Venous Thromboembolism Prophylaxis After Total Joint Arthroplasty

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Educational Objectives

As a result of reading this article, physicians should be able to:

1. Review current commonly used anticoagulant options after total joint arthroplasty.

2. Analyze the current American Academy of Orthopaedic Surgeons, American College of Chest Physicians, and Surgical Care Improvement Project guidelines for perioperative venous thromboembolism (VTE) prophylaxis after total joint arthroplasty.

3. Critically evaluate the history and most recent changes related to the current guidelines for VTE prophylaxis after total joint arthroplasty.

4. Make an informed decision on which VTE prophylaxis to use based on patient-specific factors in daily practice.

Abstract

Venous thromboembolism (VTE) prophylaxis after total joint arthroplasty is considered best practice. However, over the past 5 years, there has been considerable debate about the ideal prophylactic regimen or modality. The American Academy of Orthopaedic Surgeons and the American College of Chest Physicians published their most...
Total hip arthroplasty (THA) and total knee arthroplasty (TKA) represent some of the most successful orthopedic procedures, greatly improving quality of life for patients. However, without venous thromboembolism (VTE) prophylaxis, these procedures have an unacceptably high incidence of VTE of up to 85% as defined by deep venous thrombosis (DVT) and pulmonary embolism (PE). As a result, there is general agreement about the necessity of VTE prophylaxis after these procedures.

A recent survey of 634 orthopedic surgeons on their preferred regimen for VTE prophylaxis after THA and TKA revealed a wide variation in modalities. Low molecular-weight heparin (LMWH) was the most commonly used pharmacological prophylactic regimen, followed by warfarin, aspirin, and fondaparinux. In addition, intermittent pneumatic compression devices were used in-hospital by 83% of surgeons. However, there was a significant difference in initiation timing and total duration of VTE prophylaxis.

Historically, the American College of Chest Physicians (ACCP) and the American Academy of Orthopaedic Surgeons (AAOS) were unable to establish a consensus on indications, regimen, and duration for pharmacological VTE prophylaxis. The main criticism of the AAOS was that the ACCP’s 8th clinical practice guideline, published in 2008, focused predominantly on efficacy rather than on safety. Consequently, orthopedic surgeons voiced considerable concerns about the adverse effects of aggressive anticoagulation, resulting in postoperative bleeding, hematomas, infections, and increased reoperation rates.

In 2011 and 2012, respectively, the AAOS and ACCP published their most recent guidelines on VTE prophylaxis after THA and TKA. In contrast to previous publications, these latest recommendations have greater concordance. The ACCP’s 9th clinical practice guidelines now clearly recognize the delicate balance between efficacy and safety for any regimen used for VTE prophylaxis after total joint arthroplasty.

The purpose of this review is to discuss currently available options for pharmacological and mechanical VTE prophylaxis and briefly review the current ACCP and AAOS practice guidelines.

**Pharmacological VTE Prophylaxis**

Warfarin inhibits the vitamin K–dependent synthesis of biologically active forms of the calcium-dependent clotting Factors II, VII, IX, and X and the regulatory factors protein C, protein S, and protein Z. Warfarin continues to be one of the most commonly used pharmacotherapies of VTE prophylaxis after total joint arthroplasty. Its long track record of preventing symptomatic clot formation and ability to individualize levels of anticoagulation using international normalized ratio (INR) monitoring are appealing to orthopedic surgeons. Numerous clinical trials have compared warfarin and LMWH after THA and TKA. Of note, all of these clinical studies were performed in the 1990s and early 2000s. As an overarching theme, LMWH appeared to be more effective in reducing overall asymptomatic clot formation, whereas the incidence of symptomatic VTE showed no difference between groups. However, patients treated with LMWH displayed higher bleeding rates compared with patients receiving warfarin VTE prophylaxis.

Although warfarin allows for individual dosing and titration of VTE prophylaxis, close clinical follow-up in anticoagulation clinics is necessary for INR monitoring. This places an additional burden on health care systems in times of financial constraints. In a Markov cohort cost-effectiveness analysis, Mostafavi et al recently analyzed the cost-effectiveness of warfarin vs aspirin as pharmacological VTE prophylaxis. They found that aspirin was more cost-effective and saved more quality-adjusted life-years than warfarin in all age groups. Cost per quality-adjusted life-years gained by aspirin was $24,506.20 at age 55 years and $47,148.10 at age 85 years after THA and $15,117.20 and $24,458.10, respectively, after TKA. The authors concluded that in patients without prior VTE events, aspirin is more cost-effective than warfarin as a VTE prophylaxis; however, warfarin may be a better prophylactic agent in TKA patients with a high probability of VTE.

**Aspirin**

Aspirin is a widely used nonsteroidal anti-inflammatory drug (NSAID), which also has antiplatelet properties. The efficacy of low-dose aspirin in preventing symptomatic VTE after elective THA and femoral neck fractures has been studied in a randomized trial comparing aspirin with placebo in 16,000 patients. Although VTE incidence was significantly decreased by aspirin in the femoral neck fracture group, no significant differences were observed in the elective THA group between aspirin and placebo cohorts with regard to VTE incidence or major bleeding episodes. After the most recent ACCP guidelines recommended low-dose aspirin after THA and TKA, there has been renewed interest in using aspirin as a stand-alone or combined VTE prophylactic agent.

Recent publications present conflicting results about the efficacy of aspirin as an anticoagulating agent. In a prospective review, 281 patients were randomized into 2 groups: 152 patients received ASA, and 129 elevated-risk patients received warfarin. A comparative group of 415 patients
received warfarin without PE risk stratification. The rate of symptomatic VTE among standard-risk patients receiving aspirin was greater than the comparator group (4.6% vs 0.7% and 7.9% vs 1.2%, respectively). The authors concluded that standard-risk patients receiving aspirin had a higher rate of symptomatic VTE than did patients receiving anticoagulation in the form of warfarin.

In contrast, Bozic et al compared the risk of VTE, bleeding, surgical site infection, and mortality in patients receiving aspirin only or other pharmacological VTE agents. Out of 93,840 TKA patients, 51,923 (55%) patients received warfarin, 37,198 (40%) received LMWH/synthetic pentasaccharides, and 4719 (5%) received aspirin only. After adjustment for patient and hospital factors, patients in the aspirin cohort were found to have lower odds for VTE compared with patients in the warfarin cohort, but they had comparable odds to the LMWH/synthetic pentasaccharide group. No significant differences were found for bleeding, infection, or mortality between groups. The authors concluded that aspirin, when used in conjunction with other clinical care protocols, represents an effective agent for VTE prophylaxis for certain TKA patients.

Parvizi et al performed a retrospective analysis of 26,415 consecutive total joint arthroplasties performed at a single institution between January 2000 and April 2011, comparing aspirin (325 mg twice daily) and warfarin (aiming for INR between 1.5 and 1.8) as VTE prophylaxis. Outcome parameters were PE, bleeding, and wound complications up to 90 days postoperatively. The overall rate of PE was significantly lower in the aspirin group compared with the warfarin group (0.2% vs 1.0%, respectively). No statistically significant difference was found for hematoma and seroma formation, wound complications, DVT, acute infection, and 90-day mortality between groups. The authors concluded that aspirin appears as effective as warfarin in preventing PE, with a trend toward lower bleeding and wound complication rates.

Currently, no recent prospective, randomized trials are available in the literature that shed further light on these conflicting data.

Low-Molecular-Weight-Heparin

Low-molecular-weight-heparin represents a functional inhibitor of Factor Xa. Numerous randomized trials compared the efficacy and safety of warfarin and LMWH after total joint arthroplasty. Overall, LMWH was found to more effectively lower overall clot formation than warfarin, but no differences were found in incidences of symptomatic events. Although most studies report a higher rate of major bleeding after LMWH prophylaxis, other trials describe no difference between groups.

A Cochrane review compared direct thrombin inhibitors (eg, ximelagatran, dabigatran, desirudin) with LMWH and warfarin as prophylactic agents after THA and TKA. Fourteen studies were included, involving 21,642 patients for efficacy and 27,360 for safety. No difference was reported regarding effectiveness in VTE prevention between groups. However, direct thrombin inhibitors were found to have higher mortality and cause more bleeding than LMWH. The authors concluded that LMWH or warfarin continue to represent the standard treatment for VTE prophylaxis after total joint arthroplasty. They caution against the use of ximelagatran for VTE prevention in patients who have undergone orthopedic surgery and recommend further studies on the effectiveness and safety of dabigatran.

The attractiveness of LMWH as a VTE prophylactic agent is that no continuous monitoring is required and that it can be administered in a subcutaneous fashion, making it the most commonly used pharmacological prophylactic regimen in the orthopedic community after THA and TKA.

Novel Factor Xa Inhibitors

Factor Xa inhibitors block the intrinsic and extrinsic pathway of the coagulation cascade by direct competitive inhibition of their merging point, Factor Xa (Figure). Currently available Factor Xa inhibitors in the United States include rivaroxaban and apixaban; edoxaban is only approved for VTE prophylaxis outside the United States. These new Factor Xa inhibitors, as well as dabigatran—a Factor IIa (thrombin) inhibitor discussed later—are frequently referred to as new oral anticoagulants. Some of the reported benefits of this class of medications are their oral administration, lack of required laboratory monitoring, broad therapeutic window, and minimal drug interactions with low patient variability.

Rivaroxaban. Rivaroxaban was the first Factor Xa inhibitor approved for use in the United States for VTE prophylaxis after THA and TKA. By binding to the active site of Factor Xa, it prevents binding of substrate (prothrombin). Although no routine laboratory monitoring is required, its effects can be assessed using prothrombin time. Dosing has been recommended at 10 mg daily beginning 6 to 10 hours postoperatively for a course of 2 weeks for TKA and 5 weeks for THA.

The RECORD trials assessed the efficacy of rivaroxaban for chemical VTE prophylaxis, evaluated by DVT formation (using venogram detection), nonfatal PE, and all-cause mortality after total joint arthroplasty. The RECORD1 and RECORD2 studies compared rivaroxaban with enoxaparin after THA in more than 7000 patients and demonstrated a significant reduction in incidences of the primary outcome measures in the rivaroxaban cohorts. In the RECORD3 and RECORD4 studies, rivaroxaban was compared with enoxaparin after TKA in more than 5600 patients. Again, rivaroxaban outperformed enoxaparin with a statistically significant reduction in the primary outcome measures.

All 4 individual RECORD trials found no significant difference in the safety
profiles of enoxaparin vs rivaroxaban, as determined by wound-healing problems, major and minor bleeding, infection, blood loss, drainage, and transfusion rates.\textsuperscript{34} However, when all data from the RECORD trials were combined, a statistically significant increase in bleeding was found in the rivaroxaban cohort (3.2\% vs 2.6\% for enoxaparin). A similar trend was found in an additional study, but this did not reach statistical significance.\textsuperscript{35}

Financial analyses have revealed favorable cost-effectiveness of rivaroxaban over enoxaparin.\textsuperscript{36,37} In addition, compliance rates of rivaroxaban compared favorably with historical data of traditional anticoagulants, with noncompliance rates of only 4\%.\textsuperscript{38}

**Apixaban.** Apixaban was approved by the US Food and Drug Administration (FDA) for VTE prophylaxis after total joint arthroplasty in 2014. Like rivaroxaban, it functions by direct, competitive inhibition of Factor Xa,\textsuperscript{23} but it requires twice-daily dosing at 2.5 mg for VTE prophylaxis after total joint arthroplasty. The efficacy of apixaban vs enoxaparin as a VTE prophylactic agent has been studied in 3 large phase-III ADVANCE trials. In line with the RECORD trials, the ADVANCE trials used DVT (as determined using venogram detection), nonfatal PE, and all-cause mortality as primary outcome parameters. In ADVANCE1 and ADVANCE2, apixaban was compared with enoxaparin after TKA in more than 6200 patients.\textsuperscript{39,40} Whereas the ADVANCE1 trial failed to show any statistically significant differences between enoxaparin and apixaban, ADVANCE2 demonstrated a statistically significant superiority of apixaban. The third ADVANCE trial compared apixaban with enoxaparin after THA in more than 3800 patients, again indicating the statistically significant superiority of apixaban.\textsuperscript{41} These findings were confirmed when data sets from the ADVANCE2 and ADVANCE3 trials were combined and analyzed for incidence of VTE.\textsuperscript{42} When compared with enoxaparin, apixaban was found to have a slightly superior safety profile in a large phase-II study of more than 1200 patients,\textsuperscript{43} which was later confirmed in 3 ADVANCE trials.

A cost analysis using the ADVANCE studies indicated improved cost-effectiveness with the use of apixaban compared with enoxaparin. In line with these findings, a comparison of all Factor Xa inhibitors with the 2 LMWH agents (enoxaparin and dalteparin) found the Factor Xa inhibitors to be the economically superior option.\textsuperscript{45}

**Fondaparinux.** Fondaparinux is a synthetic indirect Factor Xa inhibitor.\textsuperscript{46} Its subcutaneous administration has been introduced as an effective prophylactic agent in various clinical trials comparing enoxaparin and fondaparinux.\textsuperscript{47-49} Although fondaparinux appears to be significantly more effective than enoxaparin in limiting asymptomatic VTE after TKA, these differences may be of limited clinical relevance.\textsuperscript{47} However, fondaparinux led to a statistically significant increase in major bleeding postoperatively when compared with enoxaparin.\textsuperscript{47} This has recently been attributed to increased fibrinolysis associated with fondaparinux.\textsuperscript{50} Moreover, the accuracy of soluble fibrin and the D-dimer test for the diagnosis of DVT was decreased by administration of fondaparinux, making the workup and diagnosis of VTE in patients receiving fondaparinux more challenging.\textsuperscript{51} These concerns have limited the widespread use of fondaparinux in total joint arthroplasty.

**Challenges of Factor Xa Inhibitors.** Several Factor Xa inhibitors have recently emerged as novel alternatives to the more traditional DVT prophylaxis agents in total joint arthroplasty.\textsuperscript{52} Their oral administration without need for laboratory monitoring represent attractive qualities, which make them unique and desirable. As outlined earlier, numerous level-I studies confirmed their efficacy as VTE prophylactic agents. A recent meta-analysis of
level-I studies summarized data of more than 24,000 patients, demonstrating the superiority of both rivaroxaban and apixaban over enoxaparin without differences in safety.53

The major, and often-cited, downside to the new oral anticoagulants is the lack of available reversal agents. However, advocates for this novel drug class argue that their relatively short half-life and predictable pharmacokinetic profile obviates the need for a true antidote. At present, there are several phase-I and phase-II studies evaluating both a recombinant Factor Xa and 4-factor prothrombin complex concentrates (PCCs) as potential reversal agents for these medications.54

**Direct Thrombin Inhibitors**

**Dabigatran.** Dabigatran was FDA approved for the treatment of VTE in the United States in 2014 but has yet to be approved by the FDA for VTE prophylaxis. As an orally administered prodrug, it is activated after ingestion and competitively inhibits thrombin by direct binding at the active site.55

Efficacy studies for dabigatran are based on 4 large phase-III trials known as RE-MODEL, RE-NOVATE, RE-MOBILIZE, and RE-NOVATE II, which used the same primary outcome parameters as the trials described earlier for the Factor Xa inhibitors.56-59 All 4 trials compared dabigatran with enoxaparin after TKA (RE-MODEL and RE-MOBILIZE) and THA (RE-NOVATE and RE-NOVATE II), respectively. Although dabigatran was found to be as effective as enoxaparin 40 mg daily, it was less effective than enoxaparin 30 mg twice daily after TKA. In THA patients, dabigatran was found to be equally effective as enoxaparin, with similar safety profiles.

Although a meta-analysis of RE-MODEL, RE-NOVATE, and RE-MOBILIZE confirmed a similar safety profile of dabigatran when compared with enoxaparin, there is concern about the increased risk for gastrointestinal bleeding and myocardial infarction associated with longer-term use of dabigatran for stroke prevention in atrial fibrillation patients.60

Similar to the Factor Xa inhibitors, dabigatran was found to be cost-saving in VTE prophylaxis in primary total joint arthroplasty61,62 but is currently without an approved reversal agent. However, a specific antidote to dabigatran has been found to be effective in animal studies but has yet to be validated in humans.54

**Mechanical VTE Prophylaxis**

The most recent amendments to the AAOS, ACCP, and Surgical Care Improvement Project (SCIP) clinical practice guidelines for VTE prophylaxis after total joint arthroplasty now include mechanical compression devices as modalities for VTE prophylaxis. As a result, there has been renewed interest in the use of mechanical devices such as venous foot pumps or calf/thigh intermittent pneumatic compression devices with or without adjunctive chemoprophylaxis after total joint arthroplasty.

Mechanical compressive devices increase the local blood flow in the lower extremities, decrease the concentration of the activated coagulation factors, and promote lymphatic drainage in adjacent tissues.53 The attractiveness of this modality lies in the absence of unwanted side effects commonly associated with the use of chemical VTE prophylaxis, such as increased risk for wound drainage and allogeneic blood transfusion, hemotoma, and gastrointestinal and intracranial bleeding.64-67 Such adverse effects can result in decreased patient satisfaction, increased cost and readmission rates, need for prolonged clinical follow-up, and/or progression to further surgical procedures.66-68 Despite the decrease in complication rates of intermittent compression devices, a distinct superiority over chemical prophylaxis has been difficult to establish, largely owing to methodological limitations of available studies.69

Historically, warfarin was considered more effective than pneumatic compression boots in limiting the formation of proximal lower extremity clots after THA,70-72 which was confirmed in the late 1990s and early 2000s, when VTE incidence was compared between venous foot pump and LMWH after THA and TKA.73-75 These studies resulted in a prevailing notion that intermittent pneumatic compression devices should not be used as the sole means of prophylaxis after total joint arthroplasty.69

However, several recent studies have challenged this dogma. Hamilton et al76 analyzed 4037 TKAs in 3144 patients who were stratified into those with a significantly increased risk for VTE events and those with a standard risk. Only patients with a significantly increased risk for VTE were prescribed chemical prophylaxis, whereas the rest received prophylaxis with foot pumps and compression stockings only. Overall, the incidence of ultrasonographically identified DVT was 2.1%, and 1 patient sustained a fatal PE. The authors concluded that this risk-stratified methodology was safe in allowing for use of isolated mechanical VTE prophylaxis in their patient population.76

In a prospective, randomized, multicenter study of 392 patients, Colwell et al77 compared a mobile compression device with LMWH with regard to safety and effectiveness for VTE prevention after THA.77 The use of the compression device began intraoperatively, and patients in the mobile compression device cohort received 81 mg of aspirin daily postoperatively. Low-molecular-weight heparin prophylaxis began between 12 and 24 hours postoperatively. Although both prophylactic regimens were found to have comparable efficacy on VTE prevention, the rate of major bleeding episodes was 0% in the compression group and 6% in the LMWH group. As a result, the authors concluded that, when compared with LMWH, use of the mobile compression device after THA resulted in a significant decrease in major bleeding events.77
Yassin et al\textsuperscript{78} recently reviewed the incidence of symptomatic VTE in 1100 patients undergoing primary or revision THA or TKA at a single hospital over a 2-year period, comparing mechanical VTE prophylaxis with pharmacological VTE prophylaxis using enoxaparin\textsuperscript{78}. The incidence of symptomatic DVT was 0.73\% in the mechanical prophylaxis cohort and 0.57\% in the pharmacological group. The rate of PE was 0.91\% in the mechanical prophylaxis group and 1.15\% in the enoxaparin cohort. These differences were not statistically significant. The authors concluded that perioperative optimization, including postoperative analgesia and immediate postoperative mobility, may be sufficient VTE prophylaxis and may help avoid unwarranted side effects of pharmacological VTE prophylaxis while having significant cost implications\textsuperscript{78}.

Zhao et al\textsuperscript{79} analyzed various pneumatic compression devices as VTE prophylaxis after THA in a Cochrane review. Only 1 quasirandomized, controlled study with 121 patients comparing 2 types of intermittent pneumatic compression devices met the inclusion criteria. No cases of symptomatic DVT or PE in either the calf-thigh compression group or the planter compression group were found during the first 3 weeks postoperatively, yet calf-thigh pneumatic compression appeared to be more effective than planter compression for reducing thigh swelling during the early postoperative stage. Given the limitations to only one trial, the authors concluded that there is a lack of evidence from randomized, controlled trials to make recommendations for an intermittent pneumatic compression device for VTE prophylaxis after THA\textsuperscript{79}.

In a recent meta-analysis, 13 prospective clinical trials comprising 1514 patients evaluating mechanical prophylaxis using venous foot pumps after THA and TKA were analyzed\textsuperscript{63}. When comparing the rate of VTE after THA, mechanical compression was found to be equally as effective as or more effective than LMWH. After TKA, mechanical compression devices were found to be equally effective as but not statistically superior to LMWH. Pooling all available data, Pour et al\textsuperscript{63} concluded that venous foot pumps decreased the rate of VTE after THA and TKA when compared with LMWH.

To improve ease of use and patient compliance with intermittent pneumatic compression devices, portable mechanical compression devices have been developed\textsuperscript{80}. This has allowed for improved compliance, enhanced rehabilitation, and the option of outpatient VTE prophylaxis using mechanical compressive devices. Finally, the cost-effectiveness of VTE prophylaxis using mobile compression devices was investigated in a recent study of hypothetical 1000- and 10,000-patient cohorts\textsuperscript{81}. The model showed a financial advantage of the compression device of $3.69 million when compared with enoxaparin in the 10,000-patient cohort.

**CURRENT AAOS, ACCP, AND SCIP GUIDELINES**

**Historical Perspective**

Despite years of research and multiple prospective, randomized trials, the ideal modality of VTE prophylaxis after THA and TKA remains elusive. To improve practice variability and inconsistency, the ACCP published their first clinical practice guidelines on this topic in 1986. In their 6th edition in 2001, all patients undergoing total joint arthroplasty were placed into the highest-risk category\textsuperscript{82}. In their 7th edition, the ACCP recommended the use of warfarin with a target INR of 2 to 3, LMWH, or fondaparinux for all THA and TKA patients\textsuperscript{83}. In 2008, the ACCP suggested a lower threshold for extended VTE prophylaxis of 35 days postoperatively after THA\textsuperscript{84}. The simultaneous formation of the SCIP mandated VTE prophylaxis as a quality measure and used the ACCP’s 8th edition as a guideline.

Despite these efforts, there were significant concerns about the ACCP’s 8th edition of VTE prophylaxis guidelines.

Venographically proven DVT was chosen as the endpoint, disregarding that the vast majority of these were asymptomatic. Parvizi et al\textsuperscript{85} described a very low correlation between the presence of DVT and PE and questioned the clinical significance of an asymptomatic DVT.

Most of the included prospective, randomized clinical studies choosing venography as an endpoint were pharmaceutical-sponsored, FDA investigational device–exempt studies. In contrast, generic options such as aspirin, warfarin, and compressive devices did not receive similar monetary research support, resulting in smaller clinical trials. As a result, these therapeutics failed to reach the highest level-1A recommendation status in the ACCP guidelines.

There was significant concern about the high bleeding risks and wound complications after aggressive VTE prophylaxis recommended by the ACCP guideline. In their 8th edition, the ACCP defined a major bleeding episode as death or a life-threatening event; intracranial, retroperitoneal, or intraocular bleeding; a transfusion requirement of more than 2 units of packed red blood cells; or a significant hemoglobin drop. This definition failed to acknowledge persistent wound drainage, wound bleeding, or hematoma, likely resulting in an underreporting of complications related to VTE prophylaxis. In an attempt to be compliant with the ACCP’s level-1A recommendations, several large centers noticed a significant increase in bleeding complications\textsuperscript{86,87}.

There was significant conflict of interest with the ACCP’s 2008 guidelines. With the exception of 1 author, all additional authors listed numerous potential conflicts of interest, which was strongly discouraged by the Institute of Medicine\textsuperscript{88,89}.

Responding to such concerns and the above-described apprehensions in the orthopedic community to the ACCP’s guidelines, the AAOS formed the DVT/PE workgroup in 2007. The goal of the
AAOS clinical practices guidelines was to minimize conflicts of interest and clinical risks while maximizing efficacy associated with anticoagulation. As a result, their methodology now used symptomatic DVT, PE, and death as endpoints for their literature review.\textsuperscript{90,91} Using symptomatic VTE events as an outcome parameter, the AAOS workgroup was unable to recommend any commonly used anticoagulant after THA or TKA. Aggressive VTE prophylaxis was recommended for the only identifiable high-risk group: patients with prior VTE. Less aggressive or no prophylaxis was recommended in the only low-risk group: patients with liver disease. Such recommendations placed the AAOS’s guidelines in direct conflict with every major recommendation provided by the ACCP’s guidelines, until the inception of the AAOS’s and ACCP’s latest guideline updates.

In 2011 and 2012, respectively, AAOS and ACCP published their most recent clinical practice guidelines. For the first time, these guidelines reached greater consensus on several previously passionately debated topics. Whereas previous ACCP guidelines typically chose asymptomatic DVT detected radiographically/ultrasonographically as an endpoint, both societies have now acknowledged that the presence of an asymptomatic DVT may be of little or no consequence to the patient. In addition, additional focus was placed on bleeding and wound drainage, and the ACCP addressed the previous conflict of interest in their latest guidelines. The latest AAOS and ACCP guideline recommendations are discussed in detail here.

## Table 1

<table>
<thead>
<tr>
<th>No.</th>
<th>Recommendation</th>
<th>Grade</th>
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<tbody>
<tr>
<td>1</td>
<td>Recommendation against routine postoperative duplex ultrasonography screening.</td>
<td>Strong</td>
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<tr>
<td>2</td>
<td>Assessing risk of VTE by determining previous VTE events should be considered.</td>
<td>Weak</td>
</tr>
<tr>
<td>3</td>
<td>Panel recommends that patients be assessed for known bleeding disorder like hemophilia and for the presence of active liver disease, which further increases risk for bleeding and bleeding-associated complications.</td>
<td>Inconclusive</td>
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<tr>
<td>4</td>
<td>Panel suggests discontinuation of antiplatelet agents (eg, aspirin, clopidogrel) before undergoing elective THA/TKA.</td>
<td>Moderate</td>
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<tr>
<td>5</td>
<td>Panel suggests use of pharmacological agents and/or mechanical compressive devices for VTE prevention in patients undergoing elective THA/TKA.</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>Panel cannot recommend for or against a specific prophylactic regimen in TKA/THA patients.</td>
<td>Inconclusive</td>
</tr>
<tr>
<td>6</td>
<td>In the absence of reliable evidence regarding the duration of prophylactic strategies, it is the opinion of the panel that patients and physicians discuss the duration of prophylaxis.</td>
<td>Consensus</td>
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<tr>
<td>7</td>
<td>In the absence of reliable evidence, it is the opinion of the panel that patients undergoing THA/TKA, who have also had a previous VTE, receive pharmacologic prophylaxis and use mechanical compressive devices.</td>
<td>Consensus</td>
</tr>
<tr>
<td>8</td>
<td>In the absence of reliable evidence, it is the opinion of the panel that patients undergoing THA/TKA, who have a known bleeding disorder and/or active liver disease, use mechanical compressive devices for prevention VTE.</td>
<td>Consensus</td>
</tr>
<tr>
<td>9</td>
<td>In the absence of reliable evidence, it is the opinion of the panel that patients undergo early mobilization following elective THA/TKA.</td>
<td>Consensus</td>
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<tr>
<td>10</td>
<td>The use of neuraxial (eg, intrathecal, epidural, spinal) anesthesia for patients undergoing elective THA/TKA is recommended to help limit blood loss, although evidence suggests that neuraxial anesthesia does not affect the occurrence of VTE.</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>Panel cannot recommend for or against the use of inferior vena cava filters because current evidence does not provide clear guidance about whether inferior vena cava filters prevent embolus in patients undergoing elective THA/TKA who also have a chemoprophylaxis and/or known residual VTE.</td>
<td>Inconclusive</td>
</tr>
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**Abbreviations:** AAOS, American Academy of Orthopaedic Surgeons; THA, total hip arthroplasty; TKA, total knee arthroplasty; VTE, venous thromboembolism.

**Data from Lieberman and Pensak,\textsuperscript{90} Mont and Jacobs,\textsuperscript{90} and Lieberman.\textsuperscript{91}**

The latest AAOS clinical practice guidelines were based on a systematic review of studies on the prevention of symptomatic VTE in patients after THA or TKA.\textsuperscript{90} This stringent and unbiased review of quality studies on this topic resulted in 10 recommendations, which are summarized in Table 1. Each recommendation was graded as strong, moderate, weak, inconclusive, or a panel consensus. The latest AAOS guidelines defined only major bleeding, PE, and all-cause mortality as the critical outcome parameters. As such, the evidence base is much weaker to guide the physician regarding optimal prophylaxis. Thus, it is not surprising that the panel could not make any recommendations with respect to the most effective prophylaxis agents. Lieberman and Pen-
sak recently published a review of these guidelines, detailing the rationale behind many of the recent changes and current recommendations, and Lieberman outlined how to best adapt the new AOS clinical practice guidelines into practice.

**ACCP Clinical Practice Guidelines**

In 2012, the ACCP issued the 9th edition of its guidelines on antithrombotic therapy and prevention of VTE. These guidelines considered the fine balance between efficacy and safety of VTE prophylaxis after total joint arthroplasty. The recommendations are summarized in Table 2. The ACCP now recommends that, instead of no prophylaxis at all, patients undergoing THA or TKA receive 1 of 9 prophylactic regimens for at least 10 to 14 days postoperatively, and they now list aspirin as one of the pharmacological options. In addition, routine screening for VTE with duplex ultrasonography before hospital discharge is not recommended. Finally, when LMWH is used as a prophylactic agent, VTE prophylaxis should be started either 12 hours or more preoperatively or 12 hours or more postoperatively, rather than 4 hours or less preoperative or postoperatively, due to bleeding concerns.

**SCIP Guidelines**

The SCIP was formed as a national organizational partnership aiming to improve quality of surgical care and reduce surgical complications. Numerous SCIP measures have been created in a collaborative effort of the Joint Commission and the Centers for Medicare and Medicaid Services (CMS) as a uniform set of national hospital quality. As such, the SCIP guidelines have been tied to CMS pay-for-performance programs. Conforming hospitals that have adapted the SCIP measures for VTE prophylaxis qualify for bonus payments; these SCIP measures for VTE prophylaxis have been referred to as the SCIP VTE-2 guidelines.

A new set of SCIP measures took effect on January 1, 2014, and include the following quality measure related to VTE prophylaxis after THA or TKA (SCIP VTE-2): patients received appropriate VTE prophylaxis within 24 hours preoperatively to 24 postoperatively.

Currently, the SCIP recommends the following agents for VTE prophylaxis for elective TKA or THA:

- LMWH
- Factor Xa inhibitor
- Oral Factor Xa inhibitor
- Vitamin K antagonist (warfarin)
- Intermittent pneumatic compression devices
- Venous foot pump
- Low-dose unfractionated heparin
- Aspirin

The current SCIP measures are based on the 2012 ACCP guidelines discussed earlier, and, as such, they provide flexibility regarding the use of different prophylactic regimens. Notably, the use of aspirin has now been included in the SCIP measures for antithrombotic prophylaxis, acknowledging its potentially decreased effectiveness as an anticoagulant but better safety profile.

Since its implementation, the effectiveness of the SCIP measures in reducing surgical complications after total joint arthroplasty has been studied. Rasouli et al investigated whether adherence to the SCIP measures would reduce rate of surgical site infection and VTE after total joint arthroplasty. Over a 10-year period, incidences of surgical site infection and VTE were evaluated in 23,907 patients undergoing primary or revision THA or TKA at a single institution. After implementation of the SCIP measures, the rate of superficial surgical site infection increased ($P = .05$), whereas the rate of deep surgical site infection was unchanged ($P = .46$). Regarding VTE, the rate of DVT was unchanged before and after implementation of the SCIP measures ($P = .51$), whereas the rate of PE increased from 0.87% to 1.30% ($P = .002$). The authors concluded that the SCIP was not successful in reducing complications in their patient population.

Similarly, in an observational study, Wang et al analyzed the rates of postoperative surgical site infection and VTE in 17,714 patients. Although compliance of the SCIP measures increased to 96% (surgical site infection) and 97.5% (VTE), higher adherence to these measures did not translate to decreased infection rates. Of note, hospitals with higher compliance rates of the SCIP VTE-2 measures were found to have significantly higher infection rates compared with less-compliant hospitals (1.60% vs 0.93%; $P < .001$). Stricter adherence to the SCIP VTE-2 measures significantly increased the risk of postoperative infection (adjusted odds ratio, 1.50; $P = .02$). As a result, the authors concluded that targeting complete compliance with the SCIP measures did not result in decreased postoperative infection rates but that SCIP VTE-2 prophylaxis may in fact significantly increase the risk of postoperative infections.

It remains to be determined whether the SCIP guidelines, albeit well intentioned, result in decreased rates of postoperative surgical site infection and VTE.

**Conclusion**

Venous thromboembolism prophylaxis after total joint arthroplasty is considered best clinical practice. The latest guidelines recommend a wide array of prophylactic agents and modalities, without evidence for clear superiority of a single regimen.

Of note, it is important to realize that, even with potent pharmacological or mechanical VTE prophylaxis, clot formation cannot be completely prevented. The US CMS recently termed postoperative VTE after THA or TKA a “never event” (ie, a condition considered to be “reasonably preventable”). This inaccurate and worrisome notion has recently been challenged as VTE continues to be a common complication of TKA and THA.
try, 30,020 TKAs were reviewed for the incidence of PE (0.45%), fatal PE (0.01%), and death (0.31%), despite state-of-the-art VTE prophylaxis.\textsuperscript{98} Variables associated with a higher incidence of PE were age, an American Society of Anesthesiologists score of 3 or higher, and the use of general anesthesia.\textsuperscript{98} This large retrospective study underscores the unpreventability of VTE after TKA despite currently recommended VTE prophylaxis, particularly in patients with numerous comorbidities.

Regardless of VTE prophylaxis used, efficacy and safety must be carefully balanced after total joint arthroplasty. Insti-
tutional protocols and a multidisciplinary approach may help optimize the desired effects of VTE prophylaxis while minimizing associated risks.

References


