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Aspirin is an Effective Prophylaxis for Venous Thromboembolism After Revision Hip and Knee Arthroplasty

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ABSTRACT

Background: Venous thromboembolism (VTE) following revision total joint arthroplasty (TJA) poses significant risks despite prophylactic measures. The optimal VTE prophylaxis agent for revision TJA remains unclear. This study aimed to compare aspirin against various anticoagulant agents regarding efficacy and safety in preventing symptomatic VTE events after revision TJA.

Methods: A retrospective analysis included 4,575 patients undergoing revision TJA between 2008 and 2020. Of these, 2,091 received aspirin, while 2,484 received other anticoagulants. Demographic, procedural, and outcome data were collected. Logistic regression models were used to identify predictors of symptomatic VTE.

Results: The aspirin group showed a significantly lower incidence of symptomatic VTE compared to the other anticoagulant group (0.53 versus 2.54%, $P < .001$). Logistic regression confirmed a higher risk of VTE with other anticoagulants (odds ratio: 0.2 to 0.26, $P < .001$), while blood transfusion (odds ratio: 2.72, $P = .001$) were identified as risk factors.

Conclusions: This study demonstrated that aspirin is a viable and potentially safer option than other anticoagulants, exhibiting comparable efficacy in preventing VTE events in revision TJA. Balancing effectiveness and safety is crucial, considering patient-specific risk factors and bleeding tendencies. This large cohort study demonstrated that aspirin was associated with a more effective and safer VTE prophylaxis agent, compared to other anticoagulants, in patients undergoing revision TJA.

Venous thromboembolism (VTE), encompassing both deep vein thrombosis (DVT) and pulmonary embolism (PE), represents a potentially life-threatening complication that can occur in the postoperative period [1,2]. The incidence of VTE following revision total joint arthroplasty is not well-documented, with estimates varying based on patient-specific factors and surgical characteristics. These events can lead to major morbidity, increased health care costs, and, in some cases, fatal outcomes [3]. Despite the use of numerous prophylactic agents, it is a known fact that it is not possible to completely prevent VTE events after TJA [4].

Although there is sufficient evidence for VTE prophylaxis after primary TJA, the current literature on VTE prophylaxis after revision TJA does not provide sufficient evidence to establish a standardized protocol for the prevention of thromboembolic events [5]. Thus, the optimum agent for VTE prophylaxis after revision TJA is not clear.

The aim of this study was to compare the efficacy and safety of aspirin and other VTE prophylactic agents, namely warfarin, LMHW (low molecular weight heparin), factor Xa, UFH (unfractioned heparin), direct thrombin inhibitors, fondaparinux, phosphodiesterase inhibitors, and their combination related to symptomatic VTE events after revision TJA.

Materials and Methods

We reviewed our prospectively collected institutional arthroplasty database to identify patients who underwent revision hip and knee arthroplasty between 2008 and 2020. Approval by the institutional review board was obtained prior to this study. The study included 4,575 consecutive patients who underwent revision

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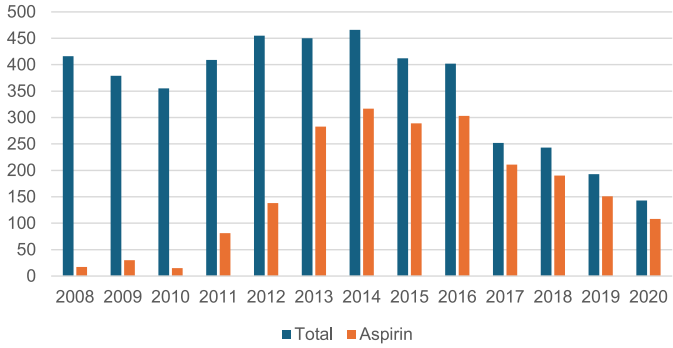

Fig. 1. Distribution of VTE agents by years. VTE, venous thromboembolism.

TJA. Of these, 2,091 patients received aspirin, and 2,484 patients received other anticoagulant agents for VTE prophylaxis (Figure 1).

Demographic data, body mass index (BMI), Charlson Comorbidity Index (CCI), comorbidities, operation time, administration of tranexamic acid, and blood transfusion were collected. The incidence of symptomatic VTEs that occurred within 90 days after the surgery was investigated using our institutional database and electronic medical records. Aspirin and other anticoagulants were compared regarding VTE.

In this study, a total of 2,091 patients (45.7%) received aspirin and 2,484 patients received other anticoagulant agents as part of the VTE prophylactic regimen. Demographic and procedural details are presented in Table 1. Other anticoagulant agents include warfarin (38.3%), low molecular weight heparin (2.69%), factor Xa (2%), unfractioned heparin (0.21%), direct thrombin inhibitors

Table 1
Demographic and Procedural Information of all Patients Undergoing Revision Total Joint Arthroplasty.

	Total Data	Other	Aspirin	*P* Value
	N = 4,575	N = 2,484	N = 2,091	
Sex: (%)				<.001
Women	2,359 (51.6)	1,342 (54.0)	1,017 (48.6)	
Men	2,216 (48.4)	1,142 (46.0)	1,074 (51.4)	
Age	63 (12.9)	64 (12.5)	62 (13.1)	<.001
Smoker Status: (%)				.155
No	2,494 (54.5)	1,347 (54.2)	1,147 (54.9)	
Occasional	2,50 (5.46)	133 (5.35)	117 (5.60)	
Heavy	196 (4.28)	93 (3.74)	103 (4.93)	
Former	1,635 (35.7)	911 (36.7)	724 (34.6)	
Alcohol Consumption (%)				<.001
No	2,374 (51.9)	1,398 (56.3)	976 (46.7)	
Occasional	1,929 (42.2)	956 (38.5)	973 (46.5)	
Heavy	272 (5.95)	130 (5.23)	142 (6.79)	
BMI	30.1 (6.43)	30.6 (6.88)	29.7 (5.81)	<.001
CCI	0.68 (1.25)	0.77 (1.37)	0.57 (1.08)	<.001
Joint: (%)				.431
Knee	1,964 (42.9)	1,080 (43.5)	884 (42.3)	
Hip	2,611 (57.1)	1,404 (56.5)	1,207 (57.7)	
Surgical Time	127 (57.0)	129 (59.6)	125 (53.7)	.006
Tourniquet: (%)				.001
No	155 (8.60)	108 (10.6)	47 (5.99)	
Yes	1,648 (91.4)	911 (89.4)	737 (94.0)	
Approach (Hips Only): (%)				.042
DA	63 (2.54)	26 (1.92)	37 (3.29)	
DL	2,417 (97.5)	1,329 (98.1)	1,088 (96.7)	
Anesthesia: Spinal (%)	2,612 (100)	1,465 (100)	1,147 (100)	.
TXA: (%)				<.001
No	3,104 (67.8)	2,237 (90.1)	867 (41.5)	
Yes	1,471 (32.2)	247 (9.94)	1,224 (58.5)	
Blood Transfusion: (%)				.035
No	3,594 (78.6)	1,981 (79.8)	1,613 (77.1)	
Yes	981 (21.4)	503 (20.2)	478 (22.9)	
Transfusion: (%)				<.001
None	3,594 (78.6)	1,981 (79.8)	1,613 (77.1)	
1	486 (10.6)	212 (8.53)	274 (13.1)	
2 or More	495 (10.8)	291 (11.7)	204 (9.76)	
VTE: (%)				<.001
No	4,501 (98.4)	2,421 (97.5)	2,080 (99.5)	
Yes	74 (1.62)	63 (2.54)	11 (0.53)	
DVT: (%)				<.001
No	4,515 (98.7)	2,434 (98.0)	2,081 (99.5)	
Yes	60 (1.31)	50 (2.01)	10 (0.48)	
PE: (%)				.001
No	4,556 (99.6)	2,466 (99.3)	2,090 (100.0)	
Yes	19 (0.42)	18 (0.72)	1 (0.05)	
Readmission: (%)				<.001
No	3,817 (83.4)	2,025 (81.6)	1,792 (85.7)	
Yes	757 (16.6)	458 (18.4)	299 (14.3)	
Time to Readmission	7.63 (20.2)	8.33 (21.0)	6.79 (19.3)	.010

BMI, body mass index; CCI, Charlson Comorbidity Index; DA, direct anterior; DL, direct lateral; TXA, tranexamic acid; VTE, venous tdhromboembolism; DVT, deep venous thromboembolism; PE, pulmonary embolism.

(0.68%), fondaparinux (0.17%), phosphodiesterase inhibitors (0.09%), and a combination of agents (0.08%). Tables 2 and 3 are presented separately for THA and TKA, respectively.

We adhered to our clinical practice protocol for VTE prophylaxis, incorporating a combination of mechanical and pharmacological strategies. Pharmacological agents included enoxaparin (40 mg every day), fondaparinux (2.5 mg every day), rivaroxaban (10 mg every day), dabigatran (220 mg every day), or apixaban (2.5 mg twice a day). In our patient group starting in 2008, surgeons mainly preferred coumadin for VTE prophylaxis, but it was abandoned over time, and aspirin was preferred in 2013 and later. Specifically, we used compression stockings and intermittent pneumatic compression devices during the inpatient period as part of mechanical prophylaxis.

Our approach to investigating pulmonary embolus adheres to our institutional protocols. We commence the evaluation process by assessing patients who have symptoms such as tachypnea, tachycardia, dyspnea, arrhythmia, or chest pain. The initial assessment includes essential diagnostic measures, including pulse oximetry, an electrocardiogram, a chest X-ray, and a panel of cardiac enzymes. Patients who have oxygen saturation levels below 90% receive immediate treatment with 2 L of oxygen delivered via a nasal cannula for a duration of 10 minutes. If hypoxia persists despite oxygen therapy, further diagnostic tests are employed. These tests may include chest-computed tomography, angiography or a ventilation-perfusion scan to assess the presence of PE. Additionally, patients suspected of having pulmonary embolus undergo an investigation for DVT using ultrasound-duplex imaging of the lower extremities. This approach ensures a thorough and systematic evaluation of patients who have suspected pulmonary embolus while also considering the possibility of concurrent DVT.

Data Analyses

The main comparison is looking at aspirin versus other medications. Continuous data were presented as medians [first quartile; third quartile] and categorical data were presented as cell counts (%). Mann-Whitney U-tests were used to compare continuous data and *Chi*-squared or Fisher's exact tests were used to compare categorical data.

Logistic regression analyses were used to identify predictors, including the patient's age, sex, Charlson Comorbidity Index, BMI,

Table 2
Demographic and Procedural Information of Revision THA Patients.

	Total Data	Other	Aspirin	*P* Value
	N = 2,611	N = 1,404	N = 1,207	
Sex: (%)				.002
Women	1,361 (52.1)	772 (55.0)	589 (48.8)	
Men	1,250 (47.9)	632 (45.0)	618 (51.2)	
Age	62 (14.3)	64 (13.8)	60 (14.7)	<.001
Smoker Status: (%)				.253
No	1,373 (52.6)	7,18 (51.1)	655 (54.3)	
Occasional	139 (5.32)	74 (5.27)	65 (5.39)	
Heavy	103 (3.94)	52 (3.70)	51 (4.23)	
Former	996 (38.1)	560 (39.9)	436 (36.1)	
Alcohol Consumption (%)				<.001
No	1,317 (50.4)	771 (54.9)	546 (45.2)	
Occasional	1,128 (43.2)	555 (39.5)	573 (47.5)	
Heavy	166 (6.36)	78 (5.56)	88 (7.29)	
BMI	28.8 (6.05)	29.0 (6.44)	28.6 (5.55)	.120
CCI	0.62 (1.22)	0.72 (1.33)	0.51 (1.05)	<.001
Surgical time	128 (61.4)	133 (64.2)	123 (57.6)	<.001
Approach: (%)				.042
DA	63 (2.54)	26 (1.92)	37 (3.29)	
DL	2,417 (97.5)	1,329 (98.1)	1,088 (96.7)	
Anesthesia: Spinal (%)	1,610 (100)	856 (100)	754 (100)	.
TXA: (%)				<.001
No	1,807 (69.2)	1,284 (91.5)	523 (43.3)	
Yes	804 (30.8)	120 (8.55)	684 (56.7)	
Blood Transfusion: (%)				<.001
No	1,960 (75.1)	1,099 (78.3)	861 (71.3)	
Yes	651 (24.9)	305 (21.7)	346 (28.7)	
Transfusion: (%)				<.001
None	1,960 (75.1)	1,099 (78.3)	861 (71.3)	
1	325 (12.4)	116 (8.26)	209 (17.3)	
2 or More	326 (12.5)	189 (13.5)	137 (11.4)	
VTE: (%)				<.001
No	2,574 (98.6)	1,373 (97.8)	1,201 (99.5)	
Yes	37 (1.42)	31 (2.21)	6 (0.50)	
DVT: (%)				.002
No	2,581 (98.9)	1,379 (98.2)	1,202 (99.6)	
Yes	30 (1.15)	25 (1.78)	5 (0.41)	
PE: (%)				.044
No	2,602 (99.7)	1,396 (99.4)	1,206 (99.9)	
Yes	9 (0.34)	8 (0.57)	1 (0.08)	
Readmission: (%)				.041
No	2,269 (86.9)	1,202 (85.6)	1,067 (88.4)	
Yes	342 (13.1)	202 (14.4)	140 (11.6)	
Time to Readmission	5.28 (16.9)	5.64 (17.3)	4.86 (16.3)	.235

THA, total hip arthroplasty; BMI, body mass index; CCI, Charlson Comorbidity Index; DA, direct anterior; DL, direct lateral; TXA, tranexamic acid; VTE, venous thromboembolism; DVT, deep venous thromboembolism; PE, pulmonary embolism.

Table 3
Demographic and Procedural Information of Revision TKA Patients.

	Total Data	Other	Aspirin	*P* Value
	N = 1,964	N = 1,080	N = 884	
Sex				.060
Women	998 (50.8)	570 (52.8)	428 (48.4)	
Men	966 (49.2)	510 (47.2)	456 (51.6)	
Age	65 (10.5)	65 (10.6)	64 (10.2)	.014
Smoker Status: (%)				.159
No	1,121 (57.1)	629 (58.2)	492 (55.7)	
Occasional	111 (5.65)	59 (5.46)	52 (5.88)	
Heavy	93 (4.74)	41 (3.80)	52 (5.88)	
Former	639 (32.5)	351 (32.5)	288 (32.6)	
Alcohol consumption (%)				<.001
No	1,057 (53.8)	627 (58.1)	430 (48.6)	
Occasional	801 (40.8)	401 (37.1)	400 (45.2)	
Heavy	106 (5.40)	52 (4.81)	54 (6.11)	
BMI	31.9 (6.49)	32.6 (6.90)	31.1 (5.84)	<.001
CCI	0.76 (1.29)	0.85 (1.42)	0.64 (1.11)	<.001
Surgical Time	126 (50.5)	124 (52.6)	127 (47.7)	.212
Tourniquet: (%)				.001
No	155 (8.60)	108 (10.6)	47 (5.99)	
Yes	1,648 (91.4)	911 (89.4)	737 (94.0)	
Anesthesia: Spinal (%)	1,002 (100)	609 (100)	393 (100)	.
TXA: (%)				<.001
No	1,297 (66.0)	953 (88.2)	344 (38.9)	
Yes	667 (34.0)	127 (11.8)	540 (61.1)	
Blood Transfusion: (%)				.052
No	1,634 (83.2)	882 (81.7)	752 (85.1)	
Yes	330 (16.8)	198 (18.3)	132 (14.9)	
Transfusion: (%)				.133
None	1,634 (83.2)	882 (81.7)	752 (85.1)	
1	161 (8.20)	96 (8.89)	65 (7.35)	
2 or More	169 (8.60)	102 (9.44)	67 (7.58)	
VTE: (%)				<.001
No	1,927 (98.1)	1,048 (97.0)	879 (99.4)	
Yes	37 (1.88)	32 (2.96)	5 (0.57)	
DVT: (%)				.003
No	1,934 (98.5)	1,055 (97.7)	879 (99.4)	
Yes	30 (1.53)	25 (2.31)	5 (0.57)	
PE: (%)				.003
No	1,954 (99.5)	1,070 (99.1)	884 (100)	
Yes	10 (0.51)	10 (0.93)	0 (0.00)	
Readmission: (%)				.002
No	1,548 (78.9)	823 (76.3)	725 (82.0)	
Yes	415 (21.1)	256 (23.7)	159 (18.0)	
Time to Readmission	10.7 (23.6)	11.8 (24.6)	9.42 (22.4)	.024

TKA, total knee arthroplasty; BMI, body mass index; CCI, Charlson Comorbidity Index; DA, direct anterior; DL, direct lateral; TXA, tranexamic acid; VTE, venous thromboembolism; DVT, deep venous thromboembolism; PE, pulmonary embolism.

operation time, tranexamic acid, and blood transfusion, for developing symptomatic VTE.

All statistical tests were performed using the R statistical software (version 3.1.1; R Foundation for Statistical Computing, Vienna, Austria). Multiple imputations and regressions were performed using the "rms" package within R.

Results

In our cohort, a total of 60 patients (1.31%) were diagnosed who had a symptomatic DVT. The rate of symptomatic DVT was higher in the other anticoagulant group (2.01%, n = 50) compared to the aspirin group (0.48%, n = 10) ($P < .001$). There were 19 patients (0.42%) who were diagnosed with symptomatic pulmonary embolus, of which 1 patient (0.05%) was in the aspirin group and 18 patients (0.72%) were in the other anticoagulant group ($P = .001$).

The incidence of symptomatic VTE was 1.62% in the total cohort, with patients receiving aspirin having a significantly lower

Table 4
Unadjusted Logistic Regression Model for VTE Focuses on Aspirin or Other Anticoagulants.

Variable	Odds Ratio	Lower 95	Upper 95	*P* Value
VTE				
Aspirin	0.20	0.10	0.37	<.001

VTE, venous thromboembolism.

Table 5
Adjusted Logistic Regression Model for VTE Focuses on Aspirin or Other Anticoagulants.

Variable	Odds Ratio	Lower 95	Upper 95	*P* Value
VTE				
Aspirin	0.26	0.12	0.51	<.001
Age	1.02	0.99	1.04	.091
Men	1.19	0.74	1.90	.475
BMI	1.00	0.97	1.04	.819
Surgical Time	1.00	0.99	1.01	.251
Joint: Hip	0.71	0.44	1.15	.166
CCI	1.09	0.94	1.25	.214
TXA	0.61	0.26	1.25	.201
Transfusion	2.72	1.64	4.47	<.001

BMI, body mass index; CCI, Charlson Comorbidity Index; TXA, tranexamic acid; VTE, venous thromboembolism.

incidence of 0.53% (11 out of 2,091) compared to other anticoagulant groups at 2.54% (6 out of 2,484) ($P < .001$).

Unadjusted (Table 4) and adjusted logistic regression models (Table 5) showed that the risk for VTE was higher in patients receiving other anticoagulants compared with those receiving aspirin (odds ratio [OR], 0.2; 95% confidence interval [CI], 0.1 to 0,37; $P < .001$) and (OR, 0.26; 95% CI, 0.12 to 0.51; $P < .001$), respectively.

A total of 3,594 patients (78.6%) did not receive blood transfusions. There were 486 (1.6%) patients who received 1 unit of blood transfusion. Of these, 274 (13.1%) patients were in the aspirin group and 212 (8.53%) patients were in the other anticoagulant group. There were 495 (10.8%) patients who received 2 or more units of blood transfusion, 204 (9.76%) in the aspirin group, and 291 (11.7%) in the other anticoagulant group. The logistic regression model identified blood transfusion as a strong risk factor for both VTEs (OR, 2.72; 95% CI, 1.64 to 4.47; $P < .001$).

Discussion

The use of aspirin, as a VTE prophylaxis is now widely accepted in primary TJA [6]. The ideal prophylactic agent for VTE after revision arthroplasty remains unclear. Revision TJA may be associated with a higher risk of VTE due to longer operating time, a larger surgical approach and wound, and longer immobilization [7]. Thus, surgeons may consider using potent anticoagulant agents in this cohort of patients. At the same time, wound related problems such as hematoma formation or persistent wound drainage, which are known to occur at a higher rate with the use of aggressive anticoagulants [8], are serious events in patients undergoing revision TJA. The lack of consensus regarding VTE prophylaxis in revision surgeries continues to be an issue. Our study compared aspirin with other potent anticoagulant agents for VTE prophylaxis in revision TJA. The findings indicate that aspirin appears to be a viable, and in fact a much better option, for patients undergoing revision TJA. The incidence of symptomatic VTE was significantly lower in the aspirin group compared to the group receiving other anticoagulant agents. This suggests that aspirin may offer comparable efficacy in preventing VTE events.

The choice of prophylactic regimen for VTE prevention in revision TJA should consider the individual patient's risk factors, bleeding tendencies, and overall health, with a focus on balancing effectiveness and safety [9]. In a previous similar study from our institution [10], the incidence of VTE after revision TJA was 1.53%. The risk of any symptomatic VTE was shown to be significantly higher in patients receiving warfarin compared with patients receiving aspirin (OR: 3.2; 95% CI: 1.03 to 16.3; $P = .03$). In another study including 6 centers [11], the incidence of VTE within 90 days after revision hip and knee arthroplasty was reported to be 0.42%, and the incidence of DVT was 0.28% and PE was 0.14%. In the study by Tang et al. [12], the incidence of VTE was reported to be 1.17% in patients given high-dose and low-dose aspirin after revision hip arthroplasty. No significant difference was found in terms of VTE in the high-dose and low-dose aspirin groups. In our study, we found the VTE incidence to be 1.62%, which is consistent with the literature. In a retrospective study of 1,917 revision arthroplasty patients by Manista et al. [13], the type of chemoprophylaxis was not associated with postoperative VTE ($P > .05$). While revision surgery did not present a significant risk factor for VTE (OR, 1.847; 95% CI, 0.423 to 8.053; $P = .414$), it is noteworthy that revision arthroplasty alone showed no association with an increased incidence of VTE. In a study including revision knee arthroplasty patients, there was no significant difference in the incidence of DVT between aspirin and other thromboprophylaxis agents. Furthermore, no statistically significant correlation was observed with other variables, including gender, age, laterality, American Society of Anesthesiologists grade, BMI, or the indication for revision [14].

It is crucial to acknowledge that transfusion was identified as a risk factor for VTE, highlighting the importance of managing these factors in the perioperative period. Shohat et al. [15] found that the incidence of VTE events was significantly higher in patients who received blood transfusions during revision TJA than in those who did not (3.34 versus 1.16%, $P < .001$). Similarly, another study using the National Surgical Quality Improvement Program data found that blood transfusion in the perioperative period was associated with a higher rate of VTE in TJA [16].

Our study has a few potential limitations. This study is retrospective in nature and suffers from the inherent limitations of such a study design, such as selection bias and incomplete or inaccurate data collection. The study was conducted at a single institution, which may limit the generalizability of the findings to other health care settings with potentially different patient populations and surgical practices. Multicenter studies with diverse patient cohorts may provide more comprehensive insights. We did not have data on weight-bearing status or length of hospital stay. Additionally, major bleeding data were not consistent due to the retrospective nature of the study. The study primarily compared aspirin to a variety of other anticoagulant agents. While providing valuable information on the effectiveness of aspirin, changes in dosages and administration protocols of specific agents in the “other anticoagulants” category may affect the results.

Conclusions

This large cohort study demonstrated that aspirin was associated with a more effective and safer VTE prophylaxis agent, compared to other anticoagulants, in patients undergoing revision TJA.

CRediT authorship contribution statement

Mehmet K. Yılmaz: Writing – original draft, Methodology, Data curation. **Ahmad Abbaszadeh:** Writing – original draft, Data curation. **Camilo Restrepo:** Methodology, Formal analysis, Data curation, Conceptualization. **Ibrahim Azboy:** Writing – original draft, Methodology. **Javad Parvizi:** Writing – review & editing, Supervision.

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