Risk of Venous Thromboembolism after Total Knee Arthroplasty in Patients with Rheumatoid Arthritis

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ABSTRACT. ***Objective.*** To compare the incidence of venous thromboembolism (VTE) following total knee arthroplasty (TKA) between patients with rheumatoid arthritis (RA) and those with osteoarthritis (OA).

Methods. The subjects were composed of 1084 Japanese patients with OA and 204 with RA. Primary effectiveness outcomes were any deep vein thrombosis (DVT) as detected by bilateral ultrasonography up to postoperative Day 10 (POD10) and pulmonary embolism (PE) up to POD28. The main safety outcomes were bleeding and death from any cause up to POD28. Plasma D-dimer levels were measured before and at POD10 after TKA.

Results. The study cohort was composed of 1288 patients from 34 hospitals. There was no death up to POD28. PE occurred in 2 patients with OA and in no patients with RA. The incidence of primary effectiveness outcome was 24.3% and 24.0% in patients with OA and RA, respectively. The incidence of major bleeding up to POD28 was 1.3% and 0.5% in patients with OA and RA, respectively. No differences in the incidence of VTE (symptomatic/asymptomatic DVT plus PE) or bleeding were noted between patients with RA and OA. D-dimer levels on POD10 were significantly higher in patients with OA compared with those with RA. Also, D-dimer levels on POD10 were significantly lower in patients receiving fondaparinux than in patients without pharmacological prophylaxis.

Conclusion. Despite some differences in demographic data, patients with RA and OA have equivalent risks of VTE and bleeding following TKA. (First Release April 15 2015; J Rheumatol 2015;42:928–34; doi:10.3899/jrheum.140768)

Key Indexing Terms:
DEEP VEIN THROMBOSIS RHEUMATOID ARTHRITIS THROMBOPROPHYLAXIS
TOTAL KNEE ARTHROPLASTY VENOUS THROMBOEMBOLISM OSTEOARTHRITIS

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After total joint arthroplasty, it is extremely important to prevent the development of venous thromboembolism (VTE), particularly pulmonary embolism (PE)[1]. Traditionally, the rate of deep vein thrombosis (DVT) after major orthopedic surgery was estimated to be 30% to 40% in patients undergoing total knee arthroplasty (TKA) without thromboprophylaxis[2]. Various thromboprophylactic measures have been introduced to reduce the incidence of these events[3]. Since the 1990s, antithrombotic therapies using agents such as unfractionated and low molecular weight heparin (LMWH) and direct factor Xa inhibitors have been provided after TKA[4]. However, despite the implementation of aggressive antithrombotic protocols, the incidence of in-hospital symptomatic PE after TKA remains at 0.27%[5]. Another study demonstrated that the incidence of PE was 0.1% in both TKA and total hip arthroplasty (THA) at Day 90 under recent thromboprophylaxis[6].

The vast majority of TKA procedures are performed for patients with osteoarthritis (OA). TKA is also indicated for the management of endstage knee arthritis in patients with rheumatoid arthritis (RA)[7]. Because RA is fundamentally different from OA in terms of pathogenesis and medical

management, differences in TKA outcomes are expected[8]. However, few studies have examined the outcomes of TKA, including the occurrence of VTE, or their predictors in patients with RA. Moreover, few have investigated whether there is a difference in the rate of VTE between patients with RA and those with OA[9]. Similar incidences of VTE have been reported between patients with RA and those with OA[10,11], whereas 1 large retrospective study indicated a potentially lower rate of thromboembolic complications in patients with RA[12].

Thromboprophylaxis is recommended in patients undergoing major orthopedic surgery[13]. The evidence for the efficacy and safety of LMWH and fondaparinux was derived from clinical trials in which patients with OA were predominantly studied[14]. Therefore, no definitive conclusion regarding patients with RA could be drawn[15]. The primary purpose of this large-scale, prospective study was to determine whether there was a difference in the incidence of postoperative VTE between patients with RA and OA undergoing TKA. The secondary purpose was to determine the risk factors predictive for the postoperative occurrence of VTE in patients with RA undergoing TKA. We evaluated the incidence of postoperative asymptomatic/symptomatic DVT in patients with RA and OA undergoing TKA.

Numerous research studies have been published evaluating the diagnostic accuracy of D-dimer for DVT[16]. We also compared the preoperative or postoperative plasma D-dimer levels between patients with RA or OA.

MATERIALS AND METHODS

Study design. The Japanese study of Prevention and Actual situation of Venous Thromboembolism after Total Arthroplasty (J-PSVT) was a hospital-based, prospective cohort study designed to document the effectiveness and safety of current standard thromboprophylactic agents approved for use in Japan, including unfractionated heparin (UFH), LMWH, fondaparinux, and antiplatelet agents[17]. Data were collected prospectively on patients undergoing primary TKA since 2007–2010 in 34 National Hospital Organization (NHO) hospitals that are all Japanese orthopedics association educational hospitals. The primary aim of the J-PSVT was to determine the rates of VTE in patients undergoing TKA, with all patients evaluated for the presence of all (symptomatic/nonsymptomatic) DVT on postoperative Day 10 (POD10). J-PSVT is a noninterventional observational study that provides a unique source of information on patient demographics and patterns and practices in THA and TKA. By documenting variations in postoperative approaches for thromboprophylaxis, it may be possible to identify factors that have important effects on VTE following arthroplasty in the real-world setting. Data on patient demographics, primary diagnosis, preexisting comorbid conditions, length of operation, type of anesthesia, VTE prophylaxis (including type and duration), and mechanical VTE prophylaxis were gathered using standard case report forms. The principal physicians were provided with the definitions of adverse events and serious adverse events. This information concerning adverse events was imputed in the case report form at each visit through a Web system. The trial was registered in the Japan University Hospital Medical Information Network Clinical Trial Registry (UMIN000001366). The study protocol was approved by the ethics committees of the NHO central Internal Review Board (No. 0623004). Written informed consent was obtained from each individual for their clinical records to be used in our study.

Patient enrollment. Patients aged ≥ 20 years were eligible if they were scheduled and underwent knee replacement surgery for primary joint diseases, such as OA and RA. Patients were excluded if they had (1) a predefined risk factor for bleeding (e.g., gastrointestinal ulcer, hemorrhagic stroke), (2) a coagulation disorder, (3) heart failure (New York Heart Association class III or IV), (4) renal impairment (creatinine clearance < 30 ml/min), or (5) liver dysfunction (aspartate aminotransferase or alanine aminotransferase ≥ 5 times the upper limit of normal, or total bilirubin ≥ 2 times the upper limit of normal). Patients were also excluded if they had undergone joint replacement within 3 months prior to hospital admission including reoperation, were scheduled to undergo bilateral joint replacement, were unable to walk, or had clinically unstable cardiovascular diseases.

Outcome measures. The primary effectiveness outcomes were the composite incidences of asymptomatic DVT up to POD10, and the incidence of symptomatic DVT and fatal/non-fatal PE up to POD28. All enrolled patients were assessed for DVT on POD10, or earlier if thrombosis was clinically suspected, by standard Doppler ultrasonography (US). DVT diagnosis required confirmation of the presence of a venous thrombus by compression US[18] performed using a standardized method[19,20,21]. All sonographers were adequately trained. Just before the start of the study, the participating sonographers received detailed instructions for standardized procedures in a specially organized conference and required a certification process. DVT was classified as being in either a proximal (i.e., the popliteal vein or any vein proximal to it) or a distal vein (i.e., any vein distal to the popliteal vein). A PE was defined as definite if computed tomography/angiography of the chest or ventilation–perfusion scintigraphy showed a characteristic intraluminal filling defect. The primary safety outcomes were the incidences of major bleeding and death from all causes up to POD28. Major bleeding was defined as hemorrhage occurring at a critical site (e.g., intracranial hemorrhage), resulting in the need for a major therapeutic intervention (e.g., surgery), causing hemodynamic compromise, requiring at least 1 unit of red-cell concentrates, or resulting in death. Minor bleeding was defined as bleeding that did not fulfill the criteria for major bleeding up to POD28.

Data collection. Data from the principal physicians were entered into the J-PSVT database at the data center of the NHO headquarters Center for Support and Education of Clinical Research through the HospNet-Internet system. Previous comorbid conditions of each patient were reviewed by the principal physicians. Mean length of stay in hospital after TKA in Japan was 35 days[22], and most patients completed the followup survey (POD28) while hospitalized.

Statistical analysis. Discrete variables were compared using chi-squared tests and continuous variables using Kruskal-Wallis rank tests. Plasma D-dimer levels were expressed as means (± SD) or medians (interquartile ranges) in Figure 1. Boxplots display the lower hinge defined as the 25th percentile, middle as 50th percentile, and upper hinge as the 75th percentile. Intergroup variations for variables were first determined by Kruskal-Wallis 1-way ANOVA. Specific comparison of variables between 2 groups was made using the Mann-Whitney U test. In multiple regression analysis, standardized regression coefficients were calculated to assess the relationship between preoperative D-dimer levels or changes of D-dimer during operation and clinical variables.

Multiple logistic regression analysis was used to estimate the risk factors independently associated with the primary composite outcome: asymptomatic/symptomatic DVT up to POD10, and PE up to POD28. Age was categorized as less than 75 or more years. Body mass index was categorized as less than 30 or greater. Other potential risk factors included sex, primary disease (categorized as OA or RA), presence or absence of previous VTE, type of anesthesia (general or regional), and presence or absence of elastic stocking, foot pump, tourniquet, and bone cement. Pharmacological prophylaxis was categorized as no medication, use of fondaparinux, enoxaparin, and others (UFH, antiplatelet agents). Multivariate logistic regression was used to calculate OR and 95% CI after controlling simultaneously for potential confounders. Individuals with missing data (n = 5) were excluded from the model. All reported p values were 2-tailed. All data processing and analysis were performed using the Statistical Analysis System (SAS) and SPSS version 18 software (SPSS).

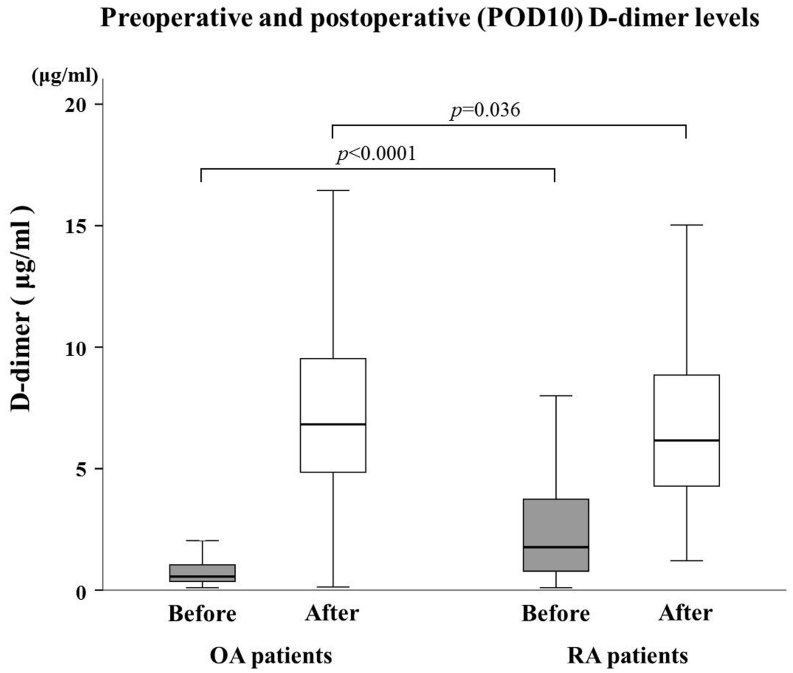

Figure 1. Preoperative and postoperative (POD10) plasma D-dimer levels in patients with RA and OA receiving TKA. P values between patients with RA versus patients with OA were calculated by the Mann-Whitney U test. POD10: postoperative Day 10; RA: rheumatoid arthritis; OA: osteoarthritis; TKA: total knee arthroplasty.

RESULTS

Patient demographic data. There were some variations in the annual volume of TKA in each hospital. Thirteen hospitals enrolled more than 40 patients (45~114), whereas 21 hospitals enrolled fewer than 40 patients (1~37). The characteristics of the study population (total patients, 1288: 204 RA, 1084 OA) undergoing TKA are presented in Table 1. The mean age at the time of TKA was 67.5 years in the RA group and 75.0 years in the OA group. Pharmacological thromboprophylaxis in patients undergoing TKA consisted of fondaparinux in 357 patients (27.7%), enoxaparin in 222 (17.2%), UFH in 71 (5.5%), and antiplatelet agents in 45 (3.5%; others: 41 aspirin, 2 ticlopidine, 2 cilostazol), whereas 593 patients (46.0%) received no medication. The mean dose (length) of thromboprophylaxis with fondaparinux, enoxaparin, and UFH were 1.7 ± 0.5 mg (10.2 ± 7.2 days), 2854 ± 992 IU (8.1 ± 4.4 days), and 13,911 ± 101 units (5.8 ± 5.8 days), respectively, in patients undergoing TKA. Among the 593 patients without medication, 590 (99.5%) received mechanical thromboprophylaxis (elastic stocking 36.8%, foot pump 14.9%, elastic stocking plus foot pump 48.3%). The risk of VTE in each patient was individually assessed based on the presence of the risk factors listed in Table 1, including age, sex, and comorbidities. The demographic data showed some differences between patients with OA and RA. Ages, percentage of males, body mass index, prevalence of comorbidities, the use of general anesthesia, and the use of antiplatelet agents (others) were significantly higher in patients with OA. Conversely, operation time and the use of cement and fondaparinux were also significantly higher in patients with OA. The 2 groups were otherwise similar.

Incidence of postoperative VTE. PE was confirmed in 1 patient with OA treated with fondaparinux (POD7) and in 1 patient with OA receiving no medication (POD13). As shown in Table 2, the rate of all DVT up to POD10 was 24.3% (263 patients) with symptomatic DVT occurring in 8 patients (0.7%) with OA and 24.0% (49 patients) with symptomatic DVT in 2 patients (1.0%) with RA, respectively. The locations of the thrombi are shown in Table 2. In both groups, most thrombi were located in the distal veins except symptomatic DVT in patients with RA. We compared the incidence of postoperative total VTE between the RA and OA groups (Table 3). There was no significant difference in the incidence of VTE between the 2 groups (24.3% OA, 24.0% RA, p = 0.941, OR 1.013, 95% CI 0.714–1.438). Multivariate analyses were also performed to identify independent predictors of VTE. Type of primary disease (RA) did not affect the risk for DVT (OR 0.948, 95% CI 0.639–1.405) in multivariate analysis (Table 4).

Incidence of postoperative bleeding. Safety analysis showed that the incidences of major bleeding up to POD28 in patients with OA and RA were 1.3% (n = 14) and 0.5% (n = 1),

Table 1. Baseline characteristics of the patients with OA or RA receiving TKA. Values are n (%) unless otherwise specified.

Characteristics	Total, n = 1288		p
	OA, n = 1084	RA, n = 204	
Male/female	197 (18.2)/887 (81.8)	24 (11.8)/180 (88.2)	0.026
Age, yrs, mean ± SD (range)	75.0 ± 6.8 (45–93)	67.5 ± 10.4 (34–86)	p < 0.0001
BMI, kg/m^2, mean ± SD	25.8 ± 3.8	23.1 ± 3.7	p < 0.0001
Venous thrombosis history	15 (1.4)	1 (0.5)	0.252
Comorbidities			
Hypertension	623 (57.5)	82 (40.2)	p < 0.0001
Ischemic heart disease	69 (6.4)	5 (2.5)	0.028
Diabetes	165 (15.2)	28 (13.7)	0.583
Cerebrovascular disease	59 (5.4)	4 (2.0)	0.034
Operation time, min, mean ± SD	126.1 ± 37.5	131.2 ± 35.1	0.019
General anesthesia	320 (29.5)	45 (22.1)	0.030
Elastic stocking use	910 (83.9)	180 (88.2)	0.119
Foot pump use	775 (71.5)	159 (77.9)	0.058
Tourniquet use	1038 (95.8)	200 (98.0)	0.122
Cement use	1004 (92.6)	199 (97.5)	0.009
Prophylaxis			
UFH	67 (6.2)	4 (2.0)	0.015
Enoxaparin	195 (18.0)	27 (13.2)	0.099
Fondaparinux	276 (25.5)	81 (39.7)	p < 0.0001
Others	43 (4.0)	2 (1.0)	0.033
No medication	503 (46.4)	90 (44.1)	0.548

OA: osteoarthritis; RA: rheumatoid arthritis; TKA: total knee arthroplasty; BMI: body mass index; UFH: unfractionated heparin.

Table 2. Incidences of primary effectiveness outcomes in patients receiving TKA. Two patients had PE complicated with DVT. Values are n (%) unless otherwise specified.

Variables	OA, n = 1084	RA, n = 204
All venous thromboembolism	263 (24.3)	49 (24.0)
Symptomatic DVT [up to POD10]	8 (0.7) [5]	2 (1.0) [0]
Distal	7 (0.6) [4]	0
Proximal	1 (0.1) [1]	2 (1.0)
Nonsymptomatic DVT, up to POD10	255 (23.5)	47 (23.0)
Distal	229 (21.1)	39 (19.1)
Proximal	26 (2.4)	8 (3.9)
PE, up to POD28	2 (0.2)	0

TKA: total knee arthroplasty; OA: osteoarthritis; RA: rheumatoid arthritis; DVT: deep vein thrombosis; POD10: postoperative Day 10; PE: pulmonary embolism; POD28: postoperative Day 28.

Table 3. Incidences of any VTE and major bleeding (up to POD28) in patients with OA and RA. Values are n (%) unless otherwise specified.

Events	OA, n = 1084	RA, n = 204	OR (95% CI)	p
VTE	263 (24.3)	49 (24.0)	1.013 (0.714–1.438)	0.941
Major bleeding	14 (1.3)	1 (0.5)	2.656 (0.359–15.956)	0.286

VTE: venous thromboembolism; OA: osteoarthritis; RA: rheumatoid arthritis; POD28: postoperative Day 28.

respectively. No fatal bleeding was observed (Table 5). We also compared the incidence of major bleeding between the RA and OA groups (Table 3). There was no significant difference in the incidence of major bleeding between the 2 groups (1.3% OA, 0.5% RA, p = 0.286, OR 2.656, 95% CI 0.359–15.956).

Changes in plasma D-dimer levels. Preoperative plasma D-dimer levels differed significantly between the OA and RA groups. As shown in Figure 1, preoperative D-dimer levels were significantly higher in patients with RA (mean ± SD, 2.70 ± 2.91 μg/ml) than in those with OA (1.03 ± 2.39 μg/ml). On POD10, however, the D-dimer levels were significantly higher (p = 0.036) in patients with OA (7.88 ± 4.70 μg/ml) than in those with RA (7.18 ± 4.21 μg/ml); however, the differences were minimal. To evaluate the effects of pharmacological thromboprophylaxis, we divided the patients without pharmacological thromboprophylaxis from those receiving enoxaparin or fondaparinux. In patients without pharmacological thromboprophylaxis, the D-dimer levels on POD10 were 8.92 ± 5.52 μg/ml in patients with OA and 8.11 ± 5.02 μg/ml in patients with RA. In patients receiving fondaparinux, the D-dimer levels on POD10 were 6.55 ± 3.34 μg/ml in patients with OA and 5.49 ± 3.42 μg/ml in patients with RA. The D-dimer levels on POD10 were significantly lower in patients receiving fondaparinux than in patients without pharmacological prophylaxis. However, there were no significant differences in the D-dimer levels on POD10 between patients with RA receiving enoxaparin and patients

Table 4. Multivariate analysis of variables associated with VTE.

Variables	OR (95% CI)	p
Age, ≥ 75 yrs	1.301 (0.987–1.716)	0.062
Male	0.633 (0.433–0.925)	0.018
BMI, ≥ 30 kg/m^2	0.884 (0.573–1.362)	0.575
Venous thrombosis history	1.136 (0.368–3.508)	0.824
RA	0.948 (0.639–1.405)	0.789
General anesthesia use	0.765 (0.560–1.045)	0.093
Elastic stocking use	0.925 (0.612–1.399)	0.712
Foot pump use	1.461 (1.049–2.034)	0.025
Tourniquet use	2.534 (1.041–6.171)	0.041
Cement use	1.386 (0.746–2.576)	0.301
Preoperative D-dimer,		
1 μg/ml increment	1.038 (0.986–1.093)	0.156
Thromboprophylaxis		
No medication	1	
Enoxaparin	0.913 (0.634–1.314)	0.624
Fondaparinux	0.495 (0.347–0.707)	p < 0.0001
UFH	1.222 (0.700–2.131)	0.480
Others	1.004 (0.495–2.039)	0.991
TKA annual volume, > 40	0.821 (0.603–1.117)	0.209

VTE: venous thromboembolism; BMI: body mass index; RA: rheumatoid arthritis; UFH: unfractionated heparin; TKA: total knee arthroplasty.

Table 5. Incidents of bleeding in patients with OA and RA receiving TKA. Values are n (%).

Bleeding Incidents	OA, n = 1084	RA, n = 204
All bleeding events	34 (3.1)	12 (5.8)
Major bleeding	14 (1.3)	1 (0.5)
Bleeding in critical organ	1 (0.1)	0
Bleeding leading to reoperation	0	0
Bleeding requiring ≥ 1 unit of transfusion	13 (1.2)	1 (0.5)
Bleeding contributing to death	0	0
Minor bleeding	20 (1.8)	11 (5.4)

OA: osteoarthritis; RA: rheumatoid arthritis; TKA: total knee arthroplasty.

without pharmacological thromboprophylaxis. The preoperative D-dimer levels and the changes of D-dimer levels (between preoperative and POD10) were subjected to multiple linear regression analysis. In regression analysis, levels of preoperative D-dimer significantly correlated with 2 baseline variables (age and RA) of 3 baseline variables (age, sex, and RA). Also, D-dimer changes significantly correlated with 4 variables (male sex, RA, use of foot pump, and use of fondaparinux) of the 6 baseline variables (age, male sex, RA, use of foot pump, use of fondaparinux, and use of tourniquet).

DISCUSSION

Patients undergoing major knee surgery are particularly prone to postoperative VTE in the form of DVT and PE[23]. Without thromboprophylaxis, the incidence of DVT in such patients exceeds 30%, and fatal PE occurs in 1% to 6% of such patients[24]. These data are based on studies in which patients with OA were predominantly investigated. Whether there is a significant difference in the risk of developing VTE between patients with RA and those with OA undergoing major orthopedic surgery remains unclear[11]. In previously reported studies, about 1.09% and 0.27% of patients after TKA experienced symptomatic VTE and PE in hospital under pharmacological prophylaxis, respectively[5]. In the present cohort study, we found that the overall rates of asymptomatic and symptomatic DVT up to POD10 and PE up to POD28 were 24.3%, 0.7%, and 0.2% in patients with OA, and 24.0%, 1.0%, and 0.0% in patients with RA, respectively. There was no statistically significant difference in the overall incidence of VTE between patients with OA and RA undergoing TKA.

In general, patients with RA have an increased burden of arterial cardiovascular events, probably because of the acceleration and triggering of atherogenesis by these proinflammatory cytokines[25,26]. Therefore, we investigated whether rheumatoid inflammatory properties affect the process of thrombosis, comparing the incidences of VTE between patients with RA and those with OA. According to our data, the incidence of compression US-confirmed DVT in patients with RA did not differ from that in patients with OA. Whether the chronic inflammation seen in patients with RA is associated with the development of VTE after TKA remains controversial.

The presence of a significant difference in the risk of developing VTE between patients with RA and those with OA undergoing major orthopedic surgery has been debated[27,28]. A metaanalysis of 2 studies revealed no difference in the risk of a VTE event within 90 days of THA in patients with RA versus OA[7]. Similarly, White, *et al* found that the unadjusted rates of in-hospital VTE events were similar between patients with RA and OA[29]. Niki, *et al* found lower incidences of Doppler US-confirmed DVT after TKA in patients with RA than in those with OA[12]. Our study demonstrated a similar risk of VTE between patients with RA and those with OA undergoing TKA. However, we cannot entirely exclude the possibility of confounded results according to the indications or presence of unmeasured confounding factors. For example, patients with RA are more likely to receive several potent medications such as methotrexate, sulfasalazine, and nonsteroidal antiinflammatory medications because of their underlying disease than are patients with OA[30]. The effect of these drugs on the risk of VTE is unclear.

We found that intermittent plantar compression (foot pumps) was an independent risk factor for VTE in patients undergoing TKA, a result not previously reported. Mechanical prophylaxis, both pneumatic compression and intermittent plantar compression, has been studied in patients undergoing TKA[31]. Although showing that mechanical prophylaxis significantly reduced thrombus formation, these studies were low powered[32,33]. There were some differences in the use of pharmacological thromboprophylaxis between patients with or without foot pump (39.9% vs 63.0%). It is possible that

these confounding factors contribute to the higher incidences of DVT in patients using foot pumps. The use of tourniquets was identified as a risk factor for DVT in patients receiving TKA in our study. These findings are consistent with the previous metaanalysis[34]. Female sex, which is defined as a risk factor for VTE after hip and knee arthroplasty[35], was also isolated as a risk factor for DVT in our study.

Patients with RA displayed significantly higher preoperative D-dimer levels than patients with OA, reflecting accelerated fibrin formation or fibrinolysis in the preoperative phase because of constitutive inflammation[36]. Conversely, postoperative D-dimer levels were not significantly different between patients with RA and OA. Thus, whether the chronic inflammatory status seen in patients with RA is associated with the development of VTE after TKA remains controversial. The inhibition of factor Xa through antithrombin by fondaparinux results in effective inhibition of thrombin generation[37]. The influence of fondaparinux on plasma markers, such as D-dimers, was demonstrated in patients without DVT in postoperative periods[38]. Similarly, our data showed that fondaparinux thromboprophylaxis significantly reduced the postoperative plasma D-dimer levels in patients with RA and OA.

There are several limitations that must be considered when interpreting these findings. The major limitation is that there was no uniformity of perioperative care or anticoagulant use because of the observational study, which adds heterogeneity. The J-PSVT does not provide detailed lifestyle information, such as smoking habits and physical activity levels, which may represent potential confounding factors in our study. Additionally, information related to the RA severity score, such as disease activity, functional impairment, and physical damage, was unavailable in our study. Another limitation could be the lack of drug data, such as antirheumatic drugs and glucocorticosteroids, to adjust for the outcomes of interest. It was reported that early mobilization after TKA reduces the incidence of DVT[39,40]. However, this information was not collected in our study. The incorporation of asymptomatic DVT in the composite primary effectiveness outcome has been questioned because a considerable imbalance exists between asymptomatic DVT, accounting for the vast majority of events, and symptomatic DVT. It is likely that our study had insufficient power to conclude that the incidences of PE and major bleeding were not different between patients with OA and RA because the incidences of these events were relatively few, especially in patients with RA. Venography is generally accepted as the gold standard in detecting DVT. A recent systematic review suggested that US is accurate for the postoperative diagnosis of DVT in asymptomatic orthopedic patients[18]. Additionally, the use of blinded investigators and independent adjudication may reduce some of the imprecision stemming from subjectivity and variability among observers[41]. Although the optimum duration of prophylaxis after hip or knee replacement surgery remains uncertain, the duration of pharmacological prophylaxis was relatively limited in our study. One of the study limitations was that the number of events was not high despite the insufficient sample size, implying the possibility of an underpowered study. For sample size calculation, we assumed, from our previously published data of the Japanese patients under recent thromboprophylaxis, a rate of DVT of about 25% after TKA[42]. Based on these assumptions, we primarily calculated that we needed 286 patients with RA and 1430 patients with OA to confirm equality within 5% difference between the 2 groups at an α error of 0.05 and a β error of 0.90. However, we could not reserve a sufficient sample size, and the possibility of an underpowered study cannot be denied.

This large prospective study assessed the incidences of VTE and bleeding in patients with OA or RA undergoing TKA under conditions reflecting real-world clinical practice in Japan. Our results showed equivalent risks of VTE and bleeding following TKA between patients with RA and those with OA.

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Corrections

Risk of Venous Thromboembolism after Total Knee Arthroplasty in Patients with Rheumatoid Arthritis

Izumi M, Migita K, Nakamura M, Jiuchi Y, Sakai T, Yamaguchi T, et al. Risk of venous thromboembolism after total knee arthroplasty in patients with rheumatoid arthritis. J Rheumatol 2015;42:928-34.

On page 928, in the author information section listing departments and institutions, at the end of the first paragraph, the following institution was omitted: Department of Molecular Immunology, Unit of Hepatology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan.

In the author affiliations, the information for Masahiro Izumi is incomplete. The affiliation should read as follows: *M. Izumi, MD; K. Migita, MD, Japanese NHO-EBM study group and J-PSVT, and Department of Molecular Immunology, Unit of Hepatology, Nagasaki University Graduate School of Biomedical Sciences;*

We regret the errors.

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