Prevention of VTE Following Total Hip and Knee Arthroplasty in Hemophilia Patients

MATTHEW I. STEIN, MD; JUSTIN PARK, MD; STEPHEN RATERMAN, MD

ABSTRACT
The often debilitating condition of hemophilic arthropathy is treated with elective total joint arthroplasty. Little has been published addressing the role of thromboembolic prophylaxis in the hemophilic patient population following total hip arthroplasty (THA) and total knee arthroplasty (TKA). Although the American College of Chest Physicians and the American Academy of Orthopaedic Surgeons have set guidelines for thromboembolic prophylaxis in the general population, no such standard of care is in place for hemophilic patients. While the

ORTHO0511Stein.indd   389
4/29/2011   8:18:36 AM
risk of thrombosis in hemophilic patients following THA and TKA is thought to be lower, cases have been reported of pulmonary embolism and deep vein thrombosis (DVT) in hemophilic patients.

Hemophilic arthropathy is an unfortunately frequent manifestation of severe hemophilia, and one that can often lead to debilitating pain, restricted range of motion, and significant functional decline. For many years, this condition presented a therapeutic dilemma for the orthopedic surgeon, as patients with such a bleeding tendency were not candidates for elective total joint arthroplasty. However, with the advancement of the hematologic care of hemophilic patients over the past several years, primarily through the use of factor replacement therapy, hemophilic arthropathy can now be effectively treated surgically. More specifically, total joint arthroplasty in this patient population has repeatedly showed beneficial outcomes, improving the quality of life with diminished postoperative bleeding episodes.

The number of hemophilic patients undergoing TKA or THA will continue to grow in the near future. Operating surgeons will have the same management dilemmas with hemophilic patients in regards to postoperative deep vein thrombosis (DVT) prophylaxis as they do when performing total joint arthroplasty in the general population. Unfortunately, currently no guidelines exist that address thromboembolic prophylaxis in hemophilic patients, and no literature to date has been published addressing the potential need for postoperative thromboembolic prophylaxis following THA and TKA. This review article summarizes the incidence of postoperative thrombosis in both the general and hemophilic population, outlines the current recommendations for postoperative thromboembolic prophylaxis following TKA and THA, and highlights the need for standard thromboembolic prophylactic guidelines in the hemophilic patient population.

INCIDENCE OF DVT FOLLOWING TKA AND THA

General Population

Elective TKA and THA carry with them a high risk of postoperative thromboembolic disease, a serious and potentially fatal complication. In the general population, this risk has been extensively studied and prophylactic guidelines have been set to best prevent such complications.

Traditionally, the rate of DVT or pulmonary embolism (PE) following total joint arthroplasty has been estimated to be between 40% and 84% in patients undergoing TKA, and 45% and 57% in those undergoing THA. Kim and Kim found that in the absence of chemoprophylaxis, 41.6% of patients following unilateral TKA, and 41.8% of patients following bilateral TKA, were positive by venography for DVT. Similarly, Cordell-Smith et al found that the combined prevalence of DVT after THA and TKA in patients who did not receive chemoprophylaxis was 46.4%. Although the reported fatal outcomes associated with such complications is far lower, the morbidity related to the high rates of DVT following TKA and THA reinforces the elevated risk of thrombotic events accompanying total joint arthroplasty and the need for effective prophylactic measures.

Hemophilic Population

The rate of DVT or PE following elective THA and TKA in hemophilic patients, however, has been only minimally addressed. This is primarily due to the fact that hemophilic patients are more at risk for postoperative bleeding than clotting, but also likely because elective joint arthroplasty in this patient population is a relatively new therapeutic option. Although only few documented cases exist of DVT or PE following total joint arthroplasty in the hemophilic population, patients diagnosed with mild to severe hemophilia are still at risk for thrombotic events.

Several case reports have highlighted instances of DVT, both spontaneous and postoperative, in patients with diagnosed hemophilia. Included among these cases, is that of a fatal PE following major pelvic surgery in a hemophilic patient. Girolami et al reviewed all 27 cases of non-catheter associated venous thrombosis in hemophilic patients, and concluded that the most frequent risk factor for thrombosis in this patient population was the administration of factor replacement therapy. Additionally, 2 patients were found to have congenital prothrombotic risk factors along with the inherited diagnosis of hemophilia.

Krause et al focused specifically on the incidence of DVT following TKA and THA, and found that, in 32 patients with hemophilia A receiving no postoperative chemoprophylaxis, there were no documented cases of venous thrombosis. Similarly, in 68 patients using no postoperative thromboprophylaxis, Silva and Luck identified only 1 nonfatal PE.

STANDARD DVT PROPHYLACTIC REGIMEN FOLLOWING TKA AND THA

General Population

Although extensive research and literature has been published on the most appropriate thromboembolic prophylaxis following TKA and THA, the exact regimen and duration of chemoprophylaxis remains controversial. According to the American College of Chest Physicians (ACCP) 2008 guidelines, patients undergoing THA should be prophylactically treated with either low-molecular-weight heparin (LMWH), fondaparinux, or a vitamin K antagonist with a target international normalized ratio of approximately 2.5. Similarly, for patients undergoing TKA, the ACCP recommends the routine use of LMWH, fondaparinux, or adjusted dose vitamin K antagonist. Additionally, the optimal use of intermittent pneumatic compression is an alternative option to anticoagulant thromboprophylaxis in TKA patients. It is important to recognize, as the source of much debate in the orthopedic community, that the ACCP specifically recommends against the use of aspirin, dextran, or venous foot pumps as the sole method of prophylaxis in both THA and TKA patients.
However, question remains regarding the effectiveness of treatment with anti-platelet agents in low-risk patients.\textsuperscript{20,21} The AAOS 2007 guidelines state that patients at standard risk of PE and major bleeding should be treated with aspirin, LMWH, synthetic pentasacharides, and warfarin. Those with elevated risk of PE, however, may not be treated with aspirin.\textsuperscript{22} Although the AAOS does not specifically designate risk factors in their recommendations, the risk-stratified recommendations of the AAOS has been further defined and frequently supported in orthopedic literature. Among the risk factors often cited are, a previous history of DVT/PE, family history of DVT/PE, history of hypercoagulable disorder, severe deep venous insufficiency, hormone replacement/birth control therapy, and severe heart disease or malignancy.\textsuperscript{23,24} Callaghan et al\textsuperscript{23} found no DVT-related deaths and a low rate of admission for thromboembolic events, with no readmissions for bleeding, in low-risk TKA patients treated with anti-platelet prophylaxis. Similarly, Dorr et al\textsuperscript{24} found that a multimodal, risk stratified, thrombo prophylactic regimen including the use of anti-platelet agents, is consistent with protecting patients, while limiting adverse clinical outcomes secondary to thromboembolic, vascular, and bleeding complications.

Although there has been extensive research on the subject, no universally agreed-upon protocol exists for the thromboembolic prophylaxis of patients undergoing TKA and THA. Similarly, extensive debate exists regarding the appropriate duration of thromboembolic prophylaxis in the postoperative period. Friedman\textsuperscript{25} reviewed the subject, and found that prophylaxis with LMWH for approximately 4 weeks following THA resulted in clinically significant reductions of DVT, but that no data exists to support extending thrombo prophylaxis beyond 10 days following TKA.

**Hemophilic Population**

The extensive discussion regarding the proper prophylactic regimen in the general population reinforces the necessity of similar, gold-standard protocols in the hemophilic population. Currently, no documented standard of care exists for the appropriate thromboembolic prophylactic protocol in the hemophilic population following THA or TKA. However, guidelines suggested by the ACCP and AAOS, regarding patients at risk of bleeding, may apply. According to the ACCP 2008 guidelines, patients with a high risk of bleeding following THA or TKA are recommended to use mechanical thromboprophylaxis with a venous foot pump or intermittent pneumatic compression only.\textsuperscript{19} The AAOS, however, recommends that patients at standard risk of PE and elevated risk of major bleeding should be treated with aspirin, warfarin, or nothing.\textsuperscript{22} Theoretically, the factor replacement therapy required during the perioperative and postoperative period in a hemophilic patient restores these patients to a normal coagulation profile with only mildly increased bleeding risks. These disparate recommendations by the ACCP and AAOS only add more confusion to the subject regarding the most appropriate thromboembolic prophylaxis in this unique patient population. Furthermore, the literature addressing THA and TKA in hemophilic patients sporadically mentions the chosen method of thrombo prophylaxis, with the majority reporting no diagnosed DVTs.\textsuperscript{1,26,27,36} In fact, a comprehensive review of total joint arthroplasty in hemophilia references DVT as a complication of THA, but fails to mention the chosen method of thromboembolic prophylaxis.\textsuperscript{28}

However, several fairly extensive published case series report the method of thromboembolic prophylaxis and any corresponding thrombotic complications. Silva et al\textsuperscript{19} found 1 non-fatal PE in 90 primary TKAs on 68 hemophilic patients with no postoperative thromboprophylaxis. Innocenti et al\textsuperscript{29} studied 24 modular TKA performed in 20 hemophilic patients, with no postoperative thromboprophylaxis, that resulted in no DVTs. Similarly, Miles et al\textsuperscript{2} found no cases of thromboembolic disease when reviewing 34 THAs performed on hemophilic patients, with only mechanical postoperative thromboprophylaxis, and Rodriguez-Merchan\textsuperscript{30} diagnosed no DVTs in 35 primary TKAs with no chemical thromboembolic prophylaxis.

**SUMMARY AND RECOMMENDATIONS**

The role of prophylactic management of postoperative thromboembolism in the hemophilic population deserves more attention. While the debate continues regarding the optimal postoperative DVT prophylactic regimen in the general population following THA and TKA, extensive research regarding prophylactic protocols in hemophilic patients is needed before evidence-based recommendations can be made.

Although hemophilic patients are generally at high risk of bleeding, the treatment required to perform elective arthroplasty increases the hemophilic patient’s risk of thrombosis. In theory, the factor replacement therapy given to hemophilic patients, perioperatively and postoperatively, returns the patient to a relatively normal clotting function, thereby exposing them to similar postoperative risks to the general population. Girolami et al\textsuperscript{16} reported that factor replacement therapy is the most common predisposing element to thrombosis in hemophilic patients. It is this careful balance between hemorrhage and thromboembolism that makes consultation with a hematologist essential.

Complicating matters further are the contradicting recommendations of the ACCP and AAOS regarding patients at an increased risk of postoperative bleeding. While the ACCP calls for mechanical thrombo prophylaxis only, the AAOS also supports the use of aspirin or warfarin.\textsuperscript{19,22} Furthermore, much of the literature addressing total joint arthroplasty in hemophilic patients fails to mention specific methods of thromboembolic prophylaxis. Although the incidence of thrombotic events in hemophilic patients following THA and TKA appears to be minimal, the relatively recent accepted use of total joint arthroplasty as a means of treating hemophilic arthropathy, has limited the capability of performing larger case series and random-
ized, controlled trials. As THA and TKA become more common in hemophilic patients, larger case series and randomized, controlled trials will be essential to determining the true incidence of DVT following TKA and THA in hemophilic patients, as well as comparing the effectiveness and need for mechanical or chemical thromboembolic prophylaxis.

Orthopedic surgeons should recognize and have a basic understanding of the thromboembolic risks associated with operating on hemophilic patients. Given the lack of well studied and proven protocols regarding this topic, it is our experience that close consultation with a hematologist, along with individualizing treatment plans based on patient risk factors, is most successful in planning appropriate thromboembolic prophylaxis in this patient population. Obtaining a detailed family history to rule out co-inherited prothrombotic genetic variations that may predispose a hemophilic patient to thrombosis is also essential. Ultimately, it is up to the operating surgeon to weigh the risks and benefits of chemoprophylaxis and take into account the recommendations of the ACCP and AAOS to determine the appropriate prophylactic regimen for their hemophilic patients.

REFERENCES