DVT Prophylaxis

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The burden of disease represented by venous thromboembolic (VTE) disease is significant, particularly in the hospitalized populations. Surgery itself represents a risk factor for VTE. A multi-modality approach achieves the best overall outcome.

VTE prophylaxis comes in three main forms: ambulation, chemical/pharmaceutical prophylaxis, and mechanical prophylaxis. These methods have synergistic effects. Patients who take regular antithrombotic medications for preexisting VTE or VTE risk factors represent a unique problem. In this population, a thorough assessment of each patient's preexisting risk factors, as well as those represented by their impending operation, needs to be made to decide when to stop their antithrombotic agents, and whether bridging therapy is required. As with many clinical decisions, cost-effectiveness of treatments has to be considered based on local circumstances.

2.1 Introduction

Virchow's triad underpins VTE pathophysiology. The clinical factors predisposing to VTE are immobilization, trauma, surgery, malignancy, and previous VTE. The nonclinical factors predisposing to VTE are age, obesity, infection, the immediate postpartum period, varicose veins, dehydration, hormone treatment, and thrombophilias. Post-thrombotic chronic venous disease is not often considered but can lead to deep venous obstruction or reflux, and the subsequent skin changes and ulceration can decrease quality of life and become quite costly over time.

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There is a low rate of appropriate VTE prophylaxis around the world, particularly for acutely ill patients. Education, hospital-wide protocols, VTE prevention audits, and clinical nurse specialists have all been shown to substantially increase the appropriate application of VTE guidelines. The risk profile for surgical patients and the associated treatments vary substantially for orthopedic and non-orthopedic procedures, and thus they will be discussed separately. There will be a brief outline of periprocedural management of anticoagulation and the cost-effectiveness of VTE prevention.

2.2 Non-Orthopedic Patients

In non-orthopedic patients, the most widely used tool for quantification of VTE risk is the modified Caprini risk assessment model from the American College of Chest Physicians (Table 2.1). The model has been validated for patients having general and abdominal/pelvic, including the critically ill among them.

One of the most important components in VTE prophylaxis decision-making is estimating the risk of bleeding. Major bleeding includes fatal bleeding, symptomatic bleeding in a critical region or organ, bleeding that causes a hemoglobin drop of ≥20 g/dL, and/or bleeding that necessitates transfusion of two or more units of packed red blood cells. The ideal method of risk assessment involves determining the patient's baseline risk of major bleeding based on the type of procedure (Table 2.2) they are having and then modifying that risk based on individual risk factors. In non-orthopedic surgical patients, the primary individual risk factors for major bleeding are bleeding as the cause for surgery; intracranial hemorrhage; development of moderate or severe coagulopathy; underlying bleeding disorder; or thrombocytopaenia. Patients at low risk (<2%) for major bleeding are those having uncomplicated general abdominal/pelvic, bariatric, vascular, and thoracic surgery. Those at high risk include patients having cardiac surgery and those with major trauma, particularly to do with the brain or spine, are considered to be at the highest risk. Also included in the high-risk category are patients in whom bleeding could be considered catastrophic such as neurosurgical patients in which thromboprophylaxis could cause spinal or intracranial hemorrhage. Mechanical prevention methods include interventions such as intermittent pneumatic compression (IPC), venous foot pumps (VFP), and graduated elastic compression (GEC) garments. Mechanical methods are thought to reduce the risk of VTE by increasing blood flow in the deep veins of the legs, inhibiting the venous stasis component of Virchow's triad. IPC increases endogenous fibrinolytic activity. Chemical prophylaxis includes drugs like vitamin K antagonists (VKA), low molecular weight heparin (LMWH), unfractionated heparin (UFH), oral factor Xa inhibitors/novel oral anticoagulants (NOAC), and fondaparinux.

The preferred options approach outlined in this chapter are consistent with the majority of reputed guidelines. It is important to note that the recommendations outlined are largely for patients at low risk for bleeding. Treatment approaches should be adapted according to the risk of major bleeding.

Table 2.1 Modified Caprini risk assessment model for VTE in general surgical patients

Risk score			
1 point	**2 points**	**3 points**	**5 points**
• Age 41–60 years • Minor surgery • BMI >25 kg/m^2 • Swollen legs • Varicose veins • Pregnancy or postpartum • History of unexplained or recurrent spontaneous abortion • Oral contraceptives or hormone replacement • Sepsis (<1 month) • Serious lung disease, including pneumonia (<1 month) • Abnormal pulmonary function • Acute myocardial infarction • Congestive heart failure (<1 month) • History of inflammatory bowel disease • Medical patient at bed rest	• Age 41–60 years • Minor surgery • BMI >25 kg/m^2 • Swollen legs • Varicose veins • Pregnancy or postpartum • History of unexplained or recurrent spontaneous abortion • Oral contraceptives or hormone replacement • Sepsis (<1 month) • Serious lung disease, including pneumonia (<1 month) • Abnormal pulmonary function • Acute myocardial infarction • Congestive heart failure (<1 month) • History of inflammatory bowel disease • Medical patient at bed rest	• Age ≥ 75 years • History of VTE • Family history of VTE • Factor V Leiden mutation • Prothrombin 20210A mutation • Lupus anticoagulant • Anticardiolipin antibodies • Elevated serum homocysteine • Heparin-induced thrombocytopenia • Other congenital or acquired thrombophilia	• Stroke (<1 month) • Elective arthroplasty • Hip, pelvis, or leg fracture • Acute spinal cord injury (<1 month)
Guide to interpretation:			
Surgical risk category		**Score**	**Estimated VTE risk in the absence of prophylaxis (%)**
Very low		0	<0.5
Low		1–2	1.5
Moderate		3–4	3.0
High		≥5	6.0

Table 2.2 Risk of major bleeding in non-orthopedic patients

Type of surgery	Risk of major bleeding (%)
General/abdominal/pelvic surgery	1
Bariatric surgery	<1
Plastic and reconstructive surgery	0.5–1.8
Vascular surgery	0.3–1.8
Cardiac surgery	5 (high risk)
Thoracic surgery	1
Neurosurgery	
• Craniotomy	1–1.5
• Spinal surgery	<0.5
Major trauma	3.4–4.7

(Source—Tables 2.1 and 2.2)

2.3 Very Low Thrombosis Risk

According to the Caprini model (Table 2.1), patients at very low risk of thrombosis are those with a score of 0 undergoing general/abdominal/pelvic surgery, or those with a score of 0–2 undergoing plastic/reconstructive surgeries. Examples include young, healthy patients having minor outpatient procedures: laser eye surgery, cataract removal, skin biopsy, benign breast biopsy, diagnostic endoscopy, nasal polypectomy, dilatation and curettage, colposcopy, or aspiration of joint effusion.

For non-orthopedic surgical patients at very low risk of VTE, the prophylaxis of choice is early and frequent ambulation. The majority of patients in this group are able to mobilize promptly after surgery, substantially reducing their risk of VTE. For exceptional circumstances in which these patients are unable to ambulate, the recommendation is mechanical prophylaxis in the form of GEC garments, VFP, or IPC. Adequate hydration is also important in this group.

2.4 Low Thrombosis Risk

Patients who are at low risk (Table 2.2) for VTE include those with a modified Caprini score of 1–2 undergoing general/abdominal/pelvic surgery, or those with a score of 3–4 undergoing plastic/reconstructive surgeries. Examples include patients having: minor elective abdominal/pelvic surgery such as appendicectomy or laparoscopic cholecystectomy; minor thoracic surgery such as diagnostic thoracoscopy or video-assisted biopsy; minor vascular procedures such as vein ablation; and elective spinal surgery such as spinal fusion. For non-orthopedic surgical patients at low risk of VTE, the prophylaxis of choice is mechanical. In these patients, the risk of VTE is sufficiently high to justify the use of prophylaxis, but not enough to warrant the risk of bleeding that comes with pharmacological methods. Pharmacological prophylaxis may be indicated for patients at low risk of major bleeding with individual risk factors for VTE.

2.5 Moderate or High Thrombosis Risk

Patients who are at moderate risk for VTE include those with a modified Caprini score of 3–4 undergoing general/abdominal/pelvic surgery, or those with a score of 5–6 undergoing plastic/reconstructive surgeries. Examples include those patients undergoing major gynecological or urological surgery, major cardiac or thoracic surgery, bariatric surgery, ankle fracture repair, neurosurgical procedures, or who have sustained non-extensive trauma which does not involve the central nervous system.

High-risk patients include those with a modified Caprini score of 5 or more undergoing general/abdominal/pelvic surgery, or those with a score of 7–8 undergoing plastic/reconstructive surgeries. Examples include patients undergoing: extensive abdominal/pelvic, thoracic surgery, distal colorectal resections, or pelvic exenteration; major trauma procedures, particularly when they involve the brain or spine; acute spinal cord injuries; and cancer surgery.

For non-orthopedic surgical patients at moderate or high risk of VTE with low bleeding risk, the prophylaxis of choice is pharmacological. In selected patients for whom the risk of VTE is particularly high (multiple risk factors, surgery for active malignancy), a multimodal approach using chemical and mechanical prophylaxis is recommended. In these patients, a combination of mechanical prophylaxis such as IPC or GEC with chemical prophylaxis such as LMWH or UFH confers greater protection against VTE than either method on its own.

For non-orthopedic surgical patients at high risk of bleeding, those who have a contraindication to pharmacologic prophylaxis, or those in whom bleeding would have catastrophic consequences (neurosurgical procedures), mechanical prophylaxis alone is recommended. In this group of patients, it is recommended adding, or switching to, a form of chemical prophylaxis as soon as the bleeding risk had adequately dropped, and/or adequate hemostasis has been achieved.

2.6 Timing of Initiation

For those patients in whom VTE prophylaxis is indicated and the bleeding risk is low, mechanical methods should be instituted just prior to surgery while pharmacological agents should ideally start 2–12 h prior to surgery (depending on the pharmacokinetics of the agent chosen). The timing, particularly for pharmacological prophylaxis, should be adjusted on an individual basis according to risk factors, and the type of prophylaxis being used. An exception to this recommendation lies in the use of neuraxial anesthetic, particularly indwelling epidural catheters, or the requirement for a spinal puncture. In these patients, there should be consultation with local anesthetic expertise, with the usual practice being to avoid preoperative pharmacologic agents in these patients, and withholding postoperative administration until 6–8 h after epidural catheter removal.

2.6.1 Duration

Around the world VTE prophylaxis appears to be prescribed for an average of 10 days, however variability in the definition, or interspersed periods of immobility may justify a longer course of prophylaxis. This is particularly important given that VTE risk does not disappear on discharge/ambulation but can continue for weeks after surgery. In patients who undergo major abdominal/pelvic surgery, particularly for active malignancy, there is evidence for VTE prophylaxis with LMWH for 10–28 days post-surgery.

2.6.2 Dosing

For dosing requirements and timing of commencement, refer to product label statements, manufacturer's recommendations, and local guidelines.

LMWH is recommended as the default pharmacologic agent of choice for VTE prophylaxis. There are a number of preparations of LMWH and none have a proven advantage over the others.

2.6.3 Enoxaparin

In patients without cancer, use 40 mg subcutaneously, 2 h prior to abdominal surgery, or 12 h prior to all other surgeries. Following this, use 40 mg subcutaneously, daily, 2–72 h postoperatively once hemostasis is achieved and the bleeding risk is acceptable. In patients with cancer, use 20 mg subcutaneously, 2–4 h prior to surgery, or 40 mg subcutaneously, 10–12 h prior to surgery. Recommence 40 mg subcutaneously, daily, 6–12 h after surgery.

2.6.4 Dalteparin

Use 5000u subcutaneously, 12 h prior to surgery and restarting the same dose daily, following surgery, once hemostasis is achieved and the bleeding risk is acceptable.

2.6.5 Tinzaparin

Use 4500u subcutaneously, 12 h prior to surgery and restarting the same dose daily, following surgery, once hemostasis is achieved and the bleeding risk is acceptable.

2.6.6 Unfractionated Heparin

Low dose heparin is a viable alternative to LMWH and is the recommended agent in the setting of renal insufficiency. Give 5000u subcutaneously, at least 2 h prior to

surgery and restarting the same dose, twice daily, following surgery once hemostasis is achieved and the bleeding risk is acceptable.

All patients having LMWH or UFH should have regular monitoring of their platelet counts to detect heparin-induced thrombocytopaenia (HIT) as early as possible. Heparin-based agents are contraindicated in all patients with active HIT or a history of HIT.

2.7 Orthopedic Patients

In orthopedic patients, the risk of VTE is significant and is related to both procedure and patient-related factors. Procedure-related factors include type of anesthesia, the likelihood of immobilization, postoperative casting, and extent/duration of surgery. Patient-related factors include age >75 years, poor ambulation prior to surgery, obesity, and cardiovascular disease.

With orthopedic operations, the risk of VTE is highest for patients who have total hip/knee arthroplasties, hip fracture surgeries, hip fractures for conservative management, pelvic fractures, and multiple fractures resulting from severe trauma. The lowest risk procedures are foot/ankle fractures, and surgery or arthroscopy of tibial/shoulder/elbow. Spinal and epidural anesthetics can reduce thromboembolism in patients undergoing hip and knee surgery but other mechanical methods should also be used.

2.8 Total Hip/Knee Arthroplasty and Hip Fracture Surgery

For patients in whom the risk of bleeding is low, many surgeons advocate for the use of combined prophylaxis with a pharmacological agent in conjunction with GEC garments or IPC. The preferred agent for these patients is LMWH or one of the NOACs (non-vitamin K antagonist oral anticoagulants), particularly rivaroxaban or apixaban. In patients having hip fracture surgery, LMWH is the preferred option.

In patients with significant renal impairment, unfractionated heparin is preferred however if patients cannot tolerate subcutaneous injections, warfarin can be used. This should be continued for 10–14 days.

Aspirin is not suitable as a single agent for VTE prophylaxis but in particularly low-risk patients, it can be used after 5 days of rivaroxaban. For patients at high risk of bleeding, or in whom chemical prophylaxis is contraindicated, use mechanical methods, ideally IPC. GEC garments can be used; however, IPC has been shown to be more effective. Specific to patients with fractures, if there is a delay in surgery, recommend starting prophylaxis with LMWH or IPC as close to the time of fracture as possible.

2.9 Timing of Initiation (for Hip/Knee Surgery)

With regards to the timing of administration, LMWH and UFH should not be given close to the time of surgery with current recommendations being 12 h or more preoperatively and postoperatively. Mechanical prophylaxis should be used just prior

to surgery and continued until hospital discharge or full ambulation. In the case of combined prophylaxis, pharmacological agents can be added as soon as adequate hemostasis has been achieved, usually 12–72 h postoperatively. Factor Xa inhibitors and VKA should be started no earlier than 8–12 h postoperatively.

2.9.1 Duration

In patients with total hip/knee arthroplasty or hip fracture surgery, VTE prophylaxis is recommended for a minimum of 10–14 days and should ideally be continued for a total of 35 days. Prophylaxis should certainly be continued at least until patients are discharged home and/or ambulating fully.

In patients whom mechanical prophylaxis is being used in place of chemical prophylaxis due to bleeding risk, it should be continued for as long as tolerated by the patient, and be replaced with pharmacologic prophylaxis as soon as it is safe to do so.

2.9.2 Dosing

For dosing requirements and timing of commencement, refer to product label statements, manufacturer's recommendations, and local guidelines.

2.9.3 Enoxaparin

In total hip arthroplasty give 30 mg subcutaneously, twice daily or 40 mg, once daily, started at least 12 h before, or after surgery. For total knee arthroplasty use 30 mg subcutaneously every 12 h, started at least 12 h before, or after surgery. Please note that dose adjustment is advised with obesity and/or renal insufficiency.

2.9.4 Unfractionated Heparin

Use 5000u subcutaneously twice daily. Again, dose adjustment is advised with obesity.

2.9.5 Warfarin

Patients should be commenced on 5 mg orally, once daily, 12–24 h after surgery. The target INR should be a range between 2 and 3, therefore many patients will need adjusted dosing.

2.9.6 Rivaroxaban

Use 10 mg orally, once daily, 6–10 h after surgery.

2.9.7 Apixaban

Use 2.5 mg orally, twice daily, 12 h after surgery.

2.10 Lower Extremity Injuries Requiring Immobilization

In most patients with lower extremity injuries requiring immobilization, use LMWH. In younger patients without significant risk factors, VTE prophylaxis can be avoided all together if early ambulation is feasible. If prophylaxis is given, it should be continued for the duration of immobilization.

2.11 Multiple Trauma

In patients without intracranial bleeding in whom hemorrhage has been controlled, use LMWH initiated within 36 h of injury. In the subset of these patients in whom anticoagulation is precluded, use IPC. Patients who receive LMWH or IPC should continue treatment until they are fully ambulant. The routine use of IVC filters is not recommended in patients without proof of DVT.

2.12 Pregnancy and VTE Prophylaxis

The risk of venous thromboembolism (VTE) is increased in all trimesters of pregnancy, and especially in the postpartum period. Although most women do not require prophylaxis, those who are considered to be at the greatest risk are generally targeted for VTE prevention.

Antepartum pharmacologic prophylaxis is considered for patients with a history of a single idiopathic, pregnancy-associated, or estrogen-associated VTE, and in those with a history of multiple VTEs, regardless of the cause. Pharmacologic prophylaxis is also considered for patients with a known thrombophilia and a history of VTE and for patients with certain “high risk” thrombophilias plus a family history of VTE.

Women who are hospitalized antenatally for nondelivery reasons, the same criteria for pharmacologic thromboprophylaxis should be used as in the outpatient setting.

Women in whom the decision is made to administer pharmacologic prophylaxis, heparin-based regimens are safer than oral anticoagulants. Therefore, low molecular weight heparin rather than unfractionated heparin is recommended provided the patient does not have renal insufficiency.

Postpartum VTE prophylaxis is initiated when a history of prior VTE (single or multiple) regardless of the provoking factor (transient or persistent) and in a subset of patients with inherited thrombophilia without a personal history of VTE. In such a situation, thromboprophylaxis should be continued for 6 weeks to 3 months. Following the cesarean section, thromboprophylaxis is continued until the patient is ambulatory.

2.13 Periprocedural Management of Antithrombotic Therapy and Bridging Anticoagulation

The periprocedural management of anticoagulants in patients requiring surgery is a very common problem. Decision-making in these patients requires careful balancing of risk of VTE when anticoagulation is ceased with the risk of bleeding during, and after, surgery. In reality, two decisions are required: firstly, whether the patient's longstanding anticoagulation needs to be ceased prior to surgery; and secondly whether temporary, or bridging, anticoagulation is needed in the perioperative period.

At present, there is no validated scoring system for the risk of bleeding related to procedures. One proposed mechanism is the use of a two-tiered system separating procedures into high and low bleeding risk. Procedures classified as high-risk are major operations lasting >45 min, vascular procedures, cardiothoracic procedures, major orthopedic surgeries, prostate/bladder surgery, and extensive cancer operations. Low-risk procedures include most operations less than 45 min, diagnostic gastrointestinal procedures, dental procedures, dermatological procedures, and ophthalmological surgeries.

If bridging therapy is being administered, usually in the form of therapeutic-dose LMWH, the final dose should be administered 24 h prior to the procedure. In the case of intravenous heparin as bridging therapy, the infusion should be ceased 4 h prior to the procedure. In terms of resuming bridging therapy, following minor procedures, LMWH should be recommenced within 24 h assuming adequate hemostasis has been achieved. For major surgery, or procedures at high risk of bleeding, there are three suggested options:

- delaying LMWH for 2–3 days after surgery,
- using low-dose LMWH within 24 h of the procedure,
- avoiding bridging therapy altogether if the VTE risk for the patient allows it.

2.14 Summary

Patients at highest risk of VTE include patients who are critically ill, patients with cancer or stroke, and patients with multiple risk factors for VTE including pregnancy, heart failure, myocardial infarction, old age (>75 years), previous VTE, prolonged immobility, renal failure, obesity, and inherited or acquired hypercoagulable states.

Special populations require an individualized approach to thromboprophylaxis during acute hospitalization. These include patients with heparin-induced thrombocytopenia, patients undergoing neuraxial anesthesia, patients with stroke or cancer, patients who are traveling for extended periods, and patients who are pregnant.

Each institution should develop a formal strategy for the prevention of VTE. This should aim to increase compliance while maintaining an equitable health care delivery system.