Complications of Anticoagulation for Thromboembolism in Early Postoperative Total Joint Arthroplasty

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Abstract

In the study reported here, we analyzed the complications associated with anticoagulation in total joint arthroplasty patients treated for venous thromboembolism (VTE) in the early postoperative period. Twenty-nine consecutive cases from a 1-year period were identified and retrospectively reviewed. VTE treatment, which in most instances (79%) consisted of a heparin drip, was begun a mean of 2.3 days after surgery. Patients received a mean (SD) of 4.4 (5.0) units of packed red blood cells.

There were no differences in bleeding parameters with respect to timing of initiation of anticoagulation. Local and systemic bleeding complications were common. The proportion of patients who were transfused was significantly (P<.0001) higher for VTE patients than for control patients, and transfused VTE patients received significantly (P = .0004) more blood products.

In total joint arthroplasty patients, VTE treatment began 2.3 days after surgery and had a high incidence of complications related to bleeding.

Venous thromboembolism (VTE) after total joint arthroplasty (TJA) is a significant clinical problem, both inherently and because of complications associated with its treatment. Rates of proximal deep vein thrombosis (DVT) and pulmonary embolism (PE) after TJA without antithrombotic prophylaxis have been estimated to range from 18% to 36% and from 0.9% to 28%, respectively.[1] Multiple studies have established the efficacy of several modalities in preventing symptomatic proximal DVT and PE.[1] However, a small but significant proportion of patients develop VTE despite adequate prophylaxis. VTE is typically treated with immediate full-dose anticoagulation as a bridge to long-term oral anticoagulation.[1-3] This aggressive treatment is widely accepted, as it reduces the rate of recurrent VTE and fatal PE.[4,5]

Unfortunately, VTE treatment can result in significant morbidity immediately after surgery, as the patient's wound may be at risk. Investigators have found high rates of local and systemic bleeding complications, increased transfusion requirements, and longer hospitalization.[6-12]

We undertook this study to further characterize complications associated with anticoagulation in the immediate postoperative period after TJA, and to evaluate whether timing of initiation of anticoagulation was a significant risk factor in the development of secondary complications.

Materials and Methods

Research Methods

We obtained institutional review board approval before starting this study. The operating room information system at our institution was queried during a 1-year period using all primary and revision hip and knee arthroplasty *Current Procedural Terminology* codes, identifying 2536 consecutive patients. This database was searched by the Pathology Informatics Department, and blood product and transfusion data were provided for the cohort as a whole. This cohort was also cross-referenced through our institution's medical records program using *International Classification of Diseases, Ninth Revision* codes for DVT and PE. Twenty-nine patients (1.1%) were diagnosed with a DVT proximal to the knee or a PE during their postoperative hospital course.

The demographic and initial postoperative hospital stay treatment data of the 29 patients in the VTE cohort were retrospectively collected and reviewed. Bleeding index (BI), defined as number of units of packed red blood cells (PRBCs) transfused + (preoperative – low hemoglobin values),[13,14] was calculated for each patient. JMP 8 (SAS Institute, Cary, North Carolina) was used for statistical analysis. Analyses were performed through χ^2 tests, t tests, analyses of variance, and linear regression. Statistical significance was determined by P<.05.

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Table I. Surgical Indications and Procedures of the Study Population

Indication	No. of Patients
Osteoarthritis	17
Failed THA	3
Avascular necrosis	2
Failed TKA	2
Developmental dysplasia	1
Perthes disease	1
Infected THA	1
Infected TKA	1
Periprosthetic fracture	1
Procedure	**No. of Patients**
THA	10
TKA	8
Revision THA	4
Revision TKA	3
Bilateral TKA	2
Bilateral THA	1
ORIF	1

Abbreviations: THA, total hip arthroplasty; TKA, total knee arthroplasty;

Clinical Methods

VTE prophylaxis was chosen at the discretion of the attending surgeon. During the study period, screening venous duplex ultrasonography was routinely performed on postoperative day 2 or 3, unless earlier investigation was clinically warranted. Patients with clinical suspicion for PE underwent immediate chest computed tomography with intravenous (IV) contrast. Treatment decisions for patients diagnosed with VTE were made in consultation with a vascular medicine attending physician. Heparin drips were used according to a standardized nomogram, maintaining the activated partial thromboplastin time between 45 seconds and 60 seconds. Bolus doses of heparin were not given coincident to initiation of a heparin drip. Patients who received full-dose anticoagulation with enoxaparin were dosed at 1 mg/kg twice a day. Surgical drains typically were not used.

Results

The overall incidence of early postoperative VTE in this series was 1.1%. Mean (SD) age was 68.2 (14.5) years (range, 24-88 years). Fifteen patients (52%) were female. Indications and surgical procedures for the cohort are listed in Table I. Patients were treated by 13 attending surgeons. Three patients (10%) had a history of previous VTE—2 with previous PE and 1 with a known hypercoaguable disorder. All patients in the cohort received pneumatic compression stockings as mechanical prophylaxis. Twenty-six patients (90%) had chemoprophylaxis with enoxaparin alone; 1 received enoxaparin and warfarin; 1 received warfarin alone; and 1 had a PE immediately after surgery, before initiation of prophylaxis. Twenty-seven patients (93%) were diagnosed with a DVT proximal to the knee. Three patients (10%) had a PE.

VTE treatment was begun a mean (SD) 2.3 (1.1) days (range, 0-6 days) after surgery. Twenty-three patients (79%) initially received a heparin drip without a bolus. Full-dose enoxaparin was used for initial treatment in 2 patients (6.9%). An inferior vena cava (IVC) filter was emergently placed in 4 patients (13.8%) without immediate full-dose anticoagulation; these patients were deemed to be at high risk for bleeding because of their operative procedures (3 revision total hip arthroplasties, 1 revision total knee arthroplasty). Two patients had their anticoagulation stopped later (after 3 days) because of negative follow-up duplex ultrasonography. The remaining patients were transitioned to warfarin (target international normalized ratio, 2-3) before discharge, for a minimum treatment duration of 3 months.

The most common complication was anemia, with 48% and 14% of patients having hemoglobin levels fall below 8 g/dL and 7 g/dL, respectively. All patients had overt bleeding, defined as BI higher than 2,[15] with a mean (SD) BI of 9.7 (4.4). BI was not significantly associated with age ($P = .87$), sex ($P = .17$), surgical procedure ($P = .27$), or indication ($P = .09$). The cohort received a mean

Table II. Bleeding Index and Transfusion Requirements in Study Cohort Analyzed by Method of Initial Treatment and Timing of Anticoagulation Initiation

Parameter	Method of Initial Treatment: Heparin Drip (n = 23)	Enoxaparin (n = 2)	IVC Filter (n = 4)	*P* Value
Bleeding index,[a] mean (SD)	9.4 (4.4)	8.8 (1.6)	10.7 (6.1)	.87
PRBC units transfused, mean (SD)	4.3 (5.2)	3.5 (3.1)	5.5 (5.7)	.88
Patients with PRBC transfusion, No. (%)	18 (78.2%)	2 (100%)	4 (100%)	.27
Patients with ≥5 PRBC units transfused, No. (%)	6 (26.0%)	1 (50%)	1 (25%)	.76
	Timing of Anticoagulation Initiation			
	Before POD 3 (n = 19)	**POD 3 or Later (n = 10)**	***P* Value**	
Bleeding index, mean (SD)	10.0 (4.6)	9.0 (4.0)	.55	
PRBC units transfused, mean (SD)	4.8 (55.6)	3.8 (3.7)	.62	
Patients with PRBC transfusion, No. (%)	14 (73%)	10 (100%)	.29	
Patients with ≥5 PRBC units transfused, No. (%)	6 (31.5%)	2 (20%)	.96	

Abbreviations: IVC, inferior vena cava; POD, postoperative day; PRBC, packed red blood cell.
[a]Bleeding index defined as number of units of PRBCs transfused + (preoperative – low hemoglobin values)

Table III. Comparison of Transfusion Rates and Amounts Between VTE and Control Cohorts

	VTE Cohort (n = 29)	Control Cohort (n = 2536)	*P* Value
Patients with PRBC transfusion, No. (%)	24 (82.7%)	748 (29.4%)	<.0001
PRBC units per transfused patient, mean (SD)	5.4 (5.0)	3.4 (2.6)	.0004

Abbreviations: PRBC, packed red blood cell; VTE, venous thromboembolism.

Table IV. Rates of Complications and Length of Stay in Study Cohort Analyzed by Method of Initial Treatment and Timing of Anticoagulation Initiation

Parameter	Method of Initial Treatment			
	Heparin Drip (n = 23)	Enoxaparin (n = 2)	IVC Filter (n = 4)	*P* Value
Reoperation, No. (%)	3 (13%)	0	0	.47
ICU stay, No. (%)	3 (13%)	0	1 (25%)	.61
Infection, No. (%)	3 (13%)	0	1 (25%)	.61
Hematoma, No. (%)	9 (39.1%)	1 (50%)	0	.14
Length of stay, mean (SD), d	12.0 (4.2)	7.5 (0.7)	10.7 (3.7)	.25
	Timing of Anticoagulation Initiation			
	Before POD 3 (n = 19)	POD 3 or Later (n = 10)	*P* Value	
Reoperation, No. (%)	2 (10.5%)	1 (10%)	.96	
ICU stay, No. (%)	2 (10.5%)	2 (20%)	.49	
Infection, No. (%)	3 (15.8%)	1 (10%)	.66	
Hematoma, No. (%)	8 (42%)	2 (20%)	.22	
Length of stay, mean (SD), d	11.6 (3.9)	11.1 (4.6)	.74	

Abbreviations: ICU, intensive care unit; IVC, inferior vena cava; POD, postoperative day.

(SD) of 4.4 (5.0) units (range, 0-19 units) of PRBCs. Table II details the comparison of bleeding parameters by treatment modality and timing of initiation of anticoagulation. There were no significant differences among the groups that received heparin, enoxaparin, or IVC filter as initial treatment, and anticoagulation timing (during or after first 2 postoperative days) was not significantly related to BI or blood transfusions.

Table III compares the transfusion parameters of the VTE cohort and the comprehensive arthroplasty population during the same period. Twenty-four patients (82.7%) in the VTE cohort and 748 patients (29.4%) in the 1-year comprehensive cohort received a PRBC transfusion ($P<.0001$). Of the patients who received blood products, those in the VTE cohort received significantly ($P = .0004$) more PRBC units.

Bleeding complications were common. Wound drainage or hematoma occurred during the hospital stay in 10 patients (34%) and was significantly ($P = .028$) associated with the number of PRBC units transfused. There was 1 death related to retroperitoneal hemorrhage and acute renal failure; this patient had a heparin drip begun on postoperative day 2. Other major bleeding complications that required discontinuation of anticoagulation were 1 case of superior gluteal artery hemorrhage that required embolization and 1 case of uncontrolled vaginal bleeding. Three patients required reoperation—1 for hemorrhage, 1 for arthrofibrosis, and 1 for deep infection. Another 3 patients developed cellulitis, which resolved with antibiotics. Table IV details the rates of complications by initial treatment method and anticoagulation timing; there were no significant differences.

Heparin-induced thrombocytopenia that required discontinuation of therapy and placement of an IVC filter occurred in 3 patients (10%). Eleven patients (38%) ultimately had a filter placed at some time during their hospitalization. A wound infection was not significantly ($P = .29$) associated with BI. Four patients (14%) required admission to the intensive care unit. For this cohort, mean (SD) stay was 11.4 (4.1) days.

Discussion

Treatment of thromboembolic disease remains a problem after TJA. Despite appropriate multimodal prophylaxis, reported rates of significant VTE events with use of both warfarin and enoxaparin range from 3% to 5%.[1-3] The results from our study are consistent with these observations, given that distal DVTs were excluded from the cohort. Nearly all symptomatic PEs are thought to arise from DVTs proximal to the knee.[2,16] Often, distal DVTs are observed with serial duplex ultrasonography without immediate full-dose anticoagulation. Therefore, these were excluded from our analysis.

Patterson and colleagues[6] reported on the largest series of complications associated with anticoagulation after TJA—112 cases of VTE treated with IV heparin bolus

and drip. When anticoagulation was started within 6 days of surgery, the incidence of bleeding complications was 45%, and therapy had to be discontinued in 35% of cases. The investigators concluded that the most influential factor was the postoperative day on which treatment was begun. Mean time to VTE diagnosis was substantially shorter in our series (2.3 vs 6 days). We found no difference in bleeding parameters between patients beginning anticoagulation on postoperative day 1 or 2 and those starting later. This indicates that, in the early postoperative course, there likely is no safe time to initiate anticoagulation.

Della Valle and colleagues[8] retrospectively compared patients who were anticoagulated with heparin for VTE, with controls who received chemoprophylaxis with enoxaparin. The heparin group had significantly higher transfusion rates, lengths of stay, and slightly higher rates of overall complications. These results were supported by our work. Compared with the control patients, a significantly higher proportion of patients diagnosed with VTE received at least 1 blood transfusion, and, among those patients who received blood, mean number of PRBC units received was also significantly higher.

Our series is unique in that time from surgery to treatment initiation is the lowest that has been reported in the literature. This is likely the result of the screening protocol using duplex ultrasonography done at our institution during the study period. There has been concern that false-positive tests in asymptomatic patients may result in overtreatment and potential harm. Two patients in our cohort were treated with anticoagulation only until repeat ultrasonography was negative. Surveillance ultrasonography was subsequently abandoned at our institution—a change supported by American College of Chest Physicians guidelines.[1]

Our study had several limitations, including those conferred by the retrospective design of the project, the relatively small sample size, and the heterogeneity of operative procedures. Data from the control group (all consecutive arthroplasties during the study period) were limited because of the very large size of the cohort. However, we were able to accurately obtain transfusion-related data, which provided for valuable group comparisons. In addition, as IVC filters without immediate full-dose anticoagulation were used only in patients at very high risk for bleeding, these patients' bleeding and complication results were likely skewed.

Emergent placement of an IVC filter as initial treatment is an alternative in selected patients with an unacceptable risk for bleeding. However, objective indications are not well defined. Filter placement is usually reserved for patients who are receiving anticoagulation and develop bleeding complications or heparin-induced thrombocytopenia, as occurred in 7 patients (24%) in our series. Some believe that, given the significant complications associated with anticoagulation, early therapeutic use of IVC filters should be expanded.[17] We believe that our series again demonstrates that considerable morbidity is associated with early anticoagulation after TJA and that there is likely no safe time in the early postoperative period to begin anticoagulation. As a result, serious consideration should be given to IVC filter placement as an alternative to early anticoagulation. A prospective study that compares the safety and efficacy of full-dose anticoagulation vs IVC filter placement without full anticoagulation in the immediate postoperative patient would thus be of considerable value.

Authors' Disclosure Statement

Dr. Froimson wishes to report that he serves on the scientific advisory board, is a paid consultant for, and has stock options in Medical Compression Systems, Inc., which manufactures a device to prevent venous thromboembolism. The other authors report no actual or potential conflict of interest in relation to this article.

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This paper will be judged for the Resident Writer's Award.