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Invited Review

Venous thromboembolism in orthopedic surgery: Global guidelines

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ABSTRACT

Venous thromboembolism (VTE) is a severe complication that can occur after major orthopedic procedures. As VTE-related morbidity and mortality are a significant concern for both medical professionals and patients, and preventative measures are typically employed. Multiple organizations, including the American College of Chest Physicians (ACCP) and the American Academy of Orthopedic Surgeons (AAOS), have developed guidelines for VTE prophylaxis specifically in patients undergoing joint replacement procedures. However, recently, the International Consensus Meeting (ICM) was convened, which brought together over 600 experts from 68 countries and 135 international societies. These experts, spanning a range of medical disciplines including orthopedic surgery, anesthesia, cardiology, hematology, vascular, and internal medicine, conducted a comprehensive review of the literature using a strict Delphi process to generate practical recommendations for VTE prophylaxis across all types of orthopedic procedures. This review article summarizes some of the recommendations of the ICM.

Level of Evidence: Level V, Expert opinion.

Venous thromboembolism: General information

Orthopedic procedure patients are at risk of developing venous thromboembolism (VTE).[1] To address this complication, numerous guidelines have been developed by several organizations including the American College of Chest Physicians (ACCP),[2] the American Academy of Orthopedic Surgeons (AAOS),[3] and others. However, many of these guidelines rely heavily on high-level studies that are often sponsored or conducted by pharmaceutical companies seeking regulatory approval for their drugs, with the detection of distal deep venous thrombosis (DVT) through venography as the primary endpoint.[4] This endpoint is of less clinical significance than symptomatic pulmonary embolism (PE), which can be fatal.[5,6] Furthermore, some guidelines may underestimate the risk of bleeding associated with potent prophylactic agents.[7]

The ICM acknowledged the limitations of existing guidelines and recognized the need for unbiased, randomized trials that use clinically significant endpoints. To address these issues, the ICM brought together a global team of experts to create guidelines that address this important issue that challenges both patients and surgeons. The team relied on a rigorous Delphi process,[8] which had been used in previous ICM initiatives,[9,10] to produce a comprehensive document. To generate recommendations for nearly 200 questions collected from the field, all published work related to VTE and orthopedics was thoroughly reviewed.

The delegates were selected either through nomination by societies or based on their interest and published expertise in VTE, with a requirement of a minimum of 3 publications in the field.

Risk analysis

Numerous research studies have been undertaken to pinpoint groups of patients who face an elevated risk of VTE. According to the most recent literature, individuals who exhibit conditions such as hypoalbuminemia, Chronic kidney disease (CKD), inflammatory diseases, an unfavorable body mass index (BMI), blood dyscrasias, hematologic malignancies and active adenocarcinoma and/or human immunodeficiency virus (HIV) are at a heightened susceptibility to experiencing VTE.[11-16] Moreover, ethnicity has also been studied for its association with VTE.[17] Table 1 provides a list of potential risk factors for VTE after orthopedic procedures based on the available data.

Contemporary literature underscores the role of inflammation as a discernible risk factor for VTE. The activation of platelets and leukocytes can set in motion the coagulation cascade by instigating the release of tissue factor.[18] A study conducted in 2018 revealed that individuals grappling with conditions such as rheumatoid arthritis and mild psoriasis faced markedly elevated VTE risks, even after accounting for conventional risk factors.[19] In addition, a higher BMI was found to be associated with a concurrent diagnosis of both PE and DVT. Notably, patients with a BMI falling below 18.5 kg/m² or exceeding 40 kg/m² demonstrated a 1.4-fold increase in the likelihood of experiencing VTE in comparison to those maintaining a BMI within the normal range.[20]

Studies have demonstrated that various types of cancer, with active adenocarcinoma being the most

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Table 1. Risk factors for venous thromboembolism

Risk factors	Increased VTE (fold)
HIV	9-20
Protein C deficiency	6.5
Factor V Leiden heterozygotes	3-8
Varicose vein	3.6
History of VTE	2.1
Congestive heart failure	2.1
CKD	2
Cardiovascular disease	1.4-5.1
Charlson Comorbidity Index ≥ 3	1.5-2.6
BMI > 25 kg/m^2	1.8
For each 10-year increase in age over 50 years	1.6
Family VTE history	1.4
Ambulation before the second postoperative day	0.7

CKD, chronic kidney disease; HIV, human immunodeficiency virus; VTE, venous thromboembolism.

common, can increase the risk of VTE by elevating levels of platelets, leukocytes, and microvesicles that carry tissue factor-positive (TF1). Ongoing investigations have proposed a categorization of cancer types into 3 groups based on their respective levels of risk for VTE. Among these, cancers classified as high-risk encompass pancreatic, ovarian, brain, stomach, gynecologic, and hematologic malignancies. Intermediate VTE risk cancers include colon and lung cancers, while those falling under the low-risk VTE category consist of breast and prostate cancer.[21] Furthermore, individuals afflicted with blood dyscrasias have also been identified as being in a heightened risk bracket for VTE.[22] Notably, Factor V Leiden thrombophilia, characterized by an inadequate anticoagulant response to activated protein C (APC), has been correlated with an increased susceptibility to VTE.[14]

Inherited deficiencies of antithrombin, protein C, and protein S have been firmly established as risk factors for VTE in adults. Considering this, it could be a prudent approach to consider screening children belonging to families with these deficiencies. This screening could aid in identifying individuals who might derive advantages from thromboprophylaxis during periods when the risk of thrombosis is heightened.[23]

Chronic kidney disease is associated with a higher risk of VTE, approximately double the risk in individuals without CKD.[12] The occurrence of VTE becomes more prevalent as one advances in age, showing a 1.6-fold rise in risk for every decade beyond 50 years. Those with a past history of VTE, encompassing both DVT and PE, exhibit a 2.1-fold heightened risk of experiencing subsequent VTE incidents.[16]

A systematic review of 54 studies with Levels I and II evidence found that several factors increase the risk of VTE after total knee arthroplasty (TKA) and total hip arthroplasty (THA). These factors include increasing age, BMI exceeding 30, undergoing bilateral surgery, being of the female gender, and undergoing surgery lasting more than 2 hours[24] Besides, TKA patients are under a higher risk than THA patients, and cemented fixation was identified as a risk factor for VTE in TKA patients. Early mobilization was identified as a protective factor for TKA patients. THA patients with a previous history of VTE have a higher risk of VTE recurrence.

Bleeding and venous thromboembolism: how to maintain an optimal balance for both risks?

On the one hand, the utilization of thromboprophylaxis seeks to curtail the risk of VTE; however, on the other hand, it introduces the potential for increased bleeding. Despite the generally favorable safety profiles exhibited by all thromboprophylaxis agents, the occurrence of bleeding events remains a significant concern for surgeons. Therefore, it is crucial to establish personalized thromboprophylaxis regimens to balance the potential risks and benefits of VTE prophylaxis.

Major bleeding event (MBE) is serious and possible complication that can occur following orthopedic procedures. These events are classified as bleeding into critical organs such as the intracranial, gastrointestinal, or intraocular regions, as well as the need for reoperation to evacuate hematoma and a requirement for more than 2 units of blood transfusion.

According to a systematic review, the rate of clinically significant bleeding after orthopedic procedures is high at 3%, which is higher than the incidence of VTE.[5] Despite this, there is a lack of research on MBE compared to VTE. Therefore, it holds paramount importance to pinpoint patients with an elevated susceptibility to MBE in order to mitigate this risk effectively. Several risk factors for MBE after total joint arthroplasty (TJA) have been identified, including perioperative blood loss, increased tourniquet and surgical times, female gender, older age, higher BMI, higher creatinine levels, TKA versus THA procedure, general anesthesia versus spinal anesthesia, and low preoperative hemoglobin levels.[25-27]

The type of chemoprophylaxis utilized may also have a significant impact on the risk of MBE. Zufferey et al[28] observed that the risk of MBE with fondaparinux thromboprophylaxis was highest in the initial days following surgery. Another study comparing aspirin and rivaroxaban showed that the rate of MBE was 0.47% in the aspirin group and 0.29% in the rivaroxaban group.[29] Parvizi et al[30] found that aspirin thromboprophylaxis was associated with less major bleeding compared to warfarin in TJA patients. The potential risk factors for bleeding after orthopedic procedures are summarized in Table 2 based on the available data.

Bleeding is a significant complication following major orthopedic operations, leading to various issues such as prolonged wound drainage, hematoma formation, increased need for blood transfusion, and

HIGHLIGHTS

- Venous thromboembolism is an important complication after major orthopedic surgery. Risk factors for VTE should be investigated properly. Also, certain groups of patients are at risk of major bleeding events. The risk of VTE and bleeding should be balanced when selecting the most appropriate prophylactic agent.
- According to most current literature, aspirin is a safe, cheap, oral, and effective option for VTE prophylaxis in a majority of patients undergoing orthopedic surgeries.
- A combined VTE and bleeding risk assessment scoring system is required to identify the best method for VTE and bleeding prophylaxis.

Table 2. Risk factors associated to a major bleeding event

Older age
Gender (female)
Active cancer
Surgical procedure type (spine > THA > TKA)
Anesthesia type (general > spinal)
Intraoperative blood loss
Increased creatinine level
Preoperative hemoglobin level
Increased surgical time
Increased tourniquet time
Hypertension history of previous bleeding

higher risk of infection. Therefore, it is essential to consider bleeding risk when choosing a VTE prophylaxis method. However, the current literature provides insufficient data to identify and grade bleeding risk factors for major orthopedic surgery adequately. Future studies may develop a grading system by combining VTE and bleeding risk factors to provide a more objective risk assessment, allowing for more effective personalized prophylaxis methods.

Tranexamic acid (TXA) is a medication designed to enhance the stability of blood clots by obstructing the lysine-binding sites on plasminogen. This action prevents the dissolution of clots.[31] Although TXA's effectiveness as a clot stabilizer is well known, concerns have been raised regarding its potential to increase the risk of VTE. However, current evidence suggests that TXA does not significantly increase VTE risk in orthopedic surgery. A recent meta-analysis conducted by Taeuber et al[32] shows that intravenous TXA did not significantly elevate the likelihood of subsequent VTE. The VTE rates in the TXA and control groups were 3.6% and 2.7%, respectively. In a study by Porter et al,[33] it was found that administering TXA to high-risk patients undergoing surgical repair for intertrochanteric hip fracture did not increase the mortality risk, stroke, PE, or DVT within 90 days after surgery, compared to those who did not receive TXA in a propensity-matched analysis. Cheriyan et al[34] concluded that intravenous administration of TXA did not raise the risk of local hematoma or VTE in individuals who underwent cervical and lumbar spine surgery. Numerous randomized controlled trials have shown that the risk of VTE in patients receiving TXA during shoulder, knee, and hip reconstruction is similar.[35-37] Moreover, no evidence has been found between TXA and an increased risk of VTE. Furthermore, administering TXA to patients undergoing orthopedic procedures does not raise the likelihood of developing subsequent VTE in individuals who don't have a history of VTE.

The available evidence is insufficient to establish a clear connection between the utilization of tourniquets during lower extremity orthopedic procedures and the occurrence of postoperative VTE. Neuraxial anesthesia, on the other hand, has been found to decrease the likelihood of VTE following lower extremity arthroplasty, and it is recommended as part of a comprehensive prophylaxis plan when possible.[38] Orthopedic procedures can frequently be managed with regional anesthesia techniques, either as a substitute for or in conjunction with general anesthesia. Performing regional anesthesia has been associated with better pain management, vasodilation mediated by sympathectomy, reduced overall stress response, and fewer incidents of both major and minor bleeding complications.[39]

Modalities for prevention of venous thromboembolism

Following major orthopedic procedures, a combination of pharmacologic and mechanical approaches is recommended for prophylaxis. Current pharmacologic agents employed for this purpose encompass warfarin, unfractionated heparin, low-molecular-weight heparin (LMWH), fondaparinux, aspirin, rivaroxaban, dabigatran, apixaban, and similar medications. Mechanical methods utilized for prophylaxis involve the use of graduated compression stockings, intermittent pneumatic compression devices, and venous foot pumps.

International consensus meeting recommendations on total joint arthroplasty

Arthroplasty: VTE after elective total TJA continues to occur despite various strategies in prophylaxis and should not be considered a "never event."

Strength of recommendation: Moderate.

Delegates vote: Agree 94.9% Disagree 5.1% Abstain 0.0% (Strong Consensus).

Historically, DVT and PE have been significant risks for patients undergoing TJA. Early studies demonstrated a higher incidence of VTE following TKA.[40] However, it is essential to acknowledge that DVT in patients with TKA commonly takes place in the lower part of the calf and is less prone to advancing into PE. The occurrence of PE has been observed at a rate of 1.3%,[19] and instances of fatalities have ranged from 0.19% to 0.4%.[41] During a prospective study that involved 34 397 consecutive THA or TKA procedures, only 32 patients (0.09%) developed a VTE after a median of 2 days, even though they were receiving ongoing thromboprophylaxis.[42]

Studies have reported that the risk of both symptomatic and asymptomatic PE after TJA in patients receiving thromboprophylaxis ranges from 0.4% to 23%.[43] Table 3 provides a summary of VTE prophylaxis agents and their associated complications.

According to several studies, when warfarin dosage is adjusted to achieve an international normalized ratio (INR) of 1.5–2.0 and is given for around 6 weeks, the incidence of DVT is between 0.2% and 1%, while the rate of nonfatal PE is between 0.1% and 0.3%.[53] However, the use of warfarin after THA or TKA has been linked to a significant risk of bleeding, despite its efficacy in reducing the incidence of VTE.[54]

Direct acting oral anticoagulants have gained widespread popularity as a preferred option for VTE prophylaxis owing to their convenient administration and the absence of a requirement for frequent monitoring.[41] Studies have shown that rivaroxaban administered after THA had in a reduced occurrence of DVT, ranging from 0.8% to 1.6%. In comparison, the incidence of DVT with LMWH was higher, ranging from 3.4% to 6.5%. Additionally, the employment of rivaroxaban showed a decreased rate of nonfatal PE at 0.1%-0.3%, whereas LMWH exhibited a slightly higher range of 0.1%-0.5%.[55]

When rivaroxaban was used after TKA, the DVT rate was higher at 6.3%-6.9% compared to 9.0%-18.2% for LMWH, while the nonfatal PE rate was lower at 0%-0.3% compared to 0.5% for LMWH.[56] Apixaban has been shown to have lower rates of DVT and nonfatal PE compared to LMWH when used for VTE prophylaxis after THA. When used for VTE prophylaxis after TKA, apixaban has a similar or lower incidence of DVT and nonfatal PE compared to LMWH,[57] with a very low rate of fatal PE.[58] Studies suggest that dabigatran could be used for prophylaxis after THA, with an incidence of DVT ranging from 5.1% to 8.0%, compared to 6.4%-8.6% for LMWH. The nonfatal PE rate was found to be 0.1%-0.4% for dabigatran and 0.2%-0.3% for LMWH, with a fatal PE rate of 0.1% observed with dabigatran in some studies.[59,60]

Aspirin has been found to be effective in preventing VTE after THA and TKA, with reported incidence rates of 2.6% for DVT, 0.14%-0.6% for nonfatal PE, and 0.2% for fatal PE.[61] The AAOS guidelines recommend aspirin as a prophylactic agent for VTE in patients at "typical" risk following THA and TKA.[62] Numerous studies have reported the efficacy of aspirin in VTE prophylaxis following TJA.[61,63-65] No notable distinctions were observed in terms of symptomatic PE, symptomatic DVT, 90-day mortality, or major bleeding incidents among patients who received either low-dose

Table 3. A summary of venous thromboembolism prophylaxis agents and related complications

		Symptomatic VTE		Symptomatic PE		Major bleeding		Mortality	
Study	**Patient number**	**%**	***P***	**%**	***P***	**%**	***P***	**%**	***P***
PEP study[44] (2000)									
Aspirin (160 mg/day)	6.679	1.07	.0003	0.3	.002	2.9	.04	6.69	
Placebo	6.677	2.5		0.6		2.4		6.90	
Parvizi et al[45] (2017)									
Aspirin (2 × 81 mg)	1.459	0.1	.34	0.1	.74	0.3β	.66	0.1	.8
Aspirin (2 × 325 mg)	3.192	0.3		0.1		0.4[β]		0.1	
Bala et al[46] (2019)									
Aspirin	649	1.7	<.01	<2		2	.94		
Enoxaparin	3.377	2.6		0.4		1			
Warfarin	3.245	3.7		0.7		2			
Factor Xa inhibitors	1.558	1.7		<1		1			
Baumgartner et al[47] (2019)									
Aspirin (80 mg vs.325 mg)	10.769	0.34	.43	0.1	.55	0.06	.006	0.06	
Anticoagulant group	22.055	0.44		0.2		0.12		0.04	
Aspirin + anticoagulant group	3.368	0.36		0.18		0.26		0.15	
EPCATII[29] (2018) (first 5 days after routine rivaroxaban)									
Aspirin (81 mg)	1.707	0.64	.84	0.29		0.47	.42	0.06	
Rivaroxaban (10 mg)	1.717	0.70		0.35		0.29		0	
Lazo-Langner et al[48] (2014)									
LMWH	11.136	1.2	.001			0.46	.6	0.22	.06
Rivaroxaban	11.823	0.7				0.41		0.14	
Senay et al[49] (2018)									
Enoxaparin	1.468	0.6	.64	0.3	.54	0.1	.033	0	
Dabigatran	904	0.8		0.3		0.6		0	
Highcock et al[50] (2020)									
Rivaroxaban (10 mg)	800	0.8	<.01	0.5	<.05	1.4	<.05		
Dabigatran (220 mg)	911	3		0.8		1.2			
Apixaban (2.5 mg)	720	2.1		1.3		0.8			
Rondon et al[51] (2019)									
Aspirin	8.061							0.2	.007
Non-aspirin	23.072							0.4	
Huang et al[52] (2016)									
Düşük riskli group									
Aspirin (2 × 81 mg vs. 2.325 mg)	4.102	0.2	<.001	0.1	<.001	0.2[β]	.64	0.1	.92
Warfarin (INR 1.8-2.0)	18.649	1.8		1.2		0.2[β]		0.2	
High-risk group									
Aspirin (2 × 81 mg vs. 2.325 mg)	796	0.6	<.001	0.1	<.001	0[β]	.054	0.1	.016
Warfarin (INR 1.8-2.0)	6.723	3.2		1.8		0.6[β]		1.1	

Anticoagulant group: unfractionated heparin, LMWH, fondaparinux, warfarin, apixaban, and rivaroxaban; INR, international normalized ratio; LMWH, low-molecular-weight heparin; PEP, pulmonary embolism prevention; PE, pulmonary embolism group; VTE, venous thromboembolism; β = Gastrointestinal bleeding and ulcer ratio.

or high-dose aspirin. The variation in the occurrence of symptomatic PE between the low-dose and high-dose aspirin groups did not demonstrate statistical significance [0.33% (95% CI 0.1%-0.8%) vs. 0.65% (95% CI 0.5%-0.9%); *P*=.161]. Likewise, the study revealed no substantial distinction in the frequency of symptomatic DVT between the low-dose and high-dose aspirin groups, as the rates were 0.52% (95% CI, 0.2%-1.5%) and 0.99% (95% CI, 0.6%-1.6%), respectively (*P* = .233). The incidence of major bleeding was 0.54% (95% CI, 0.2%-2.0%) in the low-dose aspirin group and 0.29% (95% CI, 0.2%-0.5%) in the high-dose group, and the difference was not statistically significant (*P* = .376). There was no significant difference in 90-day mortality between the low-dose and high-dose aspirin groups.[66]

Patients who received warfarin for chemoprophylaxis had a higher risk of symptomatic PE (1.24%, 95% CI, 0.8%-2.0%) compared to those who received low-dose aspirin (0.33%; 95% CI, 0.1%-0.8%) (*P* = .008). Similarly, there was a higher risk of symptomatic DVT with warfarin (1.68%; 95% CI, 1.1%-2.8%) compared to low-dose aspirin (0.52%; 95% CI, 0.2%-1.5%) (*P* = .035).[66]

Compared to low-dose aspirin, the use of LMWH (postoperative), LMWH (preoperative), and rivaroxaban did not demonstrate a significant difference in the risk of developing VTE, with odds ratio (OR) of 1.1 (0.3, 3.8), 1.4 (0.4, 4.6), and 1.4 (0.6, 3.5), respectively. On the other hand, high-dose aspirin (325 mg) had the highest risk of VTE with an OR of 7.90 (2.60, 24.05), followed by heparin [5.94 (2.28, 15.47)] and mechanical prophylaxis [5.76 (1.87, 17.73)], when compared to low-dose aspirin. In studies assessing bleeding events, low-dose aspirin (81 mg) was used as the reference and exhibited the lowest risk estimate. Mechanical prophylaxis [1.97 (0.04, 94.52)], LMWH 20 mg [2.93 (0.20, 43.80)]] and low-dose warfarin (4.32 [0.25, 75.41]) had the next lowest estimates but did not differ significantly in risk from low-dose aspirin. Thrombin inhibitors [23.91 (1.94, 295.06)] were associated with the highest risk of bleeding events, followed by LMWH (postoperative) [19.66 (1.53, 252.94)] and heparin [18.32 (1.45, 231.39)].[67,68]

Numerous nonpharmacological methods have been employed to reduce the occurrence of VTE following TJA. These encompass the utilization of regional and hypotensive anesthesia, intermittent

pneumatic compression devices, optimized strategies for managing blood loss, expedited rehabilitation protocols, and risk assessment frameworks. Together, these approaches have played a pivotal role in lowering the frequency of VTE over the course of time.[69]

The most effective prophylactic regimen for each patient remains uncertain at present.[35] Although modern surgical protocols and thromboprophylaxis have decreased DVT rates in both TKA and THA patients, they have not significantly reduced the incidence of PE.[70]

At present, there is no established consensus on the most effective prophylactic regimen to prevent VTE following arthroplasty, with individual surgeon preference being the primary determining factor. A variety of anticoagulants are commonly used in orthopedic patients for VTE prevention, including aspirin, warfarin, injectable agents like LMWH, and more recently, Factor Xa inhibitors such as rivaroxaban and apixaban.[71]

Network Meta-Analyses were employed for comparative analyses, and the resulting OR with corresponding 95% CIs were reported. Evaluating all studies across levels I-IV, it was evident that low-dose aspirin (100 mg) demonstrated the most favorable outcome with the lowest risk of VTE occurrence.[72]

Although the AAOS guidelines[73] advocate for the use of high-dose aspirin (325 mg twice daily) to prevent VTE TJA, Parvizi et al[45] discovered that low-dose aspirin (81 mg twice daily) was equally effective in VTE prevention. Moreover, this lower dosage exhibited no disparity in mortality rates within the first year post surgery. Additionally, low-dose aspirin has been linked to reduced bleeding rates compared to high-dose aspirin and could potentially mitigate gastrointestinal side effects.[74]

Pharmacological thromboprophylaxis during THA/TKA surgery is associated with bleeding complications, which is considered a safety concern that is usually assessed in clinical trials. However, the definition and adjudication of bleeding outcomes may vary across studies, leading to inconclusive results.[75] Despite this, MBE may contribute to up to 8.9% of total perioperative deaths after TJA, which highlights the seriousness of this complication.[76] The risk of bleeding was found to be similar between aspirin and LMWH in a meta-analysis that included 4 trials and 1507 patients [RR (risk ratio)=0.84 for major bleeding and RR=0.77 for minor bleeding].[77]

In a comparative analysis, pitting aspirin against non-vitamin K oral anticoagulants, including direct factor Xa inhibitors like rivaroxaban, apixaban, and dabigatran, research revealed that aspirin carried a diminished risk of necessitating blood transfusions compared to rivaroxaban (RR=0.94), as indicated by a study.[78] Additionally, a large trial involving 3,424 patients found no significant difference between aspirin and rivaroxaban in terms of clinically important bleeding (1.29% vs. 0.99%) or major bleeding (0.47% vs. 0.29%).[29]

Mechanical compressive devices can be utilized as a routine method for VTE prophylaxis in patients who undergo THA or TKA. According to the VTE prevention guidelines by AAOS,[73] the use of mechanical compressive devices is advocated for the prevention of VTE in patients undergoing elective TJA. It is essential to note that AAOS recommendations are consistent with the ACCP recommendations that mechanical compression devices can be used alone for VTE prevention, without chemical prophylaxis, especially in low-risk patients.[2] In addition, the ACCP guidelines suggest that mechanical compressive devices could be employed independently in TJA patients with an elevated risk of bleeding.[2]

Utilizing low-dose aspirin as the primary approach for VTE prophylaxis is advised for all patients undergoing TJA, encompassing those at moderate to high risk. This is currently regarded as the most efficacious and secure means of prophylaxis against VTE.

Strength of recommendation: Strong.

Delegates vote: Agree 76.9% Disagree 19.9% Abstain 3.4% (Strong Consensus).

Hip preservation surgeries: Hip preservation surgeries (HPSs), such as mini open femoroacetabular osteoplasty, hip arthroscopy (HA), surgical dislocation of the hip, and periacetabular osteotomy, are employed to address hip irregularities like femoroacetabular impingement and developmental dysplasia of the hip. However, VTE can manifest following HPS procedures. Studies have reported that the frequency of VTE during the postoperative period of patients undergoing periacetabular osteotomy ranges from 0% to 5%. Similarly, the incidence of VTE after HA has been reported to range from 0% to 9.6%, while the reported rates after mini-open femoroacetabular osteoplasty and surgical dislocation of the hip were 0.25% and 0.5%, respectively, using various VTE prophylaxis protocols. Nonetheless, there is presently a lack of consensus within the literature regarding the optimal approach for VTE prophylaxis among patients undergoing HPSs. Based on the available evidence, the majority of individuals undergoing HPS are typically youthful, in good health, and lead active lifestyles, which may not categorize them as being at a heightened risk for VTE. Aspirin or mechanical prophylaxis has been shown to be adequate for the majority of patients undergoing HPS. The use of more potent agents, which can increase the risk of bleeding, should be reserved for patients who are at high risk of VTE based on family history or prior history of VTE.[79,80]

Trauma: VTE events are a significant cause of morbidity and mortality in patients with multiple orthopedic injuries.[81] The incidence of PE, a potentially fatal form of VTE, can range from 2% to 16%.[82] Surgical interventions in the upper extremity and distal ankle are typically considered minor procedures. The risk of VTE is generally higher in surgeries performed on the lower limb, particularly in more proximal locations such as the pelvis. Other factors that should be taken into consideration for assessing the risk of VTE include the duration of the surgery and the expected level of postoperative mobility.

While there are various options for prophylaxis against VTE in patients with multiple orthopedic injuries, the available literature suggests that LMWH is the most effective choice.

Strength of recommendation: Acceptable.

Delegates vote: Agree 86.4% Disagree 9.09% Abstain 4.55% (Strong Consensus).

The Western Trauma Association guidelines suggest LMWH as the optimal prophylaxis for VTE in trauma patients, with a standard dosage of 40 mg administered subcutaneously twice daily. Nevertheless,

in specific scenarios, such as with obese patients, it is advisable to consider weight-based dosing ranging from 0.5 mg to 0.6 mg per kg, also administered twice daily. Ley et al[81] also support the use of early pharmacologic prophylaxis and suggest that it be initiated within 24 hours of injury. Additionally, patients at high bleeding risk may benefit from bilateral mechanical thromboprophylaxis if possible.

Thromboprophylaxis is crucial in trauma patients with fractures and visceral injuries, and anticoagulant-based prophylaxis should be started as soon as the bleeding risk allows. Patients who are at high bleeding risk should receive bilateral mechanical thromboprophylaxis, if possible.

Strength of recommendation: Strong.

Delegates vote: Agree 100.00% Disagree 0.00% Abstain 0.00% (Unanimous Strong Consensus)

Patients with polytrauma are at high risk of bleeding immediately and during the early period after injury. The primary focus in these patients is to manage active bleeding. While the risk of VTE also increases soon after the injury, clinically significant thrombosis is often delayed.

Recommendations

1. To reduce the risk of both bleeding and thrombosis, we suggest that all polytrauma patients undergo an evaluation upon admission.[81]
2. Patients with active bleeding are typically treated surgically or through endovascular embolization. It is recommended to delay anticoagulant thromboprophylaxis until the high risk of bleeding resolves.
3. After confirming the absence of active bleeding, we suggest initiating anticoagulant thromboprophylaxis, typically with weight-based LMWH, within 24 hours after injury.[81] In cases of traumatic brain injury, we recommend starting anticoagulant thromboprophylaxis after consecutive stable brain imaging for intracranial bleeding, usually around 24-36 hours post injury.
4. It is recommended to use sequential compression devices (SCDs) for patients at high risk for bleeding, but in polytrauma patients with lower extremity fractures, it may not be possible to use bilateral SCD. Once hemostasis is achieved, SCD can be replaced with LMWH or LMWH can be added to SCD.
5. To reduce pain, promote mobility, and decrease VTE risk, early fixation of unstable fractures is recommended.[83] However, if fracture repair is delayed, it is recommended not to delay LMWH thromboprophylaxis.
6. Encouraging early mobility and providing daily physiotherapy are also recommended to improve outcomes in polytrauma patients.[84]

Orthopedic procedures that involve the upper extremity, lower extremity, arthroscopy, and surgery distal to the ankle in patients with isolated injuries are considered nonmajor and have lower VTE risk. A large database study found that the incidence of DVT in patients undergoing upper extremity surgery was as low as 0.2%.[85]

Patients with a single lower extremity fracture who do not require surgery typically do not require routine VTE prophylaxis. However, VTE prophylaxis may be necessary for high-risk individuals with significant medical comorbidities, severely limited activity, or other coagulopathic risk factors.

Strength of recommendation: Moderate.

Delegates vote: Agree 95.65% Disagree 4.35% Abstain 0.00% (Strong Consensus).

VTE occurrence in isolated lower extremity fractures without the need for surgery is typically low, ranging from 0.1% to 4%. As a result, many believe that routine thromboprophylaxis is unnecessary for these patients.[2] The ACCP guidelines also do not recommend prophylaxis for immobilized isolated lower extremity fractures.[2]

It is recommended to use both mechanical and pharmacological VTE prophylaxis in patients who undergo internal fixation of a hip fracture after assessing their individual risk factors. In cases of surgical delay, it may be appropriate to consider preoperative pharmacological prophylaxis. To ensure effective prevention of VTE, pharmacological thromboprophylaxis should be started no later than 12 hours after wound closure and should continue for a minimum of 28 days during the postoperative period when patients remain at increased risk for thromboembolic events.

Upon admission, it is recommended that patients with hip fractures undergo medical optimization, including hydration, and receive mechanical prophylaxis using graduated compression stockings or intermittent pneumatic compression devices as long as there are no contraindications to reduce the risk of VTE.[86]

There are several agents that have been found effective in preventing VTE in patients with hip fractures, including LMWH, unfractionated heparin, fondaparinux, adjusted dose vitamin K antagonists, and aspirin.[87] The choice of prophylaxis should be individualized and based on patient factors, clinician preferences, and shared decision-making. Anticoagulation therapy should be administered for a minimum of 10-14 days, with most clinical practice guidelines recommending continuation for at least 28-35 days after surgery due to the persistently elevated postoperative VTE risk.[86] In the early postoperative period, LMWH or unfractionated heparin is often used in clinical practice, given their parenteral preparations and reliable pharmacokinetics.[88]

Currently, there is no consensus on the best pharmacological agent for VTE prophylaxis in hip fracture patients. LMWH is considered the standard of care and is often used as the comparator for new medications in clinical trials.[2] Both the ACCP and American Society of Hematology guidelines recommend the full extended course of LMWH for VTE prophylaxis in hip fracture patients.[2]

Aspirin has demonstrated a significant reduction in VTE rates during the high-risk post-fracture period when compared to placebo, but routine use of aspirin remains a topic of controversy due to the lack of evidence supporting its equivalence to the proven efficacy of LMWH.[44]

Arthroscopy: The incidence of VTE in sports surgery is generally low. However, immobilization and non-weight bearing can increase the risk of VTE. Thus, upper extremity sports procedures are typically considered to be associated with a lower VTE risk since they have a minimal impact on patient mobility. In contrast, lower extremity procedures may be considered as having a higher VTE risk if patients are unable to weight bear or mobilize postoperatively.

Strength of recommendation: Consensus.

Delegates vote: Agree 96.15% Disagree 0.0% Abstain 3.85% (Strong Consensus).

Knee arthroscopy (KA) is a frequently performed outpatient orthopedic procedure with a high global prevalence.[89] While the incidence of VTE after KA is low, ranging from 0.4% in clinically diagnosed cases to 17.9% in asymptomatic patients undergoing screening.[90]

Currently, the literature lacks studies that specifically delve into the correlation between abstaining from weight-bearing following KA and the potential incidence of VTE. Consequently, there are no targeted recommendations for prophylactic interventions aimed at this specific patient subset. However, acknowledging that avoiding weight bearing is acknowledged as a potential VTE risk factor, we propose the consideration of routine VTE prophylaxis for these patients, except in cases of heightened bleeding risk or postoperative bleeding occurrences.

Strength of recommendation: Consensus.

Delegates vote: Agree 92% Disagree 4% Abstain 4% (Strong Consensus).

The primary goal of VTE prophylaxis is to prevent the occurrence of fatal PE. However, DVT alone can cause significant pain and swelling and may result in post-thrombotic syndrome, which affects around 30% of symptomatic DVT patients within 5 years of surgery.[91] Despite this, there is no consensus on the use of VTE prophylaxis after KA procedures, and recommendations differ among countries.[2]

In the absence of sufficient evidence, healthcare providers may consider the use of prophylactic measures such as LMWH, rivaroxaban, or aspirin following non-weight-bearing KA procedures such as microfracture, autologous chondrocyte implantation, osteochondral autograft transfer surgery, or meniscal repair to reduce the risk of thrombosis associated with prolonged non-weight-bearing KA procedures. Future studies should focus on developing strategies specifically targeted at preventing VTE after non-weight-bearing KA procedures, instead of combining all KA procedures together regardless of weight-bearing status. To ascertain the most effective pharmaceutical agents and appropriate dosages for prophylaxis, it is imperative to undertake comparative clinical trials that explore various options for VTE prevention.

Anterior cruciate ligament reconstruction in healthy adult patients carries a small risk of VTE. There is moderate-to-low-level evidence supporting the use of LMWH, aspirin, or rivaroxaban for preventing PE and symptomatic DVT. However, there is very limited evidence for LMWH's effectiveness in preventing asymptomatic DVT compared to no treatment. Existing studies have limited data on adverse events, including major and minor bleeding, with no significant differences between LMWH, aspirin, and rivaroxaban. Therefore, appropriate risk stratification is necessary, considering medical comorbidities, weight-bearing status, and immobilization.

When prescribing anticoagulants to KA patients, it is important to consider the potential risks associated with thromboprophylaxis. One such risk is an increased likelihood of bleeding adverse events, as demonstrated by a significantly higher OR of 2.79 following below-knee surgery in patients receiving prophylaxis compared to those who did not receive it.[92] In order to strike a balance amidst these potential risks, clinicians must undertake thorough risk stratification. This involves taking into account factors like medical comorbidities, weight-bearing status, and the utilization of immobilization when making the decision about whether to recommend VTE prophylaxis post-surgery.

The incidence of VTE following HA is generally low and therefore routine VTE prophylaxis is not necessary. However, in patients with risk factors, the use of VTE prophylaxis should be considered. Reported rates of VTE after HA range from 0.2% to 9.5%,[93] with symptomatic DVT rates ranging from 0.4% to 3.5%.[93] Additionally, ultrasound screening detected asymptomatic DVT at a rate of 6.9%. The incidence of PE was found to be between 0.08% and 1.5%, with a corresponding mortality rate of 0.02%.[94]

A systematic review[95] was conducted to investigate the efficacy of chemoprophylaxis in patients undergoing HA, which included the use of aspirin, LMWH, or other unspecified drugs. The review found that the pooled VTE rate was 2.0% in patients who received prophylaxis compared to 3.6% in those who did not although this difference was not statistically significant. In another study with 880 patients who underwent HA, high-risk VTE patients were given chemoprophylaxis, while low-risk VTE patients received early mobilization and physiotherapy within the first 24 hours. The study found that the VTE rate in the low-risk group was 0.16% and 1.2% in the high-risk group.[96]

In conclusion, while the available evidence is limited, the risk of VTE following HA appears to be low. Therefore, routine administration of VTE prophylaxis to patients undergoing HA is not supported by the current data. However, patients at higher risk of VTE may benefit from the use of mechanical and/or chemical prophylaxis, which may include aspirin.

Spine: The risk of VTE in spine surgery varies depending on the type of procedure performed. Procedures that are deemed high-risk encompass those conducted for oncological, traumatic, or infectious conditions, alongside interventions necessitating intensive care unit admission, multiple stages, or combined approaches. Additionally, lumbar procedures involving extensive fusions or utilizing an anterior approach, as well as posterior cervical fusions, should be regarded as high-risk. Conversely, the majority of elective pediatric procedures, microdiscectomies, anterior cervical fusions, and lumbar or cervical decompressions can be categorized as low-risk procedures in terms of VTE considerations.

Strength of recommendation: Moderate.

Delegates vote: Agree 100.00%, Disagree 0.00%, Abstain 0.00% (Unanimous Strong Consensus).

The use of VTE chemoprophylaxis can be considered after elective lumbar fusions, starting within 24-48 hours. For patients who are at higher risk for bleeding, chemoprophylaxis can be initiated within 48 hours. However, the potential benefits of chemoprophylaxis should be carefully evaluated against the risks of bleeding and hematoma formation.

It is important to note that while most studies suggest no difference in epidural hematoma rates between postoperative chemoprophylaxis and no prophylaxis,[97,98] the retrospective study by Hohenberger et al[99] found that anticoagulation use (aspirin, coumadin, and rivaroxaban) was associated with an increased risk of epidural hematomas. However, the study did not provide the VTE rate, and controlling for

confounding factors was not performed. Hence, the advantages of chemoprophylaxis must be meticulously balanced against the potential hazards of bleeding and hematoma formation. The determination to prescribe chemoprophylaxis should be undertaken on an individual basis, following a comprehensive risk evaluation.

The conclusions drawn from the studies included in the review are challenging due to variations in methods of prophylaxis and VTE screening, surgical procedures, and patient populations. Furthermore, the timing and dosage of chemoprophylaxis were inconsistent across studies or not reported. Therefore, future research should include detailed information on the type, dosage, and timing of anticoagulants and provide stratified results for epidural hematoma incidence based on the indication and use of chemoprophylaxis to improve the quality and comparability of findings.

Although aspirin has been shown to reduce VTE in orthopedic procedures, there is currently no high-quality research on its effectiveness for patients undergoing spine surgery. Therefore, we recommend that surgeons carefully consider the potential benefits of chemoprophylaxis while balancing the known risks of increased bleeding.

Strength of recommendation: Consensus.

Delegates vote: Agree 96.43%, Disagree 0.00%, Abstain 3.57% (Strong Consensus).

The effectiveness of aspirin for VTE prophylaxis following hip and knee joint arthroplasty has been well-established,[77] but evidence for its use in spine surgery is limited and heterogeneous, preventing strong conclusions. There is a lack of studies investigating aspirin as a VTE prophylaxis in spine surgery, and the existing studies are of low quality and inconclusive. Despite its effectiveness in other orthopedic procedures, the efficacy of aspirin in preventing VTE in spine surgery patients remains unproven. Surgeons should carefully consider the potential benefits of chemoprophylaxis with aspirin against the known risks of increased bleeding.

Individuals who have experienced a traumatic spinal injury are exposed to an increased susceptibility to developing VTE. The suitable guidelines for VTE prophylaxis before and after spinal surgery in cases of trauma differ, contingent on various considerations including the existence of spinal cord injury (SCI), the precise spinal segment affected, and the age of the patient.

Strength of recommendation: Moderate

Delegates vote: Agree 100.00%, Disagree 0.00%, Abstain 0.00% (Unanimous Strong Consensus).

Patients with SCI are at an increased risk for VTE, with risk factors such as older age, obesity, flaccid paralysis, and cancer. Several studies have indicated that age is a particularly significant risk factor, with older patients with SCI being more likely to develop VTE.[100]

Patients with spinal trauma who also have associated SCI face an elevated likelihood of VTE. LMWH has been determined to be more efficient in preventing DVT while yielding fewer instances of bleeding complications when contrasted with unfractionated heparin. Vitamin K antagonist use is also found to be effective in preventing PE.[101] In some cases, chemical anticoagulation may be delayed after surgery due to concerns about bleeding or neurological complications. In these situations, inferior vena cava filters can be used to prevent a PE.[102]

The available evidence does not support the routine administration of pharmacologic venous VTE prophylaxis for major spinal procedures in pediatric patients. Chemoprophylaxis should be contemplated solely for patients who exhibit multiple risk factors. There is also controversy surrounding the use of mechanical prophylaxis although it poses minimal risk.

The likelihood of VTE occurring after spinal fusion in children is estimated to be 0.21%, and the risk factors include children in their adolescent years, as well as those with congenital scoliosis, syndromic spinal deformities, kyphoscoliosis, or thoracolumbar fractures.[103]

The efficacy of VTE prophylaxis in pediatric patients undergoing major spine procedures is not well-established due to the lack of available data. Nonetheless, given the rare occurrence of VTE in this patient population, studies have yet to demonstrate a significant clinical benefit for VTE prophylaxis.

A survey was conducted among 47 spine surgeons, including orthopedic and neurosurgeons, to evaluate the standard of care in perioperative thromboprophylaxis for spinal surgery. The survey found that 91% of the surgeons used pharmacologic prophylaxis for SCI patients, while only 62% used it for non-SCI patients. Comparable outcomes were noted when examining anterior thoracolumbar procedures in contrast to posterior thoracolumbar surgeries. Nevertheless, it is noteworthy that almost half of the surgeons encountered complications associated with the use of LMWH, encompassing instances such as epidural hematomas, retropharyngeal hematoma, thrombocytopenia, and wound hematoma.[104]

Pediatric

Risk factors for VTE in pediatric orthopedic patients resemble those found in adults, including advanced age (adolescents), trauma, malignancy, specific infections, coagulation disorders, and a personal or familial history of VTE. Nonetheless, certain VTE risk factors prevalent in adult literature, such as smoking, might be less prevalent among children. On the other hand, certain risk factors, like congenital thrombophilia, may be more prevalent in pediatric patients than in adults.

VTE is a rare occurrence in pediatric orthopedic patients, with reported incidence rates of 0.052% following elective procedures[105] and 0.10% when including nonelective procedures.[106] However, the incidence of VTE increases significantly to 0.68% in pediatric trauma patients, making them the subgroup with the highest risk.[107]

According to a survey on pediatric trauma practices, LMWH prophylaxis was utilized 'often' or 'always' in 13% of trauma centers for patients aged 11-15 years old and in 57% of cases for patients aged 16-20 years old.[108]

A recent meta-analysis conducted by Mahajerin et al[109] found that pharmacologic prophylaxis should be considered for children with a low risk of bleeding who are hospitalized for a traumatic injury and are over the age of 15 or younger postpubertal children with an injury severity score (ISS) greater than 25. However, routine pharmacologic prophylaxis is not recommended for prepubertal children, even those with an ISS greater than 25. The Eastern Association

of Surgery for Trauma guidelines also recommend pharmacologic prophylaxis for children over 15 years old, or postpubertal children under the age of 15 with an ISS greater than 25. It is important to note that these guidelines lack definitive evidence due to the overall low quality of available data.

It is not recommended to routinely prescribe chemoprophylaxis for VTE in patients under the age of 13 who are undergoing orthopedic procedures unless there are other identifiable risk factors for VTE.

Strength of recommendation: Weak.

Delegates vote: Agree 100.00%, disagree 0.00%, abstain 0.00% (unanimous strong consensus).

According to several studies, the incidence of DVT in pediatric patients undergoing orthopedic procedures, such as scoliosis surgery, is relatively low. For instance, a survey of Scandinavian scoliosis centers between 1963 and 1976 reported a DVT incidence of 0.65%.[110] In another study, two cases of transient thromboses were identified in 40 consecutive postpubertal adolescents undergoing posterior spinal instrumentation both of which resolved spontaneously.[111] Erkilinc et al[112] reported that the incidence of DVT was 0.13% in a study of 1471 pediatric patients undergoing scoliosis surgery. Hence, the authors of the study recommended that mechanical prophylaxis was adequate in this context. Additionally, a study by Jain et al[103] analyzing the National Inpatient Sample database reported an incidence of DVT of 0.21% in pediatric patients undergoing spine surgery. Notably, children with congenital, syndromic, or traumatic etiology of scoliosis were found to have a higher incidence of VTE compared to those with idiopathic scoliosis.[113]

Infection is a firmly established and common contributing factor to the development of VTE.[114] Specifically, infections induced by microorganisms that produce necrotizing toxins, such as Panton–Valentine leukocidin, are associated with the occurrence of extensive septic thrombosis. Consequently, in cases where infection involves methicillin-resistant *Staphylococcus aureus*, the implementation of VTE thromboprophylaxis could be warranted.[114]

The limited incidence of DVT, along with the diversity of clinical studies, multiple risk factors, and variations in risk levels due to age, make it challenging to create evidence-based guidelines for chemoprophylaxis in pediatric patients undergoing orthopedic procedures. Hence, it is advisable to contemplate thromboprophylaxis for adolescents exhibiting additional identifiable risk factors. More specifically, individuals diagnosed with osteomyelitis or widespread infection, as well as those with a central line, could be deemed suitable candidates for thromboprophylaxis.

Oncology: Individuals who receive prophylactic fixation or undergo the fixation of pathological fractures caused by metastatic bone disease face an increased likelihood of developing VTE. Multiple factors contribute to this risk, including patient age, comorbidities, and the extent and duration of surgery. To reduce this risk, thromboprophylaxis should be administered to hospitalized patients or those undergoing surgery, with or without mechanical prophylaxis, unless contraindications exist. However, there is currently insufficient evidence to recommend a specific type of thromboprophylaxis.[115]

Strength of recommendation: Limited.

Delegates vote: Agree 92.31%, Disagree 0.0%, Abstain 7.69% (Strong Consensus)

The literature regarding optimal prophylaxis for orthopedic oncology and metastasis surgery is currently limited. The American Society of Clinical Oncology has provided guidelines for the treatment of cancer patients that are categorized based on various factors, including hospitalization status, outpatient status, undergoing surgery, and having established VTE.[116] Pharmacologic thromboprophylaxis should be considered in hospitalized patients with active malignancy and acute medical illness or reduced mobility, provided that there are no contraindications, but should not be routinely administered for minor procedures or chemotherapy infusion. The need for VTE prophylaxis in cancer outpatients depends on the specific cancer being treated and the chemotherapeutic regimen used.[116]

Patients diagnosed with malignant diseases who are undergoing significant surgical procedures should be presented with the option of pharmacological thromboprophylaxis, unless contraindicated due to ongoing bleeding, heightened bleeding risk, or other medical restrictions. Thromboprophylaxis should be instated prior to the surgery, and it is advised not to rely solely on mechanical prophylaxis. Instead, a combination of mechanical and pharmacological prophylaxis is recommended for patients at high risk.[116]

There are various types of agents available for VTE prophylaxis, including LMWH, vitamin K antagonist, direct oral anticoagulants, and aspirin. According to one study, aspirin has been found to significantly lower the incidence of acute pulmonary embolism although it carries a similar risk of major bleeding as other agents.[117]

Currently, a dearth of high-quality studies prevents a conclusive determination of a specific population based on tumor characteristics or procedure type that mandates prophylaxis. Nevertheless, there exists certain evidence indicating that patients undergoing resection procedures for bone metastasis or interventions involving prosthesis reconstruction have an elevated susceptibility to VTE. Consequently, such patients should be considered for proactive prophylactic measures.

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