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Anticoagulation in Revision Total Joint Arthroplasty: A Retrospective Review of 1917 Cases

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abstract

Although several studies now support the use of aspirin for venous thromboembolism (VTE) prophylaxis in primary total hip arthroplasty (THA) and total knee arthroplasty (TKA), the optimal chemoprophylactic agent in revision THA and TKA is not clear. The purpose of this study was to determine if the type of chemoprophylaxis has an effect on the VTE rate in patients undergoing revision total joint arthroplasty (TJA). The second aim was to compare differences in rates of wound drainage in primary and revision TJA stratified by the postoperative chemoprophylaxis used. The authors retrospectively reviewed 1917 consecutive patients undergoing primary and revision TJA. Individual records were reviewed for patient demographics, medical comorbidities, type of chemoprophylaxis, VTE risk factors, intraoperative data, and postoperative complications. Outcomes, including VTE rate and wound complications, were compared between types of anticoagulant therapy used postoperatively. Of the 1917 patients, there were 742 (38.7%) primary TKAs, 326 (17%) revision TKAs, 608 (31.7%) primary THAs, and 241 (12.6%) revision THAs. The most common prophylactic agent used was rivaroxaban (40.6%), followed by warfarin (28.5%) and aspirin (27.6%). Type of chemoprophylaxis was not associated with postoperative VTE or wound drainage ($P>.05$). Although revision surgery was an independent risk factor for wound drainage (odds ratio, 3.201; 95% confidence interval, 1.594-6.426; $P=.001$), it was not a risk factor for VTE (odds ratio, 1.847; 95% confidence interval, 0.423-8.053; $P=.414$). Revision arthroplasty alone was not associated with an increased rate of VTE. Aspirin is as effective as other chemoprophylactic agents without the increased risk of bleeding in low-risk patients. [*Orthopedics*. 2019; 42(6):323-329.]

Total joint arthroplasty (TJA) carries an inherent risk for various post-surgical complications. One of the more serious complications includes thromboembolic episodes such as deep venous thrombosis (DVT) and pulmonary embolism (PE). Evidence has shown that the risk of developing such adverse events lies between 40% and 85% for patients who do not receive any postoperative thromboembolic prophylaxis.[1-3] Rates of venous thromboembolic (VTE) events following primary total hip arthroplasty (THA) and total knee arthroplasty (TKA) are reported to range from 0.41% to 4.8% for patients receiving prophylactic anticoagulation.[4-7] However, anticoagulants carry the innate risk of yielding postoperative bleeding and wound complications. Physicians must balance these risks vs clotting concerns when selecting a particular prophylactic agent. Such a balance is paramount for revision TJA patients, who are at greater risk for complications independent of the chosen anticoagulant.

Recent data suggest that aspirin is safe and effective when used as a chemopro-

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phylactic agent against VTE in primary TJA.[7] Additionally, many surgeons have moved away from low molecular weight heparin or warfarin because of their side effects, costs, and difficulty with monitoring/maintaining blood levels.[4] To the current authors' knowledge, aspirin has yet to be studied in large revision TJA patient populations. Although not clear in the literature, it is reasonable to suspect that revision TJA patients are at higher risk for VTE due to a relatively inactive preoperative state, longer operative times, greater dissection, and/or restricted postoperative activity.[8] While it is highly recommended that all TJA patients receive some form of chemoprophylaxis, the optimal VTE prophylactic agent in revision procedures is a topic of debate.

The purpose of this study was to determine if revision THA and TKA patients have higher VTE rates compared with primary TJA patients, when controlling for demographics, comorbidities, and type of chemoprophylaxis. The second aim was to compare differences in rates of wound drainage in both primary and revision TJA patients stratified by the postoperative chemoprophylaxis used. The authors hypothesized that revision THA and TKA would carry a greater risk of VTE events as compared with primary procedures regardless of postoperative prophylactic choice.

Materials and Methods

The authors retrospectively reviewed a consecutive series of patients who underwent revision TKA or THA between August 2008 and November 2016 at a single institution. This cohort was identified by reviewing the surgical database of the 2 surgeons. This study was approved by and conducted according to the institutional review board of the authors' institution. Surgical indications and procedure, demographic variables, medical comorbidities, operative time, and length of hospital stay for each patient were recorded from the notes available in the hospital and office charts.

The type of postoperative antithromboembolic therapy was recorded for each patient. Chemoprophylaxis agents used included 325 mg of aspirin twice daily, warfarin with dosing titrated to a goal international normalized ratio of 1.8 to 2.2, enoxaparin, and rivaroxaban. These were chosen based on the surgeon's assessment and the preoperative medical assessment as to the patient's risk of VTE following surgery. An additional factor that influenced choice of chemoprophylactic included preoperative use of anticoagulation, as patients receiving preoperative anticoagulation typically resume their regimen. Furthermore, in the earlier time frame of the study, coumadin was used, which was then switched to rivaroxaban once it became available. In addition, all patients did receive a sequential compression device postoperatively. As a control group, the authors also collected the same data for all primary THAs and TKAs from 2010 to 2014 using the same 2 surgeons' patient population.

Patients were included in the study if they met the following criteria: (1) a primary or revision THA or TKA; (2) follow-up of 3 months or more; and (3) aspirin, warfarin, enoxaparin, or rivaroxaban prescribed postoperatively. Patients were excluded from the study if they did not have adequate 3-month follow-up, were not administered DVT prophylaxis, or were administered a chemoprophylactic agent other than those listed above.

By reviewing the clinic notes and hospital records, the following complications were recorded: DVT/PE, wound drainage, readmission, reoperation, and other medical complications, which included cardiac myocardial infarction, respiratory failure, and in-hospital death. Wound drainage after TJA was defined by time (48 hours to beyond postoperative day 4), type of secretion (hematogenous or clear), and site content. Deep venous thrombosis and PE were identified on duplex ultrasound or spiral computed tomography scan at the hospital and considered to be associated with the procedure if they occurred within 90 days of surgery. Duplex ultrasound or spiral computed tomography scan was obtained only if a VTE or PE was suspected and was not routinely obtained for every patient.

Statistical Analysis

Categorical variables were analyzed using a chi-square test. Continuous variables such as age and body mass index were analyzed using unpaired, 2-tailed, Student's *t* tests (**Table 1**). Statistical significance was set at $P<.05$. Multivariate logistic regression was then performed to identify independent risk factors for any VTE event following TJA and risk factors for wound drainage (**Tables 2-3**). A forward, stepwise, multiple regressions analysis was also performed to identify high-risk factors for VTE and wound drainage (**Tables 4-5**). The authors started with the most significant variable and added risk factors in order of ascending *P* values. Any alpha greater than 0.10 was removed from the analysis in a stepwise fashion. Statistical analysis was performed using Excel (Microsoft, Redmond, Washington) and SPSS version 24.0 software (IBM, Armonk, New York).

Results

From August 2008 through November 2016, 1944 consecutive patients were identified from the authors' institutional database. Of these patients, 10 were excluded for lack of follow-up and 17 were excluded for receiving a different chemoprophylactic agent. There were 567 revision patients (29.6%). A total of 742 (38.7%) patients underwent a primary TKA, 326 (17%) patients underwent a revision TKA, 608 (31.7%) patients underwent a primary THA, and 241 (12.6%) patients underwent a revision THA.

Of the 778 patients who received rivaroxaban postoperatively, 236 (30.3%) patients underwent a primary TKA, 185 (23.8%) patients underwent a revision TKA, 207 (26.6%) patients underwent a

Table 1

Demographic Variables for Each Postoperative Anticoagulation Medication and Complete Descriptive Patient Statistics

Variable	Aspirin (N=529; 27.6%)	Warfarin (N=546; 28.5%)	Enoxaparin (N=63; 3.3%)	Rivaroxaban (N=778; 40.6%)	*P*
Pulmonary embolism, No. (%)	3 (0.6)	3 (0.5)	1 (1.6)	3 (0.4)	.640
Deep venous thrombosis, No. (%)	0 (0)	2 (0.4)	0 (0)	2 (0.3)	.577
Any venous thromboembolic event, No. (%)	3 (0.6)	5 (0.9)	1 (1.6)	5 (0.6)	.759
Postoperative wound drainage, No. (%)	17 (3)	15 (3)	4 (6)	35 (5)	.224
Revision arthroplasty, No. (%)	54 (10)	121 (22)	57 (91)	335 (43)	<.001
Protected or non-weight bearing, No. (%)	18 (3)	42 (8)	26 (41)	166 (21)	<.001
Body mass index, mean (SD), kg/m^2	32.0 (7.3)	33.3 (8.1)	35.7 (11.2)	33.8 (9.1)	<.001
Body mass index >35 kg/m^2, No. (%)	156 (30)	196 (36)	26 (41)	291 (37)	.016
Smoking history, No. (%)	200 (38)	212 (39)	33 (70)	338 (43)	<.001
History of deep venous thrombosis or pulmonary embolism, No. (%)	20 (4)	53 (10)	13 (21)	80 (10)	<.001
Hypertension, No. (%)	298 (56)	361 (66)	47 (75)	521 (67)	<.001
History of cancer, No. (%)	72 (14)	81 (15)	9 (14)	131 (17)	.436
Liver disease, No. (%)	15 (3)	56 (10)	8 (13)	77 (10)	<.001
Kidney disease, No. (%)	141 (27)	117 (21)	11 (18)	152 (20)	.016
Diabetes, No. (%)	77 (15)	128 (23)	17 (27)	170 (22)	.001
History of stroke, No. (%)	23 (4)	25 (5)	7 (11)	26 (3)	.028
Cardiac disease, No. (%)	133 (25)	118 (22)	14 (22)	108 (14)	<.001
Psychological disorder, No. (%)	58 (11)	92 (17)	17 (27)	146 (19)	<.001
American Society of Anesthesiologists classification, No. (%)					
I	17 (3)	10 (2)	0 (0)	5 (1)	<.001
II	366 (69)	285 (52)	14 (22)	326 (41)	
III	141 (26)	243 (44)	45 (72)	440 (56)	
IV	4 (1)	4 (1)	4 (6)	6 (1)	
Not reported	1 (1)	4 (1)	0 (0)	1 (1)	

primary THA, and 150 (19.3%) patients underwent a revision THA.

The second most commonly prescribed chemoprophylaxis was warfarin, representing 546 patients. A total of 268 (49.1%) patients taking warfarin underwent a primary TKA, 87 (15.9%) patients underwent a revision TKA, 157 (28.8%) patients underwent a primary THA, and 34 (6.2%) patients underwent a revision THA.

Aspirin was the third most used prophylactic agent, representing 529 patients. Of the patients taking aspirin, 231 (43.7%) patients underwent a primary TKA, 22 (4.2%) patients underwent a revision TKA, 244 (46.1%) patients underwent a primary THA, and 32 (6.0%) patients underwent a revision THA.

The least prescribed chemoprophylaxis was enoxaparin, representing only 63 patients. Of the patients taking enoxaparin, 6 (9.5%) patients underwent a primary TKA, 32 (50.8%) patients underwent a revision TKA, 0 (0%) patients underwent a primary THA, and 25 (39.7%) patients underwent a revision THA.

Demographic variables for each postoperative anticoagulation medication and complete descriptive statistics are presented in **Table 1**.

Controlling for all other factors, a multivariate analysis for any VTE event showed that independent risk factors for VTE were black ethnicity and history of prior VTE or DVT (**Table 2**). Revision surgery was not an independent risk factor for any VTE event (**Table 2**). A forward, stepwise, multivariate analysis for risk factors for any VTE event following TJA identified his-

Table 2

Multivariate Logistic Regression for Risk Factors for Any Venous Thromboembolism Event

Risk Factor	Odds Ratio	95% Confidence Interval	*P*
Female sex	6.569	0.815-52.923	.077
Black ethnicity	5.097	1.515-17.150	.009
Total hip arthroplasty	0.690	0.189-2.523	.575
Revision surgery	1.847	0.423-8.053	.414
Age >65 y	2.082	0.606-7.148	.244
Body mass index >35 kg/m^2	1.491	0.450-4.944	.513
American Society of Anesthesiologists classification >IV	1.000	0.000-0.000	.998
Rivaroxaban	0.374	0.072-1.935	.241
Warfarin	0.606	0.118-3.103	.548
Low molecular weight heparin (enoxaparin)	0.508	0.039-6.633	.606
Not weight bearing as tolerated	1.371	0.254-7.402	.714
History of venous thromboembolism or deep venous thrombosis	4.898	1.378-17.411	.014
Medical history of hypertension	0.743	0.197-2.805	.661
Medical history of cancer	0.000	0.000-0.000	.994
Medical history of liver disease	0.479	0.055-4.160	.505
Medical history of kidney disease	1.799	0.0494-6.556	.374
Medical history of diabetes	0.824	0.194-3.500	.794
Medical history of stroke/transient ischemic attack	1.305	0.149-11.457	.810
Medical history of myocardial infarction	1.034	0.250-4.278	.963
Medical history of depression/anxiety	2.028	0.540-7.607	.295
Current or past smoking	1.563	0.501-4.881	.442

tory of VTE or DVT, black ethnicity, and female sex as approaching statistical significance (**Table 4**).

Multivariate logistic regression for risk factors for postoperative wound drainage identified revision surgery and obesity (**Table 3**). A forward, stepwise, multivariate analysis for risk factors for wound drainage following TJA identified revision surgery, obesity, and medical history of kidney disease (**Table 5**).

Discussion

Minimization of thromboembolic events includes chemoprophylaxis through the use of pharmacological agents in addition to mechanical prophylaxis. Early ambulation, improved pain management, shorter hospital stays, and intermittent pneumatic compression devices have also been shown to decrease the risk of post-surgical DVT-related complications.[6-11] A consensus among the guidelines for DVT prevention states that a history of previous VTE is a predictable factor for having an increased risk of another VTE event.[12] The current study showed that, when controlling for all other variables, a history of prior VTE and black ethnicity were independent risk factors for the development of VTE following TJA.

When compared with primary TJA, revision TJA carries a greater clinical concern because weight bearing is more frequently restricted, pre- and postoperatively mobilization is often poor, and there is routinely a greater surgical exposure, all of which can potentially increase the rate of VTE.[8] Therefore, the current authors hypothesized that revision surgeries would evidently be more predisposed to a greater risk of VTE events. The current study supports previous literature indicating that revision surgeries alone are not a risk factor for increased postoperative VTE rates.[8,13] More specifically, the current authors found this to be evident regardless of the type of chemoprophylaxis prescribed postoperatively, thereby refuting their hypothesis. Although revision arthroplasty does carry an inherently greater risk for any adverse event,[13] the current authors found that revision arthroplasty itself did not have a higher rate of VTE events compared with primary arthroplasty with the use of any of the 4 chemoprophylactic agents assessed in this cohort.

More aggressive prophylaxis such as low molecular weight heparin and oral factor Xa inhibitors was prescribed for patients undergoing revision arthroplasty. In the current cohort, 57 (91%) of the 63 patients taking enoxaparin had a revision procedure, compared with 54 (10%) of the 529 patients taking 325 mg of aspirin. As no evidence was found of any difference in VTE rates between patients undergoing a revision procedure, the question about the necessity of more aggressive prophylaxis for revision patients becomes evident. To thoroughly assess this question, larger studies focused on the use of aspirin in revision arthroplasty must be performed. However, the current authors are able to suggest that, if minimal risk factors are present, more aggressive prophylaxis as compared with the other anticoagulants does not prevent thromboembolic events in revision patients. This is evident through lower rates of VTE among the less aggressive agents (ie, 0.6% and 0.9% in the 325 mg of aspirin and warfarin groups, respectively, vs 1.6% in the enoxaparin group; *P*=.759).

In addition to VTE, the current authors were able to consistently gather data on postoperative wound drainage. Postoperative wound drainage was defined as continuous drainage from the surgical site for greater than 48 hours.[14] Of the 4 chemoprophylactic agents in the current study, no particular prophylaxis was associated with an increased incidence of postoperative wound drainage. The rates of wound drainage among the cohort were 3%, 3%, 6%, and 5% for 325 mg of aspirin, warfarin, enoxaparin, and rivaroxaban, respectively (*P*=.224). The more aggressive prophylactic agents did have a higher incidence of wound drainage comparatively, which is supported by the likelihood of increased problems with revision arthroplasty. Although these patients are considered high risk, similar incidences of postoperative wound drainage were reported among the less aggressive agents.

Independent risk factors for wound drainage were revision surgery, obesity, and kidney disease. Understanding the role obesity plays in adverse events becomes increasingly important because obesity is the only potentially modifiable risk factor of the 3 aforementioned independent risk factors in the current study.[15,16] Current literature on the topic suggests that reoperation for wound complications and the risk of superficial wound problems are associated with increasing body mass index.[17,18] Prolonged wound drainage in primary THA has also been correlated with morbid obesity.[19] In addition to supporting current literature on the topic, the current authors have presented a link between obesity and an increased risk for wound drainage in primary as well as revision TJA. As studies on the topic of anticoagulation therapy and postoperative wound complications are lacking,[14] the current study provided insight on an independent risk factor that increased the risk for wound drainage among a cohort of patients taking 4 different types of antithromboembolic prophylaxis.

Table 3

Multivariate Logistic Regression for Risk Factors for Wound Drainage

Risk Factor	Odds Ratio	95% Confidence Interval	*P*
Female sex	1.239	0.728-2.107	.430
Black ethnicity	0.922	0.503-1.688	.792
Total hip arthroplasty	0.747	0.424-1.318	.314
Revision surgery	3.201	1.594-6.426	.001
Age >65 y	0.777	0.456-1.325	.354
Body mass index >35 kg/m^2	1.996	1.185-3.363	.009
American Society of Anesthesiologists classification >IV	1.055	0.128-8.678	.961
Rivaroxaban	0.707	0.359-1.393	.316
Warfarin	0.518	0.241-1.114	.092
Low molecular weight heparin (enoxaparin)	0.533	0.155-1.827	.317
Not weight bearing as tolerated	1.337	0.698-2.562	.381
History of venous thromboembolism or deep venous thrombosis	1.300	0.661-2.558	.448
Medical history of hypertension	1.434	0.767-2.683	.259
Medical history of cancer	0.945	0.475-1.878	.872
Medical history of liver disease	1.660	0.836-3.296	.147
Medical history of kidney disease	1.477	0.808-2.698	.205
Medical history of diabetes	1.489	0.857-2.589	.158
Medical history of stroke/transient ischemic attack	0.657	0.189-2.282	.508
Medical history of myocardial infarction	1.216	0.684-2.163	.505
Medical history of depression/anxiety	1.271	0.705-2.292	.425
Current or past smoking	1.568	0.947-2.595	.080

Other indications determined to be independent risk factors for wound drainage were revision surgery and kidney disease. A review of current literature discussed the increased risk of periprosthetic joint infections developing in individuals with chronic kidney disease.[20] The current authors have presented data highlighting kidney disease as an independent risk factor for the development of postoperative wound drainage. Revision surgery was also found to be a risk factor for increased wound drainage in patients undergoing TJA among all 4 of the prophylactic agents. As mentioned, the revision patients in the current study were more likely to be receiving a more aggressive prophylactic agent. More in-depth studies are necessary to determine whether more aggressive prophylaxis results in increased wound drainage. If wound drainage is found to persist for longer than 7 days, a reoperative procedure is warranted, which underlines the importance of identifying particular risk factors that increase the likelihood of this complication.[21]

The current study had some notable limitations. The authors did not include 81 mg of aspirin because there were too few patients taking this dose during the study period. Multiple surgeons contributed to the data used in this study, which may

Table 4

Forward, Stepwise, Multivariate Analysis for Risk Factors for Any Venous Thromboembolism Event Following Total Joint Arthroplasty

Risk Factor	Odds Ratio	95% Confidence Interval	*P*
History of venous thromboembolism or deep venous thrombosis	5.987	1.983-18.077	.002
Black ethnicity	4.747	1.629-13.831	.004
Female sex	7.233	0.934-56.026	.058

Table 5

Forward, Stepwise, Multivariate Analysis for Risk Factors for Wound Drainage Following Total Joint Arthroplasty

Risk Factor	Odds Ratio	95% Confidence Interval	*P*
Revision surgery	4.367	2.666-7.152	.000
Body mass index >35 kg/m^2	2.419	1.488-3.935	.000
Medical history of kidney disease	1.873	1.067-3.288	.029

have caused discrepancies in the consistency of outcomes reported. Retrospective studies also have some inherent limitations, one of which is the reliance on data already present in the chart. Although the authors did collect data on the type of revision each patient had undergone (ie, full revision vs poly exchange), they did not use this variable in their analysis. In general, regardless of the type of revision, the patient will be receiving some type of prophylaxis. Therefore, the authors did not limit their analysis to which type of revision the patient was undergoing. Finally, because the prevalence of VTE/PE was relatively low in this population, the study was likely underpowered regarding the cohort number and the low incidence of said adverse events. This study's sample size was similar to that of comparative studies in the literature. In addition, the sample size likely represents a single surgeon's revision population over the course of an entire surgical career, making it more applicable. A massive, nationwide database review may help alleviate this issue. However, such database reviews have internal limitations, which the authors were able to account for with diligent chart review in a large, single-center cohort.

Conclusion

This study suggests that, in low-risk patients, there is no difference in VTE rate or wound drainage for revision TJA compared with primary TJA among any of the chemoprophylaxis agents used. Controlling for other factors, independent risk factors for VTE are black ethnicity and history of prior VTE. Independent risk factors for wound drainage include revision surgery, obesity, and kidney disease. Revision arthroplasty patients should be carefully screened for particular risk factors when choosing the optimal postoperative VTE prophylaxis. If minimal risk factors are present, more aggressive prophylaxis may not be warranted in this patient population because the authors found no difference between VTE and wound drainage rates as compared with primary procedures among any of the prophylactic agents used in this study.

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