT. We recommend against routine prophylaxis with anticoagulants for CA-UEDVT for prevention of UEDVT in patients with long-term CVCs. [GRADE - 1; LEVEL OF EVIDENCE OF EVIDENCE - A]

Guideline 5.5: Prophylaxis with anticoagulation in patients with CA-UEDVT and CVCs. We recommend prophylaxis with anticoagulants for CA-UEDVT in patients with moderate-to high-risk venous thromboembolism (VTE) and long-term CVCs. We also recommend that a risk/benefit analysis should be performed based on risk of VTE and risk of bleeding to support decision-making. [GRADE - 1; LEVEL OF EVIDENCE OF EVIDENCE - B]

Guideline 6: Treatment

Guideline 6.1: Anticoagulation for the treatment of UEDVT. We recommend that UEDVT be treated with oral Xa inhibitors over vitamin K antagonists for ≥ 3 months in patients with low bleeding risk. [GRADE - 1; LEVEL OF EVIDENCE OF EVIDENCE - B]

Guideline 6.2: Anticoagulation for the treatment of UEDVT. We recommend that underlying causes such as malignancy and hypercoagulability disorders should be considered and investigated for in patients with a first, unprovoked episode of UEDVT. [GRADE - 1; LEVEL OF EVIDENCE OF EVIDENCE - B]

Guideline 6.3: Early thrombus removal for UEDVT. We suggest that acute extensive UEDVT (< 21 days) may be treated with early thrombus removal strategies in severely symptomatic patients with a life expectancy of > 1 year to reduce the incidence of PTS. [GRADE - 2; LEVEL OF EVIDENCE OF EVIDENCE - B]

Guideline 6.4: VTOS-associated with UEDVT. We recommend that VTOS-associated UEDVT with compatible imaging findings should be treated with first rib resection as the initial operative management. [GRADE - 1; LEVEL OF EVIDENCE OF EVIDENCE - B]

Guideline 6.5: Cancer-associated UEDVT treatment. We recommend that CA-UEDVT should be treated with anticoagulation and, if the indwelling catheter is no longer necessary or alternative access is feasible, catheter removal is indicated; otherwise, the catheter can remain in place. [GRADE - 1; LEVEL OF EVIDENCE OF EVIDENCE - B]

Guideline 6.6: Noncancer-associated UEDVT treatment. We recommend that NCA-UEDVT should be treated with anticoagulation for ≥ 3 months in patients with an acceptably low bleeding risk. [GRADE - 1; LEVEL OF EVIDENCE OF EVIDENCE - B]

Guideline 6.7: Noncancer-associated UEDVT treatment. We suggest that invasive interventions for NCA-UEDVT can be considered if the patient is highly

symptomatic, has low surgical risk, and has a life expectancy of >1 year. [GRADE - 2; LEVEL OF EVIDENCE OF EVIDENCE - C]

Guideline 6.8: Superior vena cava filter for patients with UEDVT. We suggest that, in highly selected patients with absolute contraindication to anticoagulation and elevated risk of life-threatening PE, temporary superior vena cava (SVC) filter placement could be considered. [GRADE - 2; LEVEL OF EVIDENCE OF EVIDENCE - C]

GRADEIFICATION OF UEDVT

Gradeification system for UEDVT

No validated Gradeification system exists for UEDVT. A distinction between proximal and distal DVT similar to lower extremity Gradeification is lacking. Therefore, the best practice has been to report UEDVT based on etiology or inciting mechanism.

Guideline 1.1. We suggest the use of a Gradeification based on etiology instead of an anatomic system to standardize the reporting and treatment of UEDVT. [BEST PRACTICE]

Gradeification system based on etiology

The first step in successfully managing UEDVT is to understand the underlying process that led to its occurrence. Although UEDVT, like LEDVT, is a result of the triad of endothelial damage, hypercoagulability, and blood stasis, specific anatomical considerations peculiar to the upper extremity influence treatment considerably. Therefore, for the correct treatment of UEDVT, the

first step is an accurate etiologic Gradeification as vTOS-associated UEDVT, catheter-associated UEDVT (CA-UEDVT), and noncatheter-associated UEDVT (NCA-UEDVT). Subsequent recommendations are based on this initial etiology Gradeification.

Guideline 1.2. We suggest Gradeifying UEDVT into vTOS-associated (vTOS), CA-UEDVT, or NCA-UEDVT for management. [GRADE - 1; LEVEL OF EVIDENCE - B5-7].

RISK FACTORS

vTOS-associated UEDVT

vTOS-associated UEDVT is defined as occurring in the absence of any other underlying conditions and is also known as unprovoked UEDVT. The most common cause is vTOS, a type of vascular compression syndrome of the subclavian vein in which upper extremity effort induces venous thrombosis, also known as Paget-Schroetter syndrome. When this is associated with intermittent upper extremity swelling in the absence of venous thrombosis, it is termed McCleery syndrome. vTOS-associated UEDVT also includes the subgroup of idiopathic UEDVT, which is exceedingly rare.

In Paget-Schroetter syndrome, as the subclavian vein exits the thoracic cavity and courses toward the upper extremity, it traverses the costoclavicular space—which contains the clavicle, costoclavicular ligament, subclavius muscle, subclavian vein, and first rib (Fig 2). This space has the anterior border of the clavicle and the inferior border of the first rib as anterior-inferior boundaries. The subclavian vein is most frequently compressed here; and with elevation of the upper extremity above

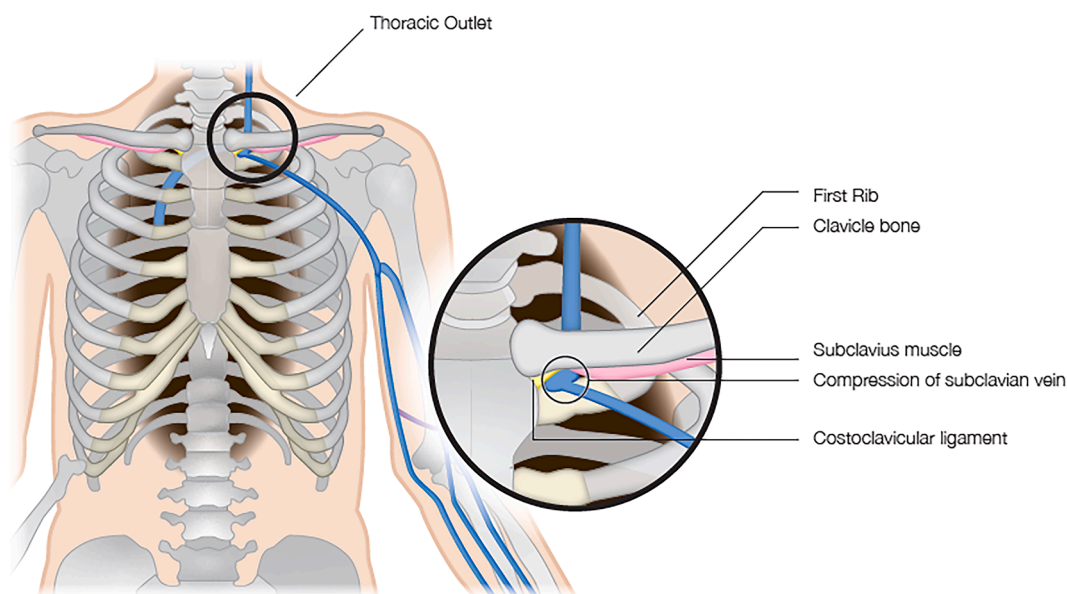


Fig 2. Costoclavicular compression in venous thoracic outlet syndrome (vTOS). Schematic depiction of subclavian vein compression within the costoclavicular space between the clavicle, first rib, subclavius muscle, and costoclavicular ligament, illustrating the pathophysiological mechanism underlying vTOS-associated upper extremity deep venous thrombosis (Paget-Schroetter syndrome).

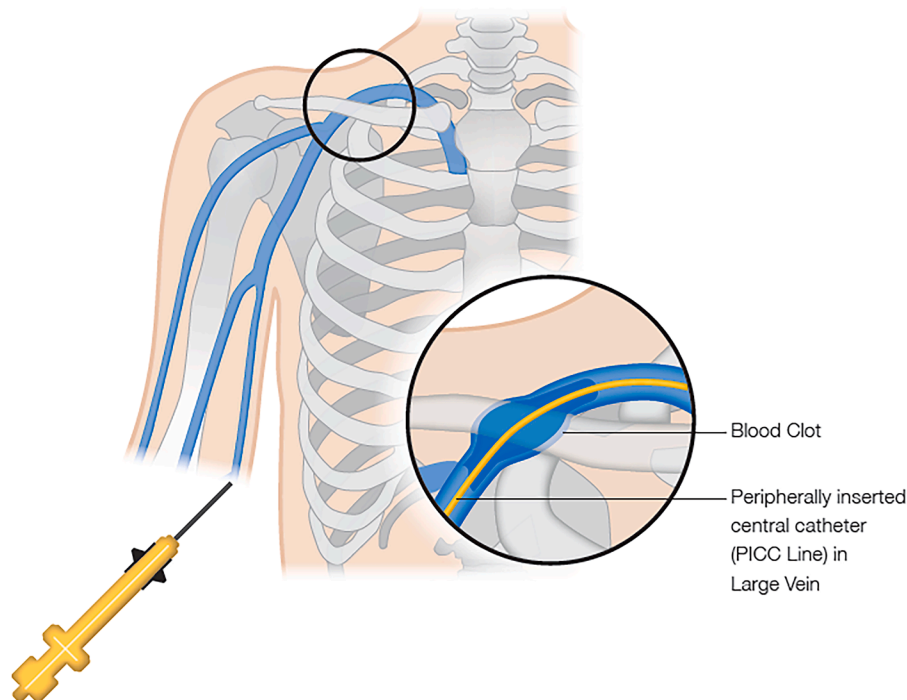


Fig 3. Catheter-associated upper extremity deep venous thrombosis (UEDVT). Illustration of a peripherally inserted central catheter (PICC) within a large upper extremity vein with associated thrombus formation, demonstrating a common mechanism of secondary catheter-associated upper extremity deep venous thrombosis (UEDVT).

the shoulder, this space is further narrowed. The repetitive nature of this compression may lead to inflammation and eventually development of thrombus in the subclavian vein, which may extend distally.

Factors that may lead to costoclavicular space narrowing include clavicular/first rib fracture, congenital narrowing or subclavius muscle hypertrophy and increase the risk of vTOS-associated UEDVT. Causes are often repetitive narrowing of costoclavicular space from overhead use of the upper extremity, whether owing to sports or occupation.^{39,40} This results in significant differences in the characteristics of the patients who have UEDVT, who are usually younger, athletic, with fewer comorbidities, and are unlikely to have other concomitant predisposing factors.

Secondary UEDVT

Secondary UEDVT, in contrast, is defined as occurring in patients with an underlying condition that directly led to the UEDVT. These causes include intravenous devices (IVDs) such as catheters, implantable cardiac devices or cannulas, malignancies, hypercoagulable disorders, or trauma. Within secondary UEDVT, there is a further subdivision of catheter-associated UEDVT (CA-UEDVT) and noncatheter-associated UEDVT (NCA-UEDVT).

Catheter-associated UEDVT is the best studied subgroup owing to its higher prevalence and need for

more active treatment, often requiring catheter removal. These CA-UEDVTs can be associated with the presence of common CVCs, or peripherally inserted central catheters (PICCs), or other intravenous devices (IVDs) such as extracorporeal membrane oxygenation cannulas, cardiac pacemaker wires, or implantable defibrillators (Fig 3). CA-UEDVT is the most common type of UEDVT in the inpatient population, because the use of IVDs is more prevalent in this group of patients. The incidence of CA-UEDVT is often correlated with the number of catheter-days and varies depending on intrinsic patient characteristics (reason for catheter placement, comorbidities, hypercoagulable disorders, etc) and catheter-related factors (bore size, number of lumens, coatings, infusate, catheter care).

Noncatheter-associated UEDVT is a large category of secondary UEDVT, which occurs owing to other underlying risk factors and predisposing conditions. These patients in general are older, with more comorbidities and greater frailty.

Epidemiology. UEDVT is less common than LEDVT and thus larger trials and higher-quality data are more difficult to obtain. This has resulted in UEDVT management frequently being based on data extrapolated from LEDVT and comparative studies.

Additionally, the prevalence of UEDVT among all of the venous thromboembolic events varies according to

whether the population is a sample of outpatients or inpatients. The prevalence of UEDVT of all DVTs ranges from 3% to 5% of all VTEs in outpatients³ and is mainly made up of vTOS-associated UEDVT, who are younger patients, or NCA-UEDVT, more frequently seen in older patients with several comorbidities.

Inpatient samples have a much greater proportion of UEDVT of all the VTEs, at around 30.4% to 36.5%.^{3,29} This occurs owing to the absolute increase in secondary UEDVT because the risk factors for secondary UEDVT are more commonly present in inpatient populations—venous access in the upper extremity and comorbid conditions.

The yearly incidence of vTOS-associated UEDVT is estimated to be between 2/100,000²⁹ and 6/100,000²⁶; however, populations that have a greater proportion of athletes in sports that elicit upper extremity muscular hypertrophy may have higher rates of vTOS-associated UEDVT. Conversely, in already hospitalized patients, vTOS-associated UEDVT is to be considered a true exception. One single-center study that reviewed all patients who under DUS study of the upper extremity with 172 diagnosed UEDVTs and 74.1% were inpatients, reported only 2 (1.1%) had vTOS-associated UEDVT.⁴

Guideline 2.1. vTOS-associated UEDVT is more common in patients who are younger, have less comorbid conditions. [GRADE - 1; LEVEL OF EVIDENCE - B⁴¹⁻⁴⁵]

Secondary UEDVT is a disease of older patients, who have more comorbidities. The main risk factor is IVD use (eg, CVCs, peripherally inserted CVCs, cannulas). In an outpatient population, the incidence is estimated at 1/100,000; however, in inpatients, secondary UEDVT is the most common, whether a CA-UEDVT or NCA-UEDVT (owing to malignancy, recent surgery or trauma, hypercoagulability, bed rest). For inpatients, incidence is often expressed in relation to patient-days or catheter-days, and the incidence of secondary UEDVT has been estimated to be 0.32/10,000 patient-days.¹⁷ For CA-UEDVT, the incidence is higher, estimated at 0.10/1000⁴⁶ to 9.5/1000 catheter-days.⁴⁷ This is variable depending on the population studied and the hospital catheter care protocols.

Additionally, the incidence of asymptomatic secondary UEDVT is much higher than symptomatic CA-UEDVT; therefore, prevalence and incidence studies show significant variability depending on whether asymptomatic patients were screened and/or included. CA-UEDVT prevalence and incidence is shown in Table IV.

Table IV. Catheter-associated upper extremity deep venous thrombosis (UEDVT)

Author, year	No. of patients	Prevalence	Incidence	Region
González et al, 2021 ⁴⁸	1142 PICCs inserted	23 (2.01%) CA-UEDVT	0.15/1000 catheter-days	Universidad de Sevilla (Seville, Spain)
Sharp et al, 2021 ⁴⁹	2438 patients with PICC insertion	26 (1.1%) CA-UEDVT	N/R	Multicentric (Australia & New Zealand)
Kuang et al, 2021 ⁴⁷	1643 ICU patients with 2114 CVC insertions	209 (10.0%) Symptomatic CA-UEDVT	9.5/1000 catheter-days	Ganzhou People's Hospital (Ganzhou, China)
Lin et al, 2021 ⁵⁰	201 patients with PICC	108 (53.7%) PICC-VT 3 (1.5%) symptomatic UEDVT	N/R	First Affiliated Hospital of Fujian Medical University (Fuzhou, China)
Chopra et al, 2018 ⁵¹	23,010 patients with PICC insertion	480 (2.1%) CA-UEDVT (PICC)	N/R	Michigan Hospital Medicine Safety Consortium (Michigan, USA)
Yeon et al, 2018 ⁵²	59 patients with CVO and PICC insertion	8 (13.6%) symptomatic CA-UEDVT 6 (10.2%) asymptomatic CA-UEDVT	N/R	2 medical centers (Seoul, South Korea)
Fracchiolla et al, 2017 ⁵³	464 PICCs and 441 CVCs	38 (8%) CA-UEDVT (PICC) 6 (1.36%) CA-UEDVT (CVC)	0.8/1000 catheter-days (PICC) 0.63/1000 catheter-days (CVC)	REL GROUP (Lombardy Hematologic Network, Italy)
Hrdy et al, 2017 ⁵⁴	308 CVCs placed in medical-surgical ICU patients	47 (26%) CA-UEDVT	N/R	University Hospital Brno (Brno, Czech Republic)
Zhang et al, 2016 ⁵⁵	8028 patients with PICC insertion	249 (3.1%) CA-UEDVT	N/R	Sun-Yat-sen University Cancer Center (Guangzhou, China)

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Table IV. Continued.

Author, year	No. of patients	Prevalence	Incidence	Region
Boersma et al, 2015 ⁵⁶	207 patients randomized to either heparin (108) or trisodium citrate (99) locking solutions.	11 (10.2%) symptomatic CA-UEDVT in the heparin group 5 (5%) symptomatic CA-UEDVT in the trisodium citrate group.	N/R	2 tertiary centers (Netherlands)
Itkin et al, 2014 ⁵⁷	332 patients with PICC insertion	197 (71.9%) CA-UEDVT (PICC) 13 (4.0%) Symptomatic CA-UEDVT 56 (16.9%) Complete CA-UEDVT	N/R	University of Pennsylvania (Pennsylvania, USA)
Maneval et al, 2014 ⁵⁸	203 acute care patients with PICC insertion	13 (6.4%) CA-UEDVT	N/R	Multicentric (Pennsylvania, USA)
Wilson et al, 2012 ⁵⁹	431 patients in the neurological ICU with PICC insertion	36 (8.4%) symptomatic CA-UEDVT (PICC)	5.5/1000 catheter-days	University of Michigan (Michigan, USA)
Goltz et al, 2012 ⁶⁰	200 patients with totally-implantable venous access ports in the forearm	21 (10.5%) CA-UEDVT	N/R	Allgemeines Krankenhaus (Hagen, Germany)
Xing et al, 2012 ⁶¹	188 patients with PICCs inserted	4 (2.1%) UEDVT	0.28/1000 catheter-days	First Affiliated Hospital, Chongqing Medical University (Chongqing, China)
Sperry et al, 2012 ⁶²	798 PICCs	10 (1.25%) symptomatic CA-UEDVT (PICC)	N/R	Georgetown University Hospital (Washington DC, USA)
Fearonce et al, 2010 ⁶³	37 PICC insertions (31 patients) in burn patients	1 (2.8%) CA-UEDVT	N/R	University of Utah (Utah, USA)
Ong et al, 2006 ²⁷	2882 patients with PICCs inserted	76 (2.6%) CA-UEDVT	N/R	Princess Alexandra Hospital (Queensland, Australia)
Abdullah et al, 2005 ⁶⁴	26 patients with PICC insertion	10 (38.5%) CA-UEDVT	N/R	University of Malaya (Kuala Lumpur, Malaysia)
Special populations				
Bertoglio et al, 2020 ⁶⁵	418 breast cancer patients with PICC	10 (2.4%) CA-UEDVT	N/R	Ospedale Policlinico San Martino (Genova, Italy)
Lee et al, 2020 ⁶⁶	314 colorectal cancer patients with CVC	11 (3.5%) CA-UEDVT	N/R	St. Mary's and St. Vincent's Hospitals (Seoul, South Korea)
Wang et al, 2020 ⁶⁷	127 patients with cancer with PICC insertion	62 (48.8%) asymptomatic PICC-VT	37.1% within 24 hours 85.49% within 1 week	Sichuan Cancer Hospital (Chengdu, China)
Suleman et al, 2019 ⁶⁸	389 cancer patients with implanted vascular access devices	5 (1.29%) symptomatic CA-UEDVT	N/R	The Ottawa Hospital (Ontario, Canada)
ALKindi et al, 2018 ⁶⁹	1337 cancer-associated VTE	138 (10.3%) CA-UEDVT 62 (4.6%) NCA-UEDVT 49 (3.7%) missing data	18.5%/4 years and 6 months	McMaster University (Hamilton, Canada)
Kang et al, 2017 ⁷⁰	328 patients with lung cancer and PICC insertion	17 (5.2%) CA-UEDVT (PICC)	0.49/1000 catheter-days	Peking Union Medical College Hospital (Beijing, China)

Table IV. Continued.

Author, year	No. of patients	Prevalence	Incidence	Region
Boddi et al, 2015 ⁴⁶	400 cancer patients with CVCs	5 (1.25%) CA-UEDVT	0.10/1000 catheter-days	Azienda Ospedaliera Universitaria (Florence, Italy)
Liu et al, 2015 ⁷¹	311 cancer patients with PICC placement	160 (51.4%) PICC-VT 87 (28.0%) symptomatic VT	N/R	2 Tertiary Referral Hospitals (China)
Lavau-Denes et al, 2013 ⁷²	420 cancer patients with CVCs	42 (10.3%) CA-UEDVT	N/R	Centre Hospitalier Universitaire (CHU) de Limoges (Limoges, France)
Aw et al, 2012 ⁷³	340 patients with cancer and PICC placement	19 (5.6%) symptomatic CA-UEDVT (PICC)	N/R	University of Ottawa (Ontario, Canada)
Nobili et al, 2010 ⁷⁴	145 patients with metastatic colorectal cancer and CVC placement	2 (1.38%) symptomatic CA-UEDVT	0.02/1000 catheter-days	University of Bologna (Bologna, Italy)
Yukisawa et al, 2010 ⁷⁵	92 patients central venous port for chemotherapy for CRC	10 (11%) CA-UEDVT	N/R	Cancer Institute Hospital (Tokyo, Japan)
Verso et al, 2008 ⁷⁶	310 cancer patients with CVC placed	50 (16.1%) CA-UEDVT	N/R	ETHIC study data (Multicentric, Italy)
COVID-19				
Mumoli et al, 2022 ⁷⁷	257 with moderate-severe COVID-19 non-ICU patients	28 (10.9%) UEDVT	10.9%/5-month period	Magenta Hospital (Italy)
Nishimoto et al, 2022 ⁷⁸	2894 patients with COVID-19	6 UEDVTs 6/18 (33%) of the isolated DVTs 6 (39) 15.4% of all VTEs	N/R	Multicentric (Japan)
Heart transplant-associated UEDVT				
Elboudwarej et al, 2015 ⁷⁹	1258 heart transplant patients screened; 117 with acute DVT	52 (4.2%) UEDVT	N/R	Cedars-Sinai Medical Center (Los Angeles, California)
Hematological malignancy-associated UEDVT				
Refaei et al, 2016 ⁸⁰	663 patients with acute leukemia and CVC or PICC insertion	82/338 (11.7%) CA-UEDVT (PICC) 41/325 (6.5%) CA-UEDVT (CVC)	1.89/1000 catheter-days (PICC) 0.52/1000 catheter-days (CVC)	University of Alberta (Alberta, Canada)
Del Principe et al, 2013 ⁸¹	71 patients with acute myeloid leukemia and 106 CVC insertions	19 (18%) CA-UEDVT	N/R	Università Tor Vergata (Rome, Italy)
Grisariu et al, 2013 ⁸²	473 patients with acute leukemia and CVC insertion	32 (6.8%) symptomatic CA-UEDVT	N/R	Hdassah Hebrew University Medical Center (Jerusalem, Israel)
Tran et al, 2010 ⁸³	899 PICCs placed in 498 patients with hematological malignancy	38 (7.8%) CA-UEDVT (PICC)	N/R	Emory University School of Medicine (Georgia, USA)
UEDVT in HIT patients				
Hong et al, 2003 ⁸⁴	260 patients with HIT	14 (5.4%) CA-UEDVT	N/A (260 consecutive HIT patients over 18 years)	Multicentric (4 academic hospitals) (Ontario, Canada)
Implantable defibrillator device-associated UEDVT				
Albertini et al, 2020 ⁸⁵	84 patients undergoing lead replacement or ICD upgrade	24 (28.6%) UEDVT	28.6%/3 years and 4 months	Heart Institute HCFMUSP (São Paulo, Brazil)
Safi et al, 2017 ⁸⁶	42 patients with transvenous pacemaker or defibrillators	9 (21%) CA-UEDVT	N/R	Modarress Hospital (Tehran, Iran)

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Table IV. Continued.

Author, year	No. of patients	Prevalence	Incidence	Region
Pediatric patients with catheter-associated UEDVT				
Menendez et al, 2016 ⁸⁷	265 pediatric patients with PICC	22 (8.3%) CA-UEDVT	2.25/1000 catheter-days	La Paz University Hospital (Madrid, Spain)
Smitherman et al, 2015 ⁸⁸	1135 pediatric central line placements	31 (2.7%) CA-UEDVT	0.25/1000 catheter-days	North Carolina Children's Hospital (North Carolina, USA)
Casior et al, 2013 ⁸⁹	1289 PICC placements in pediatric patients	24 (1.9%) CA-UEDVT (PICC)	N/R	Children's Mercy Hospital and Clinics (Missouri, USA)
Faustino et al, 2013 ³⁰	101 children in the ICU with CVC	16 (15.8%) CA-UEDVT	24.7/1000 catheter-days	Multicentric (USA)
Venovenous ECMO-associated UEDVT				
Menaker et al, 2017 ¹²	45 patients on venovenous ECMO	34 (75.6%) CA-UEDVT (ECMO)	N/R	Adams Cowley Shock Trauma Center (Maryland, USA)
Shafii et al, 2012 ⁹¹	10 patients on venovenous ECMO	8 (80%) CA-UEDVT	N/R	Cleveland Clinic (Cleveland, Ohio)
CA-UEDVT, Catheter-associated upper extremity deep venous thrombosis; CRC, colorectal cancer; CVC, central venous catheter; ECMO, extracorporeal membrane oxygenation; HIT, heparin-induced thrombocytopenia; ICU, intensive care unit; N/A, not applicable; NCA-UEDVT, noncatheter-associated upper extremity deep venous thrombosis; NR, not reported; PICC, peripherally inserted central catheter; UEDVT, upper extremity deep venous thrombosis; VT, venous thrombosis; VTE, venous thromboembolism.				

Guideline 2.2. Secondary CA-UEDVT or NCA-UEDVT is more common in inpatient populations, who are older, and have more comorbid conditions. [Grade - 1; Level Of Evidence - B^{13,14,16,28,92}]

Known risk factors for vTOS-associated UEDVT. The risk factors are considered indirect, because they are associated with narrowed costoclavicular space, in presence of scalene or subclavius muscle hypertrophy, costoclavicular ligament hypertrophy, clavicular or first rib callus formation, and repetitive exercise involving the upper extremity, especially with over-the-head movements. For secondary UEDVT, the known risk factors can be divided into patient-related factors, treatment-related factors, and venous access-related factors.

Common patient-related risk factors include race, a prior history of thrombosis, hypercoagulable disorders, hematological or oncologic disease, and gastrointestinal/liver disease. For treatment-related factors, the characteristics that have been linked to a higher risk of UEDVT include hemodialysis status, total parenteral nutrition, extracorporeal membrane oxygenation and cardiac catheterization. For CA-UEDVT, details such as catheter size, multiple lumens, type of coating, type of catheter used, location of catheterization, and presence of other catheter complications have been strongly associated with the development of UEDVT. The most consistent risk factors with the highest estimated effect are the presence of an intravenous device, active malignancy, and surgery or trauma of the upper extremity. A comprehensive review of all the known risk factors for secondary UEDVT are included in [Table V](#).

Guideline 2.3. The most consistent and common risk factors for UEDVT are the presence of an intravenous device, active malignancy, and surgery or trauma of the upper extremity. [GRADE - 1; Level Of Evidence - B^{92,19,28,51}]

RISK PREDICTION MODELS AND LABORATORY MARKERS

UEDVT is rare, comprising only 10% of thrombotic events and occurs owing to factors like indwelling lines, trauma, surgery, immobilization, or hypercoagulable states including malignancy, infection, and drug effects.^{98,99} Unlike LEDVT, risk assessment scores, such as the Wells score, are not widely accepted. Moreover, it is currently unclear if risk modeling reduces can help to prevent UEDVT.³⁰

Most of the available publications related to risk assessment in UEDVT are focused on catheter-associated DVT. The Michigan Risk Score was developed to identify factors associated with PICC-DVT.¹⁴ It is based on five predictor variables: history of DVT, active cancer, the number of PICC lumens, white cell count >12 000 at the time of PICC insertion, and presence of another CVC. It stratifies patients into four risk grades: Grade I (0 points), Grade II (1-2 points), Grade III (3-4 points), and Grade IV (>4 points). The Michigan Risk Score further distinguishes those at low vs high risk, with a five-fold greater risk of thrombosis for those in the risk Grade IV when compared with Grade I. The Michigan Risk Assessment Score for PICC-associated UEDVT is displayed in [Table VI](#).

Table V. Risk factors associated with upper extremity deep venous thrombosis (UEDVT)

Author, year	Study design	No. of patients	Risk factor	OR	95% CI	P value
Mumoli et al, 2022 ⁷⁷	Single-center retrospective cohort study. Patients with moderate-severe COVID-19 infections in the non-ICU setting.	257 (28 UEDVTs)	D-dimer (age-adjusted)	8.20	3.59-26.89	.000
			CPAP use	5.95	1.33-26.58	.019
			ARDS	3.85	1.57-9.42	.003
Tian et al, 2021 ⁹³	Systematic review and meta-analysis. CVC-related UEDVT in hospitalized children.	N/A	Patient history of thrombosis	3.88	2.57-5.85	<.00001
			Gastrointestinal/liver disease	1.85	0.99-3.46	.05
			Hematological disease	1.45	1.06-1.99	.02
			Cancer	1.58	1.01-2.48	.05
			Parenteral/total parenteral nutrition	1.70	1.21-2.39	.002
			Hemodialysis	2.17	1.34-3.51	.002
			ECMO	1.51	1.31-1.71	<.00001
			Cardiac catheterization	3.92	1.06-14.44	<.00001
			PICC vs tunneled lines	1.81	1.15-2.85	.01
			PICC vs totally implantable venous port	2.81	1.41-5.60	.003
			Multiple catheter lines	4.06	3.01-5.47	<.00001
			Multiple catheter lumens	3.71	1.99-6.92	<.00001
			Central line-associated blood-stream infection	2.66	1.15-6.16	.02
Kuang et al, 2021 ⁴⁷	Single-center retrospective cohort study. ICU inpatients with CVC-related UEDVT.	2114 (209 symptomatic CA-UEDVTs)	Trauma	2.05	1.33-3.16	.001
			Major surgery	2.46	1.64-3.68	.000
			Heart failure	2.09	1.40-3.11	.000
Sharp et al, 2021 ⁴⁹	Multicentric retrospective cohort study. Patients who had undergone PICC insertion.	2438 (39 PICC-associated UEDVTs)	Cancer as a vTOS-associated diagnosis	3.01	1.332-6.779	.008
			Chemotherapy infusion	3.78	1.66-8.623	.002
			Catheter to vein ratio >46%	2.3	1.202-4.383	.012
Chopra et al, 2018 ⁵¹	Multicentric registry retrospective cohort study. Patients with PICC insertion.	23,010 (480 PICC-associated DVTs)	Triple lumen device	2.31	1.60-3.33	<.0001
			Double-lumen device	2.06	1.59-2.66	<.0001
			PICC exchange	1.98	1.37-2.85	.0003
			Active cancer	1.68	1.15-2.46	.0077

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Table V. Continued.

Author, year	Study design	No. of patients	Risk factor	OR	95% CI	P value
Chopra et al, 2017 ¹⁴	Multicentric registry (Michigan Hospital Medicine Safety Consortium) retrospective cohort study. Patients with PICC insertion.	23,010 (475 symptomatic PICC-associated UEDVTs)	History of DVT			
			History of VTE within 30 days	2.19	1.50-3.18	<.0001
			Multilumen PICC	1.98	1.45-2.71	.002
			Active cancer	1.97	1.47-2.65	<.0001
			Presence of another CVC	1.43	1.14-1.79	.0022
			WBC >12,000	1.46	1.20-1.77	.0001
			Michigan Risk Score grade II vs I	1.68	1.19-2.37	N/R
			Michigan Risk Score Grade III vs I	2.90	2.09-4.01	N/R
			Michigan Risk Score grade IV vs I	5.20	3.65-7.42	N/R
Menaker et al, 2017 ¹²	Multicenter retrospective database study (Healthcare Cost and Utilization Project's Florida State Ambulatory Surgery and Services Database). Patients who underwent outpatient port insertion. 926 (1.81%) developed CA-UEDVT.	51,049 (926 CA-UEDVTs).	Age <65 years	1.22	1.07-1.38	.003
			Black race	2.00	1.68-2.38	<.0001
			History of DVT	1.95	1.24-3.07	.003
			End-stage renal disease	5.04	3.34-7.31	<.0001
			Lung cancer (compared with GU cancer)	1.64	1.23-2.19	.0008
			GI cancer (compared with GU cancer)	1.51	1.16-2.00	.003
			All-cause 7-day revisit	1.66	1.39-1.98	<.0001
			All-cause 30-day revisit	2.44	2.14-2.78	<.0001
			Less activity	9.583	N/R	<.001
Liu et al, 2015 ⁷¹	Multicentric prospective observational investigation. Cancer patients who underwent PICC placement.	311 (160 PICC-associated thrombosis)	Obesity	3.466	N/R	.014
			CVC	14.0	5.9-33.2	N/R
Winters et al, 2015 ¹⁹	Single-center frequency matched case-cohort study. Medical inpatients for hospital acquired VTE. Medical Inpatients and Thrombosis (MITH) study.	64,034 (91 UEDVTs)	PICC	13.0	6.1-27.6	N/R
			Centrally inserted central catheter	3.4	1.7-6.8	N/R

Table V. Continued.

Author, year	Study design	No. of patients	Risk factor	OR	95% CI	P value
Greene et al, 2015 ¹⁷	Multicentric registry (Michigan Hospital Medicine Safety consortium). Hospital patients admitted to a medicine service for 2 days or longer.	76,242 (182 UEDVTs)	PICC	10.49	7.79-14.11	<.001
			Inpatient stay within last year	1.68	1.22-2.30	.001
			Cancer within last year	2.30	1.59-3.33	<.001
			History of VTE	2.00	1.39-2.88	<.001
Wilson et al, 2012 ⁵⁹	Single-center retrospective cohort study. Neurological ICU inpatients who underwent PICC placement during their ICU stay.	431 (36 PICC-related UEDVTs)	History of surgery longer than 1 hour	3.26	1.48-7.17	.003
			Mannitol use	3.27	1.27-8.42	.014
			Placement in paretic arm	9.85	4.42-21.95	<.001
			History of VTE	6.7	2.38-18.62	<.001
Aw et al, 2012 ⁷³	Single-center retrospective cohort study. All consecutive cancer outpatients undergoing ultrasound-guided PICC placement for chemotherapy.	340 (19 PICC-related UEDVT)	Metastases	3.34	1.17-9.51	.024
			Diabetes	3.18	1.06-9.53	.039
Linnemann et al, 2008 ⁹⁴	Multicentric registry (Main-Isar-Thrombosis [MAISTHRO]) case-control study. First 150 consecutive outpatients with first-episode UEDVT in the registry. Age- and gender-matched lower extremity patients were randomly selected from the registry.	1491 (150 UEDVTs)	Elevated Factor VIII (compared with LEDVT)	0.19	0.02-0.74	.009
			Any thrombophilia (compared with LEDVT)	0.46	0.25-0.83	.009
Verso et al, 2008 ⁷⁶	Prospective single-center, double-blind, placebo-controlled study. Patients with CVCs and either undergoing CA-UEDVT prophylaxis with LMWH 40 mg once daily, or placebo for 6 weeks.	385 (191 LMWH and 194 placebo) 50 CA-UEDVTs	Chest radiotherapy	7.01	1.42-34.66	.017
			Inadequate position of CVC tip	4.05	1.64-10.02	.002
			Left-sided CVC insertion	2.29	1.01-5.51	.05

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Table V. Continued.

Author, year	Study design	No. of patients	Risk factor	OR	95% CI	P value
Blom et al, 2005 ⁹⁵	Prospective, population-based case-control study (Multiple Environmental and Genetic Assessment [MEGA] of risk factors for venous thrombosis study).	179 UEDVTs, 2399 controls	CVC present	1136	153-8448	N/A
			Malignancy (including CVC)	43.6	25.5-74.6	N/A
			Malignancy present (excluding CVC)	18.1	9.4-35.1	N/A
			Surgery of the upper extremity	13.1	2.1-80.6	N/A
			Surgery elsewhere	4.7	2.2-9.7	N/A
			Immobilization of the arm (plaster)	7.0	1.7-29.5	N/A
			Family history of VTE	2.8	1.6-4.9	N/A
			Oral contraceptive use	2.0	1.1-3.8	N/A
			Factor V Leiden/prothrombin 20210A and active cancer	177.1	17.4-1806.1	N/A
Joffe et al, 2004 ²⁸	Prospective multicentric US DVT Registry Database. All consecutive acute DVT patients.	5388 (592 UEDVTs)	In-dwelling CVC	9.7	7.8-12.2	N/A
			CVC use within 30 days	7.3	5.79-9.21	N/A
			Age <67 years (NCA-UEDVT)	2.35	1.66-3.29	<.0001
			BMI <25 kg/m ² (NCA-UEDVT)	1.70	1.25-2.31	.0007
			Hospitalization (NCA-UEDVT)	1.56	1.15-2.12	.005
Tesselaar et al, 2004 ⁹⁶	Single-center retrospective cohort study. Consecutive cancer patients with CVC placement.	243 (33 CA-UEDVTs)	Arm ports vs chest ports (with anticoagulants)	34.8	7.3-165	N/A
			Elevated homocysteine Levels of evidence	3.8	1.3-11.3	N/A
			Left-sided vs right-sided placement	3.5	1.6-7.5	N/A
			CVC tip in the SVC vs right atrium	2.7	1.1-6.6	N/A
Martinelli et al, 2004 ⁹⁷	Single-center case-control study. 115 consecutive UEDVTs, with no precipitating factors. Controls were friends or partners of the patients.	115 vTOS-associated UEDVTs 797 Healthy controls	Factor V Leiden	6.2	2.5-15.7	N/A
			Prothrombin G20210 A	5.0	2.0-12.2	N/A

Table V. Continued.

Author, year	Study design	No. of patients	Risk factor	OR	95% CI	P value
			Antithrombin, protein C, or S deficiency	4.9	1.1-22.0	N/A
			Factor V Leiden or Prothrombin G20210A and use of oral contraceptives	13.6	2.7-67.3	N/A

ARDS, Acute respiratory distress syndrome; BMI, body mass index; CA-UEDVT, catheter-associated upper extremity deep venous thrombosis; CI, confidence interval; CPAP, continuous positive airway pressure; CVC, central venous catheter; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; LEDVT, lower extremity deep venous thrombosis; LMWH, low-molecular-weight heparin; NCA-UEDVT, noncatheter-associated upper extremity deep venous thrombosis; N/R, not reported; OR, odds ratio; PICC, peripherally inserted central catheter; SVC, superior vena cava; VTOS, venous thoracic outlet syndrome; WBC, white blood cell count.

The Caprini risk model is widely used in the assessment of venous thrombosis embolism, but few studies have applied it to UEDVT. In a prospective observational study that aimed to use the Caprini thrombosis risk model in patients receiving chemotherapy via a PICC line, the risk assessment model had 74.1% sensitivity and 44.1% specificity.⁵⁰ Receiver operating characteristic analysis indicated that the area under the curve for the Caprini score risk model was 0.615 (95% confidence interval [CI], 0.537-0.693), suggesting at least moderate effectiveness as a prediction model for PICC-associated DVT. The authors propose a Caprini score of ≥ 7 as the threshold for higher risk status in the setting of PICC-related UEDVT. Notable limitations of the study were a small sample size ($n = 201$) and limited follow-up of 4 weeks.

In a retrospective cohort study, Sharp et al⁴⁹ examined 2437 PICC insertion patients with cancer to determine the effect of the catheter-to-vein ratio (CVR) on rates of symptomatic thrombosis and identify the optimal CVR

cut-off point. They analyzed the risk of thrombosis associated with a 45% CVR, which is the cut-off recommendation commonly used in clinical practice for PICC insertion. The key finding was that a 45% cut-off ($\leq 45\%$ vs $\geq 46\%$) was predictive, with the higher ratio associated with more than twice the risk of thrombosis (relative risk, 2.30; 95% CI, 1.202-4.373; $P = .01$). Of note, the cut-off was specific to patients with cancer and was not associated with the risk of thrombosis for those with an infection and other noncancer diagnoses.

In a large real-world registry from Japan, the researchers compared 74 patients with UEDVT vs 2424 with LEDVT.⁸ The prevalence of patients with UEDVT was 3.0% and patients with UEDVT more frequently had active cancer and CVC use. The cumulative 3-year incidence of recurrent VTE was not different between the two groups (9.7% and 7.4%; $P = .43$) and there was no significant difference in the risk of recurrent VTE between the groups (hazard ratio, 0.94; 95% CI, 0.36-2.01; $P = .79$). Interestingly, the latter results were found despite higher frequency of discontinuation of anticoagulation therapy in patients with UEDVT (63.7% and 29.7% at 1 year; $P < .001$).

Hong et al⁸⁴ examined all cases ($n = 260$) of heparin-induced thrombocytopenia (HIT) over a 17-year period at four Canadian academic centers. Overall, 14 of 260 patients (5.4%) with HIT developed UEDVT. The key finding was that the presence of a CVC in the setting of HIT was associated with an odds ratio of 17.1 (95% CI, 4.9-60.5; $P < .0001$) for UEDVT when compared with the control group that did not have a CVC. One study examined the utility of biomarkers in prospectively predicting CVC-related VTE.¹⁰⁰ These biomarkers are circulating procoagulant microparticles, which are microvesicles largely derived from activated platelet and endothelium, indirect markers of thrombin generation, and factor VIII. Of the 42 inpatient children with a CVC, three CVC-related VTE events were reported. Apart from circulating procoagulant microparticles, these biomarkers were significantly different in patients who developed CVC-related thrombosis in comparison with those who did not develop a CVC-related thrombosis.

Table VI. The Michigan risk assessment score for peripherally inserted central catheter (PICC)-associated upper extremity deep venous thrombosis (UEDVT)

Factor	Score
VTE within 30 days	+3 points
History of any VTE	+2 points
Triple/quad PICC lumens	+3 points
Double PICC lumens	+2 points
Active cancer	+2 points
WBC count at time of PICC insertion $>12,000$	+1 point
Presence of another CVC when index PICC placed	+1 point
Michigan Risk Score Grades	Probability of VTE
Grade I (0 points)	0.9% (95% CI: 0.7-1.2%)
Grade II (1-2 points)	1.5% (95% CI: 1.2-1.9%)
Grade III (3-4 points)	2.6% (95% CI: 2.2-3.0%)
Grade IV (>4 points)	4.5% (95% CI: 3.7-5.4%)

CI, Confidence interval; CVC, central venous catheter; VTE, venous thromboembolism; WBC, white blood cell count.

Table VII. Constans and Extended Constans Clinical Decision Making Scores¹⁰¹

Criteria	Score
CVC or pacemaker	+1
Localized pain ¹⁰¹	+1
Unilateral edema	+1
Other diagnosis at least as plausible as UEDVT	-1
Pretest clinical probability	
UEDVT likely	≥2
UEDVT unlikely	≤1
Extended Constans Clinical Decision Making Score ¹⁰¹	
CVC or pacemaker	+1
Localized pain	+1
Unilateral edema	+1
Arm swelling >1.5 cm compared with other arm	+1
Superficial vein dilatation	+1
Skin color difference	+1
Estrogen use	+1
Recent intravenous injection or peripheral catheter (past 5 days)	-1
Other diagnosis at least as plausible as UEDVT	-1
Pretest clinical probability	
UEDVT likely	≥3
UEDVT unlikely	≤2

CVC, Central venous catheter; UEDVT, upper extremity deep venous thrombosis.

For patients with clinically suspected UEDVT, Constans and colleagues developed a clinical decision score in a derivation cohort of 140 patients with suspected UEDVT of whom 50 patients (36%) had the diagnosis confirmed by ultrasound¹⁰¹ (the Constans and extended Constans can be found in Table VII). The score combines clinical presentation (signs and symptoms) with risk factors for UEDVT. The Constans Clinical Decision Score consists of four factors: intravascular foreign material presents such as CVC or pacemaker (plus 1 point); localized pain (plus 1 point); unilateral edema (plus 1 point); and other plausible diagnoses (minus 1 point). If the score is ≤1, upper extremity thrombosis is unlikely; if the score is ≥2, upper extremity thrombosis is likely. The Constans score was internally validated in a cohort of 103 patients and externally validated in a cohort of 214 patients with clinically suspected UEDVT. The area under the curve for the three cohorts (derivation, internal, and external, respectively) ranged from 0.67 in the derivation cohort to 0.77 in the external validation cohort. Taken in the appropriate context, the Constans score may help to identify higher risk patients, but it should not be used as a stand-alone tool.¹⁰² UEDVT risk-predicting models' performance are summarized in Table VIII.

Guideline 3.1. We suggest that determining the clinical probability of UEDVT using either the Constans or

Table VIII. Upper extremity deep venous thrombosis (UEDVT) scoring systems performance

Author, year	No. of patients	Associated risk factors	Patient population	Gold standard	Sensitivity/specificity
van Es et al, 2017 ¹⁰³	406 (103 UEDVTs)	Average age: 57 CVC: 23% Malignancy: 34%	Patients with suspected UEDVT	DUS	Constans score: Sensitivity: 86% Specificity: 65% Area under ROC curve: 0.81 Extended Constans score: Sensitivity: 90% Specificity: 64% Area under ROC curve: 0.85
Constans et al, 2008 ¹⁰¹	Derivation cohort of 140 patients (50 UEDVTs) Internal validation cohort of 103 patients (46 UEDVTs) External validation OPTIMEV cohort of 214 patients (65 UEDVTs)	Average age: 59 CVC: 51% Malignancy: 58% Average age: 60 CVC: 51% Malignancy: 51.5% Average age: 59 CVC: 12.1% Malignancy: NR	Patients hospitalized for UEDVT suspicion. OPTIMEV validation cohort of multi-institution outpatient and inpatient sample	DUS	Derivation cohort Sensitivity: 70% Specificity: 83% Internal validation cohort Sensitivity: 74% Specificity: 67% External validation cohort Sensitivity: 38% Specificity: 93%

AUC, Area under the receiver operating characteristic curve; CVC, central venous catheter; DUS, duplex ultrasound; NR, not reported; ROC, receiver operating characteristic.

Table IX. D-dimer use in the workup of upper extremity deep venous thrombosis (UEDVT)

Author, year	No. of patients	Associated risk factors	Patient population	Comparison standard	Sensitivity/specificity
Liu et al, 2022 ¹⁰⁴	281 (81 UEDVTs)	Average age: 44.9 PICC: 100% Malignancy: 77.4%	Patients with PICC and low venous thrombosis risk (Modified Wells score) underwent D-dimer and DUS testing.	DUS	D-dimer (cutoff of 500 µg/L): All patients: Sensitivity: 52.8% Specificity: 70.5% Cancer patients: Sensitivity: 48.8% Specificity: 78.1% Noncancer patients: Sensitivity: 66.7% Specificity: 71.0%
Sartori et al, 2015 ²⁰	239 (24 UEDVTs)	Average age: 58.3 CVC: 7.6% Malignancy: 16.3%	Patients with suspected UEDVT	DUS	D-dimer (cutoff of 500 µg/L): Sensitivity: 92% Specificity: 60%
Kleinjan et al, 2014 ¹⁰⁵	406 (103 UEDVTs)	Average age: 56 CVC: 40.9% Malignancy: 34%	Patients with suspected UEDVT	Clinical decision	D-dimer (cutoff not reported) Sensitivity: 95.6% Specificity: 71.3%
Merminod et al, 2006 ¹⁰⁶	52 (15 UEDVTs)	Median age: 61 CVC: 34.6% Malignancy: 44.2%	Patients with suspected UEDVT	DUS (CTV in 5 cases)	D-dimer (cutoff of 500 µg/L): Sensitivity: 100% Specificity: 14%

CTV, Computed tomography venography; CVC, central venous catheter; DUS, duplex ultrasound; PICC, peripherally inserted central catheter; ROC, receiver operating characteristic.

extended Constans score is preferred over the modified Wells score, and it should guide subsequent investigation. [GRADE - 2; LEVEL OF EVIDENCE - B^{101,103}]

The clinical decision-making process for diagnosing UEDVT integrates clinical prediction scores and diagnostic assays to stratify patients and guide further testing. In clinical practice, patients with a low Constans score and a negative D-dimer test can often forgo further testing, whereas those with a high Constans score or a positive D-dimer test should undergo confirmatory imaging, typically with compression ultrasonography. This combined approach minimizes unnecessary imaging and optimizes resource utilization while maintaining diagnostic accuracy. Further, predictive scoring offers a structured, evidence-based method to stratify risk and guide diagnostic pathways. The use of D-dimer in the workup of UEDVT is shown in Table IX.

Guideline 3.2. For patients unlikely to have UEDVT based on clinical probability scores, we suggest that further testing with D-dimer should not be performed, unless all other diagnoses have been excluded. [GRADE - 2; LEVEL OF EVIDENCE - B; CONSENSUS]

Guideline 3.3. We suggest that D-dimer testing should NOT be used to rule out CA-UEDVT. [GRADE - 2; LEVEL OF EVIDENCE - B¹⁰⁴]

Guideline 3.4. We recommend that D-dimer testing with a cutoff value of 500 µg/L may be used as a cost-

effective initial test for ruling out NCA-UEDVT in patients with low pretest probability. [GRADE - 1; LEVEL OF EVIDENCE - B¹⁰⁷]

DIAGNOSIS AND WORKUP

Diagnosing UEDVT relies on a combination of clinical evaluation and imaging modalities. Advanced diagnostic tools such as DUS, MRV, and catheter-based venography play critical roles in confirming the diagnosis, particularly in high-risk or complex patients. The lack of evidence on CTV for UEDVT diagnosis limits our ability to recommend this method of imaging. A comprehensive evaluation of imaging modalities utilized in the diagnosis of UEDVT is detailed in Table X.

DUS remains the first-line imaging modality for evaluating suspected UEDVT owing to its noninvasive nature, widespread availability, reproducibility, low cost, and high diagnostic accuracy. It can combine B-mode imaging to visualize thrombi and Doppler flow analysis to assess blood flow dynamics.

Ultrasound diagnostic criteria include absence of vein compressibility, visualization of thrombus echogenicity, and abnormal venous flow patterns. A significant limitation of Duplex ultrasound (DUS), which is highly effective in detecting thrombosis in distal veins such as the distal subclavian, axillary, and brachial veins, is its reduced efficacy in identifying thrombosis in the proximal subclavian vein owing to the shadowing effect caused by the

Table X. Imaging modalities in the workup of upper extremity deep venous thrombosis (*UEDVT*)

Author, year	No. of patients	Associated risk factors	Patient population	Gold standard	Anatomical location	Sensitivity/specificity
DUS						
Brownie et al, 2020 ¹⁰⁸	214 (169 UEDVTs)	CVC use: 0 Malignancy: 0 Average age: 30.7	Patients who underwent vTOS surgical treatment, that had a prior UE DUS	Surgery	Subclavian/axillary vein 100%	DUS: False-negative rate: 21% True-positive rate: 79%
Li et al, 2016 ¹⁰⁹	152 (38 UEDVTs)	CVC use: 100% Malignancy: N/A Median age: 3	Children with a CVC admitted to the ICU	Consultative DUS	Subclavian vein 19.1% Internal Jugular vein 34.9%	Point-of-care DUS: Subclavian vein: Sensitivity: 0% Specificity: 83.3% Internal jugular vein: Sensitivity: 33.3% Specificity: 93.8%
Kleinjan et al, 2014 ¹⁰⁵	406 (103 UEDVTs)	CVC use: 40.9% Malignancy: 34% Average age: 56	Inpatients and outpatients with suspected UEDVT	DUS or venography	Subclavian vein 73.8% Axillary vein 57.3% Brachial vein 34.9% Internal jugular vein 22.3% Brachiocephalic vein 9.7%	DUS: Sensitivity: 94.5% Specificity: 71%
Hanslik et al, 2008 ¹¹⁰	90 (25 UEDVTs)	CVC use: 100% Malignancy: 0% Average age: 2.7	Consecutive children with congenital heart disease requiring short-term central venous lines in the upper venous system	All imaging modalities	Internal jugular vein 88% Subclavian vein 4% Brachiocephalic vein 8% SVC 12%	DUS: Sensitivity: 88%
Baarslag et al, 2002 ¹¹¹	99 (44 UEDVTs)	CVC use: 24% Malignancy: 28% Average age: 54	Consecutive patients with suspected UEDVT	Invasive contrast venography	Brachiocephalic vein 20% Subclavian vein 43% Axillary vein 25% Basilic vein 9%	DUS: Sensitivity: 82% Specificity: 82%
Male et al, 2002 ¹¹²	66 (19 UEDVTs)	CVC use: 100% Malignancy: 100% Average age 6.8	Pediatric patients with acute lymphoblastic leukemia	Invasive contrast venography	Subclavian vein 95% Axillary vein 10.5% Internal jugular vein 21% Brachiocephalic vein 15.8%	DUS: Sensitivity: 37% Specificity: 100%
Patel et al, 1999 ¹¹³	21 (12 UEDVTs)	CVC use: 76.2% Malignancy: 71.4% Average age: 42	Patients with suspected UEDVT	Invasive contrast venography	N/A	DUS: Sensitivity: 75% Specificity: 100%
Prandoni, 1997 ¹¹⁴	58 (27 UEDVTs)	CVC use: 13.8% Malignancy: 15.5% Average age: 53	Patients with suspected UEDVT	Invasive contrast venography	N/A	CUS: Sensitivity: 96% Specificity: 93.5% DUS: Sensitivity: 100% Specificity: 93%
Koksoy et al, 1995 ¹¹⁵	44 (18 UEDVTs)	CVC use: 100% Malignancy: N/A Average age: 39	Patients with subclavian venous catheters	Invasive contrast venography	Subclavian vein 88.9% Axillary vein 16.7% Brachiocephalic vein 11.1%	DUS: Sensitivity: 94% Specificity: 96%
Haire et al, 1991 ¹¹⁶	43 (25 UEDVTs)	CVC use: 100% Malignancy: N/A Average age: N/A	Patients with CVCs and suspected UEDVT	Invasive contrast venography	Subclavian vein 100%	DUS: Sensitivity: 55.8% Specificity: 97.4%
Baxter et al, 1991 ¹¹⁷	30 (9 UEDVTs)	CVC use: 73.7% Malignancy: N/A Average age: 52	Patients on long-term renal dialysis with suspected UEDVT	Invasive contrast venography	Subclavian vein 66.6% Axillary vein 33.3% Innominate vein 55.6% Internal jugular vein 55.6%	DUS: Sensitivity: 85% Specificity: 97.8%
Knudson et al, 1990 ¹¹⁸	130 (39 UEDVTs)	CVC use: 33.8% Malignancy: 30% Average age: 49	Patients with suspected UEDVT	Concomitant imaging (n = 22) or clinical follow-up (n = 99)	N/A	DUS: Sensitivity: 78% Specificity: 92%
Falk and Smith, 1987 ¹¹⁹	22 (10 UEDVTs)	CVC use: 54.5% Malignancy: 0 Age range: 12-76	Patients with suspected central UEDVTs	Invasive contrast venography or CTV	Subclavian 80% Axillary 40% Internal jugular vein 50%	DUS: Sensitivity: 100% Specificity: 88%
Sullivan et al, 1984 ¹²⁰	33 (3 UEDVTs)	CVC use: N/A Malignancy: N/A Average age: N/A	Patients with suspected UEDVTs	Invasive contrast venography	Subclavian/axillary vein 100%	DUS: Sensitivity: 100% Specificity: 100%
Sottirurai et al, 1982 ¹²¹	42 (19 UEDVTs)	CVC use: N/A Malignancy: N/A Average age: 30	Patients with suspected UEDVT	Invasive contrast venography	N/A	DUS: Sensitivity: 89.5% Specificity: 50%
MRV						

Table X. Continued.

Author, year	No. of patients	Associated risk factors	Patient population	Gold standard	Anatomical location	Sensitivity/specificity
van Dam et al, 2021 ¹²²	60 (30 UEDVTs)	UEDVT group: Average age: 50 CVC: 23% Malignancy: 23% No UEDVT: Average age: 58 CVC: 17% Malignancy: 33%	Patients with suspected UEDVT	CUS or CTV	N/R	MR-noncontrast thrombus imaging Sensitivity: 93% Specificity: 100%
Baarslag et al, 2004 ¹²³	31 (11 UEDVTs)	Average age: 42 CVC: NR Malignancy: NR	Patients with suspected UEDVT	Invasive contrast venography	N/R	TOF MRV: Sensitivity: 71% Specificity: 89% Gadolinium-enhanced 3D MRV: Sensitivity: 50% Specificity: 80%
Haire et al, 1991 ¹¹⁶	28 (13 UEDVTs)	Average age: NR CVC: 100% Malignancy: NR	Patients with CVCs and suspected UEDVTs	Invasive contrast venography	N/R	MRI (absence of flow void) Sensitivity: 46.1% Specificity: 100%

CTV, Computed tomography venography; CUS, compression ultrasound; CVC, central venous catheter; DUS, duplex ultrasound; ICU, intensive care unit; MRI, magnetic resonance imaging; MRV, magnetic resonance venography; N/A, not applicable; N/R, not reported; SVC, superior vena cava; TOF, time-of-flight; US, ultrasound; vTOS, venous thoracic outlet syndrome.

clavicle. Therefore, a negative duplex scan does not definitively exclude UEDVT in patients with a high pre-test probability. In such cases, additional imaging, preferably MRV or CTV is warranted to avoid delays in diagnosis and treatment. This approach ensures that clinically significant thrombi in anatomically challenging regions are not missed, thereby reducing the risk of preventable complications such as PE or PTS.

Guideline 4.1. In patients with clinically suspected UEDVT, we recommend that an upper extremity DUS be the first diagnostic imaging examination. [GRADE - 1; LEVEL OF EVIDENCE - B¹⁰⁷]

Guideline 4.2. If more proximal UEDVT is suspected, upper extremity DUS may have a lower sensitivity and specificity. [GRADE - 1; LEVEL OF EVIDENCE - B^{109,108}]

Guideline 4.3. We recommend that screening for CA-UEDVT in patients with long-term indwelling catheters be guided by institutional policies, beginning with DUS, but it should not be routinely conducted in asymptomatic patients. [GRADE - 1; LEVEL OF EVIDENCE - B; CONSENSUS]

Guideline 4.4. If the initial DUS of the upper extremity is negative but clinical suspicion remains high, we recommend further investigation with MRV or, if MR is contraindicated, CTV to prevent treatment delays. [GRADE - 1; LEVEL OF EVIDENCE - B¹⁰⁸]

MRV offers superior visualization of venous anatomy and pathology, particularly in cases where DUS results are inconclusive or when deeper structures need evaluation. This modality provides high-resolution, three-dimensional images without ionizing radiation, making it ideal for patients requiring more detailed anatomical

assessment, such as those with TOS or central venous stenosis. MRV is particularly useful in evaluating thrombosis in the SVC and other central veins. However, its limited availability, higher cost, and potential contraindications, such as implanted metallic devices, may restrict its routine use.

Guideline 4.5. Owing to lack of current evidence regarding CTV, we suggest that MRV should be preferred when available for diagnosing UEDVT. [GRADE - 2; LEVEL OF EVIDENCE - B¹²²]

Catheter-based venography remains the gold standard for diagnosing UEDVT, offering unparalleled accuracy in visualizing venous structures and identifying thrombi. It can be combined with IVUS to reduce the amount of media contrast dye required. The drawbacks of this technique are its invasiveness, and potential complications such as contrast-induced nephropathy and radiation exposure. It is typically reserved for cases where noninvasive imaging is inconclusive, or intervention is planned.

Guideline 4.6. If noninvasive studies are inconclusive in patients with high index of suspicion of UEDVT, and invasive endovascular therapy is to be sought, we suggest that initial venography be considered to diagnose and document the extent of thrombus after discussing risks and benefits with the patient. [GRADE - 2; LEVEL OF EVIDENCE - B; CONSENSUS]

Guideline 4.7. We recommend that catheter-based venography be considered to better evaluate the degree of stenosis or compression of the upper extremity veins following thrombus removal if symptoms persist and with the intention to treat. [GRADE - 1; LEVEL OF EVIDENCE - B; CONSENSUS]

IVUS is an adjunct invasive imaging modality that can be used in the evaluation and management of UEDVT, particularly in complex cases. IVUS has gained acceptance in deep venous disease because it provides detailed visualization of venous anatomy, and it can assist in ruling out venous compression.¹²⁴ It can also provide information on thrombus characteristics, which can guide interventional procedures such as catheter-directed thrombolysis or thrombectomy. Although IVUS is not routinely used in all UEDVT cases, it can be valuable in assessing the extent of thrombosis, identifying underlying anatomical abnormalities, and facilitating precise delivery of therapeutic interventions. Its use should be considered on a case-by-case basis, especially in patients with severe symptoms or those who may benefit from interventional therapies.

Guideline 4.8. We recommend IVUS over venography in evaluating degree of stenosis, and for evaluation of technical success when performing endovascular interventions for UEDVT. It may also be performed at case completion to rule out or to document the presence of residual hemodynamically significant stenosis. [GRADE - 1; LEVEL OF EVIDENCE - B¹²⁵⁻¹²⁷]

PROPHYLAXIS

The three main prophylactic strategies for UEDVT are mechanical, chemical (pharmacological), and mechanochemical approaches. Mechanical methods, such as intermittent pneumatic compression devices, are often indicated in patients with LEDVT and their use has been extended to patients at high risk for UEDVT who have contraindications to anticoagulation, although infrequently.

Low-molecular-weight heparin and unfractionated heparin continue to be commonly used for DVT prophylaxis. Routine prophylaxis of UEDVT in patients with long-term indwelling central lines remains controversial based on limited data.¹²⁸ Mechanochemical approaches combining mechanical and chemical methods are also based on a paucity of evidence. Although various prophylactic strategies exist for UEDVT, the supporting evidence is limited, and recommendations are often extrapolated from LEDVT studies. Clinical decisions regarding prophylaxis should be individualized. The use of prophylaxis and its related outcomes on UEDVT are shown in [Table XI](#).

Guideline 5.1. We recommend against mechanical devices with intermittent compression as a sole prophylaxis maneuver for the prevention of UEDVT. [GRADE - 1; LEVEL OF EVIDENCE - A¹³⁰]

Guideline 5.2. We recommend against the use of pharmacomechanical prophylaxis after vTOS-associated

UEDVT has been already confirmed. [GRADE - 1; LEVEL OF EVIDENCE - B; CONSENSUS]

Guideline 5.3. We recommend avoiding mechanical prophylaxis with intermittent compression devices for CA-UEDVT. [GRADE - 1; LEVEL OF EVIDENCE - B¹³⁰]

Guideline 5.4. We recommend against routine prophylaxis with anticoagulants for CA-UEDVT for prevention of UEDVT in patients with long-term CVCs. [GRADE - 1; LEVEL OF EVIDENCE - A¹³²⁻¹³⁵]

Guideline 5.5. We recommend prophylaxis with anticoagulants for CA-UEDVT in patients with moderate-to high risk of VTE and long-term CVCs. We also recommend that a risk/benefit analysis be performed based on risk of VTE and risk of bleeding to support decision-making. [GRADE - 1; LEVEL OF EVIDENCE - B¹²⁹]

TREATMENT

UEDVT is typically managed with anticoagulation therapy, which serves as the cornerstone of treatment.^{144,145} The recommended standard regimen involves administration of oral Xa inhibitor preferably over vitamin K antagonists, with a total treatment duration of ≥ 3 months, as recommended by other consensus documents.^{144,146} In cases where a CVC is implicated and remains necessary, anticoagulation should continue for the duration the catheter is in place and extend for 3 months after its removal. For patients with cancer-associated UEDVT, extended anticoagulation is recommended as long as the malignancy remains active.^{144,146}

The evidence supporting catheter-based interventions for UEDVT is primarily derived from studies on LEDVT, with limited direct research focusing on UEDVT. The feasibility of these invasive therapies to manage UEDVT may differ from treating LEDVT because of the unique anatomical and clinical considerations of the upper extremity. Catheter-based thrombus removal with either mechanical or thrombolytic techniques or both should be individualized owing to its limited evidence. The patient's clinical status, risk factors, and the expertise and resources available must be considered.¹⁴⁴ Treatment modalities and related outcomes are summarized in [Table XII](#).

The use of SVC filters in UEDVT management is generally limited to specific scenarios. These devices may be considered for patients who have contraindications to anticoagulation therapy and are at significant risk for PE. However, the risks of SVC filters have been described as filter migration, cardiac tamponade, and the development of SVC syndrome secondary to thrombosis of the filter. Therefore, based on scarce evidence, temporary SVC filters should only be placed in highly selected patients who have absolute contraindication to anticoagulation and a high risk of life-threatening PE.¹⁵⁹

Table XI. Prophylaxis and its outcomes on upper extremity deep venous thrombosis (UEDVT)

Author, year	No. of patients	Type of study	Patient population	Prophylaxis regimen	Groups	Outcomes	Follow-up period
Brandt et al, 2022 ¹²⁹	217	Randomized, placebo-controlled, double-blind clinical trial (subgroup analysis of the AVERT trial)	Patients with intermediate to high risk of VTE with CVC and initiating chemotherapy.	Apixaban: 2.5 mg twice daily over 180 days	2 groups: Apixaban (126 patients) Placebo (91 patients)	Apixaban: 4.8% VTE rate 1.6% Major Bleeding rate Placebo: 18.7% VTE rate 2.2% Major Bleeding rate HR, 0.26 (95% CI, 0.14-0.47; $P < .0001$)	180 days
Rabinstein et al, 2020 ¹³⁰	77	Randomized, single-center controlled trial	Neurocritical intensive care patients with a PICC line that were not receiving anticoagulation	Treatment arm: Sequential compression device of the arm was applied as continuously as possible	2 groups: Sequential compression device (37 patients) Control (40 patients)	Treatment arm: UEDVT rate: 41.9% TERMINATED EARLY DUE TO EXCESS DVT Control: UEDVT rate: 16.1%	Until PICC removal
Lv et al, 2019 ¹³¹	423	Nonrandomized control trial (treatment selection was based on physician and patient preference)	Chemotherapy patients with PICC line	Enoxaparin 4000 IU/day Rivaroxaban 10 mg/day Control No placebo	3 groups: Enoxaparin (138 patients) Rivaroxaban (144 patients) Control (141 patients)	Enoxaparin: UEDVT rate: 3.03% Rivaroxaban: UEDVT rate: 3.76% Control: UEDVT rate: 12.4%	Until PICC removal
Lavau-Denes et al, 2013 ⁷²	407	Single-center, prospective, open-label, randomized trial	Consecutive patients with CVC device with planned chemotherapy	LMWH Subcutaneous LMWH (dalteparin, nadroparin or enoxaparin once daily, at recommended prevention doses) Warfarin 1 mg/day Control No anticoagulation	3 groups: LMWH (141 patients) Warfarin (135 patients) No anticoagulation (137 patients)	LMWH: UEDVT rate: 14/138 (10.1%) Warfarin: UEDVT rate: 8/134 (6.0%) No anticoagulation: UEDVT rate: 20/135 (14.8%)	90 days
Niers et al, 2007 ¹³²	87	Single-center, prospective, randomized, placebo-controlled, double-blind, study	Consecutive patients with hematological malignancies requiring intensive chemotherapy including autologous stem cell transplantation	Nadroparin: 2850 IU/day subcutaneously for 3 weeks	2 groups: Nadroparin (41 patients) Placebo (46 patients)	Nadroparin: Rate of CA-UEDVT: 17% Placebo: Rate of CA-UEDVT: 9%	21 days
Karthaus et al, 2006 ¹³³	425	Multicentric, double blind, placebo-controlled, randomized trial	Patients with cancer undergoing chemotherapy via a CVC for ≥ 12 weeks	Dalteparin: 5000 IU once daily Placebo: 0.2 mL saline once daily	2 groups: Dalteparin: (285 patients) Placebo: (140 patients)	Dalteparin: Clinically relevant CA-UEDVT rate: 3.4% Placebo: Clinically relevant CA-UEDVT rate: 3.4%	16 weeks
Verso et al, 2005 ¹³⁴	385	Multicenter, double-blind, placebo-controlled, randomized trial	Consecutive cancer patients scheduled to undergo CVC placement	Enoxaparin: 40 mg/day subcutaneously Placebo: Preloaded syringes	2 groups: Enoxaparin (191 patients) Placebo (194 patients)	Enoxaparin: CA-UEDVT rate: 14.1% Placebo: CA-UEDVT rate: 18.0%	42 $\pm$ 2 days

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Table XI. Continued.

Author, year	No. of patients	Type of study	Patient population	Prophylaxis regimen	Groups	Outcomes	Follow-up period
Couban et al, 2005 ¹³⁵	255	Randomized, placebo-controlled study	Consecutive cancer patients who required a CVC for >7 days	Warfarin 1 mg/day Placebo	2 groups: Warfarin (130 patients) Placebo (125 patients)	Warfarin: Rate of symptomatic CA-UEDVT: 4.6% Major bleeding episodes: 0% Premature CVC removal rate: 25.4% Average CVC lifespan: 63 days Placebo: Rate of symptomatic CA-UEDVT: 4.0% Major bleeding episodes: 2% Premature CVC removal rate: 23.2% Average CVC lifespan: 84 days	90 days
Mismetti et al, 2003 ¹³⁶	59	Multicentric, prospective, randomized, parallel-group	Cancer patients with CVC implantation	Warfarin: 1 mg/day for 90 days Nadroparin: 2850 IU subcutaneous daily for 90 days	2 groups: Warfarin (24 patients) Nadroparin (21 patients)	Warfarin: CA-UEDVT: 16.7% Nadroparin: CA-UEDVT: 28.6%	90 days
Massicotte et al, 2003 ¹³⁷	158	Multicentric, open-label, randomized controlled trial	Children between 36 weeks and 18 years of age with minimum duration of CVC of 5 days	Reviparin-sodium: 30 IU/kg if > 3 months of age 50 IU/kg if < 3 months of age for 30 days. Standard care: Only unfractionated heparin flushes (<3 IU/kg/hour).	2 groups: Reviparin (78 patients) Standard care (80 patients)	Reviparin: Symptomatic CA-UEDVT: 3.8% Asymptomatic CA-UEDVT: 10.3% Major bleeding event: 0 Mortality: 0 Standard care: Symptomatic CA-UEDVT: 3.8% Asymptomatic CA-UEDVT: 8.8% Major bleeding event: 1.1% Mortality: 2.1%	30 days
Carr and Rabinowitz, 2001 ¹³⁸	115	Single-center retrospective cohort study	Patients with solid tumors, and CVCs.	Warfarin: 1 mg/day No prophylaxis	2 groups: Warfarin (52 patients) No prophylaxis (65 patients)	Warfarin: Rate of CRT: 11% No prophylaxis: Rate of CRT: 21%	NR
Minassian et al, 2000 ¹³⁹	305	Single-center non-randomized retrospective chart review	Patients with gynecological malignancies who required long-term venous access catheters and ports	Warfarin: 1 mg/day No prophylaxis:	2 groups: Warfarin (96 patients) No prophylaxis (209 patients)	Warfarin: Rate of CRT: 4% No prophylaxis: Rate of CRT: 11%	>1 year
Boraks et al, 1998 ¹⁴⁰	223	Single-center case-control retrospective and prospective study	Consecutive patients with hematological malignancies requiring CVCs	Warfarin: 1 mg/day until line removal No prophylaxis	2 groups: Warfarin (108 patients) No prophylaxis (115 patients)	Warfarin: Rate of CRT: 5% No prophylaxis: 13%	NR

Table XI. Continued.

Author, year	No. of patients	Type of study	Patient population	Prophylaxis regimen	Groups	Outcomes	Follow-up period
Monreal et al, 2018 ¹⁴¹	29	Open-label, prospective, randomized controlled trial	Consecutive cancer patients undergoing long-term Port-a-Cath subclavian CVC placement	Fragmin 2500 IU daily for 90 days Control	2 groups: Fragmin (16 patients) Control (13 patients)	Fragmin: CA-UEDVT: 1/16 (6%) Control: CA-UEDVT: 8/13 (62%) RR, 6.75 (95% CI, 1.05-43.58; $P = .002$)	90 days
Pucheu et al, 1996 ¹⁴²	118	Single-center retrospective case-control study	Consecutive cancer patients requiring an implantable infusion CVC	Dalteparin: 2500 IU daily for 30 days. No prophylaxis	2 groups: Dalteparin (46 patients) No prophylaxis (72 patients)	Dalteparin: Rate of CA-UEDVT: 6.5% No prophylaxis: Rate of CA-UEDVT: 15.2%	1 year
Bern et al, 1990 ¹⁴³	82	Prospective, single center, randomized control trial	Consecutive cancer patients requiring a long-term indwelling CVC for infusion chemotherapy with an estimated survival >3 months	Warfarin 1 mg/day for 90 days	2 groups: Warfarin (42 patients) No prophylaxis (40 patients)	Warfarin: Rate of CA-UEDVT: 9.5% No prophylaxis: Rate of CA-UEDVT: 37.5%	90 days

CA-UEDVT, Catheter-associated upper extremity deep venous thrombosis; CI, confidence interval; CVC, central venous catheter; CRT, catheter-related thrombosis; HR, hazard ratio; ICU, intensive care unit; IU, international units; LMWH, low-molecular-weight heparin; NR, not reported; PICC, peripherally inserted central catheter; RR, relative risk; VTE, venous thromboembolism.

Table XII. Treatment modalities and outcomes on upper extremity deep venous thrombosis (UEDVT)

Author, year	Study design	Patient population	No. of patients	Treatment regimen	Treatment groups	Outcomes	Follow-up
Xu et al, 2023 ¹⁴⁷	Retrospective cohort study	Consecutive cancer patients with acute symptomatic PICC-related UEDVT	217 CA-UEDVTs	Initial 3-5 days of nadroparin (950 IU/10 kg every 12 hours), followed by rivaroxaban (15 mg twice daily for 21 days, then 20 mg daily for 90 days) Nadroparin therapy (950 IU/10 kg every 12 hours) for 90 days.	LMWH bridge to rivaroxaban 99 (45.6%) LMWH 118 (54.4%)	VTE recurrence rate: 1.7% Bleeding event rate: 13.1% VTE recurrence rate: 2.0% Nonmajor bleeding rate: 5.1%	180 days
Baumann Kreuziger et al, 2021 ¹⁴⁸	Multicenter retrospective cohort study	Patients with hematological malignancies and documented catheter-related thrombosis	663 CA-UEDVTs	N/A	Anticoagulation only: 124 (19%) Anticoagulation and catheter removal: 388 (58%) Catheter removal only: 119 (18%) No anticoagulation or catheter removal: 32 (5%)	All-cause death: 34% VTE recurrence rate: 15% Major bleeding rate: 5% Nonmajor bleeding rate: 5%	Median, 343 days (IQR, 159-886 days)
Vedovati et al, 2021 ¹⁴⁹	Multicentric prospective cohort studies combined into a collaborative database	Patients with objectively confirmed acute UEDVT treated with DOACs	188 UEDVTs	Any DOAC (physician preference for DOAC, dose, and duration) Mean duration of DOAC treatment: 5.1 months.	N/A	VTE recurrence: 0.9 per 100 patient-years Clinically relevant nonmajor bleeding: 10.3 per 100 patient-years Major bleeding: 1.7 per 100 patient-years All-cause death: 6.0 per 100 patient-years	Mean, 740 days (95% CI, 638-841 days)

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Table XII. Continued.

Author, year	Study design	Patient population	No. of patients	Treatment regimen	Treatment groups	Outcomes	Follow-up
Rokosh et al, 2020 ³	Single-center retrospective cohort study	All consecutive inpatients diagnosed with acute VTE	35 UEDVTs	N/A	Anticoagulation 48.6% IV heparin 22.9% warfarin 5.7% apixaban 42.9% LMWH Discharge anticoagulation 86%	All-cause mortality: 28.5% PE: 8.6%	Up to discharge only
Beiswenger et al, 2020 ⁴	Single-center retrospective cohort study	All consecutive patients undergoing UE venous duplex imaging	182 UEDVTs	N/A	Anticoagulation: 139 (76.4%) Heparin: 49.6% LMWH: 40.3% Pentassacharide: 4.3% Warfarin: (43.9% DOACs: 14.4% Direct thrombin inhibitors: 5.0% No anticoagulation: 43 (23.6%)	Death, 30 days: 12.2% PE, 30 days: 8.6% Stroke, 30 days: 0.7% Death, 6 months: 24.5% Death, 30 days: 30.2% PE, 30 days: 2.3% Stroke, 30 days: 4.7% Death, 6 months: 37.2%	6 months
Houghton et al, 2020 ¹⁵⁰	Single-center prospectively collected data, retrospectively analyzed.	Consecutive patients with VTE enrolled into the Mayo Clinic VTE Registry	210 UEDVT	N/A	Apixaban/rivaroxaban: 102 (49%) LMWH/warfarin: 108 (51%)	Recurrence: 0 Major bleeding: 0 Nonmajor bleeding: 5 (6.8%) Recurrence: 1 (1.6%) Major bleeding: 2 (3.3%) Nonmajor bleeding: 1 (1.6%)	6 months
Schastlivtsev et al, 2019 ¹⁵¹	Single-center prospective observational study.	Patients with first-episode UEDVT confirmed on DUS.	30 UEDVT	All patients received LMWH for 1-2 days, then switched to rivaroxaban for 3-6 months	Rivaroxaban: 30 (100%)	Recurrence: 0 Major bleeding: 0 Nonmajor bleeding: 2 (6.7%)	6 months
Davies et al, 2018 ¹⁵²	Multicenter prospective cohort study	Patients with cancer and CA-UEDVT	70 CA-UEDVT	Rivaroxaban 15 mg oral, twice daily for 3 weeks, followed by 20 mg daily for 9 weeks	Rivaroxaban 70 (100%)	Recurrence of VTE: 1 (1.43%) Major bleeding: 7 (10%) Nonmajor bleeding: 4 (5.7%)	12 weeks
Montiel et al, 2017 ¹⁵³	Multicenter retrospective registry (Swedish national anticoagulation registry [Auricula]) study	All patients treated with DOAC for UEDVT	55 UEDVTs	DOACs were prescribed for 3-6 months or indefinitely (provoked vs unprovoked or permanent risk factors)	Rivaroxaban (84%) Apixaban (13%) Dabigatran (4%)	Recurrence: 1 (2%) Major bleeding: 0 Nonmajor bleeding: 1 (2%)	6 months
Fan et al, 2017 ¹⁵⁴	Single-center retrospective cohort study	Patients with PICC-associated UEDVT	84 PICC-associated UEDVTs	Rivaroxaban 20 mg once daily, for 3 months. LMWH/warfarin received 40,000 IU every 12 hours, until INR ≥ 2 for 3 months	Rivaroxaban: 44 (52%) LMWH/warfarin: 40 (48%)	Recurrence: 0 Major bleeding: 0 Nonmajor bleeding: 7.3% Recurrence: 0 Major bleeding: 0 Nonmajor bleeding: 11.4%	3 months 3 patients loss of FU (rivaroxaban group) 5 patients loss of FU (LMWH/Warfarin group)

Table XII. Continued.

Author, year	Study design	Patient population	No. of patients	Treatment regimen	Treatment groups	Outcomes	Follow-up
Laube et al, 2017 ¹⁵⁵	Single-center retrospective cohort study	All patients with active cancer, and CA-UEDVT treated with rivaroxaban	83 CA-UEDVTs	55 patients had rivaroxaban solely 5 patients received <7 days of LMWH prior to rivaroxaban transition 23 patients were initially anticoagulated with LMWH and transitioned to rivaroxaban after 7 days	Rivaroxaban: 83 (100%)	Recurrence: 3 (3.6%) Major bleeding: 1 (1.2%) Nonmajor bleeding: 2 (2.4%) CVC removal owing to UEDVT: 3.6% CVC removal owing to any cause: 14%	3 months
Rathbun et al, 2011 ¹⁵⁶	Single-center prospective cohort study	Consecutive patients with confirmed UEDVT	67 patients	Dalteparin for 5-7 days followed by warfarin for 3 months Dalteparin for 3 months	LMWH/warfarin LMWH	LMWH/warfarin Recurrent VTE: 0 Major bleeding: 4% 3-month mortality: 11% LMWH Recurrent VTE: 0 Major bleeding: 0% 3-month mortality: 5%	3 months
Kovacs et al, 2007 ¹⁵⁷	Multicenter prospective cohort study	Patients with active malignancy and acute, symptomatic CA-UEDVT	74 CA-UEDVT	Dalteparin 200 IU/kg per day for 5-7 days, followed by warfarin with a target INR of 2.0-3.0	LMWH bridge + warfarin	Recurrence: 0 Major bleeding: 3 (4%) Nonmajor bleeding: 0	3 months
Savage et al, 1999 ¹⁵⁸	Single-center prospective cohort study	Patients managed as outpatients for UEDVT, most with underlying malignancy or a history of a central line	46 UEDVT	Dalteparin 200 IU/kg for a minimum of 5 days, followed by warfarin with a target INR of 2.0-3.0	LMWH bridge + warfarin	12-weeks follow-up Recurrence: 1 (2.2%) Major bleeding: 1 (2.2%) All-cause mortality: 7 (15.2%)	12 weeks

CA-UEDVT, catheter-associated upper extremity deep venous thrombosis; CI, confidence interval; CVC, central venous catheter; DOAC, direct oral anticoagulant; FU, follow-up; HR, hazard ratio; INR, international normalized ratio; IQR, interquartile range; IU, international units; LMWH, low-molecular-weight heparin; NR, not reported; PE, pulmonary embolism; PICC, peripherally inserted central catheter; VTE, venous thromboembolism.

Guideline 6.1. We recommend that UEDVT be treated with oral Xa inhibitors over vitamin K antagonists for ≥ 3 months in patients with low bleeding risk. [GRADE - 1; LEVEL OF EVIDENCE - B; CONSENSUS]

Guideline 6.2. We recommend that underlying causes such as malignancy and hypercoagulability disorders should be considered and investigated for patients with a first, unprovoked, episode of secondary UEDVT. [GRADE - 1; LEVEL OF EVIDENCE - B; CONSENSUS]

Guideline 6.3. We suggest that extensive acute UEDVT (<21 days) may be treated with early thrombus removal strategies in severely symptomatic patients with expected life expectancy >1 year to reduce the incidence of PTS. [GRADE - 2; LEVEL OF EVIDENCE - B^{160,161}]

Guideline 6.4. We recommend that management of vTOS-associated UEDVT with findings compatible with vTOS should include first rib resection. [GRADE - 1; LEVEL OF EVIDENCE - B^{41,42,162,163}]

Guideline 6.5. We recommend that CA-UEDVT be treated with anticoagulation and, if the catheter is no longer necessary or alternative access is feasible to remove the catheter. [GRADE - 1; LEVEL OF EVIDENCE - B; CONSENSUS]

Guideline 6.6. We recommend that CA-UEDVT be treated with anticoagulation and, if the catheter is no longer necessary or alternative access is feasible to remove the catheter. [GRADE - 1; LEVEL OF EVIDENCE - B; CONSENSUS]

Guideline 6.6. We recommend that NCA-UEDVT be treated with anticoagulation for ≥ 3 months in patients with acceptable bleeding risk. [GRADE - 1; LEVEL OF EVIDENCE - B; CONSENSUS]

Guideline 6.7. We suggest that interventions for NCA-UEDVT be considered if the patient is highly symptomatic, has low surgical risk, and has life expectancy >1 year. [GRADE - 2; LEVEL OF EVIDENCE - C; CONSENSUS]

Guideline 6.8. We suggest that in highly selected patients with absolute contraindication to anticoagulation and high risk of life-threatening PE, temporary SVC filter placement be considered. [GRADE - 2; LEVEL OF EVIDENCE - C^{164–166}]

AUTHOR CONTRIBUTIONS

Conception and design: RM, NM, BL

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R.D.M. serves as a consultant for Inari Medical, Boston Scientific, and Penumbra. Y.E. serves as a consultant for Cook Medical and Inari Medical. N.J.M. is a consultant for Inari Medical, Medtronic, W. L. Gore & Associates, Philips, BD Bard, and Boston Scientific. E.F. serves as a consultant for Medtronic, Boston Scientific, and Koya Medical. N.T. serves as a consultant for Boston Scientific.

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