Prophylaxis of Venous Thromboembolism in Ankle and Foot Surgeries

Profilaxia do tromboembolismo venoso nas cirurgias do tornozelo e do pé

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Abstract

Venous thromboembolism (VTE) is among the most feared complications by orthopedists both for due to its potentially lethal outcome and the uncertainties related to its prevention. Despite the vast literature on VTE prevention in major orthopedic surgeries, little is known about it in ankle and foot procedures. In orthopedics, adequate thromboprophylaxis requires a careful assessment of the thrombotic and hemorrhagic risks based on the procedure to be performed, as well as and knowledge on anticoagulant agents. The presentis review has the goal of assessing the risk of developingdiscusses VTE risk assessment, the modalities of thromboprophylaxis modalities, and the drugs used, with an emphasis on foot and ankle surgeries.

Keywords
- thrombosis
- orthopedics
- surgery
- foot
- ankle
- pre-exposure prophylaxis

Resumo

O tromboembolismo venoso (TEV) é uma das complicações mais temidas pelos ortopedistas, tanto pelo seu desfecho potencialmente letal quanto pelas incertezas relacionadas àa sua prevenção. Apesar da vasta literatura existente sobre a prevenção de TEV nas grandes cirurgias ortopédicas, pouco se sabe sobre sua prevenção nas cirurgias do tornozelo e do pé. Uma adequada prescrição da tromboprofilaxia em ortopedia exige criteriosa avaliação dos riscos trombóticos e hemorrágicos mediante com base no tipo de cirurgia a ser realizada, além do conhecimento sobre os anticoagulantes. Esta revisão tem como objetivos abordar a avaliação do risco de desenvolver TEV, as modalidades de tromboprofilaxia, e os fármacos utilizados, tendo como ênfase as cirurgias do pé e do tornozelo.

Palavras-chave
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- ortopedia
- cirurgia
- pé
- tornozelo
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Introduction

Venous thromboembolism (VTE) is the main cause of preventable death at hospital environments,[1] and one of the most known and feared complications of orthopedic surgeries. It usually presents as deep-vein thrombosis (DVT) and pulmonary thromboembolism (PTE). Deep-vein thrombosis can be complicated by postthrombotic syndrome (PTS) and PTE; in turn, PTE may result in chronic thromboembolic pulmonary hypertension (CTHP) and death.[2] The incidence of VTE in the general population is of approximately 1 to 2:1,000 people per year.[3]

Most data on VTE prevention in orthopedics relates to major orthopedic surgeries, such as knee and hip arthroplasties.[4–6] The main guidelines on the subject refer to objective recommendations for surgical prophylaxis,[1,4,7] including clear definitions on the type of drug and the duration of the treatment.

For surgeries below the level of the knee, however, the approaches and recommendations remain unclear. The guideline of the American College of Chest Physicians (ACCP) suggests not using pharmacological thromboprophylaxis for isolated lesions below the knee.[4] Similarly, the American Academy of Orthopedic Surgeons states that there is no specific guideline for prophylaxis in ankle and foot surgeries.[8] Another consensus establishes guidelines related to risk factors, but it does not define objective parameters for pharmacological thromboprophylaxis or the ideal moment to start it.[9] The most recent reccomendation of the American Society of Hematology does not mention ankle and foot injuries at all.[7]

The present review aims to present data on the incidence of VTE in ankle and foot surgeries, to identify the main risk factors in these scenarios, and to discuss the tools for the prediction of the risk and the alternatives for thromboprophylaxis.

Incidence

Lower-limb DVT (LL-DVT) rarely occurs after an ankle and foot orthopedic intervention; this is in contrast with major hip and knee surgeries, in which the incidence of LL-DVT ranges from 40% to 60%.[1]

In a meta-analysis with 43,381 patients, the incidence of symptomatic VTE was of 0.6% (95% confidence interval [95% CI]: 0.4% to 0.8%) in patients undergoing miscellaneous foot or ankle procedures, including cases of trauma or elective surgeries, with no thromboprophylaxis. Among those receiving some type of prophylaxis, the incidence of VTE was of 1.0% (95%CI: 0.2% to 1.7%),[9] possibly because these patients were in a more severe condition and/or had more risk factors for VTE.

In a retrospective cohort[10] with 22,486 patients undergoing ankle and/or foot surgery between 2008 and 2011, 173 (0.8%) patients had symptomatic VTE within 6 months following the procedure.[10] When assessed according to surgical site and the occurrence of thrombosis, 65.6% of VTE cases were associated to hindfoot and ankle surgeries, whereas 11.1% were related to midfoot surgeries, and 26.7%, to forefoot procedures.

It is known that rupture of the Achilles tendon is the foot-and-ankle condition most often associated with VTE. Data from a meta-analysis[9] show that in 1,060 patients with rupture of the Achilles tendon clinically assessed for VTE, the condition was confirmed in a total of 74 (7%) subjects.[9] From 1997 to 2015, 28,546 patients with acute rupture of the Achilles tendon submitted to surgical or non-surgical treatment were assessed for VTE.[11] Among them, 389 (1.36%) were diagnosed with thrombosis, including 278 (0.97%) cases of LL-DVT and 138 (0.48%) cases of PTE. In another prospective cohort study[12] with 291 patients with acute rupture of the Achilles tendon, 14 patients (4.81%) were diagnosed with VTE within 33 days after surgery.[12]

It is worth noting that most thromboembolic events reported in the aforementioned studies were asymptomatic, diagnosed by postoperative screening imaging tests alone. Therefore, most of these events are of little or no clinical relevance. For instance, in a prospective cohort study[13] including 114 elective foot and/or ankle surgeries performed on 111 patients, 29 subjects (25.4%) had DVT, but most cases (20/29, or 68.9%) were diagnosed on a screening ultrasound 2 weeks after surgery.[13] In another prospective cohort study,[14] 216 patients undergoing miscellaneous foot or ankle surgery were screened for DVT using an ultrasound of the lower limbs 2 to 6 weeks after surgery. The incidence of VTE was of 5.09% (11/216), and 3/11 patients had asymptomatic DVT.[14] Thus, since most asymptomatic venous thromboembolic events have little clinical repercussion and less than 10% of the cases of symptomatic distal LL-DVT present proximal extension,[15] VTE screening using ultrasound in asymptomatic patients undergoing surgery below the level of the knee should not be routinely performed. This test should be indicated for subjects with clinical suspicion of DVT.[9]

Still, the great difficulty in determining the risk of developing VTE in patients with injuries below the level of the knee stems from the following: 1) most studies are based on case series; 2) these studies provide inadequate information on the eventual use of thromboprophylaxis; 3) due to the low incidence, the number of VTE patients in these studies does not enable sufficiently robust conclusions;[16] and 4) the scarcity of studies assessing the impact of associated risk factors on the occurrence of VTE in patients submitted to surgical procedures below the level of the knee.[9,17–19]

Risk factors

Orthopedic surgeries, especially major hip and knee procedures, are high-risk interventions for VTE.[3] However, even though the thrombotic risk is lower, ankle and foot procedures usually require some time of restricted lower-limb support on the ground and/or immobilization, adding to the risk of developing VTE.[9,17]

Immobilization of a lower limb to prevent contraction of the calf muscles has been shown as an important isolated risk factor for VTE after procedures below the level of the knee.[20,21] In addition, it is known that the longer the immobilization time, the greater the risk of developing VTE.[22] Moreover, the

lack of ground support for the lower limb is associated with an increased risk of developing VTE, and, along with immobilization, it adds up as a major risk factor.[23] Immobilization with no support for a period of 2 to 8 weeks is associated with a 9-fold higher risk of developing VTE (odds ratio [OR]: 9.0; 95%CI: 1.8 to 44.3) compared to immobilization for a shorter period of time.[10] Although some authors consider that support of the lower limb on the ground enables the termination of the pharmacological prophylaxis[14] because the support provides greater mobility to the patient, this measure still requires additional studies to prove its effectiveness.

To date, the main risk factor for the development of VTE in patients submitted to procedures below the level of the knee is the history of previous thrombosis,[9–11,24] although this is considered a minor risk factor when the surgeon assesses an orthopedic patient.[17,25] The identification of this risk factor is considered the only formal indication to prescribe pharmacological thromboprophylaxis in this population.[4]

Other high risk factors for the development of VTE in ankle and foot surgeries are obesity (body mass index [BMI] above 30 kg/m^2),[9,10,18,26] age over 50 years,[9–11,17,26] and use of estrogenic compounds in women. Oral contraceptives and hormone-replacement therapy are risk factors for the development of classic VTE in the general population, being identified in most patients with VTE after ankle and foot surgeries or immobilization.[9,10,17,19] In addition, genetic risk factors, such as factor V Leiden, non-O blood type or elevated factor VIII levels must be considered when assessing the risk of developing VTE in foot and ankle surgeries, since they are known risk factors for other orthopedic procedures.[21,27,28]

An interesting question regarding ankle and foot conditions is the impact of the surgical site on the development of VTE. Patients surgically treated for injuries to the Achilles tendon appear to be those most at risk, with an incidence of VTE ranging from 1.36% to 7.00%.[9,11,18,19] The incidence of VTE also appears to be increased in ankle (1.0%),[26] hindfoot (0.14% to 1.1%)[18,29] and forefoot (0.03% to 4.00%) conditions.[14,26,30]

Risk-assessment tools

A major challenge for orthopedists treating ankle and foot injuries is to define which subjects are at greatest risk of developing VTE and, therefore, could benefit from pharmacological thromboprophylaxis. Due to the low incidence of VTE in ankle and foot surgeries and the miscellaneous VTE-related risk factors and comorbidities, this is a difficult task, since complications resulting from VTE (mainly from LL-DVT), such as PTE and PTS, although rare, are extremely harmful.[10]

Several tools have been developed to assess the patient's individual risk of developing VTE. Saragas et al.[14] analyzed the Thrombosis Risk Factor Assessment form, in which risk factors are scored and added to quantify the risk of developing VTE. These authors evaluated 216 patients with ankle and foot injuries treated by surgery, from hindfoot deformities to fractures and correction og bilateral halux valgus. They identified that the average score of the group that developed VTE was 7.7 (range, 4 to 13 points), with 90.9% of these patients scoring 5 or more points. Thus, they recommend a score of 5 as the cutoff point to initiate pharmacological thromboprophylaxis in patients undergoing ankle and foot orthopedic surgeries.

Another tool used in the assessment of the risk of developing VTE is from the National Institute for Health and Care Excellence (NICE), in the United Kingdom.[31] One of the advantages of this tool is its ability to assess all inpatients, not surgical subjects alone. In addition, the tool analyzes three important points: patient mobility, the risk factors for the development of VTE, and the risk of developing bleeding. The usefulness of this tool has been confirmed in prospective studies including patients with ankle fractures, injuries to bones of the foot, and ruptures of the Achilles tendon who received an immobilizing plaster cast or were surgically treated.[12,32] Nevertheless, despite the great advantage of considering the risk of developing bleeding in the analysis, the concept of mobility is not well defined, which can lead to misinterpretations and wrong decisions.

The Caprini score, which was developed for surgical patients in general[25,33] analyzes patient- and procedure-related risk factors; a total score $\geq$ 3 points indicates high risk (►**Figure 1**).[25] Although it has not yet been validated for general orthopedic surgery, the Caprini score has already been validated for some specific orthopedic surgeries, such as hip fractures,[34] hip and knee arthroplasties,[35] and general fractures.[36] In addition, it has also been validated for other surgical specialities, such as plastic surgery,[37,38] ear, nose and throat surgery,[39] and oncologic gynecology surgery.[40]

Since the Caprini score has already been validated in several surgical areas, it seems to be the most reliable and comprehensive for general orthopedic surgeries. However, the concept of assessment of the thrombotic risk in general orthopedic surgeries, and not in hip and knee surgeries alone, needs to be disseminated in the clinical practice. This will improve the prediction of the risk of developing VTE and result in more suitable thromboprophylaxis protocols for different groups at a higher risk of developing thrombosis.

Thromboprophylaxis modalities

Mechanical thromboprophylaxis

Mechanical thromboprophylaxis is based on gradual compression of muscles over veins, bolstering venous return.[16] In orthopedic surgeries, mechanical thromboprophylaxis can be performed using intermittent pneumatic compression devices (IPCDs) and elastic compression stockings.[41] In a recent meta-analysis[42] with 16,164 patients, IPCDs were effective in reducing VTE in hospitalized subjects when compared to placebo, with a relative risk (RR) of developing DVT of 0.43 (95%CI: 0.36 to 0.52) and an RR of developing PTE of 0.48 (95%CI: 0.33 to 0.69).[42] As advantages, these devices do not have the adverse effects presented by anticoagulant drugs, such as bleeding, nor do they require

Each risk factor represents 1 point			
Age 41-60 years		Acute myocardial infarction	
Swollen legs (current)		Congestive heart failure (<1 month)	
Varicose veins		History of prior major surgery (<1 month)	
Minor surgery planned		History of inflammatory bowel disease	
Sepsis (<1 month)		Abnormal pulmonary function (COPD)	
Obesity (BMI > 25)		Serious lung disease including pneumonia (<1 month)	
Medical patient currently at bed rest			
Oral contraceptive or hormone replacement therapy			
Pregnancy os postpartum			
History of unexplained stillborn infant, recurrent spontaneous abortion (≥3), premature birth with toxemia or growth-restricted infant			
Other risk factors			

Each risk factor represents 5 points	
Stroke (<1 month)	
Multiple trauma (<1 month)	
Elective major lower extremity arthroplasty	
Hip, pelvis or leg fracture (<1 month)	
Acute spina nord injury (paralysis) (<1 month)	

Each risk factor represents 2 points	
Age 61-74 years	
Malignancy (present or previous)	
Major surgery, including laparoscopic surgery (<45 minutes)	
Immobilizing plaster cast (<1 month)	
Central venous access	
Arthroscopic surgery	
Patient confined to bed (>72 hours)	

Each risk factor represents 3 points	
Age 75 years or older	
History of DVT/PE	
Family history of thrombosis	
Positive Factor V Leiden	
Positive Prothrombin 20210A	
Positive Lupus anticoagulant	
Heparin-induced thrombocytopenia (HIT)	
Elevated serum homocysteine	
Elevated anticardiolipin antibodies	
Other congenital or acquired thrombophilia	

Fig. 1 Caprini score. Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; DVT, deep venous thrombosis; h, hours; LLs, lower limbs; VTE, venous thromboembolism. Source: Adapted from Caprini JA. Risk assessment as a guide for the prevention of the many faces of venous thromboembolism. Am J Surg 2010;*199* (1 Suppl):S3–10[25].

laboratory monitoring.[43] However, they present an important disadvantage, that is, low postoperative adherence, since many patients undergoing ankle and foot surgery are immobilized, which prevents using these devices on the operated limb. Thus, IPCDs are reserved for the contralateral limb during hospitalization. It should be noted that the simplest mechanical method for the prevention of VTE is early walking.[22,43]

Pharmacological thromboprophylaxis

The use of drugs for VTE prophylaxis (pharmacological prophylaxis) in ankle and foot surgeries is more widespread than mechanical prophylaxis. This is due to the lower availability of compression devices, the costs of the compressive stockings, the lower ease of use and local factors, such as the need for lower-limb immobilization after these procedures.

The drugs approved for thromboprophylaxis in orthopedic surgeries include acetylsalicylic acid (ASA), heparins (both unfractionated heparin [UFH] and low-molecular-weight heparin [LMWH]), direct-acting oral anticoagulants, and warfarin. If these medications are used before surgery, it is important to observe the necessary withdrawal period prior to the procedure to avoid bleeding (►**Table 1**). Each of these drugs acts at a certain stage of the coagulation pathway, inhibiting different factors (►**Figure 2**).

Acetylsalicylic acid inhibits cyclooxygenase, decreasing the synthesis of prostaglandins and thromboxane, resulting in inhibition of platelet aggregation. It is an easily accessible, inexpensive drug with a long history of use. Although the literature is controversial on recommending ASA as a single agent for thromboprophylaxis, recent studies[44] demonstrate that it can be used after a short five-day cycle of a direct-acting oral anticoagulant (rivaroxaban) in hip and knee arthroplasties.[45,46] Studies on ASA as a thromboprophylaxis agent in ankle and foot surgeries are still scarce, as noted in a recent consensus on the subject.[17]

Unfractionated heparin and LMWH inhibit several coagulation proteases (►**Figure 2**). Unfractionated heparin acts indirectly, binding to antithrombin (a natural anticoagulant) and bolstering its inhibitory action on various coagulation proteases, including thrombin (factor IIa) and factor Xa.[41] Low-molecular-weight heparin results from the partial digestion of UFH, and it presents a reduced ability to bind to other plasma proteins and a greater specificity against factor Xa. Both forms are effective, safe, and administered by subcutaneous route. However, LMWH is easiest to use (single daily dose) and related with a lower risk of heparin-induced thrombocytopenia and lower osteopenia-inducing effects.[47] Thus, LMWH is the most recommended anticoagulant for VTE prophylaxis in ankle and foot surgeries, even according to the most recent guidelines;[9,17] so far, LMWH is the drug of choice for both surgical and non-surgical patients at risk of developing VTE as long as they are immobilized.[17]

Direct-acting oral anticoagulants (DAOAs) are a new class of drugs specifically targeted to counter factor Xa (apixaban, rivaroxaban, edoxaban, betrixaban) or factor IIa (dabigatran). Their main advantage is the lack of requirement for periodic monitoring through laboratory tests or parenteral/subcutaneous administration. In addition, they are safer drugs compared to warfarin regarding severe bleeding, even though DAOAs are more commonly related to gastrointestinal hemorrhage.

Rivaroxaban, apixaban and dabigatran have been approved for VTE prophylaxis in knee and hip arthroplasties.[48,49] Still, none of these drugs were approved for use in proximal femur and hip fractures.[4,7,50] Despite the approval of the use of DAOAs in major orthopedic surgeries, current data refer only to rivaroxaban for VTE prophylaxis in

Table 1 Drugs most used for the prophylaxis of venous thromboembolism in orthopedic surgeries

Drug	Dose	Time for withdrawal from the preoperative therapy	Notes
Acetylsalicylic acid	100 mg/day, single dose, orally	5 to 10 days before surgery	It should not be used as a monotherapy. Use as extended therapy after 5 days of rivaroxaban in patients with low thrombotic risk
LMWH - enoxaparin	40 mg/day, single dose, subcutaneous	12 hours if low risk of bleeding; 24 hours if high risk of bleeding	Start 12 hours after surgery
LMWH - dalteparin	5,000 IU/day, single dose, subcutaneous	12 hours if low risk of bleeding; 24 hours if high risk of bleeding	Start 12 hours after surgery
LMWH - nadroparin	38 IU of anti-Xa per kilogram of body weight (0.2 to 0.4 mL); increase by 50% on the fourth postoperative day (0.3 to 0.6 mL).	12 hours if low risk of bleeding; 24 hours if high risk of bleeding	Start 12 hours after surgery
Rivaroxaban	10 mg/day, orally	24 hours if low risk of bleeding; 48 hours if moderate or high risk of bleeding, or in elderly patients	Start $>$ 6 hours after surgery
Dabigatran	220 mg/day, orally	48 to 72 hours if normal renal function; minimum of 5 days for major orthopedic surgeries	Start with 110 mg 1 to 4 hours after surgery, followed by 220 mg once a day
Apixaban	2.5 mg orally, twice a day	24 hours if low risk of bleeding; 48 hours if moderate or high risk of bleeding	Start $\geq$ 12 hours after surgery
Warfarin	In most cases, 5-10 mg/day, orally	3 to 5 days	After the third day, adjust per INR with a therapeutic target of 1.5 to 2.5. Start 12 to 24 hours after surgery. We suggest a validated warfarin dose-adjustment nomogram

Abbreviations: INR, international normalized ratio; LMWH, low-molecular-weight heparin.

surgeries below the level of the knee. In a randomized study with 3,604 patients treated with 40 mg of subcutaneous enoxaparin or 10 mg of oral rivaroxaban, both administered once a day, rivaroxaban was more effective in preventing VTE than enoxaparin (RR: 0.25; 95%CI: 0.09 to 0.75), with no increased risk of bleeding.[51]

Warfarin is a vitamin K antagonist that inhibits the synthesis of calcium-dependent coagulation factors (factors II, VII, IX and X), as well as proteins C, S and Z.[41] The recommended dose varies, mostly ranging from 5 mg to 10 mg a day during the postoperative period.[41] Although cheap and widely available, warfarin should only be used as a thromboprophylactic agent in orthopedic surgeries when heparins or DAOAs are not available. Warfarin requires continuous monitoring of prothrombin time and its derivative, the international normalized ratio (INR), which should have a target value between 2 and 3 in order to be considered adequate for VTE prevention. Since its average half-life is of 2.5 days, the administration of warfarin must be terminated at least 3 days before surgery.[52]

Duration of the thromboprophylaxis

Pharmacological thromboprophylaxis must started 12 hours after surgery if the patient has no active bleeding or high risk of developing bleeding.[53]

The duration of the pharmacological thromboprophylaxis is well defined in certain orthopedic procedures, such as major orthopedic surgeries (hip and knee arthroplasties), in which postoperative anticoagulation must be performed for at least 10 to 14 days, and can reach up to 35 days.[4] Anticoagulation may be suspended until the patient starts to walk, as long as it has been performed for at least 10 to 14 days. However, the simple replication of these time periods in ankle and foot surgeries is not adequate.

The use of some sort of immobilization in the treatment of ankle and foot conditions is associated with VTE in 4.3% to 40.0% of patients, regardless of the fact that they have been treated surgically or clinically.[54] The lack of lower-limb support on the ground and the use of a partial support are risk factors for the development of DVT.[23,55] As a result, immobilization and the fact that the foot is not resting on the ground must be considered when defining the duration of the prophylaxis.

Specialists usually agree that prophylaxis must be sustained throughout the immobilization period,[17] or at least while the patient remains with no support, but immobilized. Prophylaxis may be terminated as soon as the treated lower limb is supported or after the removal of the immobilization even without support, which will enable the active contraction of calf muscles, reducing the risk of developing VTE.[14]

Complications

The major debate about prophylaxis lies on the potential complications resulting from the thr administration of anticoagulant agents, especially in major surgeries. However, information on the occurrence of pharmacological prophylaxis-related complications in ankle and foot surgeries is scarce.

A possible anticoagulant-related complication in lower-limb surgery is bleeding, which occurs in 0.3% to 1% of cases.[49,56] The factors associated with increased postoperative bleeding in this group of patients are revision surgeries, perioperative bleeding greater than expected, aggressive soft-tissue dissection, recent gastrointestinal or genitourinary bleeding, concomitant anti-platelet therapy, and advanced kidney disease.[57]

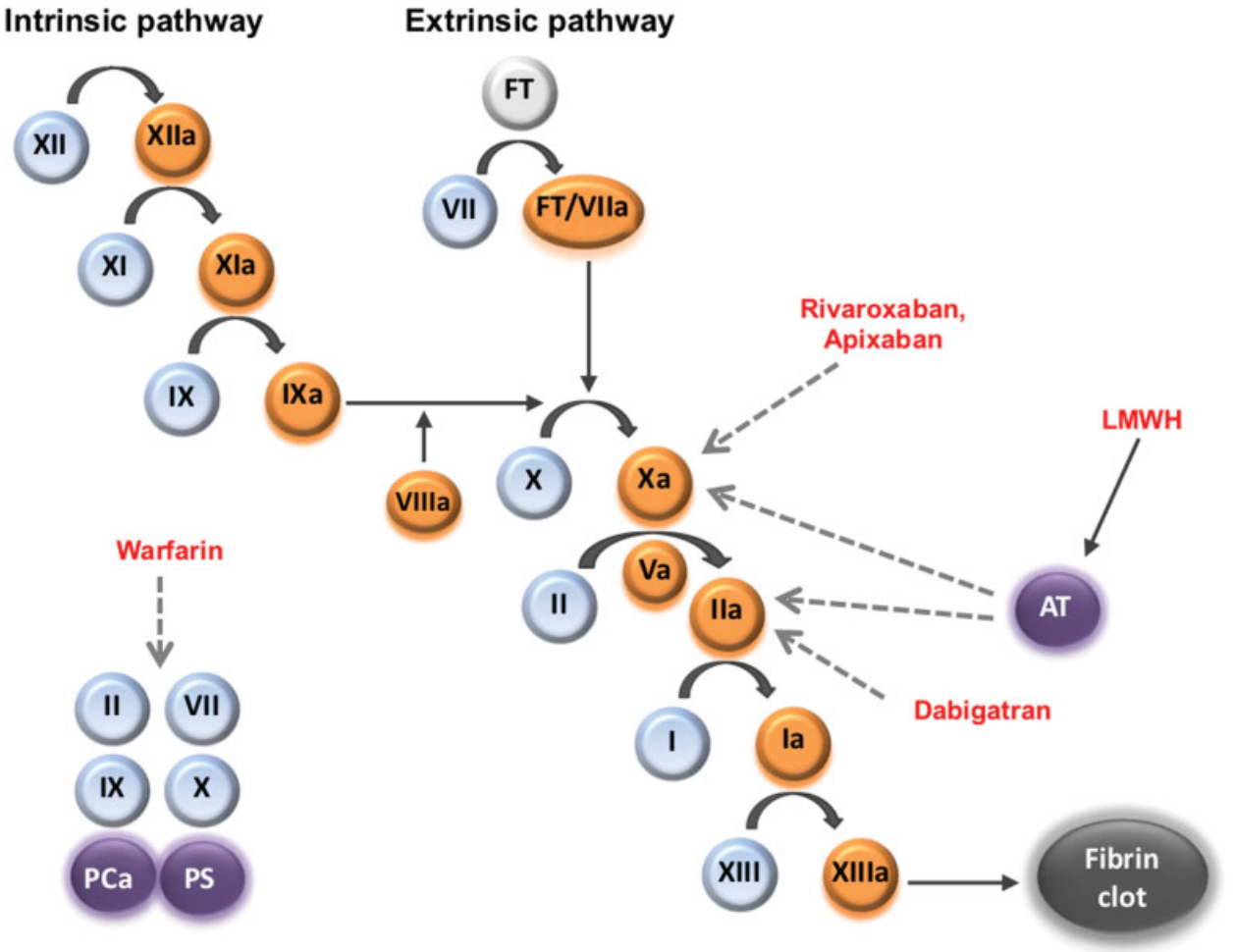

Fig. 2 Schematic representation of coagulation control and sites of activit of the main anticoagulants. Abbreviations: a, activated; AT, antithrombin; FT, tissue factor; LMWH: low-molecular-weight heparin.

Other potential local complications are bruises,[49] which can result in surgical wound dehiscence and infection, often with dramatic presentation in ankle and foot surgeries. In addition, heparin-induced thrombocytopenia, a complication considered severe due to the increased risk of thrombotic events, is more common in surgical patients, with an incidence rate of 0.20% to 0.36% in subjects treated with LMWH.[58,59]

Final Considerations

Venous thromboembolism is a complication of the treatment of ankle and foot conditions. Although its incidence is lower compared to hip and knee surgeries, robust studies are still required to assess the concomitant risk factors that interact and increase the risk of developing VTE. The assessment of risk factors associated with the type of orthopedic surgery should be individualized to substantiate and direct the focus of the thromboprophylaxis on groups at a higher risk. The current studies lack evidence for a universal thromboprophylaxis recommendation in ankle and foot surgeries.

Once pharmacological thromboprophylaxis is indicated, LMWH (usually enoxaparin) is the anticoagulant agent of choice for VTE prophylaxis in patients submitted to ankle and foot procedures. The use of DAOAs as thromboprophylactic agents in orthopedic surgeries in injuries below the level of the knee still requires further studies. To date, only rivaroxaban has been shown to be effective and safe, and its use has been approved. According to current guidelines, other DAOAs must be used only if the patient refuses heparin and rivaroxaban is unavailable. Thromboprophylaxis must be maintained throughout the period, with no limb support or immobilization, since these are recognized risk factors for the development of VTE.

Future studies should focus on the interaction of other risk factors for the development of VTE concomitantly with ankle and foot orthopedic procedures, as well as on the validation and improvement of risk-assessment tools and their automation. This will enable the identification of patients at the highest risk, resulting in an adequate indication of prophylaxis to reduce the costs and complications.

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Conflicts of Interests
The authors have no conflict of interests to declare.

References

1 Geerts WH, Bergqvist D, Pineo GF, et al. Prevention of venous thromboembolism: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest 2008;133(6 Suppl):381S–453S

2 Naess IA, Christiansen SC, Romundstad P, Cannegieter SC, Rosendaal FR, Hammerstrøm J. Incidence and mortality of venous thrombosis: a population-based study. J Thromb Haemost 2007;5 (04):692–699

3 Anderson FA Jr, Spencer FA. Risk factors for venous thromboembolism. Circulation 2003;107(23, Suppl 1):I9–I16

4 Falck-Ytter Y, Francis CW, Johanson NA, et al. Prevention of VTE in orthopedic surgery patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012; 141(2 Suppl):e278S–e325S

5 Dai WL, Lin ZM, Shi ZJ, Wang J. Venous Thromboembolic Events after Total Knee Arthroplasty: Which Patients Are at a High Risk? J Knee Surg 2020;33(10):947–957

6 Senay A, Trottier M, Delisle J, et al. Incidence of symptomatic venous thromboembolism in 2372 knee and hip replacement patients after discharge: data from a thromboprophylaxis registry in Montreal, Canada. Vasc Health Risk Manag 2018;14:81–89

7 Anderson DR, Morgano GP, Bennett C, et al. American Society of Hematology 2019 guidelines for management of venous thromboembolism: prevention of venous thromboembolism in surgical hospitalized patients. Blood Adv 2019;3(23):3898–3944

8 Jacobs JJ, Mont MA, Bozic KJ, et al. American Academy of Orthopaedic Surgeons clinical practice guideline on: preventing venous thromboembolic disease in patients undergoing elective hip and knee arthroplasty. J Bone Joint Surg Am 2012;94(08):746–747

9 Calder JD, Freeman R, Domeij-Arverud E, van Dijk CN, Ackermann PW. Meta-analysis and suggested guidelines for prevention of venous thromboembolism (VTE) in foot and ankle surgery. Knee Surg Sports Traumatol Arthrosc 2016;24(04):1409–1420

10 Richey JM, Ritterman Weintraub ML, Schuberth JM. Incidence and Risk Factors of Symptomatic Venous Thromboembolism Following Foot and Ankle Surgery. Foot Ankle Int 2019;40(01):98–104

11 Pedersen MH, Wahlsten LR, Grønborg H, Gislason GH, Petersen MM, Bonde AN. Symptomatic Venous Thromboembolism After Achilles Tendon Rupture: A Nationwide Danish Cohort Study of 28,546 Patients With Achilles Tendon Rupture. Am J Sports Med 2019;47(13):3229–3237

12 Blanco JA, Slater G, Mangwani J. A Prospective Cohort Study of Symptomatic Venous Thromboembolic Events in Foot and Ankle Trauma: The Need for Stratification in Thromboprophylaxis? J Foot Ankle Surg 2018;57(03):484–488

13 Sullivan M, Eusebio ID, Haigh K, Panti JP, Omari A, Hang JR. Prevalence of Deep Vein Thrombosis in Low-Risk Patients After Elective Foot and Ankle Surgery. Foot Ankle Int 2019;40(03): 330–335

14 Saragas NP, Ferrao PNF, Saragas E, Jacobson BF. The impact of risk assessment on the implementation of venous thromboembolism prophylaxis in foot and ankle surgery. Foot Ankle Surg 2014;20 (02):85–89

15 Parisi R, Visonà A, Camporese G, et al. Isolated distal deep vein thrombosis: efficacy and safety of a protocol of treatment. Treatment of Isolated Calf Thrombosis (TICT) Study. Int Angiol 2009;28(01):68–72

16 Chien BY, Dixon T, Guss D, DiGiovanni C. Venous Thromboembolism Disease Prophylaxis in Foot and Ankle Surgery. Orthop Clin North Am 2018;49(02):265–276

17 Fleischer AE, Abicht BP, Baker JR, Boffeli TJ, Jupiter DC, Schade VL. American College of Foot and Ankle Surgeons' clinical consensus statement: risk, prevention, and diagnosis of venous thromboembolism disease in foot and ankle surgery and injuries requiring immobilization. J Foot Ankle Surg 2015;54(03):497–507

18 Ahmad J, Lynch MK, Maltenfort M. Incidence and Risk Factors of Venous Thromboembolism After Orthopaedic Foot and Ankle Surgery. Foot Ankle Spec 2017;10(05):449–454

19 Mangwani J, Sheikh N, Cichero M, Williamson D. What is the evidence for chemical thromboprophylaxis in foot and ankle surgery? Systematic review of the English literature. Foot 2015; 25(03):173–178

20 Rosendaal FR. Venous thrombosis: a multicausal disease. Lancet 1999;353(9159):1167–1173

21 van Adrichem RA, Debeij J, Nelissen RG, Schipper IB, Rosendaal FR, Cannegieter SC. Below-knee cast immobilization and the risk of venous thrombosis: results from a large population-based case-control study. J Thromb Haemost 2014;12(09):1461–1469

22 Healy B, Beasley R, Weatherall M. Venous thromboembolism following prolonged cast immobilisation for injury to the tendo Achillis. J Bone Joint Surg Br 2010;92(05):646–650

23 Riou B, Rothmann C, Lecoules N, et al. Incidence and risk factors for venous thromboembolism in patients with nonsurgical isolated lower limb injuries. Am J Emerg Med 2007;25(05): 502–508

24 Nemeth B, Timp JF, van Hylckama Vlieg A, Rosendaal FR, Cannegieter SC. High risk of recurrent venous thrombosis in patients with lower-leg cast immobilization. J Thromb Haemost 2018;16(11):2218–2222

25 Caprini JA. Risk assessment as a guide for the prevention of the many faces of venous thromboembolism. Am J Surg 2010;199(1, Suppl)S3–S10

26 Huntley SR, Abyar E, Lehtonen EJ, Patel HA, Naranje S, Shah A. Incidence of and Risk Factors for Venous Thromboembolism After Foot and Ankle Surgery. Foot Ankle Spec 2019;12(03):218–227

27 van Adrichem RA, Nelissen RG, Schipper IB, Rosendaal FR, Cannegieter SC. Risk of venous thrombosis after arthroscopy of the knee: results from a large population-based case-control study. J Thromb Haemost 2015;13(08):1441–1448

28 Zhou X, Qian W, Li J, et al. Who are at risk for thromboembolism after arthroplasty? A systematic review and meta-analysis. Thromb Res 2013;132(05):531–536

29 Jameson SS, Augustine A, James P, et al. Venous thromboembolic events following foot and ankle surgery in the English National Health Service. J Bone Joint Surg Br 2011;93(04):490–497

30 Radl R, Kastner N, Aigner C, Portugaller H, Schreyer H, Windhager R. Venous thrombosis after hallux valgus surgery. J Bone Joint Surg Am 2003;85(07):1204–1208

31 Department of Health VTE risk assessment tool. National Institute of Health and Care Excellence (NICE), published date: 21 March 2018. Available from: https://www.nice.org.uk/guidance/ng89/chapter/Recommendations#risk-assessment

32 Haque S, Bishnoi A, Khairandish H, Menon D. Thromboprophylaxis in Ambulatory Trauma Patients With Foot and Ankle Fractures: Prospective Study Using a Risk Scoring System. Foot Ankle Spec 2016;9(05):388–393

33 Caprini JA. Thrombosis risk assessment as a guide to quality patient care. Dis Mon 2005;51(2-3):70–78

34 Luksameearunothai K, Sa-Ngasoongsong P, Kulachote N, et al. Usefulness of clinical predictors for preoperative screening of deep vein thrombosis in hip fractures. BMC Musculoskelet Disord 2017;18(01):208

35 Krauss ES, Segal A, Cronin M, et al. Implementation and Validation of the 2013 Caprini Score for Risk Stratification of Arthroplasty Patients in the Prevention of Venous Thrombosis. Clin Appl Thromb Hemost 2019;25:1076029619838066

36 Dashe J, Parisien RL, Pina M, De Giacomo AF, Tornetta P 3rd. Is the Caprini Score Predictive of Venothromboembolism Events in Orthopaedic Fracture Patients? J Orthop Trauma 2019;33(06): 269–275

37 Pannucci CJ, Bailey SH, Dreszer G, et al. Validation of the Caprini risk assessment model in plastic and reconstructive surgery patients. J Am Coll Surg 2011;212(01):105–112

38 Swanson E. Caprini Scores, Risk Stratification, and Rivaroxaban in Plastic Surgery: Time to Reconsider Our Strategy. Plast Reconstr Surg Glob Open 2016;4(06):e733
39 Shuman AG, Hu HM, Pannucci CJ, Jackson CR, Bradford CR, Bahl V. Stratifying the risk of venous thromboembolism in otolaryngology. Otolaryngol Head Neck Surg 2012;146(05):719–724
40 Stroud W, Whitworth JM, Miklic M, et al. Validation of a venous thromboembolism risk assessment model in gynecologic oncology. Gynecol Oncol 2014;134(01):160–163
41 Carr P, Ehredt DJ Jr, Dawoodian A. Prevention of Deep Venous Thromboembolism in Foot and Ankle Surgery. Clin Podiatr Med Surg 2019;36(01):21–35
42 Ho KM, Tan JA. Stratified meta-analysis of intermittent pneumatic compression of the lower limbs to prevent venous thromboembolism in hospitalized patients. Circulation 2013;128(09):1003–1020
43 Leme LE, Sguizzatto GT. Prophylaxis of venous thromboembolism in orthopaedic surgery. Rev Bras Ortop 2015;47(06):685–693
44 Anderson DR, Dunbar M, Murnaghan J, et al. Aspirin or Rivaroxaban for VTE Prophylaxis after Hip or Knee Arthroplasty. N Engl J Med 2018;378(08):699–707
45 Chu JN, Maselli J, Auerbach AD, Fang MC. The risk of venous thromboembolism with aspirin compared to anticoagulants after hip and knee arthroplasty. Thromb Res 2017;155:65–71
46 Deirmengian GK, Heller S, Smith EB, Maltenfort M, Chen AF, Parvizi J. Aspirin Can Be Used as Prophylaxis for Prevention of Venous Thromboembolism After Revision Hip and Knee Arthroplasty. J Arthroplasty 2016;31(10):2237–2240
47 Flevas DA, Megaloikonomos PD, Dimopoulos L, Mitsiokapa E, Koulouvaris P, Mavrogenis AF. Thromboembolism prophylaxis in orthopaedics: an update. EFORT Open Rev 2018;3(04):136–148
48 Eriksson BI, Borris LC, Friedman RJ, et al. RECORD1 Study Group. Rivaroxaban versus enoxaparin for thromboprophylaxis after hip arthroplasty. N Engl J Med 2008;358(26):2765–2775
49 Lassen MR, Ageno W, Borris LC, et al. RECORD3 Investigators. Rivaroxaban versus enoxaparin for thromboprophylaxis after total knee arthroplasty. N Engl J Med 2008;358(26):2776–2786
50 Raskob GE, Gallus AS, Pineo GF, et al. Apixaban versus enoxaparin for thromboprophylaxis after hip or knee replacement: pooled analysis of major venous thromboembolism and bleeding in 8464 patients from the ADVANCE-2 and ADVANCE-3 trials. J Bone Joint Surg Br 2012;94(02):257–264
51 Samama CM, Laporte S, Rosencher N, et al. PRONOMOS Investigators. Rivaroxaban or Enoxaparin in Nonmajor Orthopedic Surgery. N Engl J Med 2020;382(20):1916–1925
52 Ageno W, Gallus AS, Wittkowsky A, Crowther M, Hylek EM, Palareti G. Oral anticoagulant therapy: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012;141(2 Suppl):e44S–e88S
53 Strebel N, Prins M, Agnelli G, Büller HR. Preoperative or postoperative start of prophylaxis for venous thromboembolism with low-molecular-weight heparin in elective hip surgery? Arch Intern Med 2002;162(13):1451–1456
54 Testroote M, Stigter W, de Visser DC, Janzing H. Low molecular weight heparin for prevention of venous thromboembolism in patients with lower-leg immobilization. Cochrane Database Syst Rev 2008;(04):CD006681
55 Hanslow SS, Grujic L, Slater HK, Chen D. Thromboembolic disease after foot and ankle surgery. Foot Ankle Int 2006;27(09):693–695
56 Mayle RE Jr, DiGiovanni CW, Lin SS, Tabrizi P, Chou LB. Current concepts review: venous thromboembolic disease in foot and ankle surgery. Foot Ankle Int 2007;28(11):1207–1216
57 Francis CW. Prevention of VTE in patients having major orthopedic surgery. J Thromb Thrombolysis 2013;35(03):359–367
58 Bloemen A, Testroote MJ, Janssen-Heijnen ML, Janzing HM. Incidence and diagnosis of heparin-induced thrombocytopenia (HIT) in patients with traumatic injuries treated with unfractioned or low-molecular-weight heparin: a literature review. Injury 2012;43(05):548–552
59 Martel N, Lee J, Wells PS. Risk for heparin-induced thrombocytopenia with unfractionated and low-molecular-weight heparin thromboprophylaxis: a meta-analysis. Blood 2005;106(08):2710–2715