CURRENT CONCEPTS REVIEW

Advancements in venous thromboembolism prophylaxis strategies for total hip arthroplasty: a comprehensive narrative review

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Abstract

Worldwide, total hip arthroplasty (THA) is a widely performed procedure. However, it is associated a significant risk of venous thromboembolism (VTE), a serious and potentially life-threatening complication. As a result, VTE prophylaxis has been a focal point of ongoing clinical research and discussion. Despite extensive evaluation, there is still no definitive consensus on the optimal strategy for preventing VTE in patients undergoing THA. The absence of a clear gold standard highlights the complexity of balancing the benefits of thromboprophylaxis with the risks of bleeding and other wound complications. This review aims to address this gap by providing a thorough examination of current literature on VTE prophylaxis in the context of THA.

To explore the most effective and safest strategies for VTE prevention, we conducted a narrative review, analysing studies and guidelines from major medical databases. Our review focuses on key aspects of VTE prophylaxis, including patient-specific risk factors, diagnostic challenges, treatment-related complications, and recent advancements in both pharmacological and mechanical prevention strategies. We evaluated anticoagulants such as low molecular weight heparins, direct oral anticoagulants, and aspirin, alongside mechanical methods such as pneumatic compression devices and early mobilisation. Each prophylactic method was assessed for its effectiveness in reducing VTE incidence as well as its associated risks, including bleeding, wound complications and patient compliance.

Our synthesis of the available evidence highlights both established practices and emerging controversies in the field, offering a comprehensive understanding of the various options available to clinicians. Given the individualised nature of VTE risk in THA patients, this review emphasises the importance of tailored prophylaxis strategies, accounting for patient comorbidities, surgical factors and personal preferences. The findings of this review underscore the necessity for ongoing research and interdisciplinary collaboration to refine and optimise VTE prevention in the evolving landscape of THA. As the field progresses, it is crucial that clinicians remain updated on new evidence to make informed, patient-centred decisions that enhance safety and outcomes in THA.

Level of evidence: 5

Keywords: total hip arthroplasty, venous thromboembolism, risk assessment models, thromboprophylaxis, emerging trends

Introduction

Total hip arthroplasty (THA) is the gold standard surgical procedure for end-stage degenerative disease of the hip joint.[1] The global demand and volume of patients receiving THA surgery is projected to rise considerably due to increasing demands for improved mobility and quality of life (QoL) among the ageing population.[2] Current trends predict that the number of THAs performed annually in the United States of America (USA) will increase to 4 million by the year 2030, while in Organisation for Economic Co-operation and Development (OECD) countries, the number of THAs performed is projected to rise from 1.8 to 2.8 million per year between 2015 and 2050.[3,4]

With the increasing number of THAs performed, there is a parallel increase in associated complications. One of these complications is venous thromboembolism (VTE), which includes both deep vein thrombosis (DVT) and pulmonary embolism (PE).[5] VTE is a well-recognised and preventable cause of morbidity and mortality and is responsible for approximately 10% of hospital deaths in the United Kingdom (UK).[6,7] Globally, ten million VTE episodes are diagnosed annually, with the incidence estimated to be between 0.6 and 1.5% in patients undergoing a THA.[5,8] VTE events place a significant financial burden on both the patient and the healthcare system as a result of their recurrence and complications.[7] In the USA, it is estimated that VTE events cost the healthcare system $7–10 billion per year.[9]

While an abundance of literature and guidelines recommended by major authorities in the USA, Europe, and the UK exist, there is much controversy around which methods of VTE prophylaxis have the greatest efficiency at preventing VTE in patients undergoing THA.[10,11] There remains no clear consensus regarding the gold standard for VTE prophylaxis in THA, with difficulty finding the correct balance between eliminating VTE risk and preventing the associated complications arising with VTE prophylaxis postoperatively.

Pathophysiology

VTE encompasses a spectrum of conditions, from undetectable DVT to potentially fatal PE.[12] Venous stasis, endothelial damage, and hypercoagulable states constitute Virchow's triad, a set of three variables that contribute to thrombus formation. Two or more of the above features must be present for VTE to develop.[13] Venous stasis manifests in both the intraoperative and postoperative setting, as a result of intraoperative immobilisation during THA as well as during the postoperative period. Patients are also less mobile following joint reconstruction.[5] Endothelial damage is an inherent consequence of surgical procedures as a result of soft tissue handling and dissection, with a direct correlation existing between the degree of venous impairment and the incidence of VTE.[14] While intrinsic to the surgical process, measures can be adopted to mitigate endothelial damage by implementing minimally invasive surgical techniques, such as the direct anterior approach (DAA).[5] Inflammatory reactions and the release of prothrombotic mediators at both systemic and localised levels occur in response to tissue trauma during the intraoperative and postoperative periods, resulting in an established hypercoagulable state.[15]

In the context of THA, the surgical approach may directly cause venous stasis and endothelial injury.[16] In both the posterior approach (PA) and lateral approach (LA), flexion, adduction and external rotation of the femur during preparation of the femoral canal lead to 'scissoring' of the femoral vein and complete obstruction of flow.[16] In contrast, extension, abduction and internal rotation of the femur during canal preparation in the DAA do not alter flow through the femoral vein.[16]

Flevas et al.[10] highlighted that patients undergoing THA are at an increased risk of VTE due to bed rest and immobilisation causing venous stasis, intraoperative manipulation of the lower limb causing endothelial injury, and the use of bone cement increasing hypercoagulability through activation of the coagulation cascade.

Risk factors for VTE in patients undergoing THA

The risk factors for VTE in patients undergoing THA include patient-specific and surgical risk factors. These may be further divided into weak, moderate and strong risk factors based on their odds ratio (OR) (*Table I*).

Patient-specific risk factors

Patient factors associated with an increased risk of developing VTE after THA include age, sex, body mass index (BMI), race, American Society of Anesthesiologists (ASA) status, and the presence of comorbidities such as HIV infection, blood dyscrasias, chronic kidney disease, and malignancies.[17-19] A systematic review by Zhang et al.[18] highlighted that the most prevalent patient-related risk factors for developing VTE in THA are older age (> 70 years), female sex, higher BMI (> 30 kg/m^2), and a history of previous VTE.

Age is a non-modifiable risk factor for complications associated with THA and an independent risk factor for VTE.[18,20,21] Patients over the age of 40 years are at a significantly greater risk of VTE compared to younger patients. This may be related to the imbalance that exists with an increase in the levels of coagulation activation peptides and a reduction in the activity of the fibrinolytic system.[22] Increased age is also associated with an increase in a number of comorbid conditions, which may directly influence the risk of developing VTE.[20] Therefore, accurate diagnostic methods and strategies for preventing VTE are critical for patients preoperatively.[20]

Obesity is a moderate, independent risk factor for VTE.[18,19,23] A BMI of ≥ 30 kg/m^2 results in a constant low-grade inflammatory state, an imbalance of fibrinolysis and fibrinogen activity, and elevated levels of von Willebrand factor and factor VII, resulting in an overall prothrombotic state and increased risk of VTE.[23] A 2023 review by Uzel et al.[19] noted that 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. Therefore, it is imperative to preoperatively counsel patients about weight loss before undergoing THA.

Surgical risk factors

Surgical risk factors include the surgical approach utilised, surgical duration, cementation of the prosthesis, and anaesthetic technique.

The surgical approach utilised for THA may directly influence the risk of VTE. The manipulation of the limb during the PA and LA may explain the rate of VTE seen in patients undergoing these procedures.[16] Chen et al.[24] and Sun et al.[25] reported that the rates of VTE after DAA THA were significantly lower than those seen after PA THA and reported rates of < 1% after DAA THA. This is in contrast to Kawano et al.,[16] comparing the incidence of VTE in 109 patients who underwent THA utilising either the DAA or LA and reported a significantly higher incidence of VTE in the DAA group (19.4% vs 5%) (p = 0.014). However, a vast majority of VTE occurred during the early period after introducing the DAA, with the second half of DAA patients not showing any difference. This may be attributed to the fact that during a surgeon's early experience utilising the DAA, significantly longer operative times are noted

Table I: Risk factors for VTE according to Konstantinides et al.[82]

Weak risk factors (OR < 2)	Moderate risk factors (OR 2–9)	Strong risk factors (OR > 9)
Bed rest > 3 days	Arthroscopic knee surgery	Spinal cord injury
Cardiovascular risk factors (diabetes, hypertension, obesity)	Autoimmune diseases	Lower limb fracture
Advanced age	Blood transfusions	Arthroplasty surgery (hip or knee)
Minor surgery	Intravenous catheters	Major trauma
Pregnancy/puerperium	CCF or respiratory failure	Previous VTE
Varicose veins	Oral contraceptive therapy	Antiphospholipid syndrome
	Infection (pneumonia, UTI & HIV)	MI or heart failure requiring hospitalisation (past three months)
	Malignancy/chemotherapy	
	Superficial vein thrombosis	
	Paralytic stroke	
	Thrombophilia	

OR: odds ratio; CCF: congestive cardiac failure; UTI: urinary tract infection; HIV: human immunodeficiency virus; MI: myocardial infarction

compared to other traditional THA approaches, emphasising that duration of the procedure may contribute more than the surgical approach alone to the risk of VTE. This is in keeping with results from a recent meta-analysis comparing outcomes of the DAA, PA and LA from 24 studies that there is no difference in VTE rates between the approaches.[26]

Surgical duration has been identified as a risk factor for developing VTE, with a vast majority of the literature reporting an increased incidence of VTE associated with prolonged operative time exceeding two hours.[19,27-29] However, discrepancies exist regarding the exact cut-off time for which surgical duration influences the risk of developing VTE.[27]

Cemented versus uncemented prostheses carry different risks. Polymethyl methacrylate (PMMA) used for cementation of both femoral and acetabular components triggers the release of mononuclear cytokines, separation and deformation of endothelial cells, and subsequent coating of the endothelial surface with fibrinogen, which in turn leads to upregulation of the exogenous coagulation cascade and increases the risk of VTE.[30,31] Lindberg-Larsen et al.[32] reviewed 8 000 patients and compared the incidence of PE in individuals undergoing primary THA with either cemented or uncemented prostheses. Their findings revealed a significantly higher incidence of PE in the cemented prosthesis cohort compared to the uncemented THA counterparts (0.4% vs 0.1%, p = 0.001).

Another factor is anaesthetic technique. The association between the type of anaesthesia and the risk of VTE is complex and multifactorial, which can be influenced by various factors.[33,34] Under general anaesthesia, the occurrence of vasodilation plays a contributing role in the initiation of VTE by inducing venous stasis, increasing venous capacitance, and resulting in a reduction in venous return.[34] The use of regional anaesthesia has proven to be the most favourable anaesthetic method for patients undergoing THA, as it is associated with a lower incidence of VTE, lower volumes of perioperative blood loss, a reduction in the length of hospital stay, and an overall reduction in the risk of surgical site infection.[33,34] The 2019 International Consensus on Anaesthesia-Related Outcomes after Surgery group (ICAROS) guidelines strongly recommend using neuraxial anaesthesia as the preferred method of anaesthesia for patients undergoing THA, where possible.[35]

Diagnosis and risk stratification

To reduce the mortality from VTE as well as the morbidity associated with the unnecessary administration of thromboprophylaxis, accurate detection of VTE is crucial.[36] Risk assessment models (RAMs) have been developed to effectively stratify the VTE risk in hospitalised patients.[37] These models use clinical data extracted from the patient's medical records and physical examination to identify individuals with a heightened risk of developing VTE who stand to benefit the most from pharmacological prophylaxis.[8]

Worldwide, the Caprini score is the most widely used and validated RAM for all surgical specialities, including orthopaedic surgery.[37] This RAM estimates a patient's perioperative VTE risk and provides clinicians with recommendations for thromboprophylaxis after assessing a series of patient- and operation-specific risk factors.[38] A cumulative score is generated, based on a number of risk factors that are allocated a score of one to five points out of a total of 20 points based on their perceived variation of risk. Patients are categorised as low risk (score 0 points), intermediate risk (score 1–2 points), high risk (score 3–4 points), and very high risk (score ≥ 5).[8] All patients undergoing THA, according to the Caprini score, are considered high-risk for VTE (score≥ 5 points).[39] (See *Table II* for a summary of the Caprini RAM.)

The implementation of specific RAMs, such as the Caprini RAM, has significantly advanced VTE prophylaxis management

Table II. Summary of the Caprini RAM[9]

Risk factor		Points
Age (years)	41–60	1
	61–74	2
	≥ 75	3
Body mass index (kg/m²)	≥ 25	1
Female patients	Hormone replacement therapy/ oral contraceptive	1
	Pregnancy/puerperium	1
	Multiple unexplained miscarriages	1
Thrombophilias		3
Venous disease	Lower limb oedema/varicosities	1
	Previous VTE/family history of VTE	3
Immobilisation	Medical patient at bed rest	1
	Confined to bed > 3 days	2
	Plaster cast on lower limb	2
Surgical intervention	Elective minor surgery	1
	Arthroscopic surgery	2
	Prolonged major or laparoscopic surgery longer than 45 minutes	2
	Elective THA	5
	Pelvis, hip, or lower limb surgery	5
Other	Sepsis/pneumonia (< 30 days)	1
	Impaired pulmonary function/MI/ acute heart failure/IBD	1
	Central venous access	2
	Malignancy	2
	Stroke/spinal cord injury	5

RAM: risk assessment model; VTE: venous thromboembolism; THA: total hip arthroplasty; MI: myocardial infarction; IBD: inflammatory bowel disease

in patients undergoing THA. This approach has enabled a shift from a 'one-size-fits-all' strategy to a more individualised, risk-stratified method for VTE prevention, allowing for tailored patient-specific interventions.[40,41] Recent studies have robustly validated the efficacy of the Caprini RAM in the context of THA. In a 2019 retrospective review of 1 078 patients who underwent elective THA, Krauss et al.[41] demonstrated that the Caprini score is an accurate and reliable RAM for predicting VTE risk in THA patients. They suggested that a score of 10 points or greater should be considered high risk, noting that the dynamic nature of the scoring system can reflect changes in a patient's clinical status perioperatively, which may necessitate adjustments in VTE prophylaxis treatment. Similarly, Qiao et al.[40] analysed the incidence of VTE in 3 807 THA patients who were preoperatively evaluated using the Caprini RAM and underwent routine postoperative lower limb duplex ultrasound to detect asymptomatic VTE. They found a significant correlation between the Caprini score and VTE incidence (p = 0.003), with patients scoring over 9 points having a significantly higher likelihood of developing VTE compared to lower-risk patients (p < 0.001). Both studies underscore the model's utility in identifying patients who may benefit from more aggressive prophylactic strategies, such as anticoagulants and mechanical prophylaxis. This targeted approach not only enhances patient outcomes but also optimises resource utilisation within healthcare settings.

The ongoing refinement of the Caprini RAM further enhances its applicability.[37] Recent adaptations have considered additional risk factors and biomarkers, aiming to increase its predictive power and relevance in modern clinical practice.[42] Moreover, studies are investigating the model's performance in conjunction with contemporary THA practices, such as early postoperative mobilisation and the use of novel anticoagulants.[43,44] These efforts

Table III. Summary of the Wells score[46]

Criteria	Points
Active malignancy or treated in past six months	+1
> 3 cm discrepancy in calf swelling compared to asymptomatic calf	+1
Enlarged non-varicose veins in symptomatic limb	+1
Pitting oedema	+1
Previous DVT	+1
Swelling of entire leg	+1
Tenderness along deep venous system	+1
Recent plaster cast immobilisation of limb	+1
Bedridden > 72 hours or major surgery necessitating GA/RA in past 3 months	+1
Alternative diagnosis more likely than VTE	−2

DVT: deep vein thrombosis; GA: general anaesthetic; RA: regional anaesthetic; VTE: venous thromboembolism

are essential to ensure that the Caprini RAM remains a vital tool in the evolving landscape of THA.

An additional RAM utilised for evaluating VTE risk in patients undergoing THA is the Wells score, which is an effective, clinically validated screening tool for determining a patient's pre-test probability of developing DVT.[20] *Table III* summarises the Wells score: it assigns points by assessing ten clinical variables, with each variable contributing one point. Two points are subtracted if an alternative diagnosis is more probable than that of a DVT. The combined total is used to generate a score that ranges from −2 to 9, with a score of ≤ 0 being low risk, 1–2 being moderate risk, and > 3 being associated with a significant probability of DVT.[20,45] In low- and moderate-risk groups, a D-dimer laboratory test should be requested. If this is negative, the prevalence of DVT is < 1%, and no further imaging is required. If the D-dimer test is positive, lower limb duplex venous ultrasound (VUS), which is the gold standard initial imaging modality, should be performed.[20] In high-risk groups, diagnostic VUS should be performed irrespective of the D-dimer result. If the VUS detects the presence of a lower-limb DVT, anticoagulation therapy is strongly recommended.[20]

Luksameearunothai et al.[46] conducted an observational, analytical, case-control study comparing the accuracy of several RAMs and reported that the Wells score is more accurate and has superior sensitivity (80.6% vs 61.1%) and specificity (80.6% vs 66.7%) compared with the Caprini score at predicting the likelihood of VTE.

Management

In general, the management strategies aimed at reducing the incidence of VTE following THA include pharmacological, mechanical, or combined prophylactic measures. Nam et al.[47] reported that patients undergoing THA without VTE prophylaxis have a VTE incidence of 40–60%. In contrast, with routine thromboprophylaxis strategies, the incidence rates of VTE associated with THA range from 1.3–10%.

Currently, mechanical, pharmacological, or combined thromboprophylaxis strategies are considered the standard of care to prevent the occurrence of VTE among all hospitalised patients.[48]

Pharmacological VTE prophylaxis

The ideal agent for thromboprophylaxis should be effective in preventing VTE, easy to administer (oral), have a short half-life, be inexpensive, have a reversal agent, and be safe to use, especially with regard to bleeding complications. Another concern is persistent wound drainage (PWD) and haematoma formation, which are associated with an increased risk of prosthetic joint infection (PJI).[49] Therefore, when prescribing these agents, all the potential risks and benefits need to be considered to avoid the occurrence of adverse events.

Table IV: Summary of VTE pharmacological prophylaxis options

Pharmacological agent	Mechanism of action	Dosage	Advantage	Disadvantage	Reference
Unfractionated heparin	Potentiates the activity of antithrombin III, leading to the inhibition of thrombin and factor Xa	5 000 U IVI 8 hrly	Rapid onset of action and short half-life	Requires continuous monitoring using aPTT Increased risk of major bleeding and HIT	83
LMWH	Enhances antithrombin III activity to inhibit factor Xa and, to a lesser extent, thrombin	40 mg SC daily	No monitoring of aPTT required	Requires renal dose adjustment Subcutaneous injections	54
Warfarin	VKAs that limit clotting factors (II, VII, IX, X, protein C and S)	2–5 mg/day adjusted to a target INR of 2–3	Oral administration	Numerous drug and food interactions Requires monitoring of INR	49
Aspirin	Prevents aggregation of platelets via COX 1 and 2 inhibition	160 mg/day	Oral administration Low bleeding risk No monitoring required	No antidote Increased risk of gastrointestinal bleeding	84,85
Rivaroxaban	Directly inhibits factor Xa or thrombin	10 mg/day	Oral administration Fixed dosing	Limited availability of specific antidotes Cost considerations	85
Dabigatran	Direct thrombin inhibitor	220 mg/day	Oral administration Fixed dosing Rapid onset	Limited monitoring No reversal agent	87
Fondaparinux	Selectively inhibits factor Xa and indirectly inhibits thrombin formation	5–7.5 mg SC daily	Low risk of HIT No monitoring required	No reversal agent Subcutaneous injections	49

IVI: intravenously; LMWH: low molecular weight heparin; aPTT: activated partial thromboplastin time; HIT: heparin-induced thrombocytopenia; SC: subcutaneously; VKAs: vitamin K antagonists; INR: international normalised ratio; COX: cyclooxygenase

The most used pharmacological prophylaxis agents include low molecular weight heparin (LMWH), unfractionated heparin (UH), aspirin, vitamin K antagonists (VKAs), synthetic inhibitors of factor Xa (fondaparinux), and newer direct-acting oral anticoagulants (DOACs), namely, dabigatran, rivaroxaban, apixaban and edoxaban.[10,50] (Refer to *Table IV* for a summary of pharmacological prophylaxis options.)

Low molecular weight heparin (LMWH)

LMWH is an established pharmacological agent used for VTE prophylaxis in the setting of THA.[51,52] Numerous randomised controlled trials (RCTs) have been conducted, establishing the efficacy of LMWH in DVT prevention, not only within the arthroplasty setting but also beyond.[53] A systematic review by Lu et al.,[52] which compared the efficacy of LMWH to placebo, factor Xa inhibitors, and direct thrombin inhibitors, noted that, compared to factor Xa inhibitors, LMWH was associated with a significantly higher incidence of VTE. However, the risk of major bleeding events was lower in patients who received LMWH than in those receiving direct thrombin inhibitors. A recent meta-analysis by He et al.[54] demonstrated the effectiveness of LMWH in preventing VTE, although acknowledging limitations in patient adherence since it is administered via subcutaneous injection. This observation aligns with several meta-analyses, collectively suggesting that LMWH constitutes a robust chemoprophylactic option for patients undergoing THA.[52]

Aspirin

Aspirin exerts an anticoagulant effect through irreversible inhibition of platelet cyclooxygenase and selective inhibition of thromboxane A2.[55] It has the added advantage over other pharmacological agents in that it does not require monitoring and is inexpensive, readily available, and administered orally.[55] Globally, there has been an increase in the usage of aspirin due to the fact that it is well tolerated by patients and has been associated with lower rates of major bleeding events compared to other anticoagulants.[56] However, the recent CRISTAL trial (2021), a prospective randomised trial comparing the efficacy of LMWH and aspirin, showed that the rates of symptomatic VTE were significantly higher in the aspirin group compared to those in the LMWH group (3.4% vs 1.82%) ($p < 0.005$).[57] Aspirin has been shown to be more effective than placebo and is suggested as a suitable therapy for the prevention of VTE by the American College of Chest Physicians (ACCP) and American Academy of Orthopaedic Surgeons (AAOS); however, according to the Scottish Intercollegiate Guidelines Network (SIGN) guidelines, it should not be used as the sole pharmacological agent for VTE prophylaxis, and future studies are still needed to determine the best dosage and duration.[10] There are concerns that aspirin may not be effective for patients that are higher risk for VTE, such as patients with previous VTE, active malignancy, thrombophilia and obesity with decreased mobility.[55] The ongoing Pulmonary Embolism Prevention after hiP and kneE Replacement (PEPPER) trial comparing aspirin, rivaroxaban and warfarin will hopefully provide more valuable information, with results to be finalised in 2024.[58]

Vitamin K antagonists (VKAs)

VKAs, namely warfarin, disrupt the hepatic synthesis of factors II, VII, IX, and X.[59] Warfarin offers notable advantages over other pharmacologic agents, including a longstanding history of effective use for VTE prophylaxis in THA patients and its oral administration.[55] Drawbacks associated with the use of warfarin include the need for frequent monitoring of the international normalised ratio (INR) with a target range of 2–3, interactions with a variety of drugs and foods, and a delayed onset of action on the coagulation cascade, taking two to three days to reach the targeted INR and need overlap with other anticoagulation therapy.[60] A 2021 meta-analysis by He et al.[54] evaluating the efficacy and safety profile of eight anticoagulants, showed that warfarin had the lowest efficacy at preventing VTE and was associated with the highest risk of major bleeding events. Hughes et al.[61] reported that the use of warfarin prophylaxis in THA patients resulted in higher rates of surgical site infection and deep infections requiring reoperation compared to aspirin; however, there was no statistically significant difference noted when warfarin was compared to LMWH.

Synthetic pentasaccharide factor Xa inhibitors (fondaparinux)

Fondaparinux induces anticoagulation through selective inhibition of factor Xa, facilitated by antithrombin.[62] Notably, its advantages over LMWH include the absence of thrombin inhibition, no impact on platelet function, and the absence of cross-reactivity within the serum of patients experiencing heparin-induced thrombocytopenia (HIT). In a recent meta-analysis, which included 25 trials and a combined total of 21 000 patients, fondaparinux was found to significantly lower the incidence of symptomatic VTE compared to placebo (0.2% vs 1.2%) ($p = 0.002$).[63] However, this benefit was associated with an increased risk of major bleeding (1.2% vs 0.5%). When comparing fondaparinux to LMWHs across various trials, the rates of symptomatic VTE were comparable between the two groups. Nevertheless, fondaparinux was associated with a higher rate of major bleeding events (2.5% vs 1.8%).[63]

Direct oral anticoagulants (DOACs)

The DOACs are a group of oral anticoagulant agents that include direct factor Xa inhibitors, namely rivaroxaban, apixaban, edoxaban, and the selective, reversible, direct thrombin inhibitor, dabigatran.[64] Over the past decade, DOACs have emerged as alternative agents for both the prophylaxis and treatment of VTE.[65] The advantages of these agents include that they are administered orally, can be given at fixed doses, and do not require routine laboratory monitoring.[10] A recent meta-analysis conducted by Haykal et al.[66] reported significantly lower rates of proximal DVTs, PE, and VTE-related deaths in patients who received DOACs compared to those who received LMWH for VTE prophylaxis ($p < 0.01$). However, no statistically significant difference was noted in the incidence of major or minor bleeding events between the two cohorts. The DOACs are a safe and effective alternative to LMWH in patients undergoing THA, and due to their ease of use, rapid onset, fewer interactions with drugs and food, and the absence of the need for frequent monitoring, they are becoming increasingly popular as mainstay thromboprophylaxis agents in the field of orthopaedic surgery.[64] In a retrospective cohort study comparing the long-term outcomes of DOACs and aspirin, Simon et al.[67] identified significant differences in VTE incidence and bleeding risk

Table V: Advantages and disadvantages of mechanical VTE prophylactic strategies[88]

Advantages	Disadvantages
No risk of bleeding No laboratory monitoring is necessary No side effects Marked reduction in VTE risk when combined with pharmacological methods May enhance the efficacy of anticoagulants (IPCD)	Limits patient mobility Patient discomfort Impairment of tissue oxygenation by AES Unable to use in patients with arterial insufficiency, cardiac failure, or infection or in cases of wounds/ulcers Cost

VTE: venous thromboembolism; AES: anti-embolism stockings; IPCD: intermittent pneumatic compression

between the two agents. At 30 days, the incidence of VTE was 0.92% in the DOAC group compared to 0.83% in the aspirin group. By 90 days, these incidences were 1.63% and 1.29%, respectively. The odds of a VTE event at 30 days were similar between the DOAC and aspirin groups. However, the DOAC group exhibited a higher risk of bleeding, a trend that persisted up to 90 days, despite no significant difference in VTE odds.

Mechanical VTE prophylaxis

Mechanical methods of prophylaxis are a useful adjunct in VTE prophylaxis and are frequently used in combination with pharmacological methods. Benefits of mechanical prophylaxis strategies include the fact that they can be used in the early postoperative period and can be initiated intraoperatively with no risk of increasing bleeding or the need for any monitoring. They enhance venous blood flow, thereby creating a less favourable environment for clot formation, which may be achieved by static or dynamic systems.[68] Mechanical prophylaxis methods include patient mobilisation, anti-embolism stockings (AES), intermittent pneumatic compression devices (IPCDs), and foot impulse devices[10,50] (*Table V*).

A systematic review evaluating the incidence of VTE in patients receiving combined mechanical and pharmacological prophylaxis compared to single modality prophylaxis found that the combination prophylaxis reduced the risk of DVT compared to pharmacological methods alone.[69] However, there is insufficient evidence that mechanical prophylaxis strategies alone decrease the risk of PE.[68] In a recent large-centre retrospective study of 2 978 arthroplasty patients, Loh et al.[70] noted no statistically significant difference in VTE incidence rates between patients who received combined mechanical and chemical thromboprophylaxis and those who received chemical prophylaxis alone (5.9% vs 4.6%) (p = 0.13). Among the existing clinical literature, no randomised clinical trial exists that has investigated the utilisation of mechanical prophylaxis in combination with mobilisation and enhanced recovery protocols. A prospective study by Gill et al.[71] demonstrated that patients deemed 'low risk' preoperatively can safely be given mechanical prophylaxis alone and kept on enhanced recovery pathways, demonstrating results comparable to those of chemoprophylaxis. However, this study lacked randomisation and took place between 1999 and 2016. The improved recovery protocols for patients undergoing THA have developed significantly over the past two decades; therefore, the validity of this data is uncertain due to the influence of medical advances.

Emerging technologies in VTE thromboprophylaxis

Electronic medical records (EMRs) have created novel opportunities for VTE prevention.[72] Research demonstrates that computer-based alert interventions enhance adherence to appropriate VTE risk stratification protocols, reduce costs by preventing unnecessary thromboprophylaxis in low-risk patients, and mitigate preventable VTE-related harm.[73] The implementation of such systems should carefully evaluate whether the absolute benefits justify the additional workload imposed on healthcare providers, especially when the system's effectiveness depends on direct provider input.[74-76] Machine learning has the capacity to recognise patterns in complex sets of information that accurately predict the risk of VTE and bleeding, and this can lead to better outcomes.[77]

Current guidelines and expert opinion

There is significant global debate pertaining to VTE prophylaxis and which pharmacological agent(s) should be used for VTE prophylaxis following THA, with the need to balance cost, clinical efficacy, risk of bleeding, and wound complications.[53,78] This has led to discrepancies between the recommendations from major authorities globally, as geographic variation exists between the VTE prophylaxis guidelines followed in different countries (*Table VI*).

The ACCP recommends chemical prophylaxis using LMWH, fondaparinux or warfarin, with a target INR of 2.5 for at least 10–14 days and up to 35 days. In addition, combined prophylactic

Table VI: Global VTE prevention guidelines for THA

Organisation	Guideline	Summary of the recommendations
American College of Chest Physicians (ACCP) 9th Edition (2012)[13]	Patients who are not at an elevated risk of VTE or bleeding should receive combined mechanical and chemical prophylaxis to prevent VTE	Recommend LMWH as the optimal pharmacological agent. Acceptable alternatives include low-dose UFH, VKAs, fondaparinux, apixaban, dabigatran, rivaroxaban, or aspirin for at least 10–14 days and strongly recommend increasing to 35 days AND IPCDs recommended for 18 h a day
American Academy of Orthopaedic Surgeons (AAOS) (2011)[89]	Recommend the use of mechanical and/or chemoprophylactic measures	No specific pharmacological or mechanical prophylaxis strategy is recommended Early mobilisation is strongly advised
National Institute for Health and Care Excellence (NICE) (2018)[14]	VTE prophylaxis should be offered to individuals undergoing elective THA if the potential risk of developing VTE exceeds the potential risk of bleeding complications	Recommend LMWH or suitable alternative for ten days followed by 28 days of aspirin or LMWH along with anti-embolism stockings for 28 days Rivaroxaban, apixaban and dabigatran are suitable alternatives
Scottish Intercollegiate Guidelines Network (SIGN) (2010, updated 2015)[90]	Unless contraindicated, all patients should receive combined mechanical and pharmacological prophylaxis Extended duration prophylaxis is strongly recommended	The recommended agents include LMWH, fondaparinux, rivaroxaban and dabigatran. Aspirin is not recommended as the sole pharmacological agent IPCDs are recommended for mechanical thromboprophylaxis Extended prophylaxis is recommended; however, the optimal duration is unclear

VTE: venous thromboembolism: LMWH: low molecular weight heparin; UFH: unfractionated heparin; VKA: vitamin K antagonist; IPCD: intermittent pneumatic compression device; THA: total hip arthroplasty

strategies should be administered for 18 hours a day while the patient is admitted until discharge.[11]

The National Institute for Health and Care Excellence (NICE) guidelines recommend LMWH for ten days, followed by aspirin for 28 days, LMWH or fondaparinux for 28 days post-surgery, along with AEs until the patient is discharged, or DOACs for at least 14 days.[53]

Both the AAOS and SIGN guidelines recommend a combination of chemical and mechanical prophylaxis unless contraindicated; however, no specific agent or duration is mentioned.[79,80]

All the above-mentioned recommendations acknowledge that some form of pharmacological VTE prophylaxis is required for all patients undergoing THA, with debate around which agent is most effective, especially in high-risk individuals. Furthermore, they all recommend utilising mechanical prophylaxis with IPCD, unless contraindicated.[81] It is significant to note that some of these recommendations, such as those from the ACCP and AAOS, are at least a decade old. Although the NICE guidelines have been updated more recently, some suggestions are older than ten years. More crucially, most of the literature used to develop these recommendations was published between 1970 and the early 2000s.[81]

Latest guidelines and emerging trends

Recent guidelines and emerging trends in VTE prophylaxis for patients undergoing THA emphasise a tailored, patient-centred approach.[82] The AAOS and the ACCP now recommend risk stratification to guide prophylactic strategies, considering factors such as patient comorbidities, history of VTE, and bleeding risk.[83,84] Aspirin has gained prominence as a viable option for low- to moderate-risk patients due to its favourable safety profile and ease of administration.[85] For higher-risk individuals, DOACs such as rivaroxaban and apixaban are increasingly preferred over traditional agents such as warfarin, owing to their predictable pharmacokinetics and reduced need for monitoring.[86] An audience response poll conducted at the 2022 American Association of Hip and Knee Surgeons (AAKHS) meeting revealed that 93% of surgeons used combined VTE prophylaxis with aspirin and mechanical devices. Additionally, 4% of surgeons utilised DOACs with mechanical devices, and 3% used LMWH with mechanical devices.[87] The guidelines from the 2022 International Consensus Meeting (ICM) recommend low-dose aspirin administered at a dose of 75–100 mg per os twice daily as the most effective and safest method of prophylaxis against VTE in patients undergoing THA. It is advised to use low-dose aspirin as the primary method of VTE prophylaxis for all patients undergoing THA, including those considered to be moderate to high risk for VTE.[84] However, neither of the aforementioned guidelines specify the duration for postoperative aspirin administration, leaving clinicians without a definitive protocol. This highlights the need for more adequately powered RCTs that incorporate modern practices, such as early postoperative mobilisation, to better establish clearer clinical practice guidelines for VTE prophylaxis in THA.

Complications associated with VTE prophylaxis

While chemical prophylaxis strategies are highly effective at reducing the risk of VTE, they are not without complications.[88] The most common reported complications include bleeding, renal dysfunction and HIT.[89] The most feared complication of anticoagulation is major bleeding, which is defined as fatal or symptomatic bleeding in a critical organ system and/or bleeding resulting in a drop in haemoglobin (HB) > 2 g/dl or requiring transfusion of two or more units of packed red blood cells (PRBC), bleeding from a surgical site requiring secondary intervention, or bleeding resulting in haemodynamic instability.[90] In the context of THA, the rates of major bleeding are 0.1–3.1% respectively; this suggests that VTE prophylaxis does not significantly increase the risk of bleeding in THA patients.[90]

Anticoagulation in the setting of THA may impede wound healing, increase the risk of PWD, and increase tension on the surgical wound, resulting in wound breakdown and, overall, increasing the risk of peri-PJIs.[91] PWD may occur in response to anticoagulation disrupting haemostasis. Disrupted haemostasis results in haematoma formation, which acts as a nidus for bacteria to settle and result in infection.[92] The risk of wound complications associated with VTE prophylaxis varies considerably between different agents. Shahi et al.[93] found that, when switching from the use of warfarin to aspirin for VTE prophylaxis, the rate of PWD decreased from 6.3% to 3.1%. Jones et al.[94] showed that the use of LMWH resulted in a five-fold greater increase in wound discharge when compared with the use of no pharmacological thromboprophylaxis. Numerous studies have examined the impact of different anticoagulation therapies to determine the optimal regimen that offers sufficient VTE prevention while minimising postoperative surgical site complications.[95] Various guidelines have been recommended, and while aspirin is favoured for VTE prophylaxis due to its lower risk of wound complications, the discussion surrounding the optimal prophylactic regimen remains ongoing.[95,96]

Conclusion

The existing literature does not provide a definitive answer regarding the most effective and safest option of chemoprophylaxis for patients undergoing THA. Major guidelines concur on the importance of using some form of VTE prophylaxis for all surgical patients. It is crucial to tailor the use of VTE prophylaxis according to each patient's risk profile, considering their susceptibility to VTE and the potential for bleeding complications, either locally at the surgical site or systemically. However, to better determine the ideal pharmacological agent, dosage, duration of treatment, and outcomes of VTE prophylaxis for THA patients, additional adequately powered prospective studies evaluating large populations are needed.

Ethics statement

The authors declare that this submission is in accordance with the principles laid down by the Responsible Research Publication Position Statements as developed at the 2nd World Conference on Research Integrity in Singapore, 2010. Ethics approval was not obtained (review article).

Declaration

The authors declare authorship of this article and that they have followed sound scientific research practice. This research is original and does not transgress plagiarism policies.

Author contributions

DBG: first draft preparation, manuscript revision, manuscript preparation
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