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Complications - Other

The Effectiveness of a Risk Stratification Protocol for Thromboembolism Prophylaxis After Hip and Knee Arthroplasty

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ABSTRACT

Background: This study's purpose was to present our institution's experience with the use of a risk stratification protocol for venous thromboembolism (VTE) prophylaxis in joint arthroplasty in which "routine" risk patients receive a mobile compression device in conjunction with aspirin and "high"-risk patients receive warfarin for thromboprophylaxis.

Methods: This was a prospective study of patients undergoing primary or revision knee or hip arthroplasty. Exclusion criteria were patients with a current deep vein thrombosis, history of pulmonary embolism, chronic warfarin therapy, planned multiple surgeries, and prolonged postoperative immobilization. Patients were stratified as either routine or high risk. Routine risk patients received mobile compression devices for 10 days and aspirin twice daily for 6 weeks, whereas high-risk patients received warfarin for 4 weeks and compression stockings for 6 weeks.

Results: A total of 3143 total joint arthroplasties were enrolled (2222, 70.7% "routine"; 921, 29.3% "high risk"). The rate of symptomatic VTE within 6 weeks postoperatively was 0.7% (95% CI 0.3%-1.0%) in the standard vs 0.5% (95% CI 0.01%-1.0%) in the high-risk cohort ($P = .67$), and within 6 months postoperatively was 0.6% (95% CI 0.3%-1.0%) in the standard vs 1.1% (95% CI 0.4%-1.8%) in the high-risk cohort ($P = .23$). The rate of major bleeding events was significantly lower in the routine (0.4%; 95% CI 0.1%-0.6%) vs high-risk (2.0%; 95% CI 1.0%-3.0%; $P < .001$) cohort.

Conclusions: This study demonstrates that use of a risk stratification protocol allowed the avoidance of more aggressive anticoagulation in 70% of patients while achieving a low overall incidence of symptomatic VTE.

Venous thromboembolic events (VTEs), including deep vein thrombosis (DVT) and pulmonary embolism (PE), remain a significant cause of concern for both surgeons and patients after total hip arthroplasty (THA) and total knee arthroplasty (TKA) [1]. The reported rates of symptomatic VTE after THA and TKA range from 0.83%-15% [2-5] and 2%-10% [5], respectively. Thus, some form of VTE prophylaxis should be routinely administered after total joint arthroplasty. Recommendations from the American Academy of Orthopaedic Surgeons (AAOS) have focused on the overall safety profile of VTE prophylaxis regimens, raising concerns of postoperative bleeding, wound complications, readmission, and potential infection with the use of more potent thromboprophylactic medications [6-9]. In addition, recent guidelines from the American College of Chest Physicians (ACCP) have changed to more closely reflect AAOS recommendations [10].

Thus, orthopedic surgeons now have more flexibility regarding their choice of VTE prophylaxis regimen, yet it remains unclear which is optimal. In 2011, the AAOS clinical practice guideline noted that "the workgroup cannot recommend for or against a specific prophylactic regimen in these patients because current evidence is unclear about which strategy (or strategies) is or are optimal or suboptimal" [11,12]. In the most recent edition of ACCP guidelines, a grade-1 recommendation was made if there was certainty that the benefits of a particular

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VTE prophylaxis regimen did or did not outweigh the risk of burdens of that regimen, and a grade-2 recommendation was given if there was lower quality evidence. In addition, recommendations were graded as A, B, or C based on the quality of the randomized trials (A or B), or C, if there were only observational studies available for review. Versus the use of no antithrombotic prophylaxis, warfarin, aspirin, low-molecular-weight heparin, and oral factor Xa inhibitors were all given a 1B recommendation, whereas the use of intermittent pneumatic compression devices (MCDs) was given a 1C recommendation [10]. However, patients at low risk of VTE may receive excessive anticoagulation and unnecessarily risk further perioperative morbidity after total joint arthroplasty [8,9]. Although "risk stratification" for VTE events and/or bleeding has been recommended by the AAOS, this is difficult because of limited evidence elucidating specific risk factors that elevate VTE risk [13]. Thus, the search for the optimal balance between safety and efficacy with thromboprophylactic regimens remains elusive.

With an evolving health care landscape, emphasis on complications and readmissions, and shorter inpatient hospitalizations, it is imperative that a VTE prophylaxis regimen is simple, effective, easy to monitor, and has high patient compliance. With this in mind, MCDs have been used with greater frequency after total joint arthroplasty, with multiple reports demonstrating their effectiveness in VTE prevention with or without the addition of aspirin for chemical prophylaxis [14-19]. At our institution, a risk stratification protocol has been implemented in patients undergoing joint arthroplasty in which those deemed "routine" risk for VTE receive a MCD in conjunction with aspirin, whereas patients deemed "high" risk receive warfarin for thromboprophylaxis. The purpose of this prospective study was to present our experience with the use of this risk stratification protocol and VTE prophylaxis regimen. We hypothesized that after risk stratification, the use of MCDs with aspirin would be noninferior to warfarin in the prevention of VTE after joint arthroplasty.

Materials and Methods

This was a prospective, institutional review board–approved study of patients undergoing primary or revision TKA, unicompartmental knee arthroplasty, primary or revision THA, and surface replacement arthroplasty at a single academic medical center. Six, fellowship-trained, orthopedic surgeons enrolled patients in this study. All patients provided informed consent before their inclusion. Inclusion criteria were patients aged older than 18 years undergoing an elective, unilateral joint arthroplasty procedure. Patients were excluded if they had a positive lower extremity DVT detected on preoperative ultrasound or were being treated for a recent DVT (surgery would be delayed), a history of PE (these patients would receive low-molecular-weight heparin and warfarin postoperatively), were on chronic warfarin therapy, or were scheduled for multiple surgeries (within 3 months) in close proximity. A preoperative ultrasound was performed in all patients with a personal history of DVT. If an acute DVT was present, surgery was delayed for medical management of the DVT and the patient was excluded. This included all patients presenting with a thrombosis involving the femoral or popliteal veins or veins of the calf distal to the knee that appeared acute in nature based on Doppler ultrasound examination demonstrating abnormal vein distention and a hypoechoic or complex echo pattern [20,21]. Any patient determined to be at high risk for wound complications based on their health history (ie, poor nutritional status) were excluded at the discretion of the treating surgeon. Patients with a history of wound healing complications, patients on immunosuppressive medications for inflammatory arthritides or a solid organ transplant, or on renal dialysis were also excluded because of their potential increase of wound healing complications and to limit potential confounding variables in our analysis.

All enrolled patients were stratified to either a "routine" or "high"-risk VTE thromboprophylaxis regimen. Currently, there is no validated approach to stratify patients undergoing total joint arthroplasty based on their risk of VTE [22]. Thus, patients were stratified as "high" risk if they met any of the following criteria based on the clinical protocol at our institution (Table 1). For this study, heart disease was considered present in patients with a history of coronary artery bypass graft, cardiac stent, mechanical valve replacement, or myocardial infarction; lung disease in patients with a history of chronic obstructive pulmonary disease, restrictive lung disease, or chronic bronchitis requiring medical management; and diabetes in patients requiring medical management for type I or type II diabetes. The use of multiple medical comorbidities as an inclusion criteria in the high-risk cohort was based on National Institute for Health and Care Excellence guidelines [23] that recognize this as a potential risk factor of VTE in patients admitted for surgery. A family history of VTE was considered present if a parent or sibling had a VTE event not occurring after a specific traumatic event or surgical procedure. A patient was considered to have limited weight bearing if they were not full weight bearing on their operative extremity starting postoperative day 1. If none of these criteria were met, the patient was stratified to the "routine" risk regimen. After 2 years of patient enrollment (April 2010 to May 2012), a midterm analysis was performed to determine the effectiveness of our risk stratification protocol and to assess if inclusion criteria for the high-risk cohort could be narrowed. Low rates of VTE were seen in both the "routine" and "high"-risk cohorts with a significant increase in major bleeding, wound problems, and incisional drainage in the "high"-risk cohort. Given our encouraging preliminary results and the known difficulty in warfarin dosing and/or monitoring, age $\geq$70 years, multiple medical comorbidities, and body mass index $\geq$40 kg/m^2 were removed as inclusion criteria for the high-risk cohort for the period of study from May 2012 to October 2014. Expansion of our criteria was also influenced by concomitant reports demonstrating the effectiveness of MCDs in VTE prevention after excluding patients with a history of venous thromboembolism, coagulation disorder, active cancer, or major surgery in the past 3 months [18,24,25].

All patients in both the routine and high-risk cohorts received MCDs (Active Care+ SFT; Medical Compression Systems, Or Akiva, Israel) [17,24,26] applied to the contralateral lower extremity before the operative procedure and to the operative extremity postoperatively in the operating room. The protocol for anticoagulation therapy in the routine risk cohort consisted of use of MCDs for a goal of 23 hours a day for 10 days, along with enteric-coated aspirin (325 mg twice daily) started the evening of surgery for 6 weeks postoperatively. This dose of aspirin was already used as part of our institution's protocol and thus was not changed for the purpose of this study. During the introduction of MCDs, compliance was recorded via patient-reported responses and from

Table 1
Criteria to Determine "High"-Risk Patients.

Age $\geq$70 y
History of deep vein thrombosis with negative preoperative ultrasound examination
Active cancer
Hypercoagulable states (protein C, protein S, factor V Leiden, and so forth)
Multiple medical comorbidities (2 of the following 3 conditions: heart disease, lung disease, diabetes)
Morbid obesity (BMI $\geq$40 kg/m^2)
Family history of deep vein thrombosis or pulmonary embolism
Immobility (ie, limited weight bearing)–surgeon's discretion

BMI, body mass index.

measurements off the hard drive of the device itself. Patients in the high-risk cohort also received MCDs, but only during their inpatient stay. Warfarin therapy was initiated the night before surgery to expedite achievement of the target international normalized ratio (INR) postoperatively and adjusted for a target INR between 1.8 and 2.2 for 4 weeks postoperatively in adherence with national guidelines [13,27]. Warfarin dosing and INR monitoring were performed by our institution's anticoagulation service. As part of our institution's protocol before this study, patients receiving warfarin were also asked to wear compression stockings for a period of 6 weeks [28,29]. We elected not to alter this protocol before this study to maintain consistency with our previous regimen.

Rehabilitation protocols were identical in all patients focusing on early mobilization, range of motion, and strengthening. The primary outcome measure was the incidence of DVT or PE in both groups. Patients were monitored for any clinical signs or symptoms of VTE including increased swelling or tenderness to palpation in the lower extremity, chest pain, shortness of breath, or tachycardia. All patients were called or seen for clinical follow-up at 2 weeks postoperatively and assessed with a clinical examination at 6 weeks postoperatively. Patients with clinical symptoms of DVT underwent duplex ultrasonography, whereas patients with clinical suspicion of a PE received a spiral computed tomography scan of the lungs. These tests were not performed in the absence of clinical symptoms. Any postoperative wound, bleeding, medical complication, or readmission within 6 months of surgery was recorded. A major bleeding event was defined as bleeding that required rehospitalization or prolonged hospitalization, required any intervention such as surgery or hematoma aspiration to prevent permanent impairment or damage, endangered critical organs (intracerebral, intraocular, intraspinal, pericardial, or retroperitoneal), was life threatening, or caused death [18]. The number of days of "drainage" from the wound including any signs of discharge (blood and serous fluid) seen at the time of incisional dressing changes was also recorded. Reasons for readmission were categorized into (1) management of DVT or PE, and (2) complication related to anticoagulation (ie, prolonged wound drainage or supratherapeutic INR). Patient deaths due to VTE and all causes were also recorded. Finally, patient satisfaction with their thromboprophylaxis protocol was assessed at 2 and 6 weeks postoperatively using the following scoring system: 1 = very satisfied, 2 = satisfied, 3 = neutral, 4 = dissatisfied, 5 = very dissatisfied.

Statistical Analysis

A noninferiority power analysis was used as we hypothesized that the use of MCDs with aspirin would be as effective as warfarin in preventing VTE but would have an improved safety profile. A total sample size of 2306 patients was found to have appropriate power (beta level = 0.80, alpha level = 0.05) to detect noninferiority between the 2 treatment regimens assuming a 1.0% difference in the rate of symptomatic VTE to be clinically significant. Chi-square and Fisher's exact tests were used to assess group differences in categorical variables and independent *t*-tests were used to compare continuous variables. A *P* value of <.05 was considered statistically significant. All statistical analyses were performed using IBM SPSS software, version 22 (IBM Corp., Armonk, NY).

Results

Study Period: April 2010 to May 2012

Before modification of our inclusion criteria for the high-risk cohort, from April 2010 to May 2012 a total of 1502 patients were enrolled with 644 (42.9%) stratified to the high-risk cohort. Five hundred fifty-four patients were excluded during the initial phase of this study. As expected, based on our risk stratification criteria, patients in the routine risk cohort were younger than in the high-risk cohort (55.3 ± 9.6 vs 67.0 ± 10.8 years, $P < .001$; Table 2).

Overall, 88.1% of routine and 85.1% of high-risk patients were available for clinical follow-up at 6 weeks postoperatively. The overall rate of VTE was low in both cohorts, with a total of only 6 (0.5%; 95% CI 0.3%-0.9%) VTE events documented within 6 weeks and 8 (0.6%; 95% CI 0.4%-0.9%) VTE events within 6 months postoperatively, all in patients undergoing a primary joint arthroplasty procedure. The cumulative rate of VTE events was 0.6% (95% CI 0.1%-1.2%) in the routine risk cohort vs 0.2% (95% CI 0.0%-0.5%) in the high-risk cohort within 6 weeks postoperatively ($P = .21$), and 0.6% (95% CI 0.1%-1.2%) in the routine risk and 0.5% (95% CI 0.0%-1.1%) in the high-risk cohort within 6 months postoperatively ($P = .9$, Table 3).

The rate of major bleeding complications within 6 weeks postoperatively, wound problems within 2 weeks postoperatively, and incisional drainage lasting greater than 7 days were also lower in the routine risk cohort vs the high-risk cohort ($P < .001$-.009, Table 3). Regarding six-month readmission events, 63 patients in the routine risk (7.8%; 95% CI 6.0%-9.7%) and 97 patients in the high-risk cohort (16.2%; 95% CI 13.2%-19.1%; $P < .001$) were readmitted to the hospital, with several patients having multiple readmissions (Table 4). Two patients in the routine cohort (2.9% of all readmissions in the routine cohort; 95% CI 0.9%-6.9%) and 1 patient in the high-risk cohort (1.0%; 95% CI 0.0%-2.9%) were readmitted for a PE ($P = 0.7$). There were 2 readmissions in the routine cohort (2.9%; 95% CI 0.9%-6.9%) related to anticoagulation therapy vs 5 readmissions in the high-risk cohort (4.9%; 95% CI 0.7%-9.1%; $P = .8$).

Study Period: June 2012 to October 2014

After modification of our inclusion criteria for the high-risk cohort, from June 2012 to October 2014, a total of 1641 patients were enrolled with 277 (16.9%) stratified to the high-risk cohort. Six hundred twenty-seven patients were excluded during the second phase of this study. Again, patients in the routine risk cohort were younger than in the high-risk cohort (59.2 ± 12.0 vs 62.8 ± 11.2 years, $P < .001$; Table 5).

As during the initial study period, the overall rate of VTE was low in both cohorts. The cumulative rate of VTE events was 0.6% (95% CI 0.2%-1.1%) in the routine risk cohort vs 1.3% (95% CI 0.0%-2.7%) in the high-risk cohort within 6 weeks postoperatively ($P = .3$), and 0.6% (95% CI 0.2%-1.1%) in the routine risk and 2.4% (95% CI 0.5%-4.3%) in the high-risk cohort within 6 months postoperatively ($P = .02$, Table 6). The rate of major bleeding complications within 6

Table 2
Preoperative Demographics of the Routine and High-Risk Patient Cohorts During the Initial Study Period (Before Modification of Inclusion Criteria for the High-Risk Cohort).

April 2010-May 2012	Routine (n = 858)	High (n = 644)	*P* Value
Operative side			.51
Right	445 (51.9)	345(53.6)	
Left	413(48.1)	299(46.4)	
Revision status			**<.001**
Primary	774 (90.2)	522(81.1)	
Revision	84(9.8)	122(18.9)	
Age at surgery (y)	55.3 ± 9.6	67.0 ± 10.8	**<.001**
Gender			**<.001**
Female	433 (50.5)	402(62.4)	
Male	425 (49.5)	242 (37.6)	

Data is presented as absolute number with percentage in parentheses or mean ± standard deviation.
Bold *P* values indicate a statistically significant value.

Table 3
Rates of VTE Events and Bleeding Complications in the Routine and High-Risk Cohorts During the Initial Study Period.

April 2010-May 2012	Routine (n = 858)	High (n = 644)	*P* Value
DVT or PE within 6 wk	n = 756	n = 548	.21
No	752 (99.5%; 98.9-99.9)	547 (99.8%; 99.5-100)	
Yes	5 (0.6%; 0.1-1.2)	1 (0.2%; 0.0-0.5)	
DVT or PE within 6 mo	n = 803	n = 600	>.9
No	798 (99.4%; 98.8-99.9)	597 (99.5%; 98.9-100)	
Yes	5 (0.6%; 0.1-1.2)	3 (0.5%; 0.0-1.1)	
DVT	3 (0.4%; 0.0-0.8)	2 (0.3%; 0.0-0.8)	
PE	2 (0.2%; 0.0-0.6)	1 (0.2%; 0.0-0.5)	
Major bleeding complications within 6 wk	n = 755	n = 549	**<.001**
No	754 (99.9%; 99.6-100)	538 (98.0%; 96.8-99.2)	
Yes	1 (0.1%; 0.0-0.4)	11 (2.0%; 0.8-3.2)	
Wound problems within 2 wk	n = 771	n = 570	**.002**
No	771 (100.0%; 100-100)	563 (98.8%; 97.9-99.7)	
Yes	0 (0.0%; 0.0-0.0)	7 (1.2%; 0.3-2.1)	
Days of drainage	n = 771	n = 568	**.009**
0-3	631 (81.8%; 79.1-84.6)	442 (77.8%; 74.4-81.2)	
4-7	109 (14.1%; 11.7-16.6)	81 (14.3%; 11.4-17.1)	
>7	31 (4.0%; 2.6-5.4)	45 (7.9%; 5.7-10.1)	

Data are presented as the absolute number and the percentage of respondents in parentheses, along with the 95% CI. "n" refers to the number of patients for whom data were available for each outcome measure.
Bold *P* values indicate a statistically significant value.
DVT, deep vein thrombosis; PE, pulmonary embolism; VTE, venous thromboembolism.

weeks postoperatively, wound problems within 2 weeks postoperatively, and incisional drainage lasting greater than 7 days were again lower in the routine risk cohort vs the high-risk cohort (Table 6). During the second study period, 3 patients in the routine cohort (1.8% of all readmissions in the routine cohort; 95% CI 0.0%-3.9%) and 1 patient in the high-risk cohort (2.3%; 95% CI 0.0%-6.7%) were readmitted for a PE ($P > .9$). There were 2 readmissions in the routine cohort (1.2%; 95% CI 0.0%-2.9%) related to anticoagulation therapy vs 3 readmissions in the high-risk cohort (6.8%; 95% CI 0.0%-14.3%; $P = .1$) (Table 7).

Of note, no difference was present in the percentage of VTE events between the "routine" cohorts from the initial (April 2010-May 2012) and second (June 2012-October 2014) study periods,

Table 4
Reasons for Readmission in the Routine and High-Risk Cohorts in the Initial Study Period.

April 2010-May 2012	Routine (n = 804)	High (n = 600)	*P* Value
Number of patients readmitted	63 (7.8%; 6.0-9.7)	97 (16.2%; 13.2-19.1)	**<.001**
Reasons for readmission			
Total number of readmissions	69 (8.6%; 6.6-10.5)	102 (17%; 13.9-20.0)	
Admissions for pulmonary embolism	2 (2.9%; 0.9-6.9)	1 (1.0%; 0.0-2.9)	.7
Complication related to anticoagulation therapy	2 (2.9%; 0.9-6.9)	5 (4.9%; 0.7-9.1)	.8
Death due to VTE event	0 (0%; 0.0-0.0)	0 (0%; 0.0-0.0)	N/A
Death—all causes	1 (1.4%; 0.0-4.3)	1 (1.0%; 0.0-2.9)	>.9

Data is presented as the absolute number and the percentage of respondents in parentheses, along with the 95% confidence interval "n" refers to the number of patients for which data was available. Percentages for reason of readmission based on total number of readmissions from that, respective cohort.
Bold *P* values indicate a statistically significant value.
N/A, not applicable; VTE, venous thromboembolism.

Table 5
Preoperative Demographics of the Routine and High-Risk Patient Cohorts During the Second Study Period (After Modification of Inclusion Criteria for the High-Risk Cohort).

June 2012-October 2014	Routine (n = 1364)	High (n = 277)	*P* Value
Operative side			.99
Right	744 (54.5%)	151 (54.5%)	
Left	620 (45.5%)	126 (45.5%)	
Revision status			.47
Primary	1217 (89.2%)	243 (87.7%)	
Revision	147 (10.8%)	34 (12.3%)	
Age at surgery (y)	59.2 ± 12.0	62.8 ± 11.2	**<.001**
Gender			**<.001**
Female	752 (55.1%)	189 (68.2%)	
Male	612 (44.9%)	88 (31.8%)	

Data are presented as absolute number with percentage in parentheses or mean ± standard deviation.
Bold *P* values indicate a statistically significant value.

although incisional drainage greater than 3 days was less frequent in the second study period ($P < .001$; Table 8). When comparing the "high"-risk cohorts from the initial and second study periods, there was a slightly increased rate of VTE events within 6 months in the second study period ($P = .04$), and again incisional drainage greater than 3 days was less frequent in the second study period ($P = .02$; Table 9).

Overall Analysis: April 2010-October 2014

From April 2010 to October of 2014, a total of 3143 patients were prospectively enrolled (2222 routine risk, 70.7%; 921 high risk, 29.3%). The most common procedure was primary THA (1553), followed by primary TKA (940), revision TKA (203), revision THA (188), unicompartmental knee arthroplasty (132), and surface

Table 6
Rates of VTE Events and Bleeding Complications in the Routine and High-Risk Cohorts During the Second Study Period.

June 2012-October 2014	Routine (n = 1364)	High (n = 277)	*P* Value
DVT or PE within 6 wk	n = 1240	n = 237	.3
No	1231 (99.3%; 98.8-99.8)	234 (98.7%; 97.3-100)	
Yes	8 (0.6%; 0.2-1.1)	3 (1.3%; 0.0-2.7)	
DVT or PE within 6 mo	n = 1254	n = 248	**.02**
No	1246 (99.4%; 98.9-99.8)	242 (97.6%; 95.7-99.5)	
Yes	8 (0.6%; 0.2-1.1)	6 (2.4%; 0.5-4.3)	
DVT	5 (0.4%; 0.05-0.7)	5 (2.0%; 0.3-3.8)	
PE	3 (0.2%; 0.0-0.5)	1 (0.4%; 0.0-1.2)	
Major bleeding complications within 6 wk	n = 1236	n = 238	**.04**
No	1230 (99.5%; 99.1-99.9)	233 (97.9%; 96.1-99.7)	
Yes	6 (0.5%; 0.1-0.9)	5 (2.1%; 0.3-3.9)	
Wound problems within 2 wk	n = 1317	n = 265	**.048**
No	1312 (99.6%; 99.3-99.9)	261 (98.5%; 97.0-99.9)	
Yes	5 (0.4%; 0.05-0.7)	4 (1.5%; 0.04-3.0)	
Days of drainage	n = 1313	n = 263	**.02**
0-3	1174 (89.4%; 88.8-91.1)	224 (85.2%; 80.9-89.5)	
4-7	86 (6.5%; 5.2-7.9)	18 (6.8%; 3.8-9.9)	
>7	53 (4.0%; 3.0-5.1)	21 (8.0%; 4.7-11.3)	

Data are presented as the absolute number and the percentage of respondents in parentheses, along with the 95% CI. "n" refers to the number of patients for whom data were available for each outcome measure.
Bold *P* values indicate a statistically significant value.
DVT, deep vein thrombosis; PE, pulmonary embolism; VTE, venous thromboembolism.

Table 7
Reasons for Readmission in the Routine and High-Risk Cohorts in the Second Study Period.

June 2012-October 2014	Routine (n = 1253)	High (n = 249)	*P* Value
Number of patients readmitted	149 (11.9%; 10.1-13.7)	42 (16.9%; 12.2-21.5)	**.04**
Reasons for readmission			
Total number of readmissions	163 (13.0%; 11.2-14.9)	44 (17.7%; 12.9-22.4)	
Admissions for pulmonary embolism	3 (1.8%; 0.0-3.9)	1 (2.3%; 0.0-6.7)	>.9
Complication related to anticoagulation therapy	2 (1.2%; 0.0-2.9)	3 (6.8%; 0.0-14.3)	.1
Death due to VTE event	0 (0%; 0.0-0.0)	0 (0%; 0.0-0.0)	N/A
Death—all causes	0 (0%; 0.0-0.0)	0 (0%; 0.0-0.0)	N/A

Data are presented as the absolute number and the percentage of respondents in parentheses, along with the 95% CI. "n" refers to the number of patients for whom data were available. Percentages for reason of readmission based on total number of readmissions from that, respective cohort.
Bold *P* values indicate a statistically significant value.
N/A, not applicable; VTE, venous thromboembolism.

replacement arthroplasty (127). Patients in the routine risk cohort were younger than in the high-risk cohort (57.7 ± 11.3 vs 65.8 ± 11.1 years, $P < .001$; Table 10). The first 1834 patients in the routine risk cohort were asked about their compliance with the use of MCDs. Overall, 97.5% of patients reported compliance with the postoperative protocol, but based on the device readings, 84.5% of patients wore the MCDs for greater than 18 hours daily, with 1.5% of patients wearing them for less than 12 hours daily. The first 669 patients in the high-risk cohort were asked about their compliance with warfarin. A total of 99.0% of patients reported compliance with warfarin dosing.

Table 8
Comparison of the "Routine" Risk Cohorts From the Initial and Second Study Periods.

Outcome Measure	Routine (April 2010-May 2012; n = 858)	Routine (June 2012-October 2014; n = 1364)	*P* Value
DVT or PE within 6 wk	n = 756	n = 1240	>.9
No	752 (99.5%; 98.9-99.9)	1231 (99.3%; 98.8-99.8)	
Yes	5 (0.6%; 0.1-1.2)	8 (0.6%; 0.2-1.1)	
DVT or PE within 6 mo	n = 803	n = 1254	>.9
No	798 (99.4%; 98.8-99.9)	1246 (99.4%; 98.9-99.8)	
Yes	5 (0.6%; 0.1-1.2)	8 (0.6%; 0.2-1.1)	
DVT	3 (0.4%; 0.0-0.8)	5 (0.4%; 0.05-0.7)	
PE	2 (0.2%; 0.0-0.6)	3 (0.2%; 0.0-0.5)	
Major bleeding complications within 6 wk	n = 755	n = 1236	.4
No	754 (99.9%; 99.6-100)	1230 (99.5%; 99.1-99.9)	
Yes	1 (0.1%; 0.0-0.4)	6 (0.5%; 0.1-0.9)	
Wound problems within 2 wk	n = 771	n = 1317	.2
No	771 (100.0%; 100-100)	1312(99.6%; 99.3-99.9)	
Yes	0 (0.0%; 0.0-0.0)	5(0.4%; 0.05-0.7)	
Days of drainage	n = 771	n = 1313	**<.001**
0-3	631 (81.8%; 79.1-84.6)	1174 (89.4%; 88.8-91.1)	
4-7	109 (14.1%; 11.7-16.6)	86 (6.5%; 5.2-7.9)	
>7	31(4.0%; 2.6-5.4)	53(4.0%; 3.0-5.1)	

Data are presented as the absolute number and the percentage of respondents in parentheses, along with the 95% CI. "n" refers to the number of patients for whom data were available.
Bold *P* values indicate a statistically significant value.
DVT, deep vein thrombosis; PE, pulmonary embolism.

Table 9
Comparison of the "High"-Risk Cohorts From the Initial and Second Study Periods.

Outcome Measure	High (April 2010-May 2012; n = 644)	High (June 2012-October 2014; n = 277)	*P* Value
DVT or PE within 6 wk	n = 548	n = 237	.2
No	547 (99.8%; 99.5-100)	234 (98.7%; 97.3-100)	
Yes	1 (0.2%; 0.0-0.5)	3 (1.3%; 0.0-2.7)	
DVT or PE within 6 mo	n = 600	n = 248	**.04**
No	597 (99.5%; 98.9-100)	242 (97.6%; 95.7-99.5)	
Yes	3 (0.5%; 0.0-1.1)	6 (2.4%; 0.5-4.3)	
DVT	2 (0.3%; 0.0-0.8)	5 (2.0%; 0.3-3.8)	
PE	1 (0.2%; 0.0-0.5)	1 (0.4%; 0.0-1.2)	
Major bleeding complications within 6 wk	n = 549	n = 238	.9
No	538 (98.0%; 96.8-99.2)	233 (97.9%; 96.1-99.7)	
Yes	11 (2.0%; 0.8-3.2)	5 (2.1%; 0.3-3.9)	
Wound problems within 2 wk	n = 570	n = 265	.9
No	563 (98.8%; 97.9-99.7)	261 (98.5%; 97.0-99.9)	
Yes	7 (1.2%; 0.3-2.1)	4 (1.5%; 0.04-3.0)	
Days of drainage	n = 568	n = 263	**.02**
0-3	442 (77.8%; 74.4-81.2)	224 (85.2%; 80.9-89.5)	
4-7	81 (14.3%; 11.4-17.1)	18 (6.8%; 3.8-9.9)	
>7	45 (7.9%; 5.7-10.1)	21 (8.0%; 4.7-11.3)	

Data are presented as the absolute number and the percentage of respondents in parentheses, along with the 95% CI. "n" refers to the number of patients for whom data were available.
Bold *P* values indicate a statistically significant value.
DVT, deep vein thrombosis; PE, pulmonary embolism.

Overall, 89.8% of routine and 85.2% of high-risk patients were available for clinical follow-up at 6 weeks postoperatively. The overall rate of VTE was low in both cohorts, with a total of only 17 (0.6%; 95% CI 0.3%-0.9%) VTE events documented within 6 weeks and 22 (0.8%; 95% CI 0.4%-1.0%) VTE events within 6 months postoperatively, all in patients undergoing a primary joint arthroplasty procedure. The cumulative rate of VTE events was 0.7% (95% CI 0.3%-1.0%) in the routine risk cohort vs 0.5% (95% CI 0.01%-1.0%) in the high-risk cohort within 6 weeks postoperatively ($P = .67$), and 0.6% (95% CI 0.3%-1.0%) in the routine risk and 1.1% (95% CI 0.4%-1.8%) in the high-risk cohort within 6 months postoperatively ($P = .23$; Table 11).

The rate of major bleeding complications within 6 weeks postoperatively was significantly lower among patients in the routine risk cohort (0.4%; 95% CI 0.1%-0.6%) vs the high-risk cohort (2.0%; 95% CI 1.0%-3.0%; $P < .001$). In addition, the incidence of wound complications at 2 weeks postoperatively was significantly lower in

Table 10
Preoperative Demographics of the Routine and High-Risk Patient Cohorts for the Overall Study Period (April 2010-October 2014).

Patient Variable	Routine (n = 2222)	High (n = 921)	*P* Value
Operative side			.86
Right	1189 (53.5)	496 (53.9)	
Left	1033 (46.5)	425 (46.1)	
Revision status			**<.001**
Primary	1991 (89.6)	765 (83.1)	
Revision	231 (10.4)	156 (16.9)	
Age at surgery (y)	57.7 ± 11.3	65.8 ± 11.1	**<.001**
Gender			**<.001**
Female	1185 (53.3)	591 (64.2)	
Male	1037 (46.7)	330 (35.8)	

Data are presented as absolute number with percentage in parentheses or mean ± standard deviation.
Bold *P* values indicate a statistically significant value.

Table 11
Rates of VTE Events and Bleeding Complications in the Routine and High-Risk Cohorts During the Overall Study Period.

Outcome Measure	Routine (n = 2222)	High (n = 921)	*P* Value
DVT or PE within 6 wk	n = 1996	n = 785	.67
No	1983 (99.3%; 99.0-99.7))	781 (99.5%; 98.9-99.8)	
Yes	13 (0.7%; 0.3-1.0)	4 (0.5%; 0.01-1.0)	
DVT or PE within 6 mo	n = 2057	n = 848	.23
No	2044 (99.4%; 99.0-99.7)	839 (98.9%; 98.3-99.6)	
Yes	13 (0.6%; 0.3-1.0)	9 (1.1%; 0.4-1.8)	
DVT	8 (0.4%; 0.1-0.7)	7 (0.8%; 0.2-1.4)	
PE	5 (0.2%; 0.03-0.5)	2 (0.2%; 0.0-0.6)	
Major bleeding complications within 6 wk	n = 1991	n = 787	**<.001**
No	1984 (99.6%; 99.4-99.9)	771 (98.0%;97.0-98.9)	
Yes	7 (0.4%; 0.1-0.6)	16 (2.0%; 1.0-3.0)	
Wound problems within 2 wk	n = 2088	n = 835	**<.001**
No	2083 (99.8%; 99.6-99.9)	824 (98.7%; 97.9-99.5)	
Yes	5 (0.2%; 0.03-0.4)	11 (1.3%; 0.5-2.1)	
Days of drainage	n = 2084	n = 831	**<.001**
0-3	1805 (86.6%; 85.2-88.1)	666 (80.1%; 77.4-82.9)	
4-7	195 (9.4%; 8.1-10.6)	99 (11.9%; 9.7-14.1)	
>7	84 (4.0%; 3.2-4.9)	66 (7.9%; 6.1-9.8)	

Data are presented as the absolute number and the percentage of respondents in parentheses, along with the 95% CI. "n" refers to the number of patients for whom data were available for each outcome measure.
Bold *P* values indicate a statistically significant value.
DVT, deep vein thrombosis; PE, pulmonary embolism.

Table 12
Reasons for Readmission in the Routine and High-Risk Cohorts During the Overall Study Period.

Readmissions	Routine (n = 2057)	High (n = 849)	*P* Value
Number of patients readmitted	212 (10.3%; 9.0-11.6)	139 (16.4%; 13.9-18.9)	**<.001**
Reasons for readmission			
Total number of readmissions	232 (11.3%; 9.9-12.7)	146 (17.2%;14.7-19.7)	
Admission for pulmonary embolism	5 (2.2%; 0.3-4.0)	2 (1.4%; 0.0-3.3)	.6
Complication related to anticoagulation therapy	4 (1.7%; 0.05-3.4)	8 (5.5%; 1.8-9.2)	.1
Death due to VTE event	0 (0%; 0.0-0.0)	0 (0%; 0.0-0.0)	N/A
Death—all causes	1 (0.4%; 0.0-1.3)	1 (0.7%; 0.0-2.0)	>.9

Data are presented as the absolute number and the percentage of respondents in parentheses, along with the 95% CI. "n" refers to the number of patients for whom data were available. Percentages for reason of readmission based on total number of readmissions from that, respective cohort.
Bold *P* values indicate a statistically significant value.
N/A, not applicable; VTE, venous thromboembolism.

the routine risk cohort vs the high-risk cohort (0.2%; 95% CI 0.03%-0.4% vs 1.3%; 95% CI 0.5%-2.1%; $P < .001$) as was incisional drainage lasting greater than 7 days (4.0%; 95% CI 3.2%-4.9% vs 7.9%; 6.1%-9.8%; $P < .001$). In addition, incisional drainage lasting greater than 3 days was significantly lower in the routine risk cohort (13.4%; 95% CI 11.9%-14.8% vs 19.8%; 95% CI 17.1%-22.6%; $P < .001$).

Two thousand fifty-seven patients in the routine risk cohort (92.6% follow-up) and 849 patients in the high-risk cohort (92.2% follow-up) were analyzed regarding their 6-month postoperative readmission history. During the first 6 months postoperatively, 212 patients in the routine risk cohort (10.3%; 95% CI 9.0%-11.6%) and 139 patients in the high-risk cohort (16.4%; 95% CI 13.9%-19.8%; $P < .001$) were readmitted to the hospital, with several patients having multiple readmissions. A total of 227 readmissions occurred in the routine cohort vs 144 in the high-risk cohort (Table 12). Of note, no participants with a confirmed DVT were readmitted to the hospital for treatment, but all 7 participants with a confirmed PE were readmitted. Four readmissions in the routine cohort (1.7% of all readmissions in the routine cohort; 95% CI 0.05%-3.4%) were related to anticoagulation therapy vs 8 readmissions in the high-risk cohort (5.5%; 95% CI 1.8%-9.2%; $P = .04$). There were 2 participant deaths during the time course of the study. One patient in the routine risk cohort died of a myocardial infarction. One patient in the high-risk cohort was suspected to die of acute sepsis secondary to a periprosthetic infection, but an autopsy was not performed at the request of the family.

Patients in the routine risk cohort had superior patient satisfaction scores at 2 weeks (1.60 ± 0.64 vs 1.88 ± 0.70, $P < .001$) and at 6 weeks postoperatively (1.56 ± 0.61 vs 1.66 ± 0.63, $P < .001$) vs the high-risk cohort.

Discussion

Perioperative complications after total joint arthroplasty including wound problems, VTE, and readmissions have been increasingly scrutinized with evolving health care legislation and must be avoided for patient safety. Thus, selection of an effective VTE thromboprophylaxis regimen remains one of the most important variables in postoperative care. More potent chemical prophylactics are known to be effective in the prevention of VTE, yet they have also been shown to increase the risk of perioperative morbidity [6,8,16,30]. MCDs and aspirin are attractive forms of VTE prophylaxis as they do not require laboratory monitoring, minimally impact postoperative hemostasis, and potentially decrease the likelihood of complications associated with more potent chemical prophylactics such as warfarin and low-molecular-weight heparin [6]. The purpose of this study was to prospectively evaluate a risk stratification protocol in which patients deemed "routine" risk receive MCDs in conjunction with aspirin, whereas "high"-risk patients receive warfarin for thromboprophylaxis after total joint arthroplasty. Our findings demonstrate that after risk stratification, the use of MCDs with aspirin is noninferior to the use of warfarin in the prevention of VTE, while also enabling the avoidance of more aggressive anticoagulation in approximately 70% of patients.

This study has several limitations that must be recognized before interpretation of our results. First, the present study is not a randomized, blinded controlled trial, but this is by design. The purpose of this study was not to prove superiority of either regimen for VTE prophylaxis, but rather to assess the effectiveness of our institution's VTE prophylaxis protocol (including risk stratification) as a whole. As the AAOS recommends more aggressive anticoagulation in patients with a prior VTE, it would potentially be unethical to randomize these patients. Furthermore, surgeons were not blinded to the VTE prophylaxis regimen patients received, and thus, there is the potential for bias when evaluating these patients postoperatively. However, performing this study in a blinded fashion would be difficult, as surgeon discretion was necessary in determining how to manage these patients perioperatively. Second, this study is unable to elucidate whether the use of MCDs or aspirin is more significant in the routine risk cohort. In a prior multicenter, prospective, randomized controlled trial comparing the effectiveness of MCDs vs the use of low-molecular-weight heparin, patients in the MCD cohort were eligible to receive aspirin postoperatively at the discretion of the treating surgeon [18]. Thus, at our institution, we elect to administer aspirin concomitantly with the use of the MCDs. Again, as VTE prevention is clearly multifactorial, the

purpose of this investigation was to assess our protocol as a whole. In addition, we cannot comment on which preoperative factors truly increase a patient's risk of VTE after total joint arthroplasty given the low incidence of VTE seen in this study. Fourth, comorbidities (including a Charlson Comorbidity Index) were not collected and directly compared between the routine and high-risk cohorts, thus limiting the ability to directly compare these groups based on risk factors for VTE and bleeding postoperatively. However, we again stress that the purpose of this study was not to directly compare our 2 cohorts, but rather to assess our overall VTE prophylaxis regimen as a whole. Fifth, patients could be excluded at the surgeon's discretion if they were deemed to have poor nutritional status and potentially be at increased risk of wound complications. Thus, as 6 surgeons enrolled patients in this study, there is the potential for selection bias. Finally, during this prospective study, inclusion criteria for the high-risk cohort was modified as prior criteria for age, multiple medical comorbidities, and body mass index were removed. However, the incidence of VTE events before and after our change in risk stratification criteria was virtually identical. No difference was present in the incidence of VTE events within 6 weeks when comparing the routine cohorts from each study interval. Furthermore, our refined criteria fell further in line with concomitant reports assessing the effectiveness of MCDs published during implementation of our institution's VTE prophylaxis protocol [18,24,25]. Thus, we feel these results demonstrate use of our modified inclusion criteria is safe when determining patients eligible for the use of less aggressive anticoagulation.

Warfarin is currently the most commonly prescribed oral anticoagulant medication for both orthopedic and nonorthopedic indications [31,32] and is efficacious in preventing VTE [13,33,34]. However, its limitations include the need for monitoring of a patient's INR with frequent blood draws and difficulty in maintaining a therapeutic window because of its sensitive pharmacokinetics [35,36]. After THA or TKA, patients on warfarin were found to be within their target INR range for only 45.9%-54.4% of their therapeutic course [37]. Aspirin for chemical thromboprophylaxis requires no monitoring and has received a grade IB recommendation for its use according to the most recent ACCP guidelines [10]. Furthermore, a recent multivariate analysis accounting for direct costs of administration and subsequent complications after the use of warfarin or aspirin for VTE prophylaxis revealed aspirin to be an independent predictor of decreased total episode of care charges [38].

Reports have shown the use of MCDs after unilateral joint arthroplasty to have VTE rates similar to that of chemical thromboprophylaxis [17,18,39]. Some concerns with the use of MCDs include patient compliance and the safety of the hoses connecting the calf sleeves to the actual pump. However, based on compliance data in the first 1834 patients stratified to the routine cohort, approximately 84.5% of patients wore the MCDs for greater than 18 hours daily. In addition, patients in the routine risk cohort had superior satisfaction with their thromboprophylaxis protocol when surveyed at 2 and 6 weeks postoperatively vs patients in the high-risk cohort. As patient satisfaction continues to be a key determinant of quality of care and an important component of pay-for-performance metrics, use of a thromboprophylaxis protocol that is easy to administer with good compliance is essential.

In conclusion, this study demonstrates that use of our risk stratification protocol in which routine risk patients receive MCDs in conjunction with aspirin and high-risk patients receive warfarin allowed the avoidance of more aggressive anticoagulation in 70% of patients while achieving a low overall incidence of symptomatic VTE. In the second phase of the study, only 16.9% of patients were allocated to the high-risk cohort with little impact on the incidence of VTE events using our modified inclusion criteria. Thus, we feel that inclusion criteria for the high-risk cohort can be less stringent and remains effective. However, given that this is not a prospective, randomized controlled trial, we acknowledge that we cannot conclude that warfarin itself increases the risk of wound complications after joint arthroplasty. Despite this limitation, we believe that use of a risk stratification protocol that allows avoidance of more aggressive anticoagulation, less frequent patient monitoring, and potentially decreased wound and bleeding complications is of value. Our risk stratification protocol and VTE regimen serves as a potential starting point for future studies that elucidate specific determinants of which patients should receive more potent chemical thromboprophylaxis at the risk of potentially increased wound complications and readmission.

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