Perioperative Venous Thromboembolism Prophylaxis

Matthew A. Bartlett, MB, BCh, BAO; Karen F. Mauck, MD, MS; Christopher R. Stephenson, MD; Ravindra Ganesh, MBBS, MD; and Paul R. Daniels, MD

Abstract

Venous thromboembolism (VTE) is a preventable cause of postoperative morbidity and mortality; however, audits suggest that the use of thromboprophylaxis is underused. In this review, we describe our approach to prevention of postoperative VTE and provide guidance on how to formulate an optimal VTE prophylaxis plan. We recommend that all patients undergo thrombosis- and bleeding-risk assessment as part of their preoperative evaluation. The risk of thrombosis can be estimated based on patient- and procedure-specific factors, using validated risk-assessment models such as the Caprini score. There are no validated models to predict perioperative bleeding; however, several risk factors have been proposed. Patients should ambulate early and frequently after surgery. We recommend no additional prophylaxis in patients at very low risk of VTE (Caprini score 0). Patients at low risk of VTE (Caprini 1 to 2) are recommended to receive either mechanical or pharmacological prophylaxis. Patients at moderate (Caprini 3 to 4) to high risk of VTE (Caprini $\geq$5) are recommended pharmacological prophylaxis either alone or combined with mechanical prophylaxis. Patients at high risk of bleeding should receive mechanical prophylaxis until their risk of bleeding is reduced and pharmacological prophylaxis can be reconsidered. Populations for which the Caprini score has not been validated (such as orthopedic surgery) are recommended prophylaxis based on individual and procedure-specific risk factors. Prophylaxis is typically continued until the patient is ambulatory or until hospital dismissal; however, longer durations can be considered in certain circumstances (high-risk patients undergoing malignant abdominopelvic operations, bariatric operations, and certain orthopedic operations).

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Venous thromboembolism (VTE), defined as deep vein thrombosis (DVT) and pulmonary embolism (PE), is a serious and potentially fatal postoperative complication. The annual incidence VTE following operations in the United States following surgery is estimated to 70,000 to 600,000,[1] incurring an additional cost of approximately $12,000 per case.[2] Pulmonary emboli can be fatal and post-thrombotic syndrome, pulmonary hypertension, and heart failure are known consequences of VTE.

Clinical practice guidelines have, through the last 3 decades, systematically reviewed evidence from numerous clinical trials and concluded that appropriate use of VTE prophylaxis in postoperative patients is safe and effective.[3-6] However, the overall incidence of VTE is still high.[7,8] Although this may be in part due to the increased use of objective imaging and improved image resolution,[9] the case fatality of VTE continues to be high and, in some instances, failed to show significant decline.[7,10,11] Multiple audits from around the world have demonstrated that primary VTE prophylaxis is underused.[6] As a result, postoperative VTE prevention has become a major focus of multiple policymaking organizations including Centers for Medicare and Medicaid Services, National Quality Forum, and the Joint Commission on Accreditation of Health Care Organizations, resulting in several legislative measures

From the Division of General Internal Medicine, Department of Medicine, Mayo Clinic, Rochester, MN.

ARTICLE HIGHLIGHTS

- Venous thromboembolism is a serious and potentially fatal complication of surgery. However, preventing VTE with antithrombotic therapy may come at the cost of excess postoperative bleeding risk.
- Knowing a patient's risk of postoperative VTE and bleeding is crucial to determining an ideal postoperative VTE prevention plan. We discuss the use of risk assessment models to estimate the patient's risk of VTE as well as patient- and operation-specific risk factors for postoperative bleeding.
- Several guidelines on postoperative VTE prevention are available; however they are either outdated or do not address certain population groups or surgical specialties. This article updates available guideline recommendations based on recent studies across multiple surgical specialties.

such as making hospital reimbursement contingent on demonstration of satisfactory VTE prophylaxis metrics.[12]

In this review, we describe our approach to postoperative VTE prevention, discussing how to assess a patient's risk for postoperative VTE and bleeding, and how to balance these risks to formulate an optimal VTE prophylaxis plan. Owing to the scope of this paper and the availability of current data, we will limit these recommendations to adult, nonpregnant patients.

OUR APPROACH

Our approach to determining the most appropriate VTE prophylaxis is outlined in Table 1. Overall, this philosophy is consistent with most recommendations in the 9th edition of the American College of Chest Physicians Evidence-Based Clinical Practice Guidelines for Prevention of VTE in orthopedic and nonorthopedic surgery patients (AT9),[13,14] with iterations based on more recent data and specialty society guidelines.

A preoperative clinical assessment is the first step in the perioperative risk assessment. Coagulation studies should only be performed if there is a high clinical suspicion of an inherited or acquired coagulopathy.[15,16] Modifiable risk factors should be addressed before surgery and communicated among medical, anesthesia, and surgery teams so that the risks are well understood. The VTE prophylaxis strategy should be reassessed at various stages including immediately after the operation, at discharge, and upon posthospitalization follow-up to ensure that the risks and benefits of the current prophylaxis strategy are still balanced.

RISK ASSESSMENT

Postoperative VTE can be reduced by the use of early ambulation, mechanical methods, and pharmacoprophylaxis (ie, the use of antiplatelet and antithrombotic agents). These interventions, particularly pharmacoprophylaxis, carry the potential risk of harm (eg, bleeding). Thrombosis and bleeding risk assessments are therefore crucial for developing an appropriate prophylaxis strategy.

Thrombosis Risk Assessment

Several patient- and operation-specific risk factors of perioperative VTE have been identified.[3,13,17-23] However, consideration of individual risk factors and the level of risk that each factor contributes to overall VTE risk can be difficult. It is therefore preferred to follow a standardized, uniform approach to each patient.

Several risk-assessment models (RAMs) have been developed to estimate the risk of postoperative VTE.[24-28] These have identified over a 20-fold variation in risk of postoperative VTE and can explain more than 70% of the variation in risk of postoperative VTE.[24] The advantage of RAMs is that they not only can separate patients at a high risk of VTE who will likely benefit from prophylactic measures but that they also identify patients at very low risk of thrombosis who could avoid unnecessary pharmacoprophylaxis.

Caprini Score. The 2005 Caprini risk score[25] is the most extensively used and validated RAM in predicting postoperative VTE. It was initially developed in a 150-bed

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TABLE 1. Approach to Perioperative VTE Prophylaxis

Before hospital admission	Full history and physical examination - Assess baseline VTE risk, using Caprini score (see Figure), operation-specific risk, and other unaccounted risk factors - Assess patients bleeding risk (see Table 3), procedure-specific bleeding risk, and other unaccounted risk factors Address modifiable risk factors Thrombosis risk - Encourage ambulation and healthy weight - Avoid dehydration - Smoking cessation - Stop/hold medications associated with increased thrombosis risk, ideally 4 half-lives before surgery - Remove central lines, if not clinically indicated (PICC lines, port, etc) Bleeding risk - Control blood pressure - Stop/hold medications associated with increased bleeding risk, including over-the-counter supplements Select appropriate VTE prophylaxis strategy in collaboration with the surgical team and patient Reevaluate VTE and bleeding risk within 24 to 48 hours of admission, and adjust strategy if needed
Hospital admission	Preoperative Initiate prophylaxis strategy (mechanical, pharmacological, or combined) preoperatively, if indicated Intraoperative Address modifiable risk factors - Regional anesthesia vs general anesthesia - Limit operative time - Consider less invasive surgery (laparoscopic vs open) with a smaller impact on postoperative mobility Regular reassessments of VTE and bleeding risk, ensuring a transition to a more/less aggressive prophylaxis as indicated. Postoperative Address modifiable risk factors - Early ambulation or physical therapy if nonambulatory - Avoid dehydration - Avoid severe hypertension - Ensure prophylaxis compliance (eg, IPCD compliance; see Table 5)
Hospital discharge	Consider extended duration prophylaxis, if indicated (See Table 4 and section on extended prophylaxis) Patient/family education o Signs, symptoms of VTE and bleeding o Importance of seeking help if symptoms develop o Conservative measures to prevent VTE (ambulation, avoid dehydration)

IPCD = intermittent pneumatic compression device; PICC = peripherally inserted central line; VTE = venous thromboembolism.

community hospital[29] but has since been validated in multiple surgical specialties, including otolaryngologic surgery,[30] plastic and reconstructive surgery,[31] gynecologic surgery,[32] general surgery,[33] vascular surgery,[33] and urology.[33] A patient's risk of postoperative VTE is estimated by obtaining a score after assessing 37 to 40 patient- and operation-specific risk factors (Figure).[25] Each risk factor is weighted differently, based on perceived variations in risk. The AT9 guidelines stratify patients into 4 risk groups including very low risk (score 0), low risk (1 to 2), moderate risk (score 3 to 4), and high risk (score ≥5). Table 2 summarizes published rates of VTE stratified by the Caprini risk groups.[13,30,31,33-35]

The Caprini RAM has undergone several revisions since its original publication.[36] These revisions include adding new risk factors or making adjustments to the weight of previously included risk factors. For example, in an attempt to account for an increased risk of thrombosis following operations of longer duration, a previously published modified version assigns 5 points to operations lasting more than 6 hours, automatically stratifying patients undergoing these operations as high risk.[37] Although it may be reasonable to incorporate longer duration operations into the VTE risk assessment, we prefer to use the 2005 Caprini RAM,[25] as updated versions of the Caprini RAM have not been as extensively validated, and previous iterations have been shown to underperform compared with the original in some surgery populations.[38]

Rogers Score. The 2007 Rogers score[26] was derived from a large administrative database, which included more than 180,000 patients undergoing general, vascular, and thoracic surgery. It was validated using the same database and externally in a gynecology-oncology population.[39] The Rogers score includes fewer variables than the Caprini score and addresses the type of operation. Although endorsed by the AT9 guideline,[13] the Rogers score has not been as extensively validated as the Caprini score.

Other RAMs. Several other RAMs have been developed by using large administrative datasets.[24,27,28] These RAMs are designed for either patients undergoing any operation or operation-specific groups. A common limiting factor for these RAMs is the lack of external validation.

Although the benefits of RAMs include their standardized approach to each patient, there are potential drawbacks. They require a health-literate patient for accuracy. Although comprehensive, the RAM used may not account for additional risk factors excluded from the model, such as the complexity of the operation or postoperative complications, potentially underestimating a patient's risk. We recommended exercising caution in relying on RAMs to determine the optimal prophylaxis strategy outside the surgical populations for which they have been studied (such as after orthopedic operations), as their ability to predict postoperative VTE in these settings is unknown. However, as many of the components in the Caprini RAM pertain to individual risk factors rather than operation-specific risk factors, some clinicians still prefer to use this RAM as a reminder of common individual VTE risk factors to aid in their VTE risk assessment for these populations

RAMs have been implemented successfully and result in higher compliance with guideline-directed prophylaxis strategies.[40] The performance of existing RAMs has not been compared directly. Thus, the 2005 Caprini and 2007 Rogers scores are currently endorsed in AT9.[13] Our preferred approach is to use the 2005 Caprini risk score, given its ease of use and extensive external validation.

Bleeding-Risk Assessment

Postoperative bleeding is an important complication of pharmacoprophylaxis and increases the risk of reoperation, transfusion-related complications, surgical-site infection, flap failure, and death.

Few studies have evaluated the risk of postoperative bleeding with or without pharmacoprophylaxis. These are limited by their small sample size, lack of standardized

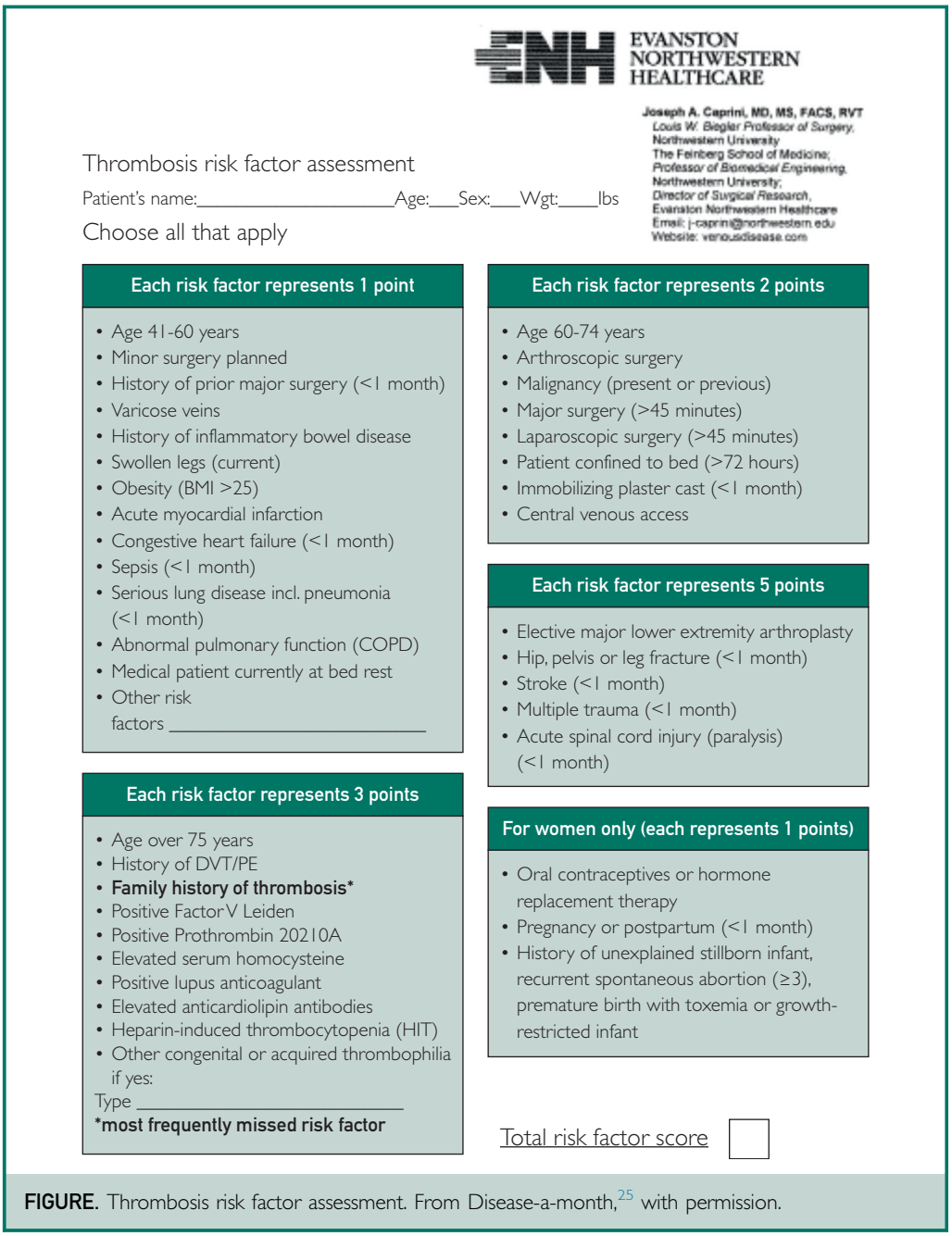

FIGURE. Thrombosis risk factor assessment. From Disease-a-month,[25] with permission.

bleeding definitions, and significant changes in surgical technique since their original study. In addition, studies of VTE prophylaxis excluded patients with high bleeding risk. Most bleeding-risk assessments are therefore based on expert opinion. Bleeding-risk assessment is often divided into patient-specific and surgery-specific risks.

Patient-Specific Bleeding Risks. The AT9 guidelines provide patient-specific bleeding risk factors that are believed to be shared among those undergoing operations (Table 3).[13,14] The weight of each risk factor is unknown, and the presence of 1 risk factor should not necessarily be an absolute contraindication for pharmacoprophylaxis.

TABLE 2. Estimated Risk of Thrombosis Without Prophylaxis by Surgery Type Stratified by Caprini Score*

	Very low	Low	Moderate	High	Highest	
	Caprini 0 (%)	Caprini 1-2 (%)	Caprini 3-4 (%)	Caprini 5-6 (%)	Caprini 7-8 (%)	Caprini ≥9 (%)
General surgery, plastic and reconstructive surgery, ENT surgery, gynecology, lumbar spine surgery, vascular surgery, surgical ICU[35]	NA	NA	0.7	1.8	4.0	10.7
General surgery[13]	0.5	1.5	3.0	6.0		
General surgery, urology, vascular surgery[†33]	<0.7	<0.7	1.0	1.3	2.6	6.5-17.3
Plastic surgery[31]	NA	NA	0.6	1.3	2.7	11.3
Gynecology (oncology)[34]	0.0	0.0	0.0	1.9	4.4	6.5
ENT surgery[30]	0.0	0.5	0.2	0.9	2.4	18.3

*Caprini 2005 version
†Percentages in patients with prophylaxis
ENT = ear, nose, and throat; ICU = intensive care unit

Operation-Specific Bleeding Risk. Operation-specific risk factors for bleeding are typically classified into low and high risk. Some operations have a low risk of bleeding overall, but because a small amount of bleeding into the surgical field could have dire consequences, they are considered to be of high risk. Examples of this include intracranial, spine, intraocular, reconstructive, and cardiac surgery. Patients who have received neuraxial anesthesia are at increased risk of spinal or epidural hematoma and should delay initiation of pharmacoprophylaxis by 1 to 12 hours, depending on the anticoagulant used.[41]

The supplemental online appendix of the 2017 ACC Expert Consensus Decision Pathway for Periprocedural Management of Anticoagulation in Patients With Nonvalvular Atrial Fibrillation[42] summarizes the bleeding-risk classification of several operations based on expert opinion from multiple professional medical and surgical societies. This document serves as an excellent resource for estimated bleeding risk and classifies operations into 4 separate risk categories (no clinically significant risk, low risk, intermediate/high risk, and uncertain risk). As the complexity of any given operation may vary, the surgeon's perceived risk of bleeding should always be considered.

There are no validated RAMs for estimating the risk of postoperative bleeding. Models to assess bleeding in other circumstances (such as the HAS-BLED score[43] for patients with atrial fibrillation) have not been studied for this purpose and should therefore not be used in this setting.

OPERATION-SPECIFIC CONSIDERATIONS

There is significant variability in the VTE and bleeding risk among some surgical specialties. These require special considerations when applying VTE prophylaxis. The following sections provide an overview of the available data on prevention of VTE, separated by surgical specialty.

General Surgery

The incidence of VTE following operations in general surgery varies with patient and surgery-specific characteristics. For example, the presence of malignancy or inflammatory bowel disease and emergent surgery are associated with increased risk. As an illustration, the incidence of symptomatic VTE following a simple elective laparoscopic appendectomy in a healthy patient is 0.5% compared with 6% in a patient who requires emergent appendectomy or one who is having an operation for inflammatory bowel disease.[13] The Caprini RAM was developed in a general surgery population and has performed well in discriminating among patients being at low, moderate, high, or highest risk of 30-day postoperative VTE.[33] Other VTE risk factors not included in the

TABLE 3. Risk Factors for Major Postoperative Bleeding

General risk factors	Procedure specific risk factors
Active bleeding	Abdominal surgery
Previous major bleeding	- Male sex
- Gastrointestinal bleed: 7 days	- Preoperative hemoglobin level <13 g/dL
- Intracranial bleed: 12 months	- Malignancy
- Recent intraocular surgery: 2 weeks	- Complex surgery (≥2 procedures, difficult dissection, more than 1 anastomosis)
- Other: 3 months	Pancreaticoduodenectomy
Previous bleeding from similar procedure	- Sepsis
Untreated bleeding disorder	- Pancreatic leak
Severe renal or hepatic failure	- Sentinel bleed
Thrombocytopenia (<50,000/<100,000 and declining)	Hepatic resection
Acute stroke	- Number of segments
Uncontrolled hypertension (>180/120 mm Hg)	- Concomitant extrahepatic organ resection
Lumbar puncture, epidural, or spinal anesthesia within previous 4 hours or next 12 hours	- Primary liver malignancy
Use of anticoagulants, antiplatelets, NSAIDs or thrombolytic drugs	- Lower preoperative hemoglobin level platelet counts (Preoperative anemia/thrombocytopenia)
Epistaxis and menstrual bleeding are NOT contraindications to pharmacological thromboprophylaxis	Cardiac surgery
Procedures in which complications may have especially severe consequences	- Older age
Craniotomy	- BMI >25 kg/m^2
Spinal surgery	- Concomitant antiplatelet therapy
Spinal trauma	- Nonelective surgery
Reconstructive procedures involving free flap	- Longer bypass time
	- Placement ≥5 grafts
	- Operation other than CABG
	Thoracic surgery
	- Pneumonectomy
	- Extended resection
	- Primary or metastatic malignancy
	Orthopedic surgery
	- Difficult to control surgical bleeding
	- Extensive surgical dissection
	- Revision surgery
	Trauma surgery
	- Severe head injuries
	- Conservatively managed liver or spleen injuries
	- Spinal column fracture with epidural hematoma
	- Pelvic fractures

BMI = body mass index; CABG = coronary artery bypass grafting; NSAID = nonsteroidal anti-inflammatory drug
Adapted from *Chest*;[13,14] with permission.

Caprini RAM include hospital stay >2 days and postoperative complications.[13]

Risk estimates for major postoperative bleeding in general surgery range between 0.7% and 1.2%.[13] In a systematic review of randomized trials, the overall rate of bleeding related to pharmacoprophylaxis requiring a change of care occurred in less than 3% of patients.[44] Additional risk factors for bleeding are included in Table 3.

Prophylaxis for VTE in general surgery (non—cancer-related) is based on patient- and surgery-specific risks with consideration of the estimated bleeding risk. The AT9 guideline recommendations for VTE prophylaxis in general surgery patients are summarized in Table 4.[13,14,19-21,23,45-56]

Bariatric Surgery and VTE Prophylaxis in the Obese Patient Undergoing Nonbariatric Surgery

Reported rates of VTE following bariatric surgery range between 0.3% and 2.2%,[17] although less invasive operations may be associated with lower risk.[49] Postoperative VTE has been found to account for 30% of postoperative mortality.[13] Risk factors for VTE include open operations, bypass surgery (compared with adjustable band), longer operative duration (>3 hours), revision surgery, and postoperative anastomotic leak.[17] Although the Caprini RAM is not validated in bariatric surgery, its use is generally considered acceptable by most experts.[13] Models specific to bariatric surgery are available but have yet to be externally validated.[27] Reported rates of major postoperative bleeding following bariatric surgery range between 0.4% and 6.7%.[17]

The AT9 recommendations for VTE prophylaxis following weight-loss surgery are similar to those for a patient undergoing other operations in general surgery.[13] The majority of patients undergoing weight-loss operations are considered to be moderate to high risk for VTE using the Caprini RAM.

Optimal heparin dosing in obese patients is unclear. Although therapeutic heparin dosing is calculated from the patient's total body weight, it is less clear whether standard prophylactic doses of heparins provide sufficient protection against VTE in the obese patient. Studies have indicated that the use of higher doses of low-molecular-weight heparin (LMWH) or low-dose unfractionated heparin (LDUH) are associated with modestly improved efficacy without a significant increase in bleeding in patients with significant obesity (Table 5).[13,14,50,55,56,58,59,60-74] The AT9 guideline does not endorse a specific dose in the obese patient;[13] however, the European Society of Anaesthesiology (ESA) guidelines suggest adjusting the dose based on the indication for operation (bariatric vs nonbariatric) and perceived risk of VTE.[75] We suggest increased doses of postoperative heparin in obese patients (Table 5), especially following low bleeding-risk procedures; however, further study would be helpful to evaluate the benefits and risks of this strategy.

The risk of postoperative VTE following weight-loss surgery is known to extend beyond the length of the patient's hospital stay.[49] Two observational studies demonstrated that extending the duration of pharmacoprophylaxis was associated with a lower risk of VTE, with no difference in bleeding; however, it is unclear whether these were symptomatic or asymptomatic VTE events.[77,78] The ESA guidelines endorse a 10- to 15-day postdischarge course of pharmacoprophylaxis for bariatric surgery patients at high risk of VTE.[75] Recommendations for VTE prophylaxis following bariatric surgery are summarized in Table 4.

Urologic Surgery

Urologists perform a diverse group of operations resulting in variable risk of VTE, with rates ranging between 0.3% and 15.7%.[79] Most nonmalignant urologic surgery is associated with a low risk of VTE, even in the setting of patient-related risk factors.[79] Conversely, cancer operations are generally associated with higher rates of VTE, especially if performed via an open approach or associated with associated with lymph-node dissection.[79] Urology operations were included in the Caprini RAM validation

TABLE 4. VTE Prophylaxis Recommendations, Stratified by Surgical Specialty and Estimated VTE Risk

Surgery type		Strategy
General abdominopelvic and gynecology	Very low/low risk	No prophylaxis (Caprini score 0)
	Caprini 0-2	Mechanical prophylaxis (Caprini score 1-2)
	Moderate risk	Average bleeding risk:
	Caprini 3-4	LMWH/ LDUH or mechanical prophylaxis
		High bleeding risk:
		Mechanical prophylaxis
	High risk	Average bleeding risk:
	Caprini ≥5	LMWH/ LDUH and mechanical prophylaxis
		High bleeding risk:
		Mechanical prophylaxis
	Considerations	
	• Prophylaxis is typically continued until the patient is ambulatory or until hospital dismissal	
	• Consider extended prophylaxis (4 weeks) in the setting of intra-abdominal malignancy[13,48-50]	
	• Fondaparinux and aspirin should only be considered if heparin is contraindicated[13]	
Bariatric	Moderate risk	Average bleeding risk:
	Caprini <4	Mechanical prophylaxis with/without LMWH/LDUH (depending on patient's VTE risk)
	Most bariatric surgery	High bleeding risk:
		Mechanical prophylaxis
	High risk	Average bleeding risk:
	Caprini ≥5	LMWH/LDUH AND Mechanical prophylaxis
	Additional VTE risk factors: age >55 years, BMI >55 kg m^2, sleep apnea, pulmonary hypertension, revision surgery, postoperative anastomotic leak[13,49]	High bleeding risk: Mechanical prophylaxis
	Considerations	
	• Prophylaxis is typically continued until the patient is ambulatory or until hospital dismissal	
	• Consider extended duration (10-15 days) prophylaxis if very high risk	
	• DOACs should not be used following bariatric surgery as absorption may be impaired[51]	
	• Consider weight-adjusting pharmacoprophylaxis in obese patients (see Table 5).	
Urology	Very low risk	No prophylaxis
	Caprini 0[13]	
	Minor day surgery (for example, circumcision, hydrocelectomy, and vasectomy)	
	0 patient risk factors*: prostatectomy without PLND, donor nephrectomy	
	One patient risk factor*: TURP, prolapse surgery or reconstructive pelvic surgery, percutaneous nephrolithotomy[52]	
	Low/moderate risk	
	Caprini 1-2[13]	Mechanical prophylaxis
	0 patient risk factors*: laparoscopic/robotic prostatectomy w/PLND (standard/extensive),	

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TABLE 4. Continued

Surgery type		Strategy
	laparoscopic nephrectomy (radical/partial) Robotic partial nephrectomy	
	1 patient risk factor*: open donor nephrectomy, prostatectomy w/o PLND	
	≥2 patient risk factors* or personal history of VTE: TURP, percutaneous nephrolithotomy, open prolapse surgery or reconstructive pelvic surgery[52]	
	High risk	
	Caprini ≥3[13]	Average bleeding risk: LMWH/ LDUH and mechanical prophylaxis
	Radical cystectomy, open prostatectomy, open nephrectomy, nephrectomy with thrombectomy or ureterectomy, primary nerve-sparing RPLND	High bleeding risk:
	1 patient risk factor*: laparoscopic/robotic prostatectomy w/extensive PLND, robotic partial nephrectomy	Mechanical prophylaxis
	≥2 patient risk factors* or personal history of VTE: laparoscopic/robotic prostatectomy with standard PLND, laparoscopic/robotic nephrectomy, open donor nephrectomy[52]	
	Considerations	
	• Prophylaxis is typically continued until the patient is ambulatory or until hospital dismissal	
	• Consider extended prophylaxis (4 weeks) in the setting of intra-abdominal malignancy[13,48,50]	
	• *Patient risk factors: previous VTE, VTE in first-degree relative, age ≥75 years, BMI ≥35 kg/m^2[52]	
Plastic and Reconstructive	Low risk: Caprini <7	Mechanical prophylaxis or LDUH/LMWH: surgeon discretion, based on individualized patient assessment
	Facial cosmetic procedures	
	High risk	Average bleeding risk:
	Caprini ≥7: extensive or combined surgical procedures, body contouring, abdominoplasty, head/neck cancer free-flap surgery, breast reconstruction, body-contouring procedures, major lower-extremity procedures	LDUH/ LMWH and mechanical prophylaxis
		High bleeding risk: Mechanical prophylaxis
	Considerations	
	• Prophylaxis is typically continued until the patient is ambulatory or until hospital dismissal	
	• Consider extended duration (up to 4 weeks) in patients with Caprini score >7	
	• LMWH is associated with an increased risk of reoperative hematoma compared with LDUH when used in non–risk-stratified patients[19,53]	
	• High bleeding risk procedures include head and neck free flap surgery, large areas of surgical dissection such as postbariatric body contouring, procedures involving highly vascular areas such as the face[19,53]	
ENT	Low risk	Mechanical prophylaxis
	Caprini <7:oral cavity or oropharynx excision, neck dissection, tonsillectomy and adenoidectomy, thyroid or parathyroid, salivary gland surgery, otologic procedures	
	High risk	Average bleeding risk:
	Caprini ≥7 or Caprini ≥ 5+ major surgery:	LMWH/LDUH and mechanical prophylaxis

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TABLE 4. Continued

Surgery type		Strategy
	(Major head and neck surgical procedures, free or regional tissue transfer, laryngectomy, oral cavity composite resection or skull-base surgery)[20,54]	High bleeding risk: Mechanical prophylaxis
	Considerations	
	• Prophylaxis is typically continued until the patient is ambulatory or until hospital dismissal	
	• Reported bleeding associated with chemoprophylaxis in ENT surgery is 2% to 8%; for this reason, anticoagulant prophylaxis is avoided by many surgeons unless the patient is thought to be very high risk[20]	
Cardiac	Moderate risk Uncomplicated CABG	Mechanical prophylaxis
	High risk Nonhemorrhagic complications, prolonged hospitalization	Average bleeding risk: LDUH/LMWH and mechanical prophylaxis High bleeding risk: Mechanical prophylaxis
	Considerations	
	• Prophylaxis is typically continued until the patient is ambulatory or until hospital dismissal	
	• Aspirin may reduce VTE but should not be used as monotherapy[21]	
Vascular	Low risk Caprini <4	Mechanical prophylaxis
	High risk Caprini ≥5	Mechanical prophylaxis or LMWH/LDUH (preferred in very high risk)
	Considerations	
	• Prophylaxis is typically continued until the patient is ambulatory or until hospital dismissal	
	• Mechanical prophylaxis may be contraindicated (lower-limb bypass procedures). If so, consider LMWH/LDUH.	
Thoracic	Low risk Diagnostic thoracoscopy, video-assisted biopsy[21]	Mechanical prophylaxis
	Moderate risk Most nonmalignant thoracic operations	Mechanical prophylaxis or LDUH/LMWH
	High risk Cancer surgery, extended pulmonary resection, pneumonectomy, extrapleural pneumonectomy, esophagectomy[13,21]	Average bleeding risk: Mechanical prophylaxis and LMWH/LDUH High bleeding risk: Mechanical prophylaxis
	Considerations	
	• Prophylaxis is typically continued until the patient is ambulatory or until hospital dismissal	
	• There are emerging data suggesting the Caprini RAM (2010 version) can predict risk of VTE following lung cancer operations and esophagectomy[45-47]	
Orthopedic	Low risk Arthroscopy, upper-extremity surgery, extremity casting, foot/ankle fractures, tibia surgery[14,55]	Mechanical prophylaxis Average bleeding risk:
	Moderate risk	

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TABLE 4. Continued

Surgery type		Strategy
	Elective, low-risk THA/TKA (unilateral, ambulatory within 24 hours) in a low-risk patient (no other VTE risk factors, including previous VTE, active cancer, known thrombophilia, lower-limb or hip fracture in the previous 3 months or expected major surgery in the oncoming 3 months)[56]	Rivaroxaban 10 mg daily for 5 days followed by an extended course of aspirin (9 to 30 days for TKA and THA, respectively)[56]
		High bleeding risk: Mechanical prophylaxis
		Average bleeding risk: Mechanical prophylaxis and • LMWH • DOAC (excluding HFS) • Second line: LDUH, aspirin, fondaparinux, VKA
	High risk THA, TKA, HFS[14]	High bleeding risk: Mechanical prophylaxis
	Considerations • Prophylaxis is typically continued for at least 10-14 days after major orthopedic surgery (THA, TKA, HFS); however, some recommend extending the duration to 35 days[14]	
Trauma	High risk Most trauma operations[13]	Average bleeding risk: LMWH/LDUH or mechanical prophylaxis
		High bleeding risk: Mechanical prophylaxis
	Very high risk Spinal cord injury, spinal trauma, traumatic brain injury, multiple fractures, pelvic fractures[13]	Average bleeding risk: LMWH/LDUH and mechanical prophylaxis
		High bleeding risk: Mechanical prophylaxis
	Considerations • Prophylaxis is typically continued until the patient is ambulatory or until hospital dismissal • Considering extended duration (up to 3 months) prophylaxis while hospitalized for rehabilitation in patients with limited mobility following spinal cord injury[57]	
Neurologic	Low risk Spine surgery (low risk, elective)[23]	Mechanical prophylaxis
	Moderate risk Craniotomy (no malignancy)[23]	Average bleeding risk: Mechanical prophylaxis, consider adding delayed LDUH/LMWH
	High risk Craniotomy (malignancy), high-risk spine surgery (malignancy, anterior-posterior approach, multiple operative levels), nontraumatic intracranial hemorrhage[23]	Average bleeding risk: Mechanical prophylaxis, LDUH/LMWH when bleeding risk is acceptable
		High bleeding risk: Mechanical prophylaxis
	Considerations • Pharmacoprophylaxis is typically delayed for at least 24-48 hours after surgery • Prophylaxis is typically continued until the patient is ambulatory or until hospital dismissal	

BMI = body mass index; CABG = coronary artery bypass grafting; DOAC = direct oral anticoagulant; ENT =ear, nose, throat; HFS = hip-fracture surgery; LDUH = low-dose unfractionated heparin; LMWH = low-molecular-weight heparin; PLND = pelvic lymph-node dissection; RAM = risk-assessment model; RPLND = retroperitoneal lymph-node dissection; THA = total hip arthroplasty; TKA = total knee arthroplasty; TURP = transurethral resection of the prostate; VKA = vitamin K antagonist; VTE = venous thromboembolism

cohort.[13,25] Major bleeding, generally defined as fatal bleeding or reoperation, occur infrequently after most urology operations, with reported rates less than 1%.[79]

There is a lack of rigorous clinical trials comparing different prophylaxis approaches in patients undergoing urology operations. Although AT9 recommends stratifying patients based on their Caprini RAM scores,[13] the more recently published European Association of Urology (EAU) guidelines incorporate both patient- and procedure-specific risk factors.[52] Recommendations are similar between AT9 and EAU for high-risk patients; however, the EAU guidelines allow for less aggressive prophylaxis in lower risk patients. Recommendations for VTE prophylaxis following urologic surgery are summarized in Table 4.

Gynecology Surgery

Contemporary VTE rates following gynecology operations range from 0.4% to 6.5%.[80-82] Risk factors for VTE among patients undergoing gynecology operations include open operations (vs laparoscopic or vaginal), underlying cancer (especially ovarian or disseminated cancer), perioperative blood transfusion, and previous pelvic radiation.[3] Validation studies of the Caprini RAM for gynecology oncology operations have been published;[32,34,39] however, because most patients fall into the highest-risk group, the RAM's ability to discriminate patients of low to moderate risk of VTE is limited (See Table 2).

The AT9 recommendations for the prevention of VTE among patients undergoing gynecology operations are presented in Table 4. Earlier iterations of AT9 have also provided the basis for the American College of Obstetrics and Gynecology practice recommendations.[48]

Extended-Duration Prophylaxis Following Abdominal or Pelvic Cancer Surgery

Extended duration thromboprophylaxis refers to the administration of pharmacologic prophylaxis for several days or weeks after hospital dismissal.[83,84] Systematic review and meta-analysis of randomized trials have demonstrated a reduction in VTE in patients undergoing abdominal or pelvic cancer operations with the administration of extended duration LMWH compared with placebo, without increases in bleeding.[50,85-87] The majority of VTE events prevented were asymptomatic DVT. Although the clinical significance of asymptomatic VTE is controversial, asymptomatic DVT has been associated with higher rates of late postthrombotic syndrome in surgical patients[88] and higher 90-day mortality in medical patients.[83,85,88,89]

Both the AT9[13] and more recent American Society for Clinical Oncology[90] guidelines endorse extended duration thromboprophylaxis for patients undergoing operations for abdominal or pelvic malignancies at high risk of VTE (defined as having restricted mobility, obesity, history of VTE, or with additional VTE risk factors).[13] Recognition that both other cancer (eg, lung, esophagus, endocrine) and non-cancer operations (eg, bariatric) carry a significant risk of postdischarge VTE will likely lead to more interest in the application of extended duration prophylaxis to other surgical populations, although additional studies would be helpful to support this practice.[91-93]

Plastic and Reconstructive Surgery

The rate of VTE in patients undergoing plastic and reconstructive operations range between 0.5% and 7.7% in observational studies.[31] Factors such as the type of operation and anesthesia as well as the patient's baseline VTE risk have significant impact on the risk of postoperative VTE. Higher-risk operations include breast reconstruction, body contouring, abdominoplasty, major operations of the lower extremity, head and neck cancer operations, and operations lasting >60 minutes.[18,19,94] Patients who undergo general anesthesia are also at increased risk for VTE compared with those who have nongeneral anesthesia.[53,94] The Caprini RAM has been validated in plastic surgery.[31] Observed risks of symptomatic VTE stratified by Caprini score are given in Table 2.

Bleeding risk associated with the use of chemoprophylaxis is a significant concern

for plastic surgeons, especially in patients with large areas of tissue dissection, such as postbariatric body contouring or highly vascular areas such as the face. However, it is estimated that chemoprophylaxis increases the rates of hematoma requiring reoperation in less than 1% of plastic surgery operations.[95]

Neither AT9[13] nor ESA[96] provide recommendations specific to plastic surgery patients. The American Society of Plastic Surgeons recommends that patients be considered for nongeneral anesthesia techniques and suggests that patients be risk stratified using the 2005 Caprini RAM.[19] Universal pneumatic compression is recommended; however, pharmacoprophylaxis is limited to patients with elevated risks of thrombosis, such as patients with Caprini scores >8. No specific recommendations are made for those patients with Caprini scores <8. Although pharmacoprophylaxis decreases the risk of VTE following head and neck free-flap surgery, it is also associated with an increased risk of hematoma. It is therefore recommended to individualize the decision about pharmacoprophylaxis in these patients.[31,38,53] Recommendations for VTE prophylaxis following plastic and reconstructive surgery are summarized in Table 4.

Otolaryngology

The overall incidence of VTE following otolaryngology (ear, nose, and throat [ENT]) operations is low; however, the available data are sparse,[20] and the wide variety of operations performed are associated with as much as a 10-fold variation in VTE risk. Although the overall incidence of VTE is approximately 0.4%, subgroups associated with increased risk of VTE include major head and neck operations, free or regional tissue transfer, laryngectomy, oral cavity composite resection, skull-base surgery, and abscess incision and drainage.[20] The Caprini RAM has been found to discriminate patients at high and low risk of VTE following ENT operations (Table 2). Reported bleeding associated with chemoprophylaxis in ENT surgery is high, with estimates ranging between 2% and 8%.[20]

There are no ENT-specific VTE prophylaxis guidelines in the United States. Routine pharmacoprophylaxis is often omitted owing to low baseline risk of VTE and increased risk of bleeding.[97] Based on a comprehensive review of the available literature, Cramer et al outlined an approach using the 2005 Caprini RAM to risk stratify patients.[20] Intraoperative intermittent pneumatic compression devices (IPCDs), nongeneral anesthesia, and limiting the time of the operative procedure are recommended. Postoperative VTE recommendations for ENT operations are summarized in Table 4.

Cardiac Surgery

The risk of VTE following cardiac surgery is highly variable, given substantial differences in surgical techniques and use of cardiopulmonary bypass. In addition, the use of intraoperative antiplatelet and antithrombotic medications is thought to reduce risk of VTE following cardiac operations. Published rates of symptomatic thrombosis range between 0.5% and 3.0%;[98] however, others have found rates 3 times higher than that of the general surgery population.[99] The Caprini RAM has not been studied in the cardiac surgery population. Identified risk factors of VTE include patient age greater than 70 years, the use of blood products, and postoperative complications.[21] Approximately 3% to 6% of patients undergoing coronary artery bypass grafting (CABG) require reoperation secondary to bleeding.[13] Risk factors for postoperative bleeding are provided in Table 3.

Given the high risk of major bleeding, the routine use of pharmacoprophylaxis is often scrutinized because of its unknown benefit. Unfortunately, the available studies comparing preventive strategies after cardiac surgery use pharmacological agents, surgical techniques, and postoperative care that are no longer standard of care, making them difficult to incorporate into current practice. Recently, a large observational study found no appreciable difference in the rate of VTE or major bleeding in patients receiving no prophylaxis, mechanical prophylaxis, or subcutaneous heparin following a CABG operation.[100]

Pharmacoprophylaxis is therefore reserved for only the highest-risk patients. The AT9[13] and ESA[21] recommendations for VTE prophylaxis in cardiac surgery patients are summarized in Table 4.

Vascular Surgery

Rates of VTE following vascular surgery range from 0.2% to 4.2%.[21,101] As with cardiac surgery, the intraoperative use of antiplatelet and antithrombotic therapy is believed to reduce the risk of postoperative VTE. Vascular surgery accounted for 16% and 18% of the patients in the Caprini and Rogers risk-assessment models, respectively, suggesting that these tools are reliable in this population.[13] Additional risk factors include preoperative steroid use, low-serum albumin, poor preoperative functional status, postoperative complications (prolonged mechanical ventilation, perioperative transfusion, postoperative pneumonia, or wound infection).[21] Operations complicated by postoperative VTE are associated with a 4-fold increase in overall mortality.[101] Reported rates of major postoperative bleeding vary depending on the type of operation, with ranges between 0.3% and 1.8%.[13]

Few high-quality studies evaluate the optimal prophylaxis strategy following vascular surgery. As such, the AT9 consensus extrapolates its recommendations based on data from general surgery.[13] Mechanical prophylaxis is often contraindicated following peripheral vascular operations. Pharmacoprophylaxis could, therefore, be considered in patients at both moderate and high risk of VTE based on the Caprini RAM. Recommendations from the AT9[13] and ESA guidelines[21] are summarized in Table 4.

Thoracic Surgery

Reported rates of VTE following thoracic surgery vary between 0.4% and 51%. Postoperative VTE is associated with an 8-fold increase in mortality after lung cancer resection.[98,102] The rate of major bleeding following thoracic surgery range from <1% and 5%.[13] The uncertainty about both thrombotic and hemorrhagic complications appears to be secondary to the inclusion of a heterogeneous group of operations (thoracotomy vs minimally invasive procedure), underlying indication (malignant vs nonmalignant disease), type of VTE prophylaxis used, and the type postoperative surveillance performed within each study. Risk factors for postoperative VTE include high ASA classification and patients undergoing certain operations such as cancer operations, extended pulmonary resections, pneumonectomy, and esophagectomies.

Although the Caprini RAM has not been extensively studied in patients undergoing chest operations, 3 recent studies found it was able to identify patients at low, moderate, or high risk of postoperative VTE following lung cancer operations and esophagectomy.[45-47] These studies used the 2010 Caprini RAM, and it is unclear whether the more commonly used 2005 Caprini would perform similarly. Shah et al used a large administrative database to derive and validate a risk-assessment tool to estimate the risk of in-hospital and postdischarge VTE specifically for the thoracic surgery population.[28]

Few studies have evaluated the optimal VTE prophylaxis strategy following thoracic surgery, leading most guidelines to be based on expert consensus.[13,21] Recommendations from AT9[13] and the current ESA guidelines[21] are summarized in Table 4.

Orthopedic Surgery

The risk of postoperative VTE following orthopedic operations is highly variable with arthroscopy and upper-extremity procedures considered to be low risk, compared with knee and hip joint arthroplasty (TKA and THA), considered to be high risk.[14,103] Although older studies report VTE rates as high as 50% after TKA and THA, advances in surgical techniques and postsurgical care has resulted in significantly reduced rates of VTE, ranging between 1% and 5% in observational studies when pharmacoprophylaxis is omitted.[3,4] Given the varying degree of VTE rates after orthopedic operations, more emphasis is placed on procedure-specific factors than patient-specific factors. Patient-specific risk factors of VTE after orthopedic

TABLE 5. VTE prophylaxis options

Medication	Dose by operation type	Considerations
Antiplatelet therapy		
Aspirin	*THA, TKA, HFS* Studies have used variable doses (75 to 1300 mg) and treatment durations (2 days to 6 weeks)[63] A highly cited study used 160 mg daily, with the first dose chewed upon admission to the hospital to complete a 35-day course[59] *THA, TKA (low-risk patients)* Aspirin 81 mg, starting after a 5-day course of rivaroxaban 10 mg every 24 hours.[56] *Other surgery* The benefit of aspirin after non-orthopedic operations is unknown as available trials are small and dated.[63]	Patient with a contraindication (eg, peptic ulcer) or preceding indication for aspirin (eg, PCI or prior stroke) were excluded from the trials using aspirin for VTE prophylaxis[63] May be associated with increased risk of myocardial infarction.[14]
Heparins	*General considerations* • *All heparins carry a risk of HIT*[64] • *Patients should undergo platelet count monitoring at day 5,7,9* • *LMWH is the preferred pharmacoprophylactic agent following most operations*[13]	
LDUH	*Most operations* 5,000 IU SQ every 8 to 12 hours, starting 2 hours before surgery,[65] most commonly administered every 8 hours *Orthopedic surgery* 5,000 IU SQ every 12 hours, starting no sooner than 12 hours before/after surgery[14,65] *High risk populations, eg, cancer surgery* 5,000 IU SQ every 8 hours, starting 2 hours before surgery, then every 8 hours postoperatively[50]	*Considerations* Preferred agent in the setting of renal impairment (CrCl <30 mL/minute) Activity rapidly reversed with protamine sulfate *Dose adjustment* *Obesity* The optimal dose is unknown. Some experts use 7500 units twice daily[61,62]
LMWH		
Enoxaparin	*Abdominal surgery* 40 mg every 24 hours, starting 2 to 12 hours before surgery[66] *TKA, THA* 30 mg every 12 hours with initial dose administered ≥12 hours preoperatively or ≥12 hours postoperatively once hemostasis is achieved[14,66] *HFS, THA* 40mg SQ, every 24 hours, with the initial dose administered ≥12 hours preoperatively or ≥12 hours postoperatively once hemostasis is achieved[14,66] *Other* 40 mg every 24 hours, starting 10 to 12 hours before surgery[13,66]	*Dose adjustments* *Renal impairment* CrCl <30 mL/minute: Avoid use. Some experts recommend enoxaparin 20 to 30 mg every 24 hours[67] *Obesity* BMI >40 kg/m^2: 40 mg every 12 hours[60-62] We do not recommend adjusting dose based on anti-Xa levels as trials have not shown a clear link between anti-Xa levels and bleeding or thrombotic events[62]
Dalteparin	*Abdominal surgery* Average risk: 2,500 IU starting 1 to 2 hours prior to surgery and repeated once daily	*Dose adjustments* Renal impairment CrCl <30 mL/min: Avoid use

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TABLE 5. Continued

Medication	Dose by operation type	Considerations
	postoperatively. High risk: 5,000 IU every 24 hours, starting the evening before surgery OR 2,500 IU started 1 to 2 hours before surgery followed by 2,500 IU 12 hours later, and then 5,000 IU every 24 hours postoperatively[76] *TKA (off-label), THA* a) 5,000 IU, every 24 hours, starting ≥12 hours preoperatively and/or ≥12 hours postoperatively once hemostasis is achieved[14]	*Obesity* BMI ≥40 kg/m^2: Some experts recommend either increasing dose by 30% or give 7,500 units once daily when patient weight >150 kg[68]
Pentasaccharides		
Fondaparinux	*Abdominal surgery, THA/TKA, HFS, Abdominal cancer (off-label)* 2.5 mg, starting 6-12 hours after surgery[69] Some experts favor administering first dose 8 to 12 hours postoperatively to reduce the risk of postoperative bleeding	*Dose adjustments* *Renal impairment* CrCL <30 mL/min: Avoid use[69] *Low body weight* Weight < 50 kg: Avoid use[69]
Direct Oral Anticoagulants (DOACs)		
General considerations	- Can be used in the setting of HIT[64] - Have not been studied in outside of orthopedic operations - There are concerns about efficacy and safety in patients weighing >120 kg - All are associated with a rapid onset of action and should not be started until hemostasis is assured *Contraindications:* - Renal disease (CrCl <30 mL/min) - Moderate-severe hepatic impairment - Significant medication interactions	
Factor Xa inhibitors		Experience is greater with apixaban and rivaroxaban
Apixaban	*THA/TKA* 2.5 mg every 12 hours, starting 12 to 24 hours after surgery[70]	
Edoxaban	*TKA (off-label use)* 30 mg, every 24 hours, starting 6 to 24 hours after surgery[73]	
Rivaroxaban	*TKA/THA* 10 mg, starting 6 to 10 hours after surgery, then every 24 hours[71]	
Direct thrombin inhibitors		
Dabigatran	*THA* 110 mg, starting 1 to 4 hours after surgery and hemostasis is assured, then 220 mg every 24 hours[72] If not started on the day of surgery, initiate treatment with 220 mg every 24 hours[74]	The capsule cannot be broken or chewed (ie, cannot be administered by nasogastric tube)[72] *Renal dose adjustment* CrCl: <50 ml/min: Do not use with concomitant P-glycoprotein inhibitors[72] CrCl <30 ml/min: Avoid use[72]
Vitamin K antagonists (VKA)		
Warfarin	*TKA, THA, HFS* Started 8-24 hours after surgery, usually continued for 4 weeks[14] Most experts recommend a therapeutic target	Can be used if DOAC/LMWH not available Associated with higher rates of bleeding, particularly when used for extended prophylaxis[14]

Continued on next page

TABLE 5. Continued

Medication	Dose by operation type	Considerations
	international normalized ratio (INR) of 2.5 (range 2-3)[14] though some advocate a lower range (1.5 to 2.5)[74]	
Mechanical prophylaxis		
General considerations	- Frequently used in the setting of high bleeding risk or in combination with pharmacological prophylaxis in patients at very high risk of thrombosis. - Its impact on symptomatic VTE (especially PE) is uncertain and varies in different clinical settings *Contraindications*[55] - Suspected or proven peripheral arterial disease - Peripheral arterial bypass grafting - Severe peripheral neuropathy or other sensory impairment - Skin disease: Fragile skin, dermatitis, gangrene or recent skin graft, Steven Johnson syndrome - Known allergy to material - Severe leg edema - Major limb deformity or unusual leg shape preventing correct fit - Lower extremity trauma with a plaster cast Some advocate using mechanical means on the unaffected contralateral leg, however ideally this should not be used as the sole means of prophylaxis	
Intermittent pneumatic compression devices (IPCDs)	Typically started before surgery and used continuously postoperatively until hospital discharge or ambulation[13] Guidelines recommend portable, battery-powered IPCDs, with a goal towards 18 h of daily compliance[13] May be removed while ambulating, but should be put back on when returning to a seated or supine position[13]	IPCDs are generally preferred over graduated compression stockings[13] Skin breakdown is a known complication. Some clinicians use loose stockinettes underneath the device to counteract this in high-risk patients (frail, underlying skin disease)[55]
Graduated compression stockings (GCS)	Pressure: 18-23 mm Hg pressure at the ankle level[13] Thigh-high stockings preferred over calf-high stockings, however, knee-high stocking can be used if there is a need to access the groin vessels during surgery (eg, AAA surgery)[13]	Studies have found a 4-fold increase in skin complications, including breaks, ulcers, blisters, and necrosis[58]
Not recommended for primary VTE prophylaxis		
Vena Cava Filters	Not recommended due to lack of evidence demonstrating benefit and considerable risk of complications.[13]	
Surveillance ultrasonography	Not recommended due to lack of evidence demonstrating a benefit[13]	

Abbreviations: BMI = Body Mass Index; CrCl = Creatinine Clearance; HFS = Hip fracture surgery; HIT = Heparin induced thrombocytopenia; IU = International units; Kg/M^2 = kilogram/meter^2; LDUH = Low dose unfractionated heparin; LMWH = Low molecular weight heparin; Mg = milligrams; PCI = Percutaneous intervention; SQ = Subcutaneous; THA = Total hip arthroplasty; TKA = Total knee arthroplasty.

operations include a previous history or strong family history of VTE, known thrombophilia; advanced cancer; morbid obesity; lower limb or hip fracture in the previous 3 months; or expected major surgery in the oncoming 3 months. The Caprini RAM is not validated in the orthopedic population[25] and is not useful for risk stratifying patients undergoing total joint arthroplasties.[104]

Bleeding risk is an essential consideration in orthopedic procedures, as a prosthetic joint hematoma significantly increases the risk of prosthetic joint infections.[105] The AT9 authors found that, in general, pharmacoprophylaxis did not have a substantial impact on major bleeding.[14] A median rate of 1.5% for major bleeding has been reported, regardless of whether or not

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patients receive pharmacoprophylaxis.[14,106] Risk factors for bleeding unique to orthopedic surgery are given in Table 3.

Interpreting the data for VTE prophylaxis following orthopedic surgery is challenging. Earlier trials were performed when surgical techniques and postoperative rehabilitation were dramatically different and most likely associated with a higher risk of VTE and bleeding. Furthermore, the use of asymptomatic DVT by screening venography or ultrasound as a surrogate marker of symptomatic DVT is frequently debated and had led to different interpretations of the literature. This is particularly true of the use of aspirin for monotherapy. Although aspirin is likely effective in preventing VTE following orthopedic surgery, it is unclear how it compares with other commonly used agents such as LMWH or direct oral anticoagulants (DOACs). Recently, a study of low-risk patients undergoing elective THA and TKA treated with 5 days of rivaroxaban followed by an extended course of aspirin had similar rates of VTE and bleeding when compared with patients who remained on rivaroxaban for the entire duration of their pharmacoprophylaxis.[56] This suggests that aspirin may be safely used in combination with a short course of an antithrombotic agent. It is not known whether these results apply to high-risk patients. When pharmacoprophylaxis was used, warfarin, fondaparinux, and rivaroxaban all appeared to have higher rates of bleeding compared with LMWH.[14]

Guidelines for VTE prophylaxis following orthopedic surgery are generally tailored to the highest-risk orthopedic operations including THA, TKA, and hip fracture surgery (HFS).[14,55,107] Anticoagulation recommendations for other procedures are individualized, given the paucity of data for these procedures. For example, patients with multiple risk factors for VTE would likely benefit from more intensive VTE prophylaxis despite undergoing "low-risk" operations. The National Institute for Health and Care Excellence (NICE) guidelines do not recommend routine pharmacoprophylaxis following most upper-limb operations or arthroscopic knee surgery.[55]

All patients undergoing THA, TKA, and HFS are recommended VTE prophylaxis, given their high risk of VTE. For patients at average risk of bleeding, AT9 gives preference to LMWH with lower-extremity compression therapy over other options.[14] For patients with increased risk of bleeding, both AT9 and NICE guidelines recommend using mechanical prophylaxis rather than pharmacoprophylaxis. The risk of VTE following orthopedic surgery is known to extend well beyond the patient's hospital stay and has been reported to last up to 3 months after surgery.[14,108,109] A Cochrane review noted a reduction in symptomatic VTE when using DOACs in an extended duration following knee and hip arthroplasties;[110] however, this was primarily supported by 2 trials that only assessed extended-duration anticoagulation after hip arthroplasty.[111,112] Consequently, there is less evidence to support the use of extended-duration anticoagulation following TKA. For major orthopedic surgery (THA, TKA, HFS), AT9 guidelines recommend that patients receive pharmacoprophylaxis and/or IPCDs for a minimum of 10 to 14 days, with a suggestion of extending pharmacoprophylaxis for up to 35 days postoperatively.[14] In contrast, the NICE guidelines recommend LMWH for 10 days, followed by aspirin for an additional 28 days following elective THR and aspirin for 14 days after elective TKR.[55] The NICE guidelines recommend LMWH or fondaparinux for 1 month following fragility fracture of the pelvis, hip, and proximal femur.[55] Recommendations for VTE prophylaxis following orthopedic surgery are summarized in Table 4.

Trauma Surgery

Patients undergoing operations for trauma are considered at high risk for both postoperative VTE and bleeding. A recent review estimated an 8.7% rate of VTE without prophylaxis.[113] Risk factors for VTE in this population include significant vascular injury,[22] soft-tissue leg injury,[22] spinal cord injury,[13] vertebral fracture,[13] and surgery requiring general

anesthesia.[22] The Caprini RAM has not been studied in the trauma surgery population. The risk of bleeding following trauma surgery is estimated to be 3.4% to 4.7%.[13]

Several randomized controlled trials have evaluated the role of VTE prophylaxis in trauma surgery. Although mechanical prophylaxis reduces the risk of VTE, rates of asymptomatic VTE were lower following the use of pharmacoprophylaxis without an increased risk of bleeding.[114-116] As such, pharmacoprophylaxis is recommended for all trauma patients, with consideration toward combined mechanical and pharmacological prophylaxis in patients at high risk for VTE.[13] Some groups recommend extending the duration of VTE prophylaxis up to 3 months or until purposeful movements of the lower extremities are regained in patients who are at elevated risk for thrombosis with significantly impaired mobility (eg, patients with spinal cord injuries).[13,57] This recommendation is based on expert opinion, as clinical trials have not evaluated the efficacy and safety of this strategy.

Some groups recommend prophylactic inferior vena cava filter placement in patients deemed at elevated risk of VTE or when operative management is delayed by more than 72 hours.[117,118] This strategy has not been found more effective over mechanical or pharmacological prophylaxis in prospective randomized controlled trials. A recent multicenter randomized controlled trial found no benefit from prophylactic vena cava filter placement in severely injured patients who have contraindications to prophylactic anticoagulation within the first 7 days of hospitalization.[119] We agree with the AT9 guidelines recommending against the use of prophylactic inferior vena cava filter placement. Recommendations for VTE prophylaxis following trauma surgery are summarized in Table 4.

Neurologic Surgery

The rate of VTE following neurosurgery depends on the type of operation and associated comorbidities. Craniotomy and nontraumatic intracranial hemorrhage are both considered high risk for VTE (1.7% to 6.7% with prophylaxis), whereas most elective operations of the spine are considered to be low risk (<1%).[23] Risk factors of postoperative VTE unique to neurosurgery include perioperative immobility and paresis as well as complicated or prolonged procedures.[23] Intracranial bleeding is thought to occur in 1% to 1.5% of patients following craniotomy without pharmacoprophylaxis. The risk of epidural hematoma is very low (0.2%) and does not appear to be associated with the use of thromboprophylaxis.[23]

Mechanical and pharmacological prophylaxis is effective in preventing VTE following operations of the spine and brain; however, the studies are old and are limited by methodological flaws.[120-122] Many surgeons are hesitant to use pharmacoprophylaxis, given the potential increased risk of bleeding and catastrophic consequences. The AT9 authors found the harm of pharmacoprophylaxis outweighs the benefits.[13] Conversely, the ESA guideline did not find strong evidence that pharmacoprophylaxis increases the risk of adverse outcomes.[23] Rather, the timing of initiation of pharmacoprophylaxis appeared to influence the risk of postoperative thrombosis and bleeding. In a recent meta-analysis, Lu et al described a reduced rate of VTE but no difference in hemorrhagic progression or mortality when pharmacoprophylaxis was initiated within 72 hours. However, the risk of VTE increased if pharmacoprophylaxis was delayed longer than 72 hours.[123]

Current guidelines recommend mechanical prophylaxis for most patients, with the possibility of adding pharmacoprophylaxis in patients at high risk of thrombosis usually, 24 to 48 hours after surgery, if it is thought safe to do so from a bleeding perspective.[13,23] Recommendations for VTE prophylaxis following neurologic surgery are summarized in Table 4.

CONCLUSION

Postoperative VTE can be a devastating and costly complication. Current strategies are unable to eliminate the risk of VTE; hence, calling it a “never event” is unreasonable.

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Prudent use of mechanical or pharmacological prophylaxis, however, can significantly reduce this risk, particularly in high-risk patients or with high-risk operations. This benefit needs to be carefully balanced with the potential harm of prophylaxis. Thoughtful risk stratification is, therefore, crucial to determine the optimal VTE prophylaxis strategy.

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Abbreviations and Acronyms: **AT9** = 9th edition of the American College of Chest Physicians Evidence-Based Clinical Practice Guidelines for Prevention of VTE in Orthopedic and Nonorthopedic Surgical Patients; **CABG** = coronary artery bypass graft; **DVT** = deep venous thrombosis; **EAU** = European Association of Urology; **ENT** = ear, nose, and throat; **ESA** = European Society of Anaesthesiology; **HFS** = hip fracture surgery; **IPCDs** = intermittent pneumatic compression devices; **LDUH** = low-dose unfractionated heparin; **LMWH** = low molecular weight heparin; **NICE** = National Institute for Health and Care Excellence; **PE** = pulmonary embolism; **RAM** = risk assessment model; **THA** = Total hip arthroplasty; **TKA** = total knee arthroplasty; **VTE** = venous thromboembolism

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Correspondence: Address to Matthew A. Bartlett, MB, BCh, BAO, Division of General Internal Medicine, Mayo Clinic, 200 First Street SW, Rochester, MN 55905 (Bartlett.matthew@mayo.edu).

ORCID

Matthew A. Bartlett: https://orcid.org/0000-0001-7246-9324; Christopher R. Stephenson: https://orcid.org/0000-0001-8537-392X; Ravindra Ganesh: https://orcid.org/0000-0002-6877-1712

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