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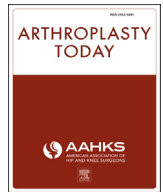
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Guidelines

Time for an Update? A Look at Current Guidelines for Venous Thromboembolism Prophylaxis After Hip and Knee Arthroplasty and Hip Fracture

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ABSTRACT

Venous thromboembolism is a well-established complication of total hip and knee arthroplasty and hip fracture surgery. Clinical practice guidelines have been proposed to help clinicians provide prophylaxis against this risk. However, most guidelines reference data that are becoming outdated because of new advances in perioperative protocols. Recent data would suggest that aspirin may be appropriate for most patients after total hip and knee replacement and a more potent chemoprophylaxis for higher risk patients. Low-molecular-weight heparin remains the recommended choice after hip fracture surgery, although there is a paucity of recent literature in this patient population. There are randomized trials currently underway in the arthroplasty population that may guide clinicians in the appropriate choice of chemoprophylaxis. These studies should inform updates to the current clinical practice guidelines.

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Introduction

Venous thromboembolism (VTE), comprised of deep venous thrombosis and pulmonary embolism, can be a devastating complication of orthopedic surgery and may occur due to surgical trauma and perioperative immobility. We aim to briefly review current clinical practice guidelines (CPGs) for the prevention of VTE after hip and knee replacement and hip fracture surgery (HFS) and highlight evidence that supports an update to these CPGs.

Postoperative VTE may be suspected clinically when patients present with acute leg pain, swelling, erythema, warmth, hypotension, hemoptysis, chest pain, or dyspnea. Diagnosis may be supplemented with laboratory tests, but deep venous thrombosis is typically confirmed with venous ultrasound, and pulmonary embolism with computed tomography angiogram of the pulmonary arteries. In addition to the morbidity and possible mortality that can result from VTE, a significant financial burden is placed on the health-care system, with an estimated cost of \$33,000 US dollars

per VTE event after 1 year [1]. VTE is of particular concern after total joint arthroplasty (TJA) and HFS because of the increasing volume of these procedures, the older age of the patients, and their associated comorbidities. Orthopedic surgeons and hospitalists often comanage these patients because of evidence of improvements in care and reduced costs [2]; therefore, knowledge of the safety and efficacy of chemoprophylaxis after TJA and HFS is necessary for all teams involved. Fortunately, the incidence of VTE after HFS and TJA has declined in recent decades with combined pharmacologic and mechanical prophylaxis, advances in surgical and anesthetic techniques, improvements in perioperative pain control, and early mobilization [3]. Current rates have been reported as 0.83%–1.5% after HFS, 0.6%–1.2% after total hip arthroplasty (THA), and 0.3%–1.4% after total knee arthroplasty (TKA) [4–6].

Problem statement

Many medical societies have created CPG for VTE prophylaxis in orthopedic surgery, including after TJA and HFS. Guidelines from the American Academy of Orthopedic Surgeons, the American College of Chest Physicians, the National Institute for Health and Care Excellence from the Department of Health in England, and the American Society of Hematology are summarized in Table 1. These

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Table 1
Summary of pharmacologic recommendations in CPGs for VTE prevention after TKA, THA, and HFS.

Clinical practice guideline	AAOS (TJA 2011, HFS 2014) [31,32]	ACCP (2012) [33]	NICE (2021) [34]	ASH (2019) [35]
Surgical procedure				
TKA	Recommends pharmacologic prophylaxis but does not recommend specific agents <i>Duration: Does not specify</i>	LMWH, ASA, fondaparinux, apixaban, dabigatran, rivaroxaban, UH, VKA <i>Duration: minimum 10–14 d</i>	LMWH, ASA, or rivaroxaban (consider apixaban or dabigatran if others cannot be used) <i>Duration: 14 d</i>	ASA or anticoagulants (AC) When AC used DOAC preferred over LMWH which is preferred over UH. <i>Duration: Beyond 3 wk (19–42 d)</i>
THA	Recommends pharmacologic prophylaxis but does not recommend specific agents <i>Duration: Does not specify</i>	Same as TKA	LMWH (10 d) followed by ASA (28 d), LMWH (28 d), or rivaroxaban (consider apixaban or dagibatan if others cannot be used)	Same as TKA
HFS	Recommends pharmacologic prophylaxis but does not recommend specific agents <i>Duration: Does not specify</i>	LMWH, ASA, fondaparinux, UH, VKA <i>Duration: minimum 10–14 d</i>	LMWH or fondaparinux <i>Duration: 1 mo</i>	LMWH or UH. <i>Duration: Beyond 3 wk (19–42 d)</i>

Although not listed, all recommend IPC.

AAOS, American Academy of Orthopedic Surgeons; ACCP, American College of Chest Physicians; ASA, aspirin; ASH, American Society of Hematology; fondaparinux, fondaparinux sodium; IPC, intermittent pneumatic compression device; NICE, National Institute for Health and Care Excellence; UH, unfractionated heparin; VKA, adjusted-dose vitamin K antagonist.

guidelines all agree that some form of prophylaxis is necessary; however, there is no consensus on choice of agent or duration. All suggest more potent prophylaxis in patients who have risk factors for VTE, especially in patients with prior history of VTE. In addition, all suggest the use of mechanical prophylaxis with intermittent pneumatic compression unless contraindicated.

It is important to recognize that some of these guidelines (American Academy of Orthopedic Surgeons and American College of Chest Physicians) are nearly 10 years old or older. In addition, although the National Institute for Health and Care Excellence guidelines are more recently updated, some recommendations are over 10 years old, and more importantly, the majority of the literature cited to create the recommendations dates from the 1970s to early 2000s. Although the American Society of Hematology TJA guidelines include citations dated in the 2010s, this is not the case for the HFS guidelines. In fact, all HFS CPGs mentioned almost exclusively cite literature dated 2000 or earlier. This statement is not to place fault on the CPG but rather to highlight the paucity of new research directed in this area. The past 10 years have been marked by significant advances in recovery after TJA and HFS, including multimodal pain management, regional anesthesia, blood conservation with medications such as tranexamic acid, and early ambulation [7]. These older CPG risk and benefit assessments, therefore, may not be based on the current VTE risk.

Proposed solution

The optimal chemoprophylactic agent would minimize both the risks of VTE and bleeding, while being cost-effective and easy to administer. While no single medication has yet to be identified, aspirin, for example, has been gaining clinical acceptance for prophylaxis after TJA as its safety and efficacy have been demonstrated repeatedly [8–13]. A recent systematic review and meta-analysis of randomized controlled trials found no difference in VTE or adverse events when comparing aspirin with other anticoagulants after TJA [14]. Registry studies have shown aspirin to be noninferior to other forms of anticoagulation after both TKA [15] and THA [16]. However, controversy surrounding aspirin remains [17,18]. The direct oral anticoagulants (DOACs) have gained acceptance given their ease of administration and potential for fewer VTE events. A recent study using the National Joint Registry for England Wales, Northern Island, and the Isle of Man compared DOACs to aspirin after THA and TKA

and found that DOACs were associated with a lower risk of VTE and no higher risk of mortality or complications except for renal injury [19]. These medications were not approved during the time period of many of the studies referenced in the preparation of the referenced CPGs. DOACs are more potent anticoagulants, however, and there are reports of increased wound complications and reoperation with their use [20,21]. In HFS, 2 recent studies compared DOACs to low-molecular-weight heparin (LMWH) and found either no difference [22] or reduced [23] VTE rates in the DOAC group, although these studies included small sample sizes. Another recent study in HFS compared aspirin to rivaroxaban after 5 days of LMWH and found no difference in VTE or bleeding events [24].

With the current pharmacologic prophylaxis strategies available, providers seek to balance low VTE rates while minimizing other complications related to anticoagulation such as bleeding and wound complications. In recent years, with patients mobilizing earlier postoperatively, the balance has shifted toward using less-potent anticoagulation such as aspirin after TJA in low-risk patients. Interest in identifying patient risk factors to tailor the appropriate VTE prophylaxis to individual patients has been rising [25,26]. There is much focus on one agent over another, but the real challenge is determining the appropriate threshold of risk factors for the use of a given agent in a particular patient. For TJA, recent data [8–16] support that aspirin is appropriate for most patients with modern pain management and mobilization protocols. Low-dose aspirin appears to be sufficient [27,28]. Still, there is a small group of patients that should likely receive more aggressive anticoagulation [29], possibly DOACs, after primary TJA. In HFS, despite the outdated evidence and given the advances in perioperative management, there are currently no recent well-designed studies or ongoing trials being conducted to help provide updated recommendations.

Future direction and long-term focus

Furthermore, high-quality research is necessary to help provide more detailed guidelines; however, this remains challenging because of the low event rates, need for large sample sizes, and costs associated with performing large-scale studies. In TJA, there is currently one ongoing trial nested within the Australian Orthopaedic Association National Joint Replacement Registry, known as CRISTAL, which is a cluster randomized, crossover trial comparing aspirin and LMWH after TKA and THA in over 15,000 patients

(ACTRN12618001879257). In addition, the Pulmonary Embolism Prevention after Hip and Knee Replacement trial (PEPPER; NCT02810704) is a randomized trial comparing aspirin, rivaroxaban, and warfarin in 20,000 patients undergoing THA and TKA in the United States. Studies such as these will hopefully help elucidate the optimal agent for these patients given their individual risk factors. We hope to see the development of similar studies for the hip fracture population as well.

Recommendations

Patients undergoing TJA or HFS are frequently on preoperative anticoagulation. A comprehensive discussion of preoperative management is out of the scope of this review but was well detailed in a recent review by Barlow et al. [30]. The choice of VTE prophylaxis after TJA and HFS is ultimately at the discretion of the treating physician but should be tailored to the individual patient and should continue for at least 14 days, with consideration of a 4-week duration in high-risk patients. Low-dose aspirin is likely appropriate after primary, lower extremity TJA for the vast majority of patients without an increased personal risk of VTE. DOACs are preferred in higher risk patients. Although no consensus exists to define high risk, the treating physician may consider a high-risk patient to be one with a personal or family history of VTE, active cancer, hypercoagulable state, or multiple medical comorbidities such as cardiac disease, pulmonary disease, diabetes mellitus, and morbid obesity [26]. For HFS, LMWH is recommended for most patients, but aspirin is supported in some guidelines. As further high-quality clinical trials are completed, and guidelines are updated to reflect current practice, clinical practice can be modified accordingly.

Conflicts of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

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