Mod Rheumatol (2008) 18:359–365
DOI 10.1007/s10165-008-0068-6

ORIGINAL ARTICLE

Disease-specific screening for deep venous thrombosis and pulmonary thromboembolism using plasma D-dimer values after total knee arthroplasty

Teruhito Yoshitaka · Nobuhiro Abe · Hiroshi Minagawa · Hirokazu Date · Yoshimasa Sakoma · Keiichiro Nishida · Toshifumi Ozaki

Received: 17 December 2007 / Accepted: 3 March 2008 / Published online: 8 May 2008

Abstract We prospectively evaluated the disease-specific features of the early postoperative plasma D-dimer value and the relationship with deep venous thrombosis and/or pulmonary thromboembolism (DVT/PE) in 95 patients following total knee arthroplasty. Patients in whom DVT/PE was highly suspected were diagnosed by high-resolution multi-detector row computed tomography scanning (MDCT). Forty-nine knees in 46 patients with rheumatoid arthritis (RA, 24 knees) or osteoarthritis (OA, 25 knees) were finally recruited. DVT/PE was detected in 28 (57.1%) of the 49 cases examined by diagnostic MDCT: 12 (50.0%) of the 24 cases of RA, and 16 (64.0%) of the 25 cases of OA. Of these, PE was found in 11 cases (39.2%), but none of them showed clinical symptomatic signs of dyspnea or chest pain. In both RA and OA cases, there were statistically significant differences in the D-dimer value on postoperative day 3 ($P = 0.027$) and after day 28 ($P = 0.037$) between the groups with and without DVT/PE. In OA cases, there were significant differences between the two groups on postoperative days 1 ($P = 0.034$), 3 ($P = 0.020$), 5 ($P = 0.005$), and 7 ($P = 0.045$), respectively. At the baseline, perioperative D-dimer levels in the RA group without DVT/PE were higher than in the OA group. However, multivariate logistic regression analysis showed that RA was not a significant risk factor of DVT/PE in comparison with OA. In conclusion, individual evaluation of the D-dimer level between RA and OA should provide a more precise predictive indicator of early postoperative DVT/PE.

Keywords Plasma D-dimer · Deep venous thrombosis · Pulmonary thromboembolism · Total knee arthroplasty · Rheumatoid arthritis · Osteoarthritis

T. Yoshitaka · N. Abe (✉)
Department of Orthopaedic Surgery, Okayama University Hospital, 2-5-1 Shikata-cho, Okayama 700-8558, Japan
e-mail: nobuabe@md.okayama-u.ac.jp

H. Minagawa · H. Date · Y. Sakoma · T. Ozaki
Department of Orthopaedic Surgery, Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences, 2-5-1 Shikata-cho, Okayama 700-8558, Japan

K. Nishida
Department of Human Morphology, Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences, 2-5-1 Shikata-cho, Okayama 700-8558, Japan

Introduction

Deep venous thrombosis (DVT) and pulmonary thromboembolism (PE) are common complications following total hip and knee arthroplasty (THA and TKA). Numerous studies have investigated the incidence and prediction of DVT/PE after TKA, especially in patients with osteoarthritis (OA) [1–3]. Plasma D-dimer measurement has been widely used for screening of DVT/PE [4, 5]. However, the D-dimer value varies depending on the general condition of the patient, the sampling time point after surgery, and also in inflammatory diseases such as rheumatoid arthritis (RA). However, disease-specific screening for DVT/PE has received little attention [6].

Recently, aggressive early postoperative rehabilitation has been commonly adopted to aid more rapid recovery

after TKA. On the other hand, 90.4% of fatal or near-fatal complications, including DVT/PE, have been reported to occur within the first four postoperative days after TKA [7]. It is therefore important to predict the occurrence of DVT/PE as early as possible to ensure safe rehabilitation.

The purpose of the present study was to evaluate the disease-specific features of early postoperative D-dimer levels in patients with RA and OA in order to allow precise prediction of DVT/PE.

Patients and procedures

Demographic data

We prospectively recruited 105 knees in 95 patients with RA or OA who underwent primary TKA at our institution between September 2004 and November 2006. Informed consent and institutional review board approval were obtained for the series. Four patients (four knees) who received preoperative anticoagulant therapy were excluded. One patient (one knee) who received a postoperative autologous transfusion of filtered shed blood was also excluded, because high concentrations of D-dimer after retransfusion of shed blood have been reported [8]. The remaining 100 knees in 90 patients (86 in women, 14 in men, 65 knees with RA, and 35 with OA) were enrolled for this study. Of these, 49 knees in 46 patients (median age 71.0 years, range 37–82 years) underwent multi-detector row computed tomography scanning (MDCT), and were subjected to further study (Table 1). There were 24 knees in 23 patients (median age 62.5 years, range 37–81 years) with RA, and 25 knees in 23 patients (median age 75.0 years, range 53–82 years) with OA. Among the risk factors for DVT/PE, there were significant differences between the RA and OA groups in median age (RA 62.5 years, OA 75.0 years, $P < 0.001$) and body mass index (RA 22.7 kg/m^2, OA 25.7 kg/m^2, $P = 0.012$), but no significant differences in gender or other predisposing factors (congestive heart failure, chronic obstructive pulmonary disease, nephrosis, stroke, previous history of DVT/PE, previous major surgery within 6 months).

Surgical data

Cemented arthroplasty was performed in all cases. Forty-one patients received spinal and epidural anesthesia in principle, and eight patients (five with RA and three with OA) received general anesthesia because of specific clinical conditions. A pneumatic tourniquet was applied in all cases. Total tourniquet time averaged 126.2 min (median 122.5 min; range 80–170 min). Pneumatic foot pumps were placed on the contralateral side from the start of surgery and on both feet just after surgery. Continuous passive motion exercise was started on the first or second postoperative day according to the patient's general condition. Patients were encouraged to perform active ankle and foot exercise as early as possible after surgery. All patients were allowed to walk with weight-bearing as far as could be tolerated. The suction drain was removed within 48 postoperative hours. No patient received any chemical anticoagulant therapy before contrast CT scanning. Substantial thrombi and PE were treated with anticoagulation using parenteral heparin, followed by oral warfarin.

Study procedure

Timing of blood sampling

The hemoglobin level (normal value: males 13.5–17.0 g/dl, females 11.5–15.0 g/dl), platelet count (normal value: 150–350 $\times$ 10^3/μl), C-reactive protein (CRP) level (latex turbidimetric method; normal value $\leq$0.3 mg/dl), and D-dimer

Table 1 Background characteristics of the present study population

	Total (n=49)	Rheumatoid Arthritis (n=24)	Osteoarthritis (n=25)	*P*
Age (years)	71.0 (37–82)	62.5 (37–81)	75.0 (53–82)	<0.001 *
Gender				0.413 †
Female, n (%)	43 (87.8)	22 (91.7)	21 (84.0)	
Male, n	6	2	4	
Body mass index (kg/m²)	24.5 (18.0–35.7)	22.7 (18.0–35.7)	25.7 (20.4–33.2)	0.012 *
Predisposing risk factors, n (%)	5 (10.2)	3 (6.1)	2 (4.1)	0.672 †
Congestive heart failure	0	0	0	
COPD	0	0	0	
Nephrosis	1	0	1	
Stroke	4	3	1	
Previous history of DVT/PE, n (%)	3 (6.1)	1 (2.0)	2 (4.1)	0.576 †
DVT	2	0	2	
PE	0	0	0	
DVT and PE	1	1	0	
Previous major surgery within 6 months, n (%)	8 (16.3)	4 (8.2)	4 (8.2)	0.950 †

Values are median (range) or n (%). *P* values are given using Mann–Whitney U test (*) or Chi-squared test (†)

COPD Chronic obstructive pulmonary disease, *DVT/PE* deep venous thrombosis and/or pulmonary thromboembolism

level (latex turbidimetric method) were measured. Venous blood samples were taken serially on preoperative days 3–1, and on postoperative days 1, 3, 5, 7, 14, 21, and after day 28. Although the normal range of the D-dimer value is ≤1.0 μg/ml at our institution, the cut-off values after TKA for diagnostic second tests were set at 15 μg/ml on postoperative day 5, [9] and 10 μg/ml on postoperative day 7, in accordance with a previous study [10].

Detection of DVT/PE

After the operation, primary screening for VTE was undertaken by meticulous check of clinical signs, and elevation of the plasma D-dimer level. For the clinical signs of DVT/PE, we carefully examined the patient for swelling of the entire leg or localized leg swelling, localized tenderness along the distribution of deep veins, acute cardiovascular dysfunction, dyspnea, chest pain, and loss of consciousness. Patients who showed a high plasma concentration of D-dimer exceeding the cut-off values, or suspected clinical signs of DVT/PE, were subjected to CT scanning using MDCT (Toshiba, Tokyo, Japan) from the chest to the ankle for detection of DVT/PE. Pulmonary arteries were scanned with helical acquisition increment, 300 mAs and 120 kVp, starting 20 s after the beginning of intravenous injection of 100–120 ml of 30% iodinated contrast material (Iopamiron®370, Bayer Schering Pharma, Berlin, Germany) at a flow rate of 3 ml/s. The images were obtained using helical acquisition with 1.0-mm collimation, 2.0-mm-thick reconstructed slices, and a 2.0-mm reconstruction increment. CT venography was performed 200 s after the start of injection, extending from the ankle to diaphragm, using helical acquisition with 2.0-mm collimation, 5.0-mm-thick reconstructed slices, a 5.0-mm reconstruction increment, 300 mAs and 120 kVp. When the acquisitions showed non-homogeneous luminal enhancement, a second scan was performed at the corresponding venous level 60–120 s later. At least two radiologists assessed each of the CT scan images.

Outcome events

Objectively documented DVT/PE using MDCT scans were considered outcomes.

Statistical analysis

Statistical analysis was performed with StatView version 5.0 (SAS Institute, Cary, NC, USA) or SPSS 11.0 for Windows (SPSS Inc., Chicago, IL, USA). Data are presented as medians with ranges.

Crude associations for categorical variables were evaluated through the use of a Chi-squared test. For continuous variables, differences between groups were evaluated by Mann–Whitney *U* test. Multivariate analysis was conducted by fitting logistic regression analysis models to adjust for the effects of confounding factors while identifying significant predictors of DVT/PE. The variables on multiple logistic regression analysis were selected from variables showing a P value of <0.5 in univariate analyses. The exact confidence intervals and probability values are reported for the multivariate models. For all other tests, a P value of <0.05 was considered statistically significant. The performance of the D-dimer value as a diagnostic test in the early postoperative period was assessed using the receiver operating characteristic (ROC) curve.

Results

Deep venous thrombosis and/or pulmonary thromboembolism was detected in 28 (57.1%) of the 49 cases subjected to diagnostic MDCT: 12 (50.0%) of the 24 cases of RA, and 16 (64.0%) of the 25 cases of OA. Of these, PE was found in 11 cases (39.2%), but none of them showed clinical symptomatic signs of dyspnea or chest pain.

On postoperative day 1, both groups showed an increased D-dimer value, with a wide variation (Fig. 1). In both RA and OA patents, the D-dimer value initially decreased on postoperative day 3, peaked on postoperative days 5–14, and then decreased. In RA patients, there were statistically significant differences in the D-dimer value between DVT/PE-positive and negative patients on postoperative day 3 (median 11.2 μg/ml for DVT/PE-positive patients, and 6.7 μg/ml for negative patients; $P = 0.027$) and after day 28 (median 8.4 μg/ml for positive patients, and 3.0 μg/ml for negative patients; $P = 0.037$). In OA patients, there were significant differences between the two groups on postoperative day 1 (median 15.5 μg/ml for positive patients, 6.5 μg/ml for negative patients; $P = 0.034$), day 3 (median 7.7 μg/ml for positive patients, 4.4 μg/ml for negative patients; $P = 0.020$), day 5 (median 18.6 μg/ml for positive patients, 11.4 μg/ml for negative patients; $P = 0.005$), and day 7 (median 22.6 μg/ml for positive patients, 17.4 μg/ml for negative patients; $P = 0.045$). At the baseline, the D-dimer levels in RA patients without DVT/PE were significantly higher than in OA patients without DVT/PE on preoperative days 3–1 (median 2.9 μg/ml in RA, 0.95 μg/ml in OA; $P = 0.029$), postoperative day 1 (median 19.0 μg/ml in RA, 6.5 μg/ml in OA; $P = 0.041$), day 3 (median 6.7 μg/ml in RA, 4.4 μg/ml in OA; $P = 0.048$), and day 5 (median 15.4 μg/ml in RA, 11.4 μg/ml in OA; $P = 0.019$).

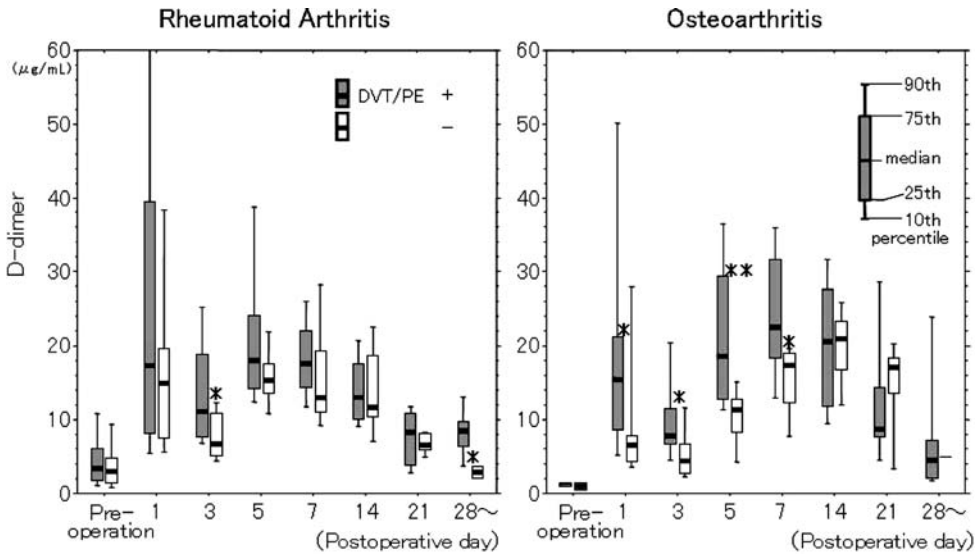

Fig. 1 Course of plasma D-dimer levels in patients with rheumatoid arthritis and osteoarthritis. The median is identified within a boxplot by a *horizontal line* inside the box. The *lower* edge of the whisker, the *lower* end of the box, the *upper* end of the box, and the *upper* edge of the whisker represent the 10th, 25th, 75th, and 90th percentile, respectively. ** $P < 0.01$, * $P < 0.05$ (Mann–Whitney U test)

Risk factors for DVT/PE

To detect the occurrence of DVT/PE early, it is preferable to perform screening on postoperative days 1–3. Using preoperative, intraoperative, and postoperative parameters, predictors of DVT/PE were analyzed using multivariate logistic regression analysis.

First, several variables obtained in the perioperative period were selected through univariate analysis according to the P value < 0.5 (Table 2, middle column), and these selected parameters were then subjected to multivariate analysis. The parameters included were: age ($P = 0.438$), gender ($P = 0.208$), body mass index ($P = 0.455$), diagnosis group (RA/OA; $P = 0.322$), previous major surgery ($P = 0.265$), previous DVT/PE ($P = 0.122$), preoperative hemoglobin value ($P = 0.449$), CRP value ($P = 0.352$), blood transfusion ($P = 0.071$), and postoperative D-dimer value (day 3; $P = 0.005$). The other parameters excluded were: predisposing cardiopulmonary disorders, duration of pneumatic tourniquet inflation, platelet count on preoperative days 3–1, and postoperative days 1 and 3, hemoglobin value on postoperative days 1 and 3; D-dimer value, $P = 0.458$ and 0.096 (data not shown in the table) for preoperative and postoperative day 1, respectively; and CRP value on postoperative day 3.

Logistic regression multivariate analysis revealed only gender ($P = 0.038$) and D-dimer value ($P = 0.011$) as significant risk factors (Table 2, right column). No significant difference in the occurrence of DVT/PE was detected between RA and OA patients.

Prediction of DVT/PE

The diagnostic performance of D-dimer values was assessed in patients with RA and OA on postoperative days 1 and 3, using the ROC curve. On postoperative day 1, areas under the curve in patients with RA and OA were 0.554 and 0.766, respectively (ROC curve not shown). On postoperative day 3, these values were 0.852 and 0.794, respectively (Fig. 2). The predictive efficiency of the D-dimer value on postoperative day 3 was superior to that on day 1, especially in patients with RA.

The cut-off values were chosen for optimal performance of at least >80% sensitivity and >50% specificity using the D-dimer values on postoperative day 3. The resulting cut-off values were 7.25 μg/ml (sensitivity 83.3%; specificity 54.5%) for RA and 4.55 μg/ml (sensitivity 85.7%; specificity 55.6%) for OA.

Discussion

The D-dimer is a fibrin-specific degradation product that detects cross-linked fibrin resulting from endogenous fibrinolysis, and hence DVT/PE [20]. In general, the D-dimer assay has been reported to be a sensitive but nonspecific marker of DVT, thus making it a good "rule out" test with appropriate pretest probability [5, 21]. In the present study, the diagnostic performance of the D-dimer was assessed in patients with RA and OA, respectively, in the early postoperative period. On postoperative day 1, the D-dimer level varied widely due to differences in surgical procedure, including bleeding, transient coagulation, or internal hypercoagulability. The usefulness of the D-dimer value was partially restricted to patients with OA because of the variation evident on postoperative day 1 in RA patients. The preoperative D-dimer level in patients with RA was higher than that in patients with OA. Increased D-dimer levels in patients with RA may reflect accelerated fibrin formation and/or fibrinolysis. So et al. [22] and

Table 2 Predictors of DVT/PE identified through univariate and multivariate analysis

Characteristic	DVT/PE		Univariable analysis	Multivariable analysis		
	+ $n = 28$ (57.1%)	− $n = 21$ (42.9%)	*P*	OR	(95% CI)	*P*
Preoperative factors						
Age (per year)	72.5 (37–82)	68.0 (47–78)	0.438*	0.96	(0.87–1.06)	0.448
Gender						
Female ($n = 43$)	26 (53.1)	17 (34.7)	0.208†	72.39	(1.26–4147.04)	0.038
Male ($n = 6$)	2 (4.1)	4 (8.2)		1.00		
Body mass index (kg/m^2)	24.7 (18.9–35.7)	23.6 (18.0–33.2)	0.455*	1.15	(0.92–1.45)	0.217
Diagnosis group						
Rheumatoid arthritis ($n = 24$)	12 (24.5)	12 (24.5)	0.322†	0.29	(0.17–4.86)	0.389
Osteoarthritis ($n = 25$)	16 (32.7)	9 (18.4)		1.00		
Predisposing risk factors						
+ ($n = 5$)	3 (6.1)	2 (4.1)	0.892†			
− ($n = 44$)	25 (51.0)	19 (38.8)				
Previous major surgery (<6 months)						
+ ($n = 8$)	6 (12.2)	2 (4.1)	0.265†	0.17	(0.01–2.58)	0.203
− ($n = 41$)	22 (44.9)	19 (38.8)		1.00		
Previous DVT/PE						
+ ($n = 3$)	3 (6.1)	0	0.122†	3.28×10^{-8}	(0.00−)	0.997
− ($n = 46$)	25 (51.0)	21 (42.9)		1.00		
D-dimer (μg/ml)	2.1 (0.9–14.2)	2.1 (0.2–12.6)	0.458*			
Hemoglobin (g/dl)	12.6 (9.2–14.9)	12.1 (9.8–15.3)	0.449*	1.31	(0.47–3.64)	0.603
Platelet (counts/mm^3)	263 (131–436)	260 (121–440)	0.832*			
CRP (mg/dl)	0.2 (0.0–4.6)	0.25 (0.0–4.7)	0.352*	0.68	(0.22–2.17)	0.519
Intra/post-operative factors						
Blood transfusion						
+ ($n = 4$)	4 (8.2)	0	0.071†	1.65×10^{8}	(0.00−)	0.996
− ($n = 45$)	24 (49.0)	21 (42.9)		1.00		
Tourniquet time (min)	105 (60–165)	115 (65–155)	0.965*			
Postoperative factors (day 3)						
D-dimer (μg/ml)	9.1 (4.3–33.1)	5.3 (6.8–3.7)	0.005*	1.54	(1.10–2.16)	0.011
Hemoglobin (g/dl)	8.2 (5.6–11.1)	8.1 (5.9–11.0)	0.797*			
Platelet (counts/mm^3)	207 (56–345)	190 (92–371)	0.974*			
CRP (mg/dL)	12.7 (5.4–25.6)	14.2 (4.8–21.6)	0.487*			

Values are median (range) or *n* (%). *P* values are given using Mann–Whitney U test (*) or chi-squared test (†)

DVT/PE Deep venous thrombosis and/or pulmonary thromboembolism, *CRP* C-reactive protein, *OR* odds ratio, *CI* confidence interval

Weinberg et al. [23] reported a tendency for D-dimer deposition on the articular synovium in patients with RA. The level of D-dimer in patients with RA is reportedly higher than normal, independent of surgery [24, 25]. Mukubo et al. [6] reported that the high D-dimer level in patients with RA was maintained from the preoperative period for up to 1 week after TKA. However, the present study showed no significant difference between patients with RA and those with OA in terms of risk factors for DVT/PE, and that D-dimer levels in the former differed from those in the latter. On postoperative day 1, the accuracy of the D-dimer value for prediction of DVT/PE was relatively lower than on postoperative day 3 because of the wide range. ROC curve analysis showed that DVT/PE patients were clearly detected by the D-dimer level in both the RA and OA groups on postoperative day 3.

Early postoperative rehabilitation has been recommended for quick recovery after TKA. Although calf and foot pumping is useful for preventing DVT, it may detach existing DVT and consequently lead to PE [11].

Kearon [3] reported that a large proportion (perhaps one half) of DVT/PE cases occurred between the intraoperative period and the first three postoperative days, although many of these cases resolved spontaneously, approximately

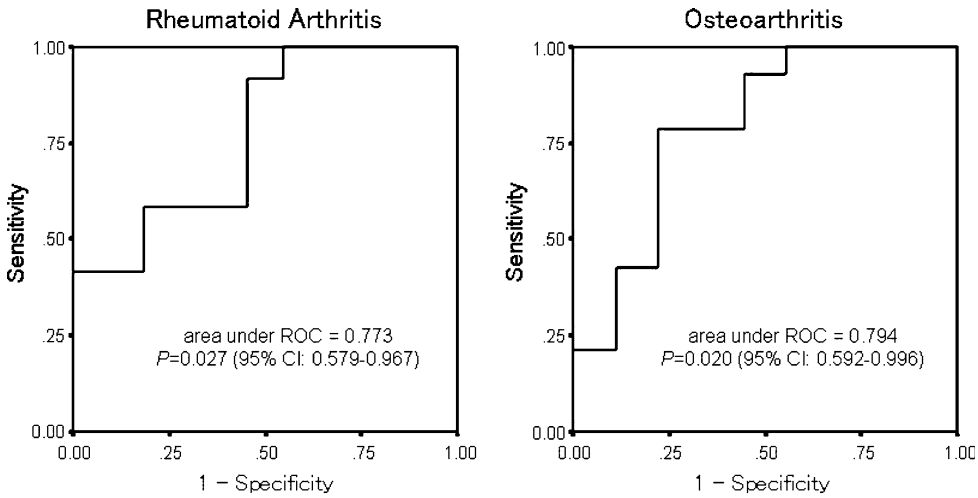

Fig. 2 Receiver operating characteristics curve analysis of plasma D-dimer value. Receiver operating characteristic curve of plasma D-dimer assay as a diagnostic test for deep venous thrombosis and/or pulmonary thromboembolism 3 days after total knee arthroplasty. *RA* rheumatoid arthritis, *OA* osteoarthritis. Area under the ROC curve is 0.852 in RA and 0.794 in OA

half within 72 h. Parvizi et al. [7] demonstrated that 90.4% of life-threatening complications including PE resulting from lower-extremity total joint arthroplasty occurred within 4 days of index surgery. Thus, it is extremely important to check for the clinical signs of DVT/PE carefully within the first four postoperative days. In the present study, although the D-dimer level on postoperative day 1 differed significantly between DVT/PE-positive and negative patients with OA, its clinical value for screening seemed to be less effective than on day 3, because half of all cases of asymptomatic DVT/PE resolve spontaneously within the following 48 h, and de novo DVT/PE may occur after invasive MDCT examination on postoperative day 1.

Ascending venography and venous compression ultrasonography have been widely used to detect DVT [12]. However, the use of CT scan for diagnosis of DVT/PE is an evolving field [13, 14]. MDCT has the potential to reveal more detail about DVT/PE [15–19]. Winter-Muram et al. [19] reported 100% sensitivity and 89% specificity for 4 × 2.5 mm collimation MDCT when used for detection of PE referenced by pulmonary arteriography. Perrier et al. [17] reported the usefulness of a diagnostic strategy for PE on the basis of D-dimer testing and MDCT instead of lower-limb ultrasonography. Loud et al. [16] reported that CT venography was 97% sensitive and 100% specific for femoropopliteal DVT. In the present study, DVT/PE was detected with 16 × 1–2 mm collimation MDCT, and its diagnostic value appeared to be sufficiently high.

In conclusion, we have demonstrated that perioperative D-dimer levels are higher in patients with RA than in those with OA, though there was no significant difference in the occurrence of DVT/PE between the two groups. In both RA and OA patients, after TKA, the D-dimer value at postoperative day 3 provides a critical diagnostic parameter indicating that early postoperative aggressive exercise can be continued without any anxiety about possible DVT/PE.

Acknowledgments We wish to thank Dr. Toru Miyoshi for critical reading of the manuscript, and in particular statistical analysis of the data. No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

References

1. Maynard MJ, Sculco TP, Ghelman B. Progression and regression of deep vein thrombosis after total knee arthroplasty. Clin Orthop Relat Res. 1991;1:125–30.
2. Schiff RL, Kahn SR, Shrier I, Strulovitch C, Hammouda W, Cohen E, et al. Identifying orthopedic patients at high risk for venous thromboembolism despite thromboprophylaxis. Chest. 2005;128:3364–71.
3. Kearon C. Duration of venous thromboembolism prophylaxis after surgery. Chest. 2003;124:386S–92.
4. Kelly J, Hunt BJ. A clinical probability assessment and D-dimer measurement should be the initial step in the investigation of suspected venous thromboembolism. Chest. 2003;124:1116–9.
5. Stein PD, Hull RD, Patel KC, Olson RE, Ghali WA, Brant R, et al. D-dimer for the exclusion of acute venous thrombosis and pulmonary embolism: a systematic review. Ann Intern Med. 2004;140:589–602.
6. Mukubo Y, Kawamata M. Higher preoperative D-dimer value remain high postoperatively in patients with rheumatoid arthritis compared with those with osteoarthrosis. J Anesth. 2006;20:51–3.
7. Parvizi J, Mui A, Purtill JJ, Sharkey PF, Hozack WJ, Rothman RH. Total joint arthroplasty: when do fatal or near-fatal complications occur? J Bone Joint Surg Am. 2007;89:27–32.
8. Helwig U, Schaub S, Berghold A, Ziervogel H. Coagulation parameters after retransfusion of unwashed blood. J Arthroplasty. 2006;21:385–91.
9. Nasu Y, Takeda K, Yorimitsu M, Abe N, Sato T, Hashizume H. D-dimer testing for a early screening for the diagnosis of deep vein thrombosis after total knee arthroplasty. J Jpn Knee Soc. 2005;30:120–3.
10. Shiota N, Sato T, Nishida K, Matsuo M, Takahara Y, Mitani S, et al. Changes in LPIA D-dimer levels after total hip or knee arthroplasty relevant to deep-vein thrombosis diagnosed by bilateral ascending venography. J Orthop Sci. 2002;7:444–50.
11. Siddiqui AU, Buchman TG, Hotchkiss RS. Pulmonary embolism as a consequence of applying sequential compression device on legs in a patient asymptomatic of deep vein thrombosis. Anesthesiology. 2000;92:880–2.

12. Fraser JD, Anderson DR. Deep venous thrombosis: recent advances and optimal investigation with US. Radiology. 1999;211:9–24.
13. Segal JB, Eng J, Tamariz LJ, Bass EB. Review of the evidence on diagnosis of deep venous thrombosis and pulmonary embolism. Ann Fam Med. 2007;5:63–73.
14. Nakamura M. Diagnosis of deep vein thrombosis in the perioperative period. Masui. 2006;55:1371–81.
15. Cham MD, Yankelevitz DF, Henschke CI. Thromboembolic disease detection at indirect CT venography versus CT pulmonary angiography. Radiology. 2005;234:591–4.
16. Loud PA, Katz DS, Bruce DA, Klippenstein DL, Grossman ZD. Deep venous thrombosis with suspected pulmonary embolism: detection with combined CT venography and pulmonary angiography. Radiology. 2001;219:498–502.
17. Perrier A, Roy PM, Sanchez O, Le Gal G, Meyer G, Gourdier AL, et al. Multidetector-row computed tomography in suspected pulmonary embolism. N Engl J Med. 2005;352:1760–8.
18. Stein PD, Fowler SE, Goodman LR, Gottschalk A, Hales CA, Hull RD, et al. Multidetector computed tomography for acute pulmonary embolism. N Engl J Med. 2006;354:2317–27.
19. Winer-Muram HT, Rydberg J, Johnson MS, Tarver RD, Williams MD, Shah H, et al. Suspected acute pulmonary embolism: evaluation with multi-detector row CT versus digital subtraction pulmonary arteriography. Radiology. 2004;233:806–15.
20. Caprini JA, Glase CJ, Anderson CB, Hathaway K. Laboratory markers in the diagnosis of venous thromboembolism. Circulation. 2004;109:I4–8.
21. Wells PS, Anderson DR, Rodger M, Forgie M, Kearon C, Dreyer J, et al. Evaluation of D-dimer in the diagnosis of suspected deep-vein thrombosis. N Engl J Med. 2003;349:1227–35.
22. So AK, Varisco PA, Kemkes-Matthes B, Herkenne-Morard C, Chobaz-Peclat V, Gerster JC, et al. Arthritis is linked to local and systemic activation of coagulation and fibrinolysis pathways. J Thromb Haemost. 2003;1:2510–5.
23. Weinberg JB, Pippen AM, Greenberg CS. Extravascular fibrin formation and dissolution in synovial tissue of patients with osteoarthritis and rheumatoid arthritis. Arthritis Rheum. 1991;34:996–1005.
24. Wallberg-Jonsson S, Cvetkovic JT, Sundqvist KG, Lefvert AK, Rantapaa-Dahlqvist S. Activation of the immune system and inflammatory activity in relation to markers of atherothrombotic disease and atherosclerosis in rheumatoid arthritis. J Rheumatol. 2002;29:875–82.
25. Ichikawa Y, Yamada C, Horiki T, Hoshina Y, Uchiyama M. Serum matrix metalloproteinase-3 and fibrin degradation product levels correlate with clinical disease activity in rheumatoid arthritis. Clin Exp Rheumatol. 1998;16:533–40.