

2026 American Association for Thoracic Surgery Expert Consensus Document: Diagnosis and management of heparin-induced thrombocytopenia in patients who undergo cardiac surgery

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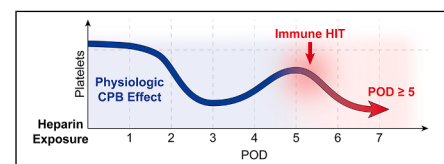
ABSTRACT

Background: Heparin-induced thrombocytopenia (HIT) in patients who undergo cardiac surgery presents unique diagnostic and management challenges due to universal perioperative heparin exposure, postoperative platelet kinetics, and the high prevalence of critical illness in this population. Current guidelines do not fully address these cardiac surgery-specific features, leading to practice variation in screening, diagnosis, anticoagulation management, and perioperative planning. Consolidated, practical, and evidence-based recommendations are needed that are tailored to cardiac surgery and to temporary mechanical circulatory support after cardiac surgery.

Methods: The American Association for Thoracic Surgery Clinical Practice Standards Committee convened a multidisciplinary panel of 16 experts in cardiac surgery, hematology, critical care, anesthesiology, perfusion, and pharmacology. A comprehensive literature review was performed with medical librarian support. Using a modified Delphi methodology, the panel evaluated the evidence, developed clinical statements, and assigned a class of recommendation and a level of evidence to each recommendation.

Results: Consensus was achieved for 32 recommendations across 5 domains: epidemiology and natural history of HIT after cardiac surgery; diagnostic evaluation, including appropriate Thrombocytopenia, Timing, Thrombosis, oTher cause (4Ts) score use, time-dependent platelet count patterns, and integration of immunoassay and functional testing; therapeutic management with nonheparin anticoagulants, including the selection of direct thrombin inhibitors, factor Xa inhibitors, and adjunctive therapies; perioperative management of patients with HIT who require cardiac surgery, including the timing of surgery, intraoperative anticoagulation strategy, and adjunctive therapies; and screening, testing, and anticoagulation strategies for patients supported by extracorporeal membrane oxygenation or temporary mechanical circulatory support after cardiac surgery. Additional best practices are included for cardiopulmonary bypass circuit management for patients with HIT.

Conclusions: This American Association for Thoracic Surgery Expert Consensus Document provides practical, cardiac surgery-specific guidance for the diagnosis and management of HIT across the continuum of cardiac surgical care. By addressing the complexities unique to cardiac surgery, high-risk anticoagulation environments, and extracorporeal and temporary mechanical circulatory support, these recommendations aim to improve diagnostic accuracy, standardize care, reduce complications, and support safe heparin re-exposure or alternative anticoagulation strategies when surgery is required. (J Thorac Cardiovasc Surg 2026; ■:1-23)



Postcardiac surgery HIT algorithm: platelet trends, testing, and treatment.

CENTRAL MESSAGE

The diagnosis and management of HIT after cardiac surgery requires context-specific nuance. This AATS consensus provides practical guidance to improve safety across the perioperative continuum.

PERSPECTIVE

Treating patients for HIT after cardiac surgery poses unique challenges. This consensus bridges the gap between general HIT guidance and the realities of perioperative cardiac surgical care, offering multidisciplinary, cardiac surgery-specific recommendations to support accurate diagnosis, safer anticoagulation, and better outcomes.

See Commentary on page XXX.
See Discussion on page XXX.

Abbreviations and Acronyms

4Ts	= Thrombocytopenia, Timing, Thrombosis, oTher cause
AATS	= American Association for Thoracic Surgery
ASH	= American Society of Hematology
CoR	= class of recommendation
CPB	= cardiopulmonary bypass
DOAC	= direct oral anticoagulant
DTI	= direct thrombin inhibitor
DVT	= deep vein thrombosis
ECMO	= extracorporeal membrane oxygenation
ELISA	= enzyme-linked immunosorbent assay
HIT	= heparin-induced thrombocytopenia
IgG	= immunoglobulin G
IVIg	= intravenous immunoglobulin
LMWH	= low-molecular-weight heparin
LoE	= level of evidence
NPV	= negative predictive value
OD	= optical density
PF4	= platelet factor 4
POD	= postoperative day
PPV	= positive predictive value
SRA	= serotonin-release assay
TPE	= therapeutic plasma exchange
UFH	= unfractionated heparin
VKA	= vitamin K antagonist
VTE	= venous thromboembolism



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Heparin-induced thrombocytopenia (HIT) is an immune-mediated, prothrombotic reaction that carries substantial morbidity—especially in cardiac surgery, wherein near-universal heparin exposure and expected postoperative thrombocytopenia complicate the diagnosis of HIT. Although existing HIT guidelines offer broad direction, they do not address procedure-specific issues in cardiac surgery or postoperative extracorporeal circulatory support.^{1,2} HIT with thrombosis represents a subset of cases; the diagnostic framework and recommendations herein apply to both, with thrombosis-specific management distinctions noted where relevant.

This American Association for Thoracic Surgery (AATS) Consensus Statement provides focused guidance for diagnosing and managing HIT in these circumstances. It emphasizes timely identification, judicious continuation or cessation of heparin, appropriate use of alternative anticoagulants, and strategies for patients with acute or prior HIT who require cardiac surgery.

METHODS AND RESULTS

The AATS/Society of Thoracic Surgeons methodology for developing clinical practice documents was followed.³ A writing committee consisting of a 17-member multidisciplinary panel was convened comprising cardiothoracic surgeons, hematologists, intensivists, cardiac anesthesiologists, pharmacists, and perfusionists, including 2 authors (AC and TEW) of the 2018 American Society of Hematology (ASH) HIT Guidelines.¹ The panel developed expert consensus statements and assigned each one a class of recommendation (CoR) and level of evidence (LoE). The CoR reflects the estimated risk-benefit balance, and the LoE describes the quality, quantity, and consistency of supporting data (Figure 1).³

Consensus statements were created across 5 domains relevant to HIT in cardiac surgery: epidemiology and natural history of postoperative HIT; diagnostic evaluation, including use of the Thrombocytopenia, Timing, Thrombosis, oTher cause (4Ts) score, time-dependent platelet trends, and integration of immunoassay and functional

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Class of Recommendation

Suggested phrases for writing recommendations	
I Strong recommendation Benefit >>> risk	- Is recommended - Is indicated
IIa Moderate recommendation Benefit >> risk	- Should be considered - Is reasonable - Can be useful/effective/beneficial
IIb Weak recommendation Benefit ≥ risk	- May/might be reasonable - May/might be considered
III Moderate recommendation No benefit: risk = benefit Strong recommendation Harm: risk > benefit	- Is not recommended - Is contraindicated - Should not be performed/administrated

Level of Evidence

A	High-quality evidence from more than one RCT with no concern for high risk of bias, or meta-analyses of high-quality RCTs with no concerns for significant bias.
B	Randomized (B-R): Moderate-quality evidence from 1 or more RCT or meta-analysis of RCTs. Non-Randomized (B-NR): Moderate-quality evidence from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies or meta-analyses of such studies.
C	Limited data (C-LD): Studies with limitations of design or execution, meta-analyses of such studies, case series, or physiological or mechanistic studies in human subjects. Expert opinion (C-EO): Consensus of expert opinion based on clinical experience.

AATS, American Association for Thoracic Surgery; EACTS, European Association for Cardio-Thoracic Surgery; ESTS, European Society of Thoracic Surgeons; STS, Society of Thoracic Surgeons; RCT, randomized controlled trial.

FIGURE 1. Adopted definitions of classes of recommendation and levels of evidence. Adapted from reference.³ RCT, Randomized controlled trial.

testing; therapeutic management with nonheparin anticoagulants, including the selection of direct thrombin inhibitors (DTIs), factor Xa inhibitors, and adjunctive therapies; perioperative management of patients with HIT who require cardiac surgery, including surgical timing, intraoperative anticoagulation strategies, and preoperative adjuncts; and screening, testing, and anticoagulation approaches in patients supported by extracorporeal membrane oxygenation (ECMO) or temporary mechanical circulatory support after cardiac surgery (Table 1).

A scholarly communications librarian performed comprehensive PubMed/MEDLINE searches, reviewing all publications from January 1, 2000, through December 31, 2024, as

well as earlier landmark studies identified by the panel. The writing committee reviewed the evidence and developed recommendations through iterative discussion. Consensus required at least 80% participation and 75% agreement. This process was repeated for each section, with unresolved issues addressed through scheduled online meetings and formal voting, using a Delphi framework.⁴

All authors contributed to drafting and revising their assigned sections. The writing committee chairs synthesized the final document, which was reviewed and approved by the full writing committee and the AATS Adult Cardiac Clinical Practice Standards Committee before submission to the AATS Board of Directors.

TABLE 1. Complete list of 32 statements across 5 clinical domains with class of recommendation (CoR) and level of evidence (LoE)

Section	Statement	CoR	LoE
Natural history	1.1) Daily platelet count monitoring is recommended for early detection of HIT while hospitalized after cardiac surgery.	I	C-EO
	1.2) LMWH should be considered an alternative to UFH for VTE prophylaxis after cardiac surgery, as it confers a lower risk of developing HIT.	IIa	B-NR
Diagnosis	2.1) In the first 4 d after cardiac surgery, the 4Ts score should not be used to guide HIT testing.	III	C-EO
	2.2) In the first 4 d after cardiac surgery, it is recommended to order a HIT immunoassay (without prior 4Ts score) in a patient exposed to unfractionated heparin in the prior 5-10 days with a new thrombosis.	I	B-NR
	2.3) In the first 5-30 d after cardiac surgery, it is recommended to calculate a 4Ts score in patients with 1 or more of the following (Note: the “baseline” platelet count is the highest postoperative platelet count that immediately precedes the fallen platelet count under consideration): A. an unexpected platelet count fall ($\geq 30\%$) in a biphasic pattern (second fall begins on or after postoperative day 5); B. an early and persistently low pattern ($< 100 \times 10^9/L$), when a superimposed $\geq 30\%$ fall occurs on or after day 5; or C. a new thrombosis	I	B-NR
	2.4) It is recommended that in centers performing cardiac surgery, HIT immunoassay testing should be available 7 days a week with a turnaround time within 24 hours.	I	C-EO
	2.5.) In patients with a low-probability 4Ts score (≤ 3) after cardiac surgery, discontinuation of heparin, laboratory testing for HIT, and empiric treatment with a nonheparin anticoagulant are not recommended.	III	B-NR
	2.6) In patients with an intermediate- or high-probability 4Ts score (≥ 4) after cardiac surgery, discontinuation of heparin and obtaining initial laboratory testing with a HIT immunoassay is recommended.	I	B-NR
	2.7) In patients with an intermediate-probability 4Ts awaiting an immunoassay after cardiac surgery, it is reasonable to postpone the initiation of a nonheparin anticoagulant until the immunoassay result is available in the absence of thrombosis.	IIa	C-EO
	2.8) Patients with a negative immunoassay test (ELISA or rapid immunoassay) after cardiac surgery do not require further testing, or empiric treatment in the absence of compelling clinical or laboratory features.	III	B-NR
	2.9) In patients with a positive immunoassay after cardiac surgery, confirmatory testing with a functional assay is recommended.	I	B-NR
	2.10) For patients with an intermediate-probability 4Ts score and a “weakly positive” immunoassay (ie, OD of 0.40-0.99 units for labs using an ELISA), it is reasonable to delay initiation of nonheparin anticoagulant until confirmatory functional testing is available in the absence of thrombosis.	IIa	C-EO
	2.11) For patients with a high-probability 4Ts score or a strongly positive immunoassay (ie, OD ≥ 1.0 units for labs using an ELISA) or positive rapid immunoassay (> 1.0 U/mL), initiation of a nonheparin anticoagulant at therapeutic-intensity is recommended pending the results of the functional assay.	I	B-NR
Treatment	3.1) In patients with confirmed HIT who are critically ill, at increased risk of bleeding, or may require additional procedures, treatment with intravenous direct thrombin inhibitors (ie, bivalirudin, argatroban) may be reasonable due to their shorter half-life.	IIb	C-LD
	3.2) In patients with confirmed HIT who are at lower risk of bleeding and are unlikely to need additional procedures, treatment with fondaparinux, danaparoid, or DOACs may be considered if medication-specific eligibility criteria are met.	IIb	B-NR
	3.3) VKAs should not be used for treatment of HIT until after platelet count recovery has occurred (above $150 \times 10^9/L$).	III	B-NR
	3.4) IVIg or TPE may be considered for refractory or progressive acute HIT in addition to therapeutic nonheparin anticoagulation.	IIb	C-LD
	3.5) Temporary cessation of nonheparin therapeutic anticoagulation is reasonable with active bleeding and HIT.	IIa	C-EO
	3.6) Routine platelet transfusion is not recommended in nonbleeding patients with HIT.	III	C-LD
	3.7) It is reasonable to transfuse platelets in patients with HIT and active bleeding.	IIa	C-EO
	3.8) In patients with HIT, noninvasive 4-limb ultrasound should be considered for assessment of proximal deep venous thrombosis to guide the duration of anticoagulation.	IIa	B-NR

(Continued)

TABLE 1. Continued

Section	Statement	CoR	LoE
Needing cardiac surgery	3.9) In patients with HIT without associated thrombosis, anticoagulation is indicated until platelet recovery to a stable plateau, for up to 3 months.	IIa	B-NR
	3.10) Patients with HIT and thrombosis should be treated with anticoagulation for 3 to 6 months.	IIa	B-NR
	4.1) In patients with a history of HIT undergoing nonemergency cardiac surgery, it is recommended to perform an immunoassay assay.	I	C-EO
	4.2) In patients with confirmed HIT, it is recommended that nonemergency cardiac surgery be delayed until the functional assay is negative.	I	B-NR
	4.3) In patients with HIT and a positive functional assay requiring urgent/emergency cardiac surgery, it may be reasonable to use either intraoperative bivalirudin alone or heparin with additional measures (eg, preoperative IVIg and/or TPE).	IIb	C-LD
ECMO/MCS	4.4) Intraoperative heparin is recommended in patients with a history of HIT and a negative immuno- or functional assay; intraoperative heparin is also appropriate if the immunoassay is positive, but the functional test is negative.	I	C-LD
	5.1) The 4Ts should not be used to guide HIT testing in patients receiving post-cardiotomy ECMO.	III	B-NR
	5.2) HIT testing should be considered in patients receiving ECMO for post-cardiotomy shock who experience persistent thrombocytopenia 5-14 d after their first exposure to unfractionated heparin.	IIa	B-NR
	5.3) A direct thrombin inhibitor is a reasonable strategy for anticoagulation during post-cardiotomy ECMO as it reduces the risk of developing HIT.	IIa	B-NR
	5.4) It is recommended that patients on ECMO requiring anticoagulation with suspected HIT are switched to a direct thrombin inhibitor and all heparin products should be discontinued.	I	C-EO
	5.5) In post-cardiotomy patients requiring a micro-axillary flow pump with a concern for HIT, sodium bicarbonate-based purge solutions should be considered over heparin-based solutions.	IIa	B-NR

HIT, Heparin-induced thrombocytopenia; EO, expert opinion; LMWH, low-molecular-weight heparin; UFH, unfractionated heparin; VTE, venous thromboembolism; NR, non-randomized; 4Ts, Thrombocytopenia, Timing, Thrombosis, oTher cause; ELISA, enzyme-linked immunosorbent assay; OD, optical density; DOAC, direct oral anticoagulant; VKA, vitamin K antagonist; IVIg, intravenous immunoglobulin; TPE, therapeutic plasma exchange; ECMO, extracorporeal membrane oxygenation; MCS, mechanical circulatory support.

Section 1: Natural History/Epidemiology

Statement 1.1: Daily platelet count monitoring is recommended for early detection of HIT during hospitalization after cardiac surgery. (CoR I, LoE C-expert opinion). HIT is an immune-mediated adverse reaction in which antibodies against platelet factor 4 (PF4)-heparin complexes trigger platelet activation and a paradoxical prothrombotic state.^{1,5} In cardiac surgery patients, HIT causes substantial morbidity due to near-universal perioperative heparin exposure, expected postoperative thrombocytopenia, and the physiologic stresses of cardiopulmonary bypass (CPB) and critical illness.⁵

The incidence of HIT after cardiac surgery ranges from 0.5% to 3%, which is markedly higher than the <0.1% rate observed in most other hospitalized populations.⁵⁻⁷ Although up to 50% of cardiac surgery patients develop anti-PF4/heparin antibodies, only a minority progress to clinical HIT, highlighting the importance of clinical context and platelet trend interpretation in the diagnosis of HIT.^{2,6} When HIT occurs in this population, 30% to 60% of cases are complicated by arterial or venous thrombosis, reinforcing the need for early detection.⁸

Thrombocytopenia is common after CPB; up to 50% of patients develop significant platelet count decline.^{9,10} This early postoperative thrombocytopenia is typically not immune-mediated and reflects hemodilution, platelet activation and consumption, and mechanical destruction. Platelet recovery is expected by postoperative day (POD) 3 or 4. Persistent thrombocytopenia beyond POD 4 or a new platelet decline beginning on or after POD 5 should prompt concern for HIT.^{2,9} In this circumstance, HIT can present either as a classic biphasic pattern or as a new, superimposed >30% platelet count decline beginning on or after POD 5.

HIT can be divided into distinct clinical phases: suspected HIT, acute HIT, subacute HIT A, subacute HIT B, and remote HIT (Table 2). Recognizing these phases is essential for diagnostic evaluation, therapeutic decision making, and perioperative management, especially in patients who undergo cardiac surgery.¹ Early detection of HIT is critical because delayed recognition can result in severe thrombotic complications. Daily platelet count monitoring enables timely identification of the postoperative platelet count fall that is often the earliest indicator of

TABLE 2. The phases of heparin-induced thrombocytopenia (HIT)

Phase	Brief explanation	Diagnostic tests useful for identification
Suspected HIT	Clinical suspicion based on new thrombocytopenia and recent heparin exposure	Platelet count monitoring, 4Ts score (clinical probability)
Acute HIT	Thrombocytopenia (50% fall from peak), usually 5-10 days postheparin Highest risk for thrombosis	Platelet count monitoring, immunoassay (positive), functional assay (positive)
Subacute HIT A	Platelet count recovers HIT antibodies persist; risk of thrombosis probably remains but is lower than in acute HIT	Immunoassay (positive), functional assay (positive)
Subacute HIT B	Platelet count recovers Antibodies persist, but platelet-activating antibodies are no longer detectable Risk of HIT recurrence with intraoperative heparin re-exposure is low	Immunoassay (positive), functional assay (negative)
Remote HIT	Platelet count recovers Antibodies are no longer detectable Risk of recurrence with intraoperative heparin re-exposure is low	Immunoassay (negative), functional assay (negative)

4Ts, Thrombocytopenia, Timing, Thrombosis, oTher cause.

HIT. The ASH guidelines emphasize that postoperative cardiac surgery patients are at elevated risk due to intensive and prolonged unfractionated heparin (UFH) exposure and the proinflammatory environment of surgery, which may potentiate immune responses to PF4-heparin complexes.¹

Statement 1.2: Low-molecular-weight heparin should be considered an alternative to UFH for venous thromboembolism prophylaxis after cardiac surgery because it confers a lower risk of developing HIT. (CoR IIa, LoE B-nonrandomized). Chemoprophylaxis for venous thromboembolism (VTE) is recommended after cardiac surgery.¹¹ Low-molecular-weight heparin (LMWH) has a smaller molecular size than UFH and is less likely to form large PF4/heparin complexes, resulting in fewer pathogenic immunoglobulin G (IgG) antibodies and diminished platelet activation.¹² HIT is therefore consistently less common when LMWH is used instead of UFH, a benefit that extends to cardiac surgery patients.

A recent Cochrane systematic review involving 1398 postoperative patients found that compared with UFH, LMWH was associated with a significantly lower risk of HIT (risk ratio, 0.23; 95% CI, 0.07-0.73) and of HIT complicated by thrombosis (risk ratio, 0.22; 95% CI, 0.06-0.84).¹³ Consistent with these findings, a quality-improvement program at a high-volume Canadian tertiary care center produced dramatic reductions in the rates of HIT and HIT with thrombosis after transitioning from UFH to LMWH as part of routine practice.¹⁴ In cardiac surgery specifically, a retrospective study of heart valve surgery patients showed that those bridged to warfarin with LMWH postoperatively had fewer HIT events (3 out of 100) than a prior cohort that received UFH (6 out of 103), with correspondingly fewer thrombotic complications.¹⁵ These findings suggest that LMWH is less immunogenic than UFH.

Mechanistic and immunologic data also support the lower immunogenicity of LMWH. After CPB using UFH, anti-PF4/heparin antibodies develop commonly, but clinical HIT is far more frequent in patients who continue UFH than in those switched to LMWH.¹⁶ Furthermore, narrative reviews of the cardiac surgery literature suggest that HIT incidence can be up to 10-fold higher with UFH than with LMWH.¹⁷

The decision to use LMWH should be individualized. LMWH has a longer half-life and may be cleared less efficiently by the kidneys than UFH; furthermore, rapid reversal during bleeding emergencies is more difficult and may increase the risk that re-exploration will be needed. Protamine sulfate partially reverses LMWH, fully neutralizing anti-IIa activity but achieving only 60% to 80% anti-Xa reversal.¹⁸ Andexanet alfa may provide more complete reversal when protamine is insufficient, but its use before CPB has been associated with heparin resistance and is not recommended in the preoperative cardiac surgery setting.¹⁹ Therefore, close monitoring is necessary when LMWH is used in patients with acute or chronic kidney disease, including periodic assessment of antifactor Xa activity and renal function, particularly in those with advanced impairment or fluctuating renal clearance.⁵ A complete discussion of the reversal of anticoagulant agents is beyond the scope of this document.

Section 2: Diagnostic Approach

Statement 2.1: During the first 4 days after cardiac surgery, the 4Ts score should not be used to guide HIT testing. (CoR III, LoE C-expert opinion). In patients with suspected HIT who have not undergone cardiac surgery, it is standard to calculate a pretest probability score, most commonly the 4Ts score, before ordering an immunoassay test (Figure 2).²⁰ In contrast, thrombocytopenia

4Ts Scoring:**4Ts Interpretation:****Thrombocytopenia Component Scoring (0-2)**

Criteria	Score
Platelet fall >50%	2
Platelet fall 30–50%	1
Platelet fall <30% or absolute count <10K	0

- Biphasic pattern: Calculate change between highest postoperative platelet count and new decrease
- Early/persistent pattern: Calculate change from the last preop value
- A >50% fall from the postoperative peak is highly suspicious for HIT even if the absolute count is ≥150.

Timing Scoring (0-2)

Criteria	Score
New (biphasic) platelet count fall beginning within PODs 5-10; or Fall after POD 10 that is ≤1 after day of a new, postoperative heparin exposure	2
Consistent with POD 5-10 fall but not clear timing; or Onset after day 10; or Fall ≤1 day with preop UFH exposure in prior 5-10 days	1
Fall ≤ POD 4 without any recent heparin exposure.	0

Thrombosis Scoring (0-2)

Findings	Score
New confirmed thrombosis (venous or arterial); skin necrosis at heparin injection sites; acute systemic reaction after IV heparin bolus; adrenal hemorrhage; acute limb ischemia	2
Progressive or recurrent thrombosis; suspected thrombosis; non-necrotizing skin lesions; catheter-associated thrombosis; superficial thrombophlebitis	1
No thrombosis or other sequelae	0

Other Causes for Thrombocytopenia Scoring (0-2)

Assessment of Other Causes	Score
No other apparent cause for thrombocytopenia	2
Possible other cause* present (> POD 3)	1
Definite other cause* present (POD 1-3)	0

*CPB hemodilution/consumption; sepsis; DIC (eg, secondary to cardiogenic shock); IABP, ECMO, CRRT, massive transfusion; drug-induced thrombocytopenia (e.g., GP IIb/IIIa inhibitors, beta-lactams, vancomycin [note: D-ITP usually causes platelet count falls to >20K beginning at least 5 days after immunizing drug exposure]).

Total Score	Interpretation	Management
1–3	Low	Continue heparin PRN; do not send immunoassay.
4–5	Intermediate	Send immunoassay; stop heparin; consider nonheparin anticoagulant.
6–8	High	Send immunoassay; stop heparin; begin nonheparin anticoagulant.

FIGURE 2. Adapted Thrombocytopenia, Timing, Thrombosis, oTher cause (4Ts) scoring system for the evaluation of suspected heparin-induced thrombocytopenia (HIT) in postoperative cardiac surgery patients. The figure highlights timing considerations unique to cardiopulmonary bypass, including early postoperative thrombocytopenia and biphasic platelet count patterns, and incorporates common alternative causes of thrombocytopenia in this population. Score interpretation and corresponding management recommendations are shown. *EIA*, Enzyme immunoassay; *POD*, postoperative day; *UFH*, unfractionated heparin; *IV*, intravenous; *IABP*, intra-aortic balloon pump; *ECMO*, extracorporeal membrane oxygenation; *CRRT*, continuous renal replacement therapy; *PRN*, pro re nata (ie, as needed).

during the first 4 days after cardiac surgery is expected and usually not immune-mediated. Hemodilution, blood loss, platelet activation and consumption, and mechanical destruction from CPB or mechanical circulatory support devices account for the typical 25% to 50% decline in platelet count that occurs within 48 to 72 hours after surgery, followed by spontaneous recovery by about POD 5.²¹

As an immune-mediated event, HIT typically requires at least 5 days after an initial immunizing heparin exposure for clinically significant, platelet-activating antibodies to form. Accordingly, thrombocytopenia developing within the first 4 days after cardiac surgery is unlikely to represent HIT unless the patient had recent preoperative heparin (typically UFH) exposure within the preceding 5 to 10 days before cardiac surgery. In this early postoperative window, the 4Ts score may overestimate HIT probability because cardiac surgery patients receive intraoperative heparin and have unrelated expected thrombocytopenia, resulting in automatic assignment of points for both heparin exposure and platelet count decline. Such misclassification can lead to unnecessary heparin discontinuation and inappropriate initiation of long-acting or irreversible nonheparin anticoagulants.^{22,23} Modified versions of the 4Ts score limit

assignment of points to those patients with a >50% platelet decline within 72 hours after CPB.^{24,25} If such a modified 4Ts scoring system is used, then an intermediate score (4 points) will be reached only if a thrombotic event occurs during the first 4 days after cardiac surgery, in a patient who has also received heparin in the recent preoperative period (see Statement 2.2) (Table 3).

Statement 2.2: During the first 4 days after cardiac surgery, it is recommended to order a HIT immunoassay (without 4Ts score) in a patient who has a new thrombosis and has been exposed to UFH during the 5 to 10 days before surgery. (CoR I, LoE B-nonrandomized). Preoperative heparin exposure should be carefully reviewed whenever thrombocytopenia or thrombosis occurs after cardiac surgery. Patients who received UFH within 5 to 10 days before surgery (eg, for acute coronary syndrome, catheterization procedures, or bridging from other anticoagulants) may present with early HIT postoperatively due to preformed anti-PF4/heparin antibodies, leading to platelet activation and thrombosis.²⁶ Although early HIT accounts for only 10% of postoperative HIT cases after cardiac surgery, it is associated with clinically significant morbidity and mortality.⁸ Thus, in patients with recent preoperative

TABLE 3. Thrombocytopenia, Timing, Thrombosis, oTher cause (4Ts) scoring system for heparin-induced thrombocytopenia (HIT): Key notes on timing (day 0 reference)

Clinical scenario		Day 0 for timing calculation	
Typical biphasic HIT (2nd fall onset POD 5-10)		Day of cardiac surgery (intraoperative UFH)	
Early/persistent thrombocytopenia with preop UFH		First day of recent preoperative UFH exposure	
Late-onset HIT (after POD 10) or rapid-onset with re-exposure		Day heparin was restarted	
Component	Score 2	Score 1	Score 0
Thrombocytopenia	Platelet count fall >50% (and nadir $\geq 20 \times 10^9/L$)	Platelet count fall 30-50% (or >50% with nadir $< 20 \times 10^9/L$)	Platelet count fall <30%
Timing of platelet fall	Clear onset on POD 5-10 or ≤ 1 day (with heparin exposure 5-30 days prior) or biphasic pattern	Consistent with POD 5-10 but not clear or onset after POD 10 or ≤ 1 day (heparin exposure 30-100 d prior)	Platelet fall $\leq$ POD 4 without recent heparin exposure (past 100 days)
Thrombosis or other sequelae	New proven thrombosis, skin necrosis, or acute systemic reaction after IV heparin bolus	Progressive/recurrent thrombosis, non-necrotizing skin lesions, or suspected thrombosis (not proven)	None
oTher causes of thrombocytopenia	None evident	Possible other cause (especially after POD 3)	Definite other cause (especially on POD 1-3)

POD, Postoperative day; UFH, unfractionated heparin; IV, intravenous.

UFH exposure and new thrombosis, immunoassay testing should be promptly performed, and the 4Ts score should not be used to guide testing.

It remains unclear how isolated thrombocytopenia (without thrombosis) should be approached during the early postoperative period in patients with recent UFH exposure, given the high prevalence of non-HIT-related platelet declines after cardiac surgery. In patients with atypical features—such as persistent or worsening thrombocytopenia beyond the expected postoperative nadir, failure of platelet recovery, a biphasic platelet pattern, or other clinical features inconsistent with routine postoperative thrombocytopenia—consultation with hematology or vascular medicine specialists may provide additional guidance regarding the timing and appropriateness of a HIT workup.

Statement 2.3: During the 5 to 30 days after cardiac surgery, it is recommended to calculate a 4Ts score in patients with 1 or more of the following.

- An unexpected platelet count fall ($\geq 30\%$ of baseline) in a biphasic pattern (second fall beginning on or after POD 5);
- An early and persistently low platelet count below $100 \times 10^9/L$ followed by a superimposed decline of 30% or more from baseline occurring on or after day 5; and
- New thrombosis. (CoR I, LoE B-nonrandomized)

Note that the “baseline” platelet count is the highest postoperative platelet count that precedes the low platelet count under consideration.

PODs 5 to 30 encompass the immune-mediated phase of HIT, when anti-PF4/heparin antibody formation peaks. A biphasic platelet trajectory is strongly suggestive of HIT. This pattern consists of an initial postoperative platelet decline with partial or complete recovery, followed by a

second decline beginning approximately between PODs 5 to 10. This pattern should prompt formal calculation of the 4Ts score.^{22,26,27} HIT presents between PODs 5 and 10 after cardiac surgery in about 75% of cases, whereas late-onset HIT occurs in roughly 10% to 15% of cases.⁸

The postoperative platelet “peak” is defined as the highest platelet count after cardiac surgery. Percentage platelet decline should be calculated relative to this peak when a subsequent, unexpected decrease is assessed. When platelet counts fall early and remain persistently low ($< 100 \times 10^9/L$), calculating the 4Ts score is recommended if a superimposed $\geq 30\%$ decline occurs on or after day 5 in the absence of other plausible causes. Any new thrombosis during this period should similarly prompt 4Ts-based risk assessment.

The 4Ts pretest score reduces unnecessary and potentially false-positive HIT immunoassay testing. Although the 4Ts score has an outstanding negative predictive value (NPV) ($> 99\%$), it has only a modest positive predictive value (PPV) (14% for intermediate probability; 64% for high probability).¹⁷ Because 22% to 52% of patients who undergo cardiac surgery develop nonpathogenic anti-PF4/heparin antibodies within the first postoperative week,^{17,28} inappropriate immunoassay testing increases the risk of false-positive results and unnecessary exposure to nonheparin anticoagulant agents. In patients treated empirically with alternative nonheparin anticoagulants while awaiting confirmatory functional testing, major bleeding occurs at an estimated rate of approximately $\sim 1\%$ per day, and most agents lack readily available target-specific reversal agents.^{21,29,30}

Although other cardiac surgical-specific scoring tools exist, incorporating factors such as the use of an intra-aortic balloon pump or CPB within 96 hours, they have

not demonstrated superior diagnostic performance to the 4Ts score in prospective validation studies.^{31,32} Clinical judgment regarding the timing and magnitude of platelet fall remains essential.

Statement 2.4: It is recommended that, at centers performing cardiac surgery, HIT immunoassay testing should be available 7 days a week, with a turnaround time within 24 hours. (CoR I, LoE C-expert opinion).

Timely availability of HIT immunoassay testing is essential at cardiac surgery centers, where postoperative thrombocytopenia is common and thrombotic complications of HIT can evolve rapidly. When test turnaround times are prolonged, clinicians may feel compelled to initiate diagnostic testing preemptively, before the clinical picture has fully evolved, out of concern that delayed results would preclude timely intervention. This practice contributes to overtesting, unnecessary interruption of heparin administration, premature initiation of alternative anticoagulants, higher bleeding risk, and higher health care costs. In critically ill and cardiac postoperative patients, Fiorenza and colleagues³³ showed that structured, timely testing markedly improved diagnostic accuracy and reduced unnecessary HIT evaluations. Likewise, Chaturvedi and colleagues³⁴ reported substantial overtesting and clinical misclassification when HIT assays were not efficiently available, leading to avoidable exposure to alternative anticoagulants and complications. Studies of rapid or automated HIT immunoassays demonstrate that modern assays provide high diagnostic sensitivity with rapid turnaround, enabling same-day clinical decision making.³⁵⁻³⁷

The 2018 ASH HIT guidelines likewise highlight the need for timely laboratory confirmation to reduce thrombotic risk and prevent unwarranted use of alternative

anticoagulants. Collectively, these data support maintaining 7-day-a-week HIT immunoassay capability, with results available within 24 hours, across all centers performing cardiac surgery.

Statement 2.5: In patients with a low-probability 4Ts score (≤ 3) after cardiac surgery, discontinuation of heparin, laboratory testing for HIT, and empiric treatment with a nonheparin anticoagulant is not recommended. (CoR III, LoE B-nonrandomized). The 4Ts score is a widely used and well-validated scoring system for estimating the probability of HIT. Patients are evaluated across 4 domains: thrombocytopenia, timing of the platelet count fall in relation to heparin exposure, the presence of thrombosis or other clinical sequelae, and the likelihood of other causes of thrombocytopenia. Scores of 0 to 3, 4 to 5, and 6 to 8 correspond to a low, intermediate, and high probability of HIT, respectively (Figure 3).³⁸

A systematic review and meta-analysis showed that a low-probability 4Ts score robustly excludes HIT, with an NPV of 99.8% (95% CI, 97.0%-100%). Even in studies with a substantial proportion of cardiac surgery patients, the NPV remained high (99.6%; 95% CI, 87.7%-100%).³⁹

Because of its strong NPV, a low-probability 4Ts score generally excludes HIT and supports no further HIT laboratory testing or empiric treatment. Immunoassay testing is discouraged in this circumstance because positive results are far more likely to be false than to indicate true HIT, leading to inappropriate clinical decisions.⁴⁰

Nevertheless, a low-probability 4Ts score alone should not entirely preclude a diagnosis of HIT because false-negative diagnoses made on this basis have been identified.⁴¹ Clinicians should therefore maintain a low threshold for

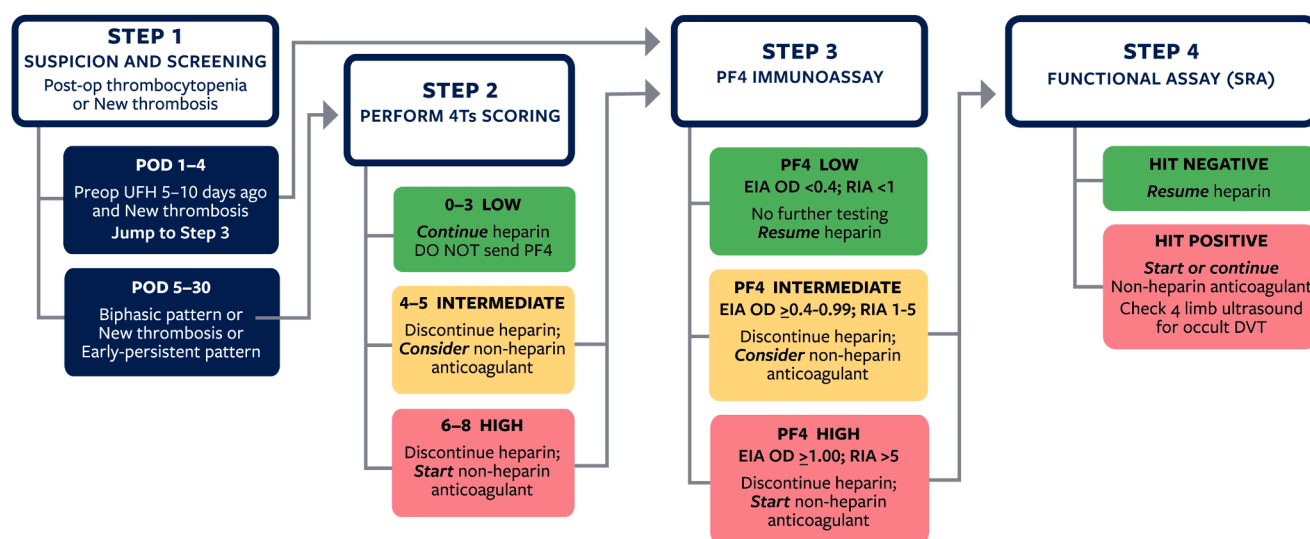


FIGURE 3. Diagnostic and management algorithm for suspected heparin-induced thrombocytopenia after cardiac surgery, incorporating Thrombocytopenia, Timing, Thrombosis, Other cause (4Ts) scoring, immunoassay strength, and functional testing to guide anticoagulation decisions. EIA, Enzyme immunoassay; OD, optical density; RIA, rapid immunoassay.

reassessment and repeat scoring if the clinical trajectory changes, including when thrombocytopenia deepens unexpectedly, new thrombosis develops, or platelet recovery fails to materialize in the expected postoperative time course. In such cases, further workup is reasonable even when the initial 4Ts score was low. This statement is aligned with the ASH and British Committee for Standards in Haematology clinical practice guidelines on HIT.^{1,42}

Statement 2.6: In patients with an intermediate- or high-probability 4Ts score (≥ 4) after cardiac surgery, discontinuing heparin and obtaining initial laboratory testing with a HIT immunoassay is recommended. (CoR I, LoE B-nonrandomized). Although the NPV of a low-probability 4Ts score is nearly absolute (99.8%), the PPV of the 4Ts score is more modest. A systematic review and meta-analysis showed that the PPVs of intermediate and high 4Ts scores were 14% (95% CI, 9%-22%) and 64% (95% CI, 40%-82%), respectively (Figure 4).³⁹ Given its low PPV, the 4Ts score should not be used in isolation to diagnose HIT. Laboratory testing, initially with a HIT immunoassay, is needed to confirm the diagnosis.

Diagnostic delay in HIT can have dangerous consequences. In a historical study, initial delay in diagnosis and treatment was associated with a 6.1% daily risk of thrombosis, amputation, or death.⁴³ Therefore, patients with an intermediate or high 4Ts score should have heparin discontinued empirically. Whether to initiate a nonheparin anticoagulant at this stage is addressed in Statements 2.7, 2.10, and 2.11. This statement is aligned with the ASH and British Committee for Standards in Haematology clinical practice guidelines on HIT.^{1,42}

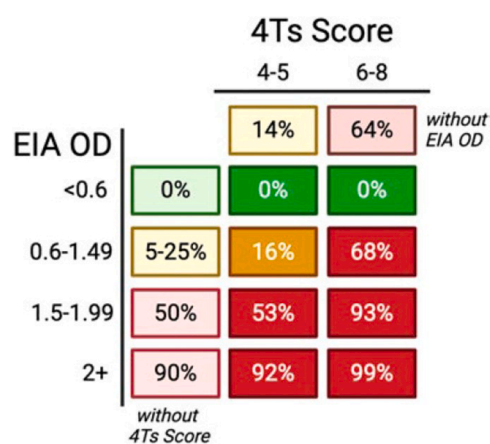


FIGURE 4. Estimated probability of heparin-induced thrombocytopenia (HIT) based on combined Thrombocytopenia, Timing, Thrombosis, oTher cause (4Ts) score and enzyme immunoassay optical density (EIA OD). Color intensity reflects increasing likelihood of HIT when clinical probability (4Ts score) and immunoassay strength are considered together, compared with either measure alone. Probability estimates vary by assay and are shown for illustrative purposes. Reproduced from May and colleagues.²⁰

Statement 2.7: In patients with an intermediate-probability 4Ts score who are awaiting an immunoassay after cardiac surgery and who do not have thrombosis, it is reasonable to postpone initiating a nonheparin anticoagulant until the immunoassay result is available. (CoR IIa, LoE C-expert opinion). The decision to start a nonheparin anticoagulant in patients with suspected HIT must balance the thrombotic risk of untreated HIT against the substantial bleeding risk that accompanies postoperative nonheparin anticoagulation. HIT is highly prothrombotic—approximately half of untreated patients develop thrombosis.⁴⁴ However, most patients with an intermediate 4Ts score do not have HIT; its prevalence in this group is only 14% (95% CI, 9%-22%).³⁹

On the other hand, nonheparin anticoagulation carries a high incidence of major bleeding. In a retrospective cohort study of patients treated with nonheparin alternatives (80% received argatroban), major bleeding occurred in 35.7% of patients with confirmed HIT and 44.0% of those in whom HIT was ultimately ruled out.⁴⁵ Risk factors associated with major bleeding—intensive care unit admission, renal dysfunction, and platelet count $<25 \times 10^9/L$ —are common after cardiac surgery.

Given the low PPV of an intermediate-probability 4Ts score and the high bleeding risk with nonheparin anticoagulation in patients after cardiac surgery, deferring treatment until immunoassay results are available appears reasonable when no thrombosis is present, particularly in patients considered to be at high bleeding risk. In contrast to the 2018 ASH guidelines panel, the writing committee for this consensus document judged that individualized anticoagulation decisions, including selective withholding or initiation of therapy based on bleeding and thrombotic risk, are more appropriate for this postoperative population (Figure 3).

Statement 2.8: For patients with an appropriately timed negative immunoassay test (enzyme-linked immunosorbent assay or rapid immunoassay) after cardiac surgery, further testing or empiric treatment is not recommended in the absence of compelling clinical or laboratory features. (CoR III, LoE B-nonrandomized). PF4/heparin immunoassays have high sensitivity ($>95\%$) for HIT at manufacturer-recommended thresholds.⁴⁶⁻⁴⁸ The most widely used immunoassays in the United States, the polyspecific enzyme-linked immunoassay (ELISA) and IgG-specific ELISA, were both found to have an NPV of 99% (95% CI, 99%-100%) in a systematic review and meta-analysis.⁴⁶ Therefore, a negative immunoassay, particularly ELISA, essentially rules out HIT; such patients do not warrant additional HIT testing and may receive heparin when clinically indicated.

Rapid immunoassays such as the PF4/polyanion chemiluminescence immunoassay⁴⁹ and latex-enhanced immunoturbidimetric immunoassay⁵⁰ are available on-demand at some centers, with results available within 1 hour.

Compared with ELISA, these assays may offer modestly higher specificity but slightly lower sensitivity (~95%-98% vs >99%), although published data from patients after cardiac surgery remain limited. Consistent with these results, the recent towards precise and rapid diagnosis of heparin-induced thrombocytopenia study found a 4.5% false-negative rate for the chemiluminescence immunoassay alone.⁴¹ The manufacturer's cutoff for a positive result is 1.0 U/mL; results in the 0.40 to 0.99 U/mL range should be considered high-negative, and further evaluation with a platelet activation assay is warranted if clinical suspicion persists.

Statement 2.9: In patients with a positive immunoassay after cardiac surgery, confirmatory testing with a functional assay is recommended. (CoR I, LoE B-non-randomized). Immunoassays are widely available and are the appropriate first laboratory test in evaluating suspected HIT. However, nonpathogenic anti-PF4/heparin antibodies are common after cardiac surgery, making immunoassay positivity alone insufficient to establish the diagnosis (Figure 4).⁴⁸ Functional assays, prototypically the serotonin-release assay (SRA), have high sensitivity and specificity for HIT and are considered the diagnostic gold standard.

Accurate classification is essential because misdiagnosis carries significant long-term consequences. In a retrospective review of 239 patients with a new heparin allergy

documented due to suspicion of HIT, 100 (42%) were HIT-negative. Sixty-eight of these patients were unnecessarily treated with an alternative anticoagulant, and the erroneous allergy documentation persisted in the medical record for more than 3 years.⁵¹ Such mislabeling exposes patients to avoidable bleeding risk from nonheparin anticoagulation and complicates future hospitalizations in which heparin may be the safest or most effective agent.

Given the downstream consequences of inaccurate heparin allergy labeling, the writing committee offers the following best practice guidance for institutions performing cardiac surgery on the documentation and removal of heparin allergy in the medical record (Table 4).

Statement 2.10: For patients with an intermediate-probability 4Ts score, a "weakly positive" immunoassay (ie, optical density, 0.40-0.99 U for labs using an ELISA), and no thrombosis, it is reasonable to delay initiating a nonheparin anticoagulant until confirmatory functional testing is available. (CoR IIa, LoE C-expert opinion). In a study of nearly 500 patients who underwent ELISA testing, a screening threshold of >0.40 was compared with a threshold of 1.00, using a positive SRA as the reference standard. Although both thresholds showed 100% sensitivity and NPV, an optical density (OD) cutoff of 0.4 had a specificity of only 86.5% and a PPV of only 13.2%.⁵² These findings are consistent with those from

TABLE 4. Best practice: Documentation and removal of heparin allergy in the medical record

Domain	Key actions	Rationale/evidence
At the time of allergy listing	• Distinguish confirmed HIT (positive functional assay) from suspected HIT—workup pending • Document: date, 4Ts score, immunoassay result, functional assay result • Use provisional label until confirmatory testing is complete	42% of 239 patients labeled with heparin allergy due to suspected HIT were ultimately HIT-negative; most were labeled based on immunoassay alone without functional assay confirmation. ⁵¹
Criteria for removal	Remove label if HIT is excluded: (1) Negative immunoassay (2) Negative functional assay	Anti-PF4/heparin antibodies become undetectable at a median of 85 days. Persistent labeling beyond this window unnecessarily restricts heparin use, including during future cardiac surgery.*
Criteria to update label as HIT resolve	Update (not simply remove) when confirmed HIT has resolved: • Negative immunoassay AND functional assay (≥85-100 days after episode) • Note that intraoperative heparin re-exposure is permissible per Statements 4.1 and 4.4	Anti-PF4/heparin antibodies become undetectable at a median of 85 days. Persistent labeling beyond this window unnecessarily restricts heparin use, including during future cardiac surgery.*
Institutional stewardship	• Prospective pharmacist or hematology review of new heparin allergy entries • Link allergy documentation to 4Ts score and laboratory results in the EMR • Structured removal protocol when diagnosis is excluded or antibodies have waned • Require co-signature for both allergy listing and removal	Erroneous labels persisted a median of 7.5 years after discharge, prompting unnecessary alternative anticoagulant use, with 66% major bleeding rate, during subsequent admissions. ⁵¹

Given the downstream consequences of inaccurate heparin allergy labeling, the writing committee offers the following best practice guidance for institutions performing cardiac surgery. HIT, Heparin-induced thrombocytopenia; 4Ts, Thrombocytopenia, Timing, Thrombosis, other cause; EMR, electronic medical record. *Cuker A, Arepally GM, Chong BH, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: heparin-induced thrombocytopenia. *Blood Adv*. 2018; 2(22):3360-3392.

another cohort, in which the prevalence of HIT in patients with an OD of 0.4 to 1.0 was <2%.⁵³

Although this non-0 prevalence warrants confirmatory functional testing, empiric treatment decisions during this interval should be individualized. In patients without true HIT, nonheparin anticoagulation in the postoperative period unnecessarily exposes patients to a substantial risk of major bleeding.⁴⁵ Accordingly, when HIT remains unconfirmed and no thrombosis is present, deferring anticoagulation until functional testing is completed is reasonable. If anticoagulation is required for an indication unrelated to HIT before confirmatory results are available, a nonheparin anticoagulant should be selected.

Although Statement 2.10 references ELISA-based OD thresholds, similar principles apply to other immunoassays. For rapid latex immunoassay or chemiluminescence immunoassay platforms, lower positive values (1.0 U/mL) are generally analogous to a weakly positive ELISA result and indicate a low probability of true HIT. As with ELISA, these findings should prompt confirmatory functional testing, with interim anticoagulation decisions individualized to bleeding risk, thrombotic risk, and clinical context.

Statement 2.11: In patients with a high-probability 4Ts score, a strongly positive immunoassay (ELISA OD ≥ 1.0 U), or a positive rapid immunoassay (>1.0 U/mL), therapeutic-intensity nonheparin anticoagulation is recommended pending the results of the functional assay. (CoR I, LoE B-nonrandomized). A missed or delayed diagnosis of HIT carries a substantial risk of life- or limb-threatening thrombosis. Functional assays, the definitive tests for HIT, are complex, are performed only in specialized reference laboratories, and typically take several days to yield results.¹⁷ In patients with a high-probability 4Ts score, a strongly positive ELISA (optical density ≥ 2.0) or highly positive results on rapid latex immunoassay or chemiluminescence immunoassay platforms (particularly values ≥ 16.0 U/mL), the likelihood that true platelet-activating antibodies are present is sufficiently high that the thrombosis risk outweighs the bleeding risk. Therefore, therapeutic-intensity anticoagulation with a nonheparin agent should be initiated promptly while confirmatory functional testing is pending.⁵²

Section 3: Treatment of HIT

Statement 3.1: In patients with confirmed HIT who are critically ill, are at elevated risk of bleeding, or may require additional procedures, treatment with intravenous DTIs (ie, bivalirudin or argatroban) may be reasonable due to their short half-life. (CoR IIB, LoE C-limited data). Managing confirmed HIT in patients who undergo cardiac surgery is challenging and requires balancing the high thrombotic risk of the syndrome with the substantial risk of postoperative bleeding. Many of these patients are clinically unstable or are at risk of requiring

urgent reoperation or other invasive procedures. Renal or hepatic dysfunction and impaired enteral absorption are also common in this population and can influence the safety and effectiveness of various anticoagulants (Table 5).

Bivalirudin and argatroban are continuous intravenous infusion DTIs that can be used to treat HIT.^{1,63-65} Bivalirudin is approved in Canada for the treatment of HIT, whereas in the United States, HIT is an off-label indication.⁵⁴ Argatroban is approved for the treatment of HIT in both countries.⁵⁵ In a single-center, retrospective analysis of data from 108 patients (including 61 patients in a cardiothoracic surgery intensive care unit) treated with an intravenous DTI for confirmed or suspected HIT, bivalirudin and argatroban showed similar efficacy, safety, and anticoagulation profiles.⁶⁵

Bivalirudin's elimination half-life is prolonged in patients with renal dysfunction, necessitating dose adjustment.⁶⁶ In patients with renal dysfunction, either dose-reduced bivalirudin or argatroban is acceptable. Argatroban, by contrast, is hepatically cleared, and its half-life is markedly prolonged in patients with hepatic impairment, critical illness, or heart failure, necessitating substantial dose reductions.⁶⁷ Despite being prolonged in certain populations, these drugs' elimination half-lives remain considerably shorter than those of other long-acting agents used to treat HIT, such as direct-acting oral anticoagulants (DOACs), fondaparinux, and danaparoid (see Table 5).⁵⁶⁻⁶¹ This shorter half-life is advantageous in patients at elevated bleeding risk and in those who may require urgent procedures, potentially reducing exposure to costly reversal strategies, minimizing the duration of critical bleeding, and avoiding procedural delays.¹

Although intravenous DTIs offer flexibility and rapid titratability, they require continuous infusion and frequent laboratory monitoring. See Figure 4 regarding anticoagulation strategies for treating HIT in patients who undergo cardiac surgery.

Statement 3.2: In patients with confirmed HIT who are at lower risk of bleeding and are unlikely to need additional procedures, treatment with fondaparinux, danaparoid, or DOACs may be considered if medication-specific eligibility criteria are met. (CoR IIB, LoE B-nonrandomized). Fondaparinux, danaparoid (not available in the United States), and DOACs offer practical advantages, including infrequent dosing and no requirement for routine laboratory monitoring. These agents are effective for treating acute HIT; however, there are several patient-specific considerations for safety and efficacy.^{1,64} Fondaparinux, danaparoid, and DOACs have limited data supporting their use for treatment of acute HIT in critically ill patients; in such cases, intravenous DTIs may be preferred.¹ See Table 4 for a detailed overview of these drugs' pharmacokinetic properties and important patient-specific considerations for use.

TABLE 5. Properties of anticoagulants for treatment of heparin-induced thrombocytopenia (HIT)

Medication	Mechanism of action*	Route*	Half-life	Monitoring	Metabolism and elimination	Additional considerations
Bivalirudin ⁵⁴	Direct thrombin inhibitor	Continuous intravenous infusion	25 min (34-57 min in moderate to severe renal impairment; ~3-5 h on dialysis)	aPTT (target 1.5-2.5 × baseline) for systemic anticoagulation; ACT during CPB (target >300-400 s depending on protocol)	Proteolytic cleavage; 20% excreted unchanged in urine	Dose reduction in renal dysfunction
Argatroban ⁵⁵			39-51 min (181 min in hepatic impairment)	aPTT (target 1.5-3.0 × baseline); ACT during CPB; note: argatroban artificially elevates PT/INR, complicating warfarin transition	Hepatic hydroxylation and aromatization; minor CYP3A4/5 metabolism	Dose reduction in hepatic dysfunction, heart failure, or critical illness
Fondaparinux ⁵⁶	Indirect factor Xa inhibitor	Subcutaneous	17-21 h (prolonged in renal impairment and elderly)	Anti-Xa activity (fondaparinux-calibrated assay); no routine monitoring needed at prophylactic doses	~77% excreted unchanged in urine	Renal dysfunction†; body weight‡; drug interactions
Danaparoid ⁵⁷			~25 h (29-35 h in renal impairment)	Danaparoid-specific anti-Xa activity (target 0.5-0.8 anti-Xa units/mL)	Primarily renal excretion	Renal dysfunction†; body weight‡; drug interactions
Rivaroxaban ⁵⁸	Direct factor Xa inhibitor	Oral	5-9 h (11-13 h in elderly)	No routine monitoring; anti-Xa activity when needed	Hepatic metabolism (CYP3A4/5, CYP2J2); ~36% unchanged in urine	Avoid in severe renal dysfunction†; not dialyzable; caution at extremes of weight‡; drug interactions; do not administer postpylorus
Apixaban ⁵⁹			8-15 h	No routine monitoring; anti-Xa activity when needed	Hepatic metabolism (CYP3A4/5; minor CYP1A2, 2C8, 2C9, 2C19, 2J2); P-gp substrate; ~27% unchanged in urine	Not dialyzable; body weight‡; drug interactions
Dabigatran ⁶⁰	Direct thrombin inhibitor		12-17 h (15-28 h in renal impairment; 14-17 h in older patients)	No routine monitoring; aPTT provides qualitative estimate	Hepatic/plasma esterases to active form; primarily excreted in urine	Avoid in severe renal dysfunction†; partially dialyzable; body weight‡; drug interactions; do not open capsules; ↑ GI bleeding risk; contraindicated with mechanical heart valves
Edoxaban ⁶¹	Direct factor Xa inhibitor		10-14 h	No routine monitoring; anti-Xa activity when needed	Minimal hepatic metabolism; primarily renal excretion	Avoid in severe renal dysfunction†; avoid if CrCl >95 mL/min; not significantly dialyzable; body weight‡; drug interactions
Warfarin ⁶²	Vitamin K antagonist		20-60 h (factor II 42-72 h, VII 4-6 h, IX and X 27-48 h)	PT/INR (therapeutic range typically 2.0-3.0 for most indications); avoid initiating before platelet recovery in HIT	CYP2C9 (major); minor CYP2C8, 2C18, 2C19, 1A2, 3A4; PK affected by genomic variants	Drug interactions; initiate only after platelet recovery; requires bridging with nonheparin anticoagulant; reverse if already receiving warfarin at HIT diagnosis

aPTT, Activated partial thromboplastin time; ACT, activated clotting time; CPB, cardiopulmonary bypass; PT/INR, prothrombin time/international normalized ratio; P-gp, P-glycoprotein; GI, gastrointestinal; CrCl, creatinine clearance; PK, pharmacokinetics. *In rows where mechanism of action or route is not listed, the entry follows that of the most recently preceding agent in the same drug class. †Renal dysfunction: Avoid in severe renal impairment or unstable renal function. ‡Body weight: use caution in extremes of body weight.

Reversal considerations further influence agent selection. Fondaparinux and danaparoid lack fully effective reversal agents, and DOAC reversal strategies can be costly or associated with thrombosis. Accordingly, these agents should be used cautiously in patients with meaningful bleeding risk or potential need for urgent invasive procedures.

Evidence supporting the postoperative use of DOACs in cardiac surgical patients, although limited, is favorable. Evidence supporting the postoperative use of nonheparin

anticoagulants after cardiac surgery is limited but generally favorable. In a retrospective cohort study of 16 patients (14 after cardiovascular surgery) treated with fondaparinux for confirmed HIT, no patient developed new or progressive thrombosis; 1 patient experienced major bleeding, and 1 patient required limb amputation related to irreversible tissue necrosis present before fondaparinux initiation.⁶⁸ In another retrospective cohort study of 93 patients treated with danaparoid for HIT after valve surgery, thrombus resolved in all

cases, with 1 possibly related major bleeding event.⁶⁹ Additional clinical experience describing fondaparinux use in patients with HIT after cardiac surgery has been reported.⁷⁰

After cardiac surgery, HIT most often begins on POD 7 (median), with 1 or 2 days thereafter required for a sufficient platelet count fall to occur to trigger consideration of HIT. Therefore, patients after cardiac surgery typically do not require therapeutic-dose anticoagulation for potential HIT until at least 1 week after surgery, which is generally a time when therapeutic-dose anticoagulation can be safely administered.

Experience with DOACs—primarily rivaroxaban and apixaban, with fewer reports for dabigatran and edoxaban—in treating acute HIT is growing.^{1,71} A retrospective cohort study that included 15 patients (11 after cardiovascular surgery) treated with DOACs for confirmed HIT found no recurrent thrombosis or major bleeding at 30 days; 1 patient had persistent thrombocytopenia.⁷²

Dosing strategies for treating HIT should follow established VTE treatment regimens. Dabigatran and edoxaban require at least 5 days of initial parenteral anticoagulation before oral therapy is initiated. In contrast, rivaroxaban and apixaban are started without a parenteral lead-in and use a higher initial dose (rivaroxaban for 21 days, apixaban for 7 days) before transitioning to maintenance dosing to reduce early recurrent thrombosis. In patients with isolated HIT without thrombosis, limited data support continuing the higher dose only until platelet recovery, then switching to maintenance doses.^{1,71}

Statement 3.3: Vitamin K antagonists should not be used to treat HIT until after platelet count recovery (to $>150 \times 10^9/L$). (CoR III, LoE B-nonrandomized). Vitamin K antagonists (VKAs) inhibit hepatic synthesis of vitamin K-dependent clotting factors (II, VII, IX, and X) as well as natural anticoagulants (proteins C and S). Initiating warfarin can result in an initial prothrombotic state due to rapid protein C depletion (half-life ~6 hours) and delayed thrombin inhibition (half-life ~72 hours).⁷³

This prothrombotic imbalance has serious implications in acute HIT. A retrospective case-control study found an association between warfarin administration and venous limb gangrene in patients with HIT. All 8 patients presented with HIT and VTE but then developed venous limb gangrene after heparin therapy was discontinued and treatment with warfarin was initiated or continued.⁷³ The highest risk of thromboembolism in patients with isolated HIT occurs before platelet recovery.⁴⁴ Initiating VKA before platelet count recovery is not recommended due to the risk of life- or limb-threatening thrombosis in patients with acute HIT.¹

If a VKA is selected as the long-term anticoagulant after platelet recovery (when HIT has become subacute), bridging (overlap) with a nonheparin parenteral anticoagulant is required, as patients with HIT remain at risk for

thromboembolism. Bridging should be continued until the international normalized ratio is therapeutic for at least 2 days, with a typical overall bridging duration of at least 5 days.⁶² Bridging from argatroban (and to a lesser extent bivalirudin) increases the international normalized ratio and makes transitioning more complicated. Specialized protocols can be followed to standardize this transition.⁷⁴ If patients are receiving warfarin at the time of HIT diagnosis, warfarin should be immediately reversed with intravenous vitamin K, and nonheparin anticoagulation should be initiated concomitantly.¹

Statement 3.4: Intravenous immunoglobulin or therapeutic plasma exchange may be considered for refractory or progressive acute HIT in addition to therapeutic nonheparin anticoagulation. (CoR IIB, LoE C-limited data). In most patients with acute HIT, platelet counts recover after heparin cessation, and the risk of thrombosis is mitigated with therapeutic nonheparin anticoagulation. Patients who have persistent thrombocytopenia beyond 1 week, or who develop new or progressive thrombosis despite therapeutic anticoagulation, may have heparin-independent antibody-mediated platelet activation.^{75,76} Before initiating adjunctive therapy, clinicians should first assess the adequacy and effectiveness of nonheparin anticoagulation and transition to an alternative agent if needed.⁷⁵

Intravenous immunoglobulin (IVIg) is the most commonly used adjunctive therapy for refractory or progressive acute HIT because it inhibits Fc γ RIIa-mediated platelet activation by binding to platelet Fc receptors.^{20,75} A review of 21 cases found that high-dose IVIg was mainly used for delayed-onset or persistent autoimmune HIT.⁷⁷ Approximately 80% of patients had a platelet count increase of $>50 \times 10^9/L$ within 1 week after IVIg initiation. One patient experienced a thrombotic event the day after IVIg was started, potentially attributable to ineffective anticoagulation. The most common dosing strategy was a total dose of 2 mg/kg (eg, 1 mg/kg/day for 2 days).

In patients with refractory or progressive acute HIT who have an inadequate response to IVIg, therapeutic plasma exchange (TPE) can be considered.^{75,76} A systematic review of studies of refractory HIT included 9 cases treated with TPE alone and 1 case with IVIg and TPE. On average, patients underwent 4 TPE procedures with 1 to 1.5 plasma volumes exchanged, and the majority received fresh-frozen plasma, either alone or combined with albumin, as replacement fluid. This review also included 49 patients who received IVIg and/or TPE for initial or refractory HIT; all of these patients' platelet counts improved, and platelet recovery ($>150 \times 10^9/L$) occurred at similar rates at an average of 6 days after treatment initiation with IVIg (55%) and TPE (60%).⁷⁸ Accordingly, IVIg and TPE appear to achieve comparable rates of platelet recovery to $\geq 150 \times 10^9/L$; however, the supporting evidence is derived from heterogeneous, case-level reports and does not allow

definitive conclusions about their comparative efficacy. Clinically, IVIg has most often been employed in refractory HIT, whereas TPE has been preferentially applied to enable safe intraoperative heparin administration during CPB. When TPE is used, fresh-frozen plasma may be preferable to albumin for several reasons.

Repletion of clotting factors during therapeutic anticoagulation may mitigate excessive anticoagulant effect and reduce bleeding risk in the postexchange period. Fresh-frozen plasma also restores natural anticoagulants such as protein C and protein S and provides IgG, which can inhibit FcγRIIa-mediated platelet activation, whereas albumin contains neither clotting factors nor immunoglobulins.⁷⁶

Statement 3.5: Temporary cessation of nonheparin therapeutic anticoagulation is reasonable with active bleeding and HIT. (CoR IIa, LoE C-expert opinion). Contemporary cohort data and expert consensus support temporary cessation of nonheparin anticoagulation during active bleeding in patients with HIT. Although HIT is a highly prothrombotic state, real-world evidence shows that short, clinically supervised interruptions in anticoagulation can be safely undertaken when bleeding risk exceeds thrombotic risk. In a multicenter cohort of 310 patients with acute HIT, Kuter and colleagues⁷⁹ found that bleeding complications were a common indication for adjusting or temporarily discontinuing nonheparin anticoagulants. Such interruptions were not associated with an excess of new thrombosis when therapy was resumed promptly once hemostasis improved. Additional contemporary analyses of empiric HIT management confirm that clinicians frequently reduce or briefly hold bivalirudin or argatroban in patients with major bleeding, hepatic dysfunction, or hemodynamic instability; with careful monitoring and timely reinstatement of anticoagulation, rates of thrombotic progression are low.^{66,80} Systematic reviews and clinical guidelines explicitly acknowledge the necessity of individualized dosing and temporary cessation during life-threatening bleeding, emphasizing that the priority in such situations is stabilizing hemorrhage and then reinitiating a nonheparin agent once bleeding risk is controlled.^{1,81} In patients with acute HIT and clinically significant bleeding, which contraindicate therapeutic anticoagulation, alternative treatments such as IVIg and TPE can be considered.⁷⁸

Given the competing risks of thrombosis and hemorrhage inherent to HIT, temporary cessation of nonheparin therapeutic anticoagulation is reasonable in carefully selected, actively bleeding patients, accompanied by close reassessment and early reinitiation once bleeding stabilizes. Multidisciplinary decision making is advised regarding anticoagulation during the perioperative period.

Statement 3.6: Routine platelet transfusion is not recommended in nonbleeding patients with HIT. (CoR III, LoE C-limited data). Routine platelet transfusion should be avoided in nonbleeding patients with HIT. Mechanistically, transfused platelets may provide additional substrate for

anti-PF4/heparin antibodies, potentially amplifying FcγIIa-mediated platelet activation and increasing thrombotic risk.

Observational data support this concern. In a large, multicenter cohort of 310 patients with HIT, Kuter and colleagues⁷⁹ found that platelet transfusion was independently associated with arterial thrombosis and mortality. These findings align with the 2018 ASH HIT guidelines, which advise against prophylactic platelet transfusion in the absence of bleeding, citing its lack of proven benefit and its potential to exacerbate antibody-mediated platelet activation.^{1,80,82} Other reports have not demonstrated a clear association between platelet transfusion and thrombosis in patients with HIT,⁸³ highlighting the limitations of available data. Importantly, no study has shown that prophylactic platelet transfusion reduces bleeding risk or improves outcomes in this population. Thus, although in other clinical conditions empiric platelet transfusion is recommended when counts fall below 10 000 or 20 000, no such recommendation has been made or validated in HIT.⁸⁴

Systematic reviews and empiric management analyses provide further evidence that platelet transfusion is rarely indicated in HIT patients without active bleeding.^{81,85} The observed associations between platelet transfusion and adverse outcomes may reflect confounding by disease severity because more profound thrombocytopenia probably signifies more severe HIT and independently confers higher thrombotic risk while also increasing the likelihood of transfusion. Accordingly, although definitive causality cannot be established, the absence of demonstrated benefit and the potential for harm support a recommendation against routine platelet transfusion in nonbleeding patients with HIT.

Statement 3.7: It is reasonable to transfuse platelets in patients with HIT and active bleeding. (CoR IIa, LoE C-expert opinion). Although routine platelet transfusion is discouraged in stable, nonbleeding patients with HIT (Statement 3.6), platelet transfusion may be appropriate for patients with clinically significant bleeding. Observational studies of real-world HIT management indicate that selective platelet transfusion for major hemorrhage, procedural hemostasis, or severe thrombocytopenia with bleeding has not been associated with a clear increase in thrombotic complications when transfusion is accompanied by close monitoring and timely resumption of nonheparin anticoagulation after hemostasis is achieved.^{1,86}

Contemporary expert reviews, including perioperative, cardiac, and vascular surgery perspectives, consistently support targeted platelet transfusion for patients with HIT and active bleeding when urgent hemostatic support is required.¹ In this scenario, immediate control of bleeding appropriately takes precedence, with the understanding that therapeutic anticoagulation will typically need to be reinitiated once bleeding is controlled. Accordingly, although platelet transfusion should be avoided in stable, nonbleeding HIT because of

potential thrombotic risk, it is reasonable in patients with HIT and active bleeding, for whom the anticipated benefit of achieving hemostasis outweighs theoretical thrombotic concerns.⁸²

Statement 3.8: In patients with HIT, noninvasive 4-limb ultrasonography should be considered to assess for proximal deep venous thrombosis and to guide the duration of anticoagulation. (CoR IIa, LoE B-nonrandomized). Thrombosis is the most frequent complication of HIT; lower-extremity deep vein thrombosis (DVT) is found in up to 50% of affected patients.⁸⁷ Identifying silent DVT in patients with HIT is clinically meaningful because the presence, extent, and location of thrombosis influences both the duration and intensity of anticoagulant use.

Upper-extremity thrombosis is also relevant in postoperative and critically ill patients. In a study of postoperative orthopedic and intensive care unit patients with HIT, upper-extremity DVT occurred in 9.7% of patients with a central venous catheter versus none of the patients without such a catheter ($P < .001$). All events arose at the catheter insertion site. Because central venous access is used in nearly all cardiac surgery patients during their perioperative course, targeted evaluation of central venous catheter sites is particularly important.⁸⁸

For these reasons, a 4-limb venous duplex ultrasonogram is reasonable in patients with confirmed HIT to detect occult thrombosis, establish a baseline for follow-up, and inform anticoagulation management. This approach supports individualized clinical decision making while avoiding routine screening in patients with only suspected HIT.

Statement 3.9: In patients with HIT without associated thrombosis, anticoagulation is indicated until platelet recovery to a stable plateau, for up to 3 months. (CoR I, LoE B-nonrandomized). Patients with isolated HIT (ie, HIT without clinically apparent thrombosis) remain at meaningful risk for thromboembolism even after heparin cessation. In a cohort study of patients with HIT and no DVT identified by screening ultrasonography, the risk of thromboembolic events was highest in the first 30 days after heparin was stopped.⁴⁴ Approximately 80% of thromboembolisms occurred in the first week, as platelets were recovering.

Evidence to guide the optimal duration of anticoagulation in isolated HIT is limited, and no randomized trials exist. Contemporary national guidelines recommend continuing nonheparin anticoagulation at least until platelet recovery, with a total duration not exceeding 3 months in the absence of thrombosis.^{1,42,89} Within that range, duration should be individualized based on each patient's bleeding risk, thrombotic profile, and clinical trajectory. For many patients, discontinuation shortly after platelet stabilization is appropriate; for others, extending therapy beyond platelet recovery (up to 3 months) may be reasonable (Figure 5).

Statement 3.10: For patients with HIT and thrombosis, 3 to 6 months of anticoagulation should be considered. (CoR IIa, LoE B-nonrandomized). No studies have specifically attempted to determine the optimal duration of anticoagulation for arterial or VTE in patients with HIT. HIT-associated thrombosis is generally considered a reversible, provoked thrombotic event, and recommended treatment durations align with standard management for thrombosis provoked by other transient risk factors. Current national guidelines support 3 months of therapeutic anticoagulation for HIT-associated thrombosis, with consideration of extending therapy to 6 months in selected patients depending on clot burden, ongoing risk factors, or comorbidities that may predispose them to recurrence.^{1,89}

Section 4: Management of Patients With HIT Before Cardiac Surgery

Patients with past or present HIT who need cardiac surgery pose a unique perioperative challenge. Diagnostic and management approaches are outlined, as are best practices (Table 5).

Statement 4.1: In patients with a history of HIT undergoing nonemergency cardiac surgery, it is recommended to perform an immunoassay. (CoR I, LoE C-expert opinion). In patients with a history of HIT who undergo nonemergency cardiac surgery, immunoassay testing is essential to determine whether anti-PF4/heparin antibodies are still present. This information directly influences perioperative planning, including any further functional testing, timing of surgery, and the selection of intraoperative anticoagulation (eg, UFH vs nonheparin alternatives), thereby optimizing patient safety during cardiac surgery.⁷

This recommendation reflects the elevated thrombotic risk associated with inadvertent heparin re-exposure in patients with prior HIT. Determining whether anti-PF4/heparin antibodies persist is essential because immunoassay positivity may continue for months after an episode of HIT. Re-exposure to heparin during the acute or subacute A phase, when platelet-activating antibodies are still present, can trigger rapid platelet activation, severe thrombocytopenia, and life-threatening thrombosis.^{2,90} Immunoassay testing helps identify patients in whom intraoperative UFH remains unsafe.

Statement 4.2: In patients with confirmed HIT, it is recommended that nonemergency cardiac surgery be delayed until the functional assay is negative. (CoR I, LoE B-nonrandomized). In patients with confirmed HIT, it is recommended to postpone nonemergency cardiac surgery until the functional assay becomes negative because persistent platelet-activating anti-PF4/heparin antibodies are the primary drivers of recurrent thrombocytopenia and perioperative thrombosis when heparin is reintroduced in the presence of a strong prothrombotic stimulus such as

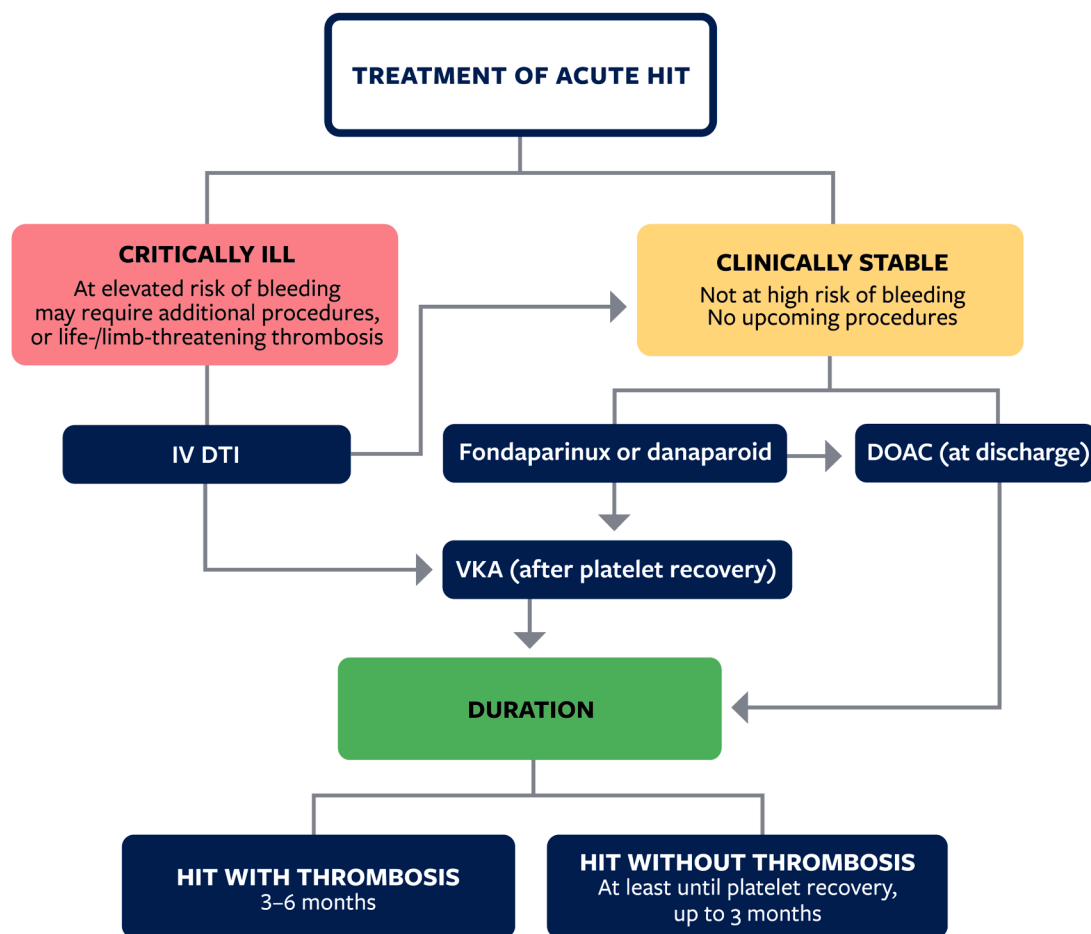


FIGURE 5. Therapeutic anticoagulation options for acute heparin-induced thrombocytopenia, stratified by clinical stability and bleeding risk, with guidance on agent selection and duration of therapy. IV, Intravenous; DTI, direct thrombin inhibitor; VKA, vitamin K antagonist; DOAC, direct oral anticoagulant.

CPB. Serial cohort studies have shown that the risk of HIT-related arterial and venous thrombosis is highest during the acute and subacute A phases, when functional assays remain positive.⁹¹⁻⁹⁴

Delaying surgery until functional assays are negative reduces the risk of perioperative thrombotic complications and allows safe re-exposure to heparin during CPB. Because HIT antibodies can persist for 60 to 90 days, deferring elective procedures until platelet-activating antibodies are no longer detectable can mitigate antibody-mediated thrombotic risk.⁷

Statement 4.3: In patients with HIT and a positive functional assay who require urgent/emergency cardiac surgery, it may be reasonable to use either intraoperative bivalirudin alone or heparin with additional measures; for example, preoperative IVIg and/or TPE. (CoR IIb, LoE C-limited data). In patients with acute or subacute HIT and a positive functional assay and for whom cardiac surgery cannot be delayed, measures should be taken to mitigate the marked prothrombotic risk associated with

intraoperative heparin exposure. Positive functional assays indicate the continued presence of platelet-activating antibodies, and re-exposing patients to heparin in this situation can precipitate rapid platelet activation and life-threatening venous or arterial thrombosis. To reduce the likelihood of thrombotic complications in patients requiring urgent/emergency cardiac surgery, 2 broad approaches have been described:

- Using a nonheparin anticoagulant during CPB, most commonly the direct thrombin inhibitor bivalirudin, for which the most data have been published regarding its use in cardiac surgery requiring CPB.⁹⁵⁻⁹⁷ The major challenges with DTIs are proper monitoring, venous reservoir management,⁹⁸ and lack of a target-specific reversal agent after CPB, as well as the risk of stagnant blood clotting (eg, within clamped conduits as a result of time-dependent degradation of bivalirudin).
- Heparin-based strategies combined with antibody-modifying interventions to reduce PF4-heparin antibody

levels or activity before heparin exposure. In this approach, UFH is restricted to the CPB period, with non-heparin anticoagulation used outside CPB as needed. Adjunctive interventions include TPE to remove circulating antibodies and preoperative intravenous immunoglobulin, which can neutralize platelet-activating effects of HIT antibodies through Fc receptor blockade and attenuate downstream activation.^{99,100}

A recent case report described the use of intraoperative heparin for urgent cardiac surgery after 2 doses of IVIg, with platelet activation studies of pre- and post-IVIg blood samples confirming that high-dose IVIg inhibited platelet activation, particularly at the high heparin concentrations used during cardiac surgery.¹⁰¹ This finding is mechanistically relevant because HIT antibody-induced platelet activation is maximal at 0.1 to 0.5 U/mL heparin, whereas cardiac surgery is usually performed at 2 to 5 U/mL—a concentration range at which IVIg-mediated inhibition appears most effective. These observations support the theoretical basis for high-dose IVIg as an adjunct to inhibit platelet-activating HIT antibodies when heparin anticoagulation is required for cardiac surgery in a patient with acute HIT. Intraoperative platelet inhibition with epoprostenol or tirofiban coadministered with UFH has been reported in small case series with variable results; evidence is of very low certainty, and a recent retrospective cohort raised concern about thrombotic risk with epoprostenol in patients with confirmed platelet-activating antibodies,¹⁰² whereas tirofiban may pose bleeding risk in patients with renal impairment.⁸¹ These strategies may warrant consideration in highly selected cases when other options are not feasible or based on institutional experience with these agents.

Statement 4.4: Intraoperative heparin is recommended in patients with a history of HIT and a negative immunoassay and functional assay; intraoperative heparin is also appropriate if the immunoassay is positive but the functional assay is negative. (CoR I, LoE C-limited data). Once platelet-activating antibodies are no longer detectable, the risk of HIT recurrence with short-term, intraoperative UFH exposure is very low.¹⁰³ Immunoassays for HIT (eg, PF4/heparin ELISAs) are highly sensitive and often detect nonpathogenic antibodies, whereas functional assays such as the SRA and the heparin-induced platelet activation test provide greater specificity for platelet-activating antibodies, making them more clinically relevant.¹⁰⁴

In a series of patients with previous HIT and negative immunoassays, minimal to no recurrence of HIT or new thrombotic events were reported in those patients for whom heparin was restricted to the intraoperative period ($n = 17$).¹⁰³ Patients with a positive immunoassay but a negative functional test typically have nonactivating antibodies and, similarly, have a minimal risk of HIT-related thrombosis or platelet fall. The benefits of heparin use

(predictable performance on CPB, established dosing/reversal, and extensive clinician experience) are substantial and outweigh the risks associated with less familiar anticoagulation drugs and strategies.

Section 5: HIT and Extracorporeal and Temporary Mechanical Circulatory Support After Cardiac Surgery

Statement 5.1: The 4Ts should not be used to guide HIT testing in patients receiving postcardiotomy ECMO. (CoR III-no benefit, LoE B-nonrandomized). No clinical scoring system has demonstrated adequate performance in estimating HIT probability or guiding laboratory testing in patients supported with postcardiotomy ECMO.¹⁰⁵ The 4Ts score has been studied most extensively; its PPV is only 21% to 25% in patients supported by ECMO.¹⁰⁶⁻¹⁰⁸ This low PPV is probably due, in part, to inevitable thrombocytopenia from exposure to ECMO. Observational studies show that, in patients supported by ECMO, 4Ts scores tend to be similar among both those with confirmed HIT and those with HIT excluded.^{109,110} In contrast, several other observational studies have identified ECMO-supported patients who had high OD values, positive HIT-IgG, or positive SRA despite having a low-probability 4Ts score.^{106-108,111} Other scoring systems such as the HIT Expert Probability score and the Lillo-Le Louët score have less supporting evidence and even poorer predictive value than that of the 4Ts score and also should not be used to guide HIT testing in patients receiving postcardiotomy ECMO.¹⁰⁵

Statement 5.2: HIT testing should be considered in patients receiving ECMO for postcardiotomy shock who experience persistent thrombocytopenia 5 to 14 days after their first exposure to UFH. (CoR IIa, LoE B-nonrandomized). Thrombocytopenia is nearly universal in patients with postcardiotomy shock requiring ECMO support.^{106,112} Therefore, platelet trends alone are generally unreliable; however, a failure of platelet recovery after day 5 or a continued decline is more characteristic of HIT than of ECMO-related consumption. Further, screening scores have poor predictive value during ECMO, reinforcing the need for immunoassay and confirmatory functional assays (eg, SRA), particularly in the 5- to 14-day window after first exposure to UFH.^{106,108}

Previous studies have reported HIT rates in patients on ECMO ranging from 0.36% to 8.3%,^{106,110,113} with more recent reports indicating a prevalence of 2% to 4%.^{105,108,114,115} Thromboembolic complications, particularly arterial ones, have been reported in more than 50% of patients with postcardiotomy shock requiring ECMO.^{106,110,116} Mortality remains high at 33% to 60%, although several series indicate similar mortality rates between patients receiving ECMO with and without HIT.^{109,114-117} Early recognition of HIT, prompt cessation

of heparin, and transition to a DTI improve platelet recovery, decrease device-related complications, and may reduce mortality.^{110,113,116,117}

Statement 5.3: Administering a DTI is a reasonable strategy for anticoagulation during postcardiotomy ECMO because it reduces patients' risk of developing HIT. (CoR IIa, LoE B-nonrandomized). Although heparin is the most-used agent for maintenance anticoagulation during ECMO,¹¹⁸ DTIs such as bivalirudin and argatroban are increasingly used as alternatives. Evidence from observational studies suggests that compared with heparin, these agents may be associated with fewer circuit-related thrombotic events and similar or lower bleeding risk in patients supported by ECMO.^{119,120} These effects may be due to DTIs' engagement with not only circulating thrombin, as with heparin, but also clot-bound thrombin,^{121,122} which is relevant given that ECMO circuitry components have a substantial propensity for fibrin deposition.¹²³ Further, in patients supported by ECMO, bivalirudin has been shown to achieve anticoagulation targets faster and maintain them more consistently than heparin.¹²⁴ Potential reasons include bivalirudin not relying on a cofactor,¹²⁵ not interacting with plasma proteins,¹²⁶ and not having batch-to-batch variability in potency due to the manufacturing process.¹²⁷ DTIs should be used cautiously or avoided when the activated partial thromboplastin time might be inaccurate (eg, due to a lupus anticoagulant) unless alternative monitoring assays are available, such as the dilute thrombin time or the ecarin chromogenic assay.¹²⁸

Statement 5.4: It is recommended that patients on ECMO requiring anticoagulation with suspected HIT Are switched to a direct thrombin inhibitor and all heparin products should be discontinued. (CoR I, LoE C-expert opinion). When HIT is suspected, termination of all heparin anticoagulation is recommended, and an alternative nonheparin anticoagulant should be initiated to mitigate thrombotic risk.^{115,117,129} DTIs offer distinct advantages over heparin by providing more predictable anticoagulant effects due to their relative independence from dynamic plasma protein concentration and cell counts and their ability to bind both clot-bound and circulating thrombin.¹²⁹ The DTIs most frequently used during ECMO support are argatroban and bivalirudin. Bivalirudin has emerged as the preferred agent for anticoagulation in ECMO-supported patients with HIT because its short half-life and predictable pharmacokinetics are well suited to the frequent interruptions and resumptions of anticoagulation necessitated by bleeding events and procedural interventions.¹²⁹⁻¹³¹ The effect of heparin coating within ECMO circuits on HIT development and severity is worth considering. However, at present, there is no evidence to support the transition from a heparin-coated ECMO circuit to a circuit that is not heparin coated upon suspicion or diagnosis of HIT (Table 6).^{115,117,131}

TABLE 6. Cardiopulmonary bypass (CPB) and extracorporeal membrane oxygenation (ECMO) circuit management considerations for patients with heparin-induced thrombocytopenia (HIT)

Best practices
Use CPB components (eg, circuit tubing, cannulas, oxygenators) and intravascular catheters with nonheparin-bonded surface coatings where available.
When DTIs are used for anticoagulation during CPB, use ultrafiltration to reduce DTI concentration after weaning from CPB.
Transfer residual CPB circuit blood to a cell-washing device to remove residual anticoagulant before reinfusion.
Do not use heparin flush for intraoperative cell salvage.
Use citrate-based anticoagulant flush solutions for intraoperative cell salvage as an alternative to heparin.
The necessity to replace a heparin-bonded ECMO circuit in a patient with suspected or confirmed HIT has not been established.

DTI, Direct thrombin inhibitor.

Statement 5.5: In postcardiotomy patients with suspected HIT who require a microaxial flow pump, sodium bicarbonate-based purge solutions should be preferred over heparin-based solutions. (CoR IIa, LoE B-nonrandomized). Microaxial flow pumps require a counter-current purge solution that provides component lubrication and creates a positive pressure barrier to prevent thrombosis and failure due to protein deposition and blood leakage into the pump motor housing.¹³²⁻¹³⁴ Historically, heparin-based solutions were used for this purpose, but ionic charge, rather than the anticoagulant effect, has been identified as the important characteristic of purge solutions.^{133,135} Sodium bicarbonate provides a similar ionic environment, stabilizes blood proteins, and reduces protein deposition on pump components.¹³²⁻¹³⁴ Furthermore, sodium bicarbonate may disrupt fibrinogen-to-fibrin conversion, further limiting biomaterial deposition within the pump.¹³² Observational studies have demonstrated comparable device viability with dextrose-based sodium bicarbonate purge solutions and heparin-based solutions.^{132,134,136-138}

Summary of Take-Home Points

- 1) New thrombosis, consider HIT
- 2) Early post-CPB platelet drop is normal — usually not HIT
- 3) Second platelet fall begins on or after day 5 — classic HIT pattern
- 4) 4Ts Score unreliable in the first 4 days after CPB
- 5) 4Ts Score unreliable during ECMO — poor predictive value
- 6) Positive immunoassay ≠ HIT — needs functional assay to confirm HIT
- 7) Intermediate 4Ts/Weakly positive immunoassay — may not necessitate nonheparin anticoagulation
- 8) Avoid routine platelet transfusions — may increase thrombosis risk
- 9) Treatment duration varies — depends on HIT ± thrombosis
- 10) If preop HIT* & urgent surgery — use bivalirudin or TPE/IVIG/UHF strategy

FIGURE 6. Ten key take-home principles for heparin-induced thrombocytopenia (HIT) in cardiac surgery. CPB, Cardiopulmonary bypass; 4Ts, Thrombocytopenia, Timing, Thrombosis, oTher cause; ECMO, extracorporeal membrane oxygenation; TPE, therapeutic plasma exchange; IVIg, intravenous immunoglobulin; UHF, unfractionated heparin.

CONCLUSIONS

Heparin-induced thrombocytopenia in cardiac surgery presents distinct diagnostic and therapeutic challenges driven by universal heparin exposure, postoperative platelet kinetics, and the complexity of perioperative care. A summary of major take-home points is provided in [Figure 6](#). This interdisciplinary, multispecialty AATS consensus provides cardiac surgery-specific, evidence-informed recommendations to improve diagnostic accuracy, guide appropriate immunoassay and functional testing, optimize selection of nonheparin anticoagulants, and standardize perioperative management for patients with acute or prior HIT, including those requiring CPB or ECMO support. By integrating clinical context with the best available evidence, these recommendations aim to reduce misdiagnosis, prevent avoidable thrombosis and bleeding, and support safer re-exposure or alternative anticoagulation strategies across the continuum of cardiac surgical care.

Webcast

You can watch a Webcast of this AATS meeting presentation by going to: Xxx.



Conflict of Interest Statement

See [Appendix E1](#). Dr Arora consults or advises Medtronic, Edwards Lifesciences, Renibus Therapeutics Inc, Serb Pharmaceuticals, HLS Therapeutics Inc, Bioparto, and Alexion. Drs Chatterjee and Grant serve on the executive board of the ERAS–Cardiac Society (non-remunerated). Dr Cuker consults for Pfizer and Sanofi and receives authorship royalties from UpToDate (Wolters Kluwer). Dr Engelman serves on a device safety monitoring board for Edwards Lifesciences; executive steering committees for Alexion, Genentech, and Bayer; and medical advisory boards for Medela, Arthrex, Atricure, Johnson & Johnson, Pharmacosmos, and Chugai, and provided expert review in medical malpractice cases. Dr Mims owns stock in Amgen and Biogen; received an honorarium from OncLive; received travel support from the Binaytara Foundation; serves on committees for the American Society of Hematology, the American College of Physicians, and a National Institutes of Health study section; and provides compensated leadership on the external advisory boards of the cancer centers at Ohio State University and the University of Vermont. Dr Moon consults for Edwards

Lifesciences. Dr Sultan consults for and participates in clinical research for Abbott, Atricure, Artivion, Edwards Lifesciences, Medtronic, Terumo Aortic, and W.L. Gore. Dr Warkentin consults for Arbor Biotechnologies; provides Device Safety Monitoring Board consulting for Paradigm Biopharmaceuticals; provides study executive committee consulting and holds stock options with Veralox Therapeutics; consults for and receives research support from Instrumentation Laboratory/Werfen; receives authorship royalties from Informa (Taylor & Francis) and UpToDate (Wolters Kluwer); and provided expert witness testimony for legal firms. Dr Wieruszewski receives consulting fees from Wolters Kluwer/UpToDate and previously received consulting fees from Viatrix Inc. He receives research funding from the ZOLL Foundation. All other authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: heparin-induced thrombocytopenia, cardiac surgery, cardiopulmonary bypass, anticoagulation, direct thrombin inhibitors, immunoassay, functional testing

APPENDIX E1

Writing group member and primary affiliation	Grants	Royalties	Consulting	Payment or honoraria for speaking	Payment for expert testimony	Support for meetings	Patents	Participation advisory board	Leadership role	Stock	Receipt other services	Other financial or non-financial interests	All entities with whom the author may have the indicated relationships, and if payments were made to the author or institution
Rakesh C. Arora, Department of Surgery, Northwestern University, Feinberg School of Medicine, Chicago, Ill			x	x				x					Medtronic, Edward's LifeSciences, Renibus Therapeutics Inc, Serb Pharmaceuticals, HLS Therapeutics Inc, Bioportro, Alexion
Leora Balsam, UMass Memorial Medical Center, Worcester, Mass													
Busra Cangut, Department of Cardiovascular Surgery, Icahn School of Medicine at Mount Sinai, New York, NY													
Subhasis Chatterjee, Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, Tex									x				ERAS-Cardiac Executive Board, nonremunerated
Jessica Crow, Department of Pharmacy, The Johns Hopkins Hospital, Baltimore, Md													
Adam Cuker, Department of Medicine and Department of Pathology & Laboratory Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pa		x	x										Consultant for Pfizer and Sanofi; authorship royalties from UpToDate
Daniel T. Engelman, Department of Surgery, Baystate Medical Center, University of Massachusetts Chan Medical School-Baystate, Springfield, Mass			x		x			x					Paid to me: Device Safety Monitoring Board: Edwards Lifesciences Transcatheter Valves Research Trial Executive Steering Committees: Alexion, Genentech, Bayer Medical Advisory Boards: Medela, Arthrex, Atricure, J & J, Pharmacosmos, Chugai Expert review for medical malpractice case.
Natalia I. Girardi, Department of Anesthesiology, Weill Cornell Medicine, New York, NY													
								x					

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Writing group member and primary affiliation	Grants	Royalties	Consulting	Payment or honoraria for speaking	Payment for expert testimony	Support for meetings	Patents	Participation advisory board	Leadership role	Stock	Receipt other services	Other financial or non-financial interests	All entities with whom the author may have the indicated relationships, and if payments were made to the author or institution
Michael C. Grant, Department of Anesthesiology and Critical Care Medicine, Johns Hopkins University School of Medicine, Baltimore, Md													Executive Board - ERAS Cardiac Society
Jillian F. Holler, Department of Congenital Perfusion, Atrium Health Levine Children's Hospital, Charlotte, NC													
Mark Martin, Redline Perfusion & Consulting, LLC, Gainesville, Fla													
Martha Mims, Department of Medicine, Baylor College of Medicine, Houston, Tex	x			x		x			x	x			Grants: Victory Inc, National Institutes of Health, Cancer Prevention and Research Institute of Texas, ASCO Stock ownership: Amgen, Biogen IDEC Talks paid: OncLive: AML talk, Binaytara Foundation (travel/hotel only), PriMed Conference Talks unpaid: American College of Physicians, Binaytara Foundation, Texas Heart Advances in Critical Care Committee work: American Society of Hematology, American College of Physicians, National Institutes of Health study section Leadership unpaid: Board of Pensions of the Presbyterian Church, Board of the Weiss School of Natural Sciences, Rice University Leadership paid: External Advisory Board of Cancer Centers at Ohio State University and University of Vermont

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Writing group member and primary affiliation	Grants	Royalties	Consulting	Payment or honoraria for speaking	Payment for expert testimony	Support for meetings	Patents	Participation advisory board	Leadership role	Stock	Receipt other services	Other financial or non-financial interests	All entities with whom the author may have the indicated relationships, and if payments were made to the author or institution
Marc R. Moon, Texas Heart Institute/Baylor College of Medicine, Houston, Tex			x										Edwards Lifesciences
Arabesque Parker, Department of Critical Care, University of Alberta, Edmonton, Alberta, Canada													
Ibrahim Sultan, Division of Cardiac Surgery, Heart and Vascular Institute, Department of Cardiothoracic Surgery, University of Pittsburgh Medical Center, Pittsburgh, Pa	x		x										Research grants and consults for Abbott, Atricure, Artivion, Edwards Lifesciences, Medtronic, Terumo Aortic and WL Gore
Theodore E. Warkentin, Department of Pathology and Molecular Medicine, McMaster University, Hamilton, Ontario, Canada	x	x	x	x	x			x		x			Arbor Biotechnologies (consulting, self) Paradigm Biopharmaceuticals (DSMB consulting, self) Veralox Therapeutics (study executive committee consulting, self; stock options) Instrumentation Laboratory/Werfen (research support-to my institution); Instrumentation Laboratory/Werfen (consulting, self) Informa (Taylor & Francis) (royalties, self) UpToDate (Wolters Kluwer) (royalties, self) Expert witness testimony (consulting, testimony, legal firms, self)
Patrick M. Wieruszewski, Department of Pharmacy, Department of Anesthesiology, Mayo Clinic, Rochester, Minn	x		x										Consulting fees from Wolters Kluwer/UpToDate, previous consulting fees from Viatrix Inc. Research funding from ZOLL Foundation