Upper Extremity Deep Venous Thrombosis Prophylaxis After Elective Upper Extremity Surgery

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abstract

Historically, upper extremity deep venous thromboses (DVTs) have been rare; however, their incidence has increased as awareness has increased. Patients who develop upper extremity DVTs often have multiple comorbidities. However, in the past decade, studies have found a small risk of upper extremity DVTs associated with orthopedic procedures involving the upper extremity. The risk of complications following a DVT, including post-thrombotic syndrome and pulmonary embolism, is substantially higher with a DVT of the upper extremity compared with a DVT of the lower extremity. Furthermore, there is no consensus regarding the role and efficacy of prophylactic measures in preventing upper extremity DVT after upper extremity surgery. This article discusses the use of prophylactic agents after elective upper extremity surgery, with an emphasis on the efficacy of commonly used interventions. [Orthopedics. 201x; xx(x):xx-xx.]

Epidemiology of Venous Thromboembolism

The development of venous thromboembolism is multifactorial, with the risk increasing with age.14-16 In the United States, the average annual incidence is 0.1%, ranging from 0.01% for young adults to more than 1% for adults older than 60 years.14-16 Deep venous thrombosis, in which a clot forms in a deep vein, accounts for more than half of these cases.17 In addition to age, trauma (13-fold), surgery (6- to 22-fold), and malignancy (5-fold) are known risk factors for the development of a DVT (Table 1). The thromboembolic risk of surgery alone, including abdominal surgery, pelvic surgery, orthopedic surgery, neurosurgery, and oncologic surgery, has been estimated as approximately 1.6%.18

Most orthopedists have encountered or will encounter a patient with an upper extremity deep venous thrombosis (DVT) following surgery. Although this condition is understudied, it is known that patients who develop an upper extremity DVT tend to have poorer outcomes. Patients who develop a lower extremity DVT have a higher rate of complications and a higher short-term mortality rate than patients who do not develop DVTs.1-7 Several factors, including age, anatomy, central venous catheters, trauma, and diagnosis of cancer, may predispose patients to developing an upper extremity DVT.1-8-10 During the past decade, some studies have reported an increased risk of upper extremity DVT in patients undergoing elective orthopedic procedures of the upper extremity.11-13 This finding has generated questions regarding the role of prophylactic agents for patients undergoing upper extremity surgery. Although guidelines and evidence supporting the use of prophylactic agents are lacking, prophylactic agents may be justified for properly selected patients.

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Virchow’s Triad

Virchow’s triad was first proposed in the 19th century in an attempt to explain the pathogenesis of thrombosis. Three factors—venous stasis, endothelial injury, and hypercoagulability—work in concert to promote the formation of a clot. Reduced blood flow, which occurs in immobilization, obesity, and pregnancy, leads to venous stasis, which increases the risk of thrombus formation. Vessel wall alterations can provide a surface on which a clot may form and grow. Additionally, hypercoagulable states, such as those found in patients with genetic abnormalities or cancer, have been shown to promote the clotting process.

Upper Extremity DVT

Most DVTs involve the lower extremities. The upper extremities may be affected in a small number of cases. The upper extremities are thought to be at a decreased risk for DVT compared with the lower extremities because the venous circulation of the arms is located at nearly the same level as the heart. Eighteen to 69% of upper extremity DTVs involve the subclavian vein, 5% to 42% involve the axillary vein, and 4% to 13% involve the brachial vein (Figures 1-2). Factors such as anatomy (e.g., Paget–Schroetter syndrome, an effort thrombosis associated with increased activity of the upper extremity that accounts for 20% of upper extremity DTVs), infection, central venous catheters, trauma, hypercoagulable states, and upper extremity surgery all increase the risk for development of an upper extremity DVT. The rate of upper extremity DVT has increased from 2% of all cases of DVT between 1966 and 1986 to 4% to 10% of all cases currently, largely being attributed to the growing use of central venous catheters. The mortality rate after development of an upper extremity DVT is high (34% at 3 months and 48% at 6 months) and likely a reflection of the substantial comorbidities harbored by these patients.

Clinical Manifestations

Upper extremity and lower extremity DVTs have similar clinical manifestations. The most common symptoms of upper extremity DVT are edema and pain, occurring in 98% and 63% of cases, respectively. Patients can also experience skin discoloration, numbness, pruritus, and limited range of motion. However, patients with an upper extremity DVT may also be asymptomatic. This is problematic for physicians, as an estimated 12% to 36% of patients with an upper extremity DVT will develop a pulmonary embolism (PE) or postthrombotic syndrome. Patients with an upper extremity DVT may have more than twice the risk of developing a PE compared with patients with a lower extremity DVT. Thus, it is vital that physicians remain vigilant in assessing for upper extremity DTVs, especially in patients with risk factors.

Surgery and Upper Extremity DVTs

Historically, the relationship between upper extremity DVTs and surgery was not recognized; only in the past decade have studies established a better understanding of the association between the two. Surgical procedures, especially those that lead to immobilization, are thought to be a risk factor for the development of both lower extremity and upper extremity DTVs. In a retrospective study of patients with upper extremity DVTs, Lee et al found that 27% had undergone surgery within 30 days of presentation. Other studies have found similar associations.

Studying specifically examining patients undergoing upper extremity surgery have also found that these patients are at an increased risk of developing an upper extremity DVT. In 2010, Smith et al performed a systematic review to analyze all cases of upper extremity DVT presented in the literature. They identified 38 cases of upper extremity DVT and 19 cases of PE from 20 different journals. Notably, 47% of the upper extremity DVTs that they identified occurred in patients following shoulder arthroplasty or arthroscopic shoulder surgery. Additionally, all cases of documented PE secondary to an upper extremity DVT occurred after shoulder surgery.

Although upper extremity DVTs may be more common after shoulder surgery than after elbow or wrist surgery, the overall risk of developing an upper extremity DVT after an orthopedic procedure of the upper extremities is low. In 2013, Dattani et al conducted a systematic review and found that the overall risk of DVT, in both the lower and the upper extremities, was 0.038% after shoulder arthroscopy, 0.52% after shoulder arthroplasty, 0.64% after proximal humerus procedures (open reduction and internal fixation or hemiarthroplasty), and 0.26% after elbow arthroplasty. When the location of the thrombus was identified, the upper extremities were affected in 58% of the cases. In 2014, Hastie et al reported that the risk of upper extremity DVT after arthroscopic shoulder surgery was 0.64%.
Similarly, Willis et al.\textsuperscript{13} found that, at an academic institution, the risk of subclinical DVT in any extremity was 13.0% after shoulder surgery, lower than the 27.2% risk associated with knee arthroplasty but higher than the 10.3% risk associated with hip arthroplasty. Other than a few case reports, little to no literature exists about DVT after fixation of other upper extremity fractures, including the elbow and humerus.

Historically, most patients at risk of developing an upper extremity DVT have not received prophylaxis. The DVT FREE Steering Committee study found that only 33% of patients who ultimately developed an upper extremity DVT had received prophylaxis in the previous 30 days.\textsuperscript{25} However, given the increased risk of PE associated with DVT of the upper extremity, physicians must carefully consider the risks for patients undergoing upper limb surgery. For selected patients, it may be beneficial to consider the use of prophylactic agents postoperatively.

**GUIDELINES FOR PROPHYLAXIS**

In general, guidelines governing the use of prophylactic agents after elective upper extremity surgery recommend against the routine use of prophylaxis or are nonexistent.\textsuperscript{4} In the United Kingdom, the National Institute for Health and Care Excellence recommends that physicians not routinely offer prophylaxis for patients undergoing upper limb surgery. However, it does recommend that physicians consider prophylaxis for patients who are at a higher risk for DVT.\textsuperscript{36} The British Society for Surgery of the Hand recommends no prophylaxis for patients at low risk and mechanical prophylaxis for patients at medium or high risk; additionally, chemical prophylaxis should also be considered for patients at high risk.\textsuperscript{37}

In contrast, both the American Academy of Orthopaedic Surgeons and the American College of Chest Physicians do not make specific recommendations for patients undergoing elective upper extremity surgery.\textsuperscript{38,39} However, the American College of Chest Physicians does recommend DVT prophylaxis for patients undergoing other orthopedic surgeries, including total hip arthroplasty, total knee arthroplasty, and hip fracture surgery.\textsuperscript{38} The Scottish Intercollegiate Guidelines Network, the Institute for Clinical Systems Improvement, the International Consensus Statement, the National Health and Medical Research Council, and the Australia and New Zealand Working Party have not developed guidelines regarding prophylaxis following upper extremity surgery.\textsuperscript{37} After a review of the Medicare database of shoulder arthroplasties, Day et al.\textsuperscript{40} recommended that the routine use of anticoagulation was not warranted following shoulder arthroplasties because of

![Figure 1: Color Doppler ultrasound of the right subclavian vein revealing a clot and no flow as indicated by the absence of color (white arrow) and waveform (blue arrow).](image1)

![Figure 2: Color Doppler ultrasound obtained a few days later after anticoagulation in the patient of Figure 1 revealing the absence of a clot and the return of flow with the presence of color (white arrow) and waveform (blue arrow).](image2)
the risk of bleeding. However, mechanical prophylaxis and aspirin may be used for patients with normal risk and other agents may be used for patients with increased risk for DVT.\textsuperscript{40}

Despite the lack of clarity provided by these guidelines, surgeons have increasingly prescribed prophylactic agents for patients undergoing elective upper limb surgery. In addition to the consequences of upper extremity DVT potentially being severe, not prescribing prophylactic treatment could result in medical malpractice litigation against physicians.\textsuperscript{4}

**Mechanical Prophylaxis**

Mechanical prophylactic devices, including compression stockings, intermittent pneumatic compression devices, and foot pumps, are widely used by hospitals.\textsuperscript{4} No one of these three modalities has been shown to be superior.\textsuperscript{38} When used correctly, these devices have been shown to reduce the rate of asymptomatic DVT, but they do not change the risk of PE developing.\textsuperscript{27,41-43}

**Chemical Prophylaxis**

The efficacy of chemical prophylactic agents for preventing upper extremity DVT after elective upper extremity surgery has not been studied. However, many different agents, including aspirin, factor Xa inhibitors, unfractionated heparin and low-molecular-weight heparin (LMWH), and vitamin K antagonists, can be used.

Low-molecular-weight heparin is relatively safe and has been reported to be superior to both unfractionated heparin and aspirin in preventing lower extremity DVTs and PE.\textsuperscript{36,44} In the absence of renal failure, the National Institute for Health and Care Excellence guidelines recommend prophylactic treatment with LMWH.\textsuperscript{36}

Warfarin is a vitamin K antagonist that has known efficacy against the development of DVTs. However, it may not reach therapeutic levels for 5 days, limiting its use in outpatient surgery. Additionally, warfarin carries an increased risk of bleeding and requires monitoring, which could complicate treatment among patients for whom follow-up is challenging.\textsuperscript{4}

Factor Xa inhibitors have not been approved for use in preventing upper extremity DVT. However, they have been found to be equivalent to LMWH in preventing DVT after hip and knee arthroplasty.\textsuperscript{43,44} These medications can be particularly useful when prophylaxis is needed for longer periods.\textsuperscript{4}

Aspirin

Aspirin is commonly used by orthopedists as prophylaxis against upper extremity DVTs.\textsuperscript{29} The terms “high-dose” and “low-dose” aspirin are vague in practice and in the literature. There is no agreed on dosing or frequency of aspirin for DVT prophylaxis (range, 81 to 325 mg once or twice per day). However, the mechanism of aspirin allows for understanding of appropriate dosing. Aspirin irreversibly inhibits cyclooxygenase (cyclooxygenase 1 and cyclooxygenase 2). Cyclooxygenase is a component of prostaglandin H synthase, which produces prostaglandin H\textsubscript{2}, leading to the production of thromboxane A2 and endothelium-derived prostacyclin. Thromboxane A2 is produced by platelets and causes platelet aggregation and vasoconstriction. Endothelium-derived prostacyclin inhibits platelet aggregation and induces vasodilation.\textsuperscript{45} With low doses of aspirin (75 to 150 mg/d), its antiplatelet effect can be achieved by inhibition of cyclooxygenase 1. However, cyclooxygenase 2 (analogic and anti-inflammatory properties) inhibition requires high-dose aspirin, which can be up to 10- to 100-fold higher.\textsuperscript{46} Thromboxane A2 is mostly derived from cyclooxygenase 1 and is highly sensitive to aspirin inhibition, which can be seen with low dosage. Although endothelium-derived prostacyclin can be created from cyclooxygenase 1, it mainly comes from cyclooxygenase 2 activity, which is inhibited by high doses of aspirin.\textsuperscript{47} It has not been proven that decreased formation of endothelium-derived prostacyclin with higher doses of aspirin can predispose to thrombosis. Therefore, it can be inferred that doses of at least 75 to 150 mg/d of aspirin may be sufficient for DVT prophylaxis.

Donohoe et al\textsuperscript{48} reported that aspirin was inferior when compared with other forms of prophylaxis. The relative risk of developing a DVT was 0.36 for patients receiving LMWH, 0.64 for those receiving vitamin K antagonists, and 0.66 for those receiving high-dose aspirin (defined as 325 mg twice per day). Likewise, the relative risk of developing a PE was 0.12 for those receiving LMWH, 0.10 for those receiving vitamin K antagonists, and 0.16 for those receiving high-dose aspirin. However, patients receiving aspirin had a 60% lower risk of a major bleeding event compared with patients receiving LMWH and vitamin K antagonists.\textsuperscript{48}

There is some disagreement regarding the relative benefits of aspirin.\textsuperscript{49} The American College of Chest Physicians’ 2012 guidelines included aspirin as a potential option for chemoprophylaxis against DVT in patients undergoing total hip arthroplasty, total knee arthroplasty, or hip fracture surgery.\textsuperscript{38} The American Academy of Orthopaedic Surgeons has also endorsed the use of aspirin for prophylaxis after total hip and knee arthroplasty.\textsuperscript{50} A 2015 review of the literature by Sahebally et al\textsuperscript{51} concluded that aspirin may be as effective as LMWH as prophylaxis for orthopedic patients with a lower risk of bleeding. Although aspirin may be a controversial prophylactic option for use in elective upper extremity surgery, its utility for preventing lower extremity DVT has been confirmed by multiple national organizations. Studies of patients undergoing orthopedic surgery seem to support its use as a prophylactic agent.\textsuperscript{51-53}

**Length of Use**

Literature and recommendations are lacking regarding how long chemical prophylaxis for DVT should be used. Sweetland et al\textsuperscript{54} studied 947,454 middle-aged women to assess the duration and increased risk of venous thromboembolism after different types of surgery. Patients undergoing outpatient surgery were 10 times more like-
ly to be admitted with a venous thromboembolism in the first 6 weeks after surgery; the risk decreased thereafter. For orthopedic surgery, the peak incidence of DVT is 5 to 10 days after hip or knee arthroplasty.\textsuperscript{55} For hip and knee arthroplasty, the American College of Chest Physicians guidelines recommend a minimum of 10 to 14 days of prophylaxis but suggest extending thromboprophylaxis to 35 days during the outpatient period (grade 2B).\textsuperscript{38} Given the lack of specific recommendations, physicians must use their clinical judgment in deciding the correct length of chemical prophylaxis after any upper extremity surgery.\textsuperscript{54}

### Previous Recommendations

Due to the paucity of studies evaluating the efficacy of prophylaxis for upper extremity DVT, specific recommendations cannot be made regarding the choice of chemical prophylaxis and the length of use after upper extremity surgery. However, after evaluating the evidence pertaining to the risk of developing an upper extremity DVT after elective upper limb surgery, Anakwe et al\textsuperscript{4} recommended that physicians start with a detailed DVT risk assessment for every new patient. Despite the costs, all patients undergoing elective upper extremity surgery should be offered mechanical prophylaxis. Although there is little evidence to support this practice, mechanical agents have been shown to be effective in preventing DVTs.

Anakwe et al\textsuperscript{4} recommended that chemical prophylaxis be considered for patients with a high risk of developing an upper extremity DVT. However, there is likely no need for chemical prophylaxis if such patients are able to quickly return to their prior level of mobility. For those who cannot, chemical prophylaxis with LMWH is suggested with no recommendation regarding length of use after surgery.\textsuperscript{4} In a review of the literature regarding the risk of DVT among patients undergoing elbow, wrist, and hand surgery, Roberts and Warwick\textsuperscript{37} recommended mechanical prophylaxis for patients with medium or high risk and that chemical prophylaxis only be considered for patients with high risk because these medications have adverse effects.

Although there is no evidence supporting the use of a specific prophylactic agent, the National Institute for Health and Care Excellence recommends beginning with LMWH or unfractionated heparin for patients with poor renal function. According to the National Institute for Health and Care Excellence guidelines, risk factors for DVT include malignancy, age older than 60 years, receiving intensive care, dehydration, known thrombophilia, obesity, history of DVT, oral contraceptive or hormonal therapy, varicose veins with phlebitis, multiple comorbidities, and pregnancy.\textsuperscript{56} Patients already receiving warfarin can continue prophylaxis at the same or at a modified dose, depending on their specific history. With all forms of chemical prophylaxis, the risk of bleeding must be weighed carefully before beginning therapy.\textsuperscript{5}

Although the efficacy of aspirin as a prophylactic agent has been the source of extensive debate, there is increasing evidence that aspirin may be appropriate for use among orthopedic patients. Aspirin has been found to be safe and efficacious in preventing DVT for orthopedic patients undergoing total hip arthroplasty, total knee arthroplasty, and hip fracture surgery.\textsuperscript{53} Therefore, although aspirin could also be useful in preventing upper extremity DVT, additional studies are warranted.

The current authors recommend performing a detailed risk assessment for every patient undergoing elective upper extremity surgery. For patients with an average risk of developing an upper extremity DVT who undergo high-risk procedures (eg, total shoulder arthroplasty, proximal humerus open reduction and internal fixation, and elbow arthroplasty), physicians should consider beginning low-dose aspirin (325 mg/d) because once daily dosing leads to better patient compliance. Chemical prophylaxis should be administered for at least 2 weeks because the risk of DVT is highest in the first 2 weeks following surgery. Chemical prophylaxis is not needed for lower-risk procedures (eg, shoulder arthroscopy and elbow, wrist, and hand procedures). For patients at the highest risk for

### Table 2

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<thead>
<tr>
<th>Recommendations for Upper Extremity Deep Venous Thrombosis Prophylaxis for Patients Undergoing Elective Upper Extremity Surgery</th>
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</thead>
<tbody>
<tr>
<td>All patients</td>
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<tr>
<td>Detailed risk assessment for deep venous thrombosis</td>
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<tr>
<td>Mechanical prophylaxis</td>
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<tr>
<td>Patients with average risk undergoing low-risk procedures (shoulder arthroscopy and elbow, wrist, and hand procedures)</td>
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<tr>
<td>No chemical prophylaxis needed</td>
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<tr>
<td>Patients with average risk undergoing high-risk procedures (total shoulder arthroplasty, proximal humerus open reduction and internal fixation, and elbow arthroplasty)</td>
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<tr>
<td>Aspirin (325 mg/d) for at least 2 weeks</td>
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<tr>
<td>Patients with high risk undergoing low-risk procedures</td>
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<td>Aspirin (325 mg/d) for at least 2 weeks</td>
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<tr>
<td>Patients with high risk undergoing high-risk procedures</td>
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<tr>
<td>Aspirin (325 mg/d) or consider low-molecular-weight heparin, unfractionated heparin, or warfarin for at least 2 weeks</td>
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upper extremity DVT (ie, those with cancer, a prior history of DVT, or thrombophilia) undergoing high-risk procedures, physicians should consider beginning LMWH, unfractionated heparin, or warfarin. Mechanical prophylaxis is a low-risk treatment and should be started for all patients in the operating room, regardless of risk for upper extremity DVT (Table 2).

**CONCLUSION**

Although upper extremity DVT is a rare complication after upper extremity surgery, it can have serious consequences. Thus, physicians must carefully manage at-risk patients, paying close attention to signs and symptoms that may suggest development of an upper extremity DVT. The American Academy of Orthopaedic Surgeons and the American College of Chest Physicians do not offer specific guidelines regarding the use of prophylactic agents after elective orthopedic procedures of the upper extremity. The current authors recommend that all patients undergoing upper extremity surgery receive a detailed risk assessment and be offered mechanical prophylaxis. Physicians should consider beginning low-dose daily aspirin for patients with average risk undergoing high-risk procedures. Chemical prophylaxis is not recommended for lower-risk procedures. For patients with multiple risk factors undergoing high-risk procedures, physicians should consider beginning LMWH, unfractionated heparin, or warfarin; however, the risk of bleeding should be carefully weighed. No evidence exists regarding the length of use; however, the authors recommend at least 2 weeks if chemical prophylaxis is given because the risk of DVT is highest in the first 2 weeks following surgery.

**REFERENCES**


