

## Venous Thromboembolism after Total Hip Arthroplasty Diagnosed by Enhanced Computed Tomography: Comparison of Selective Thromboprophylaxis and No Thromboprophylaxis

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Total hip arthroplasty (THA) is the most effective treatment for advanced or end-stage hip osteoarthritis. However, venous thromboembolism (VTE) remains one of its unresolved complications. We reviewed the records of 322 patients undergoing primary THA and investigated the efficacy of anticoagulant prophylaxis for VTE. Our study cohort consisted of 60 patients who received no anticoagulants, 100 patients who received a factor Xa inhibitor (fondaparinux), 100 patients who received low molecular weight heparin (enoxaparin), and 62 patients who selectively received no anticoagulant prophylaxis due to perioperative bleeding, weight, and/or hemoglobin concentration. Enhanced 64-slice multidetector row computed tomography was performed postoperatively for 7 days in all cases. The incidence of VTE in the four groups was 15%, 9.0%, 6.0%, and 6.4%, respectively. The incidence of VTE was significantly lower in the groups receiving anticoagulant prophylaxis and the group selectively receiving no anticoagulant prophylaxis than in the group receiving no anticoagulants. Complications of fondaparinux therapy included hepatic dysfunction in 4 cases (4.0%), minor bleeding in 2 cases (2.0%), persistent wound drainage in 3 cases (3.0%), and eruption in 1 case (1.0%). The complications of enoxaparin therapy were persistent wound drainage in 1 case (1.0%) and progression of anemia in 1 case (1.0%). The incidence of VTE was low in patients who selectively received no anticoagulant prophylaxis, so we conclude that anticoagulant prophylaxis should be used selectively in THA cases.

**Key words:** total hip arthroplasty, venous thromboembolism, anticoagulant prophylaxis, complications

Venous thromboembolism (VTE) is a perioperative complication of total hip arthroplasty (THA). According to the Japanese guideline for the prevention of venous thromboembolism [1], patients

undergoing THA are at high risk for developing VTE and are recommended to receive preventive therapy. The recommended methods of preventing VTE are the use of compression stockings, intermittent pneumatic compression (IPC), anticoagulants, and other thera-

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pies. The usefulness of anticoagulants for the prevention of VTE has been described by the American Academy of Orthopedic Surgeons (AAOS) and the American College of Chest Physicians (ACCP) [2], as well as in recent studies [3–5]. However, complications such as bleeding can be serious [6]. In Japan, secondary osteoarthritis of the hip is the leading reason for THA [7]. The operation for secondary osteoarthritis is more complicated than that for primary osteoarthritis of the hip, so the operative time and levels of perioperative bleeding are different in each case.

Duplex ultrasonography (US) is commonly used for VTE screening [8], but it cannot detect pulmonary thromboembolism (PE). In our institute, enhanced computed tomography (e-CT) was performed one week after surgery to screen for deep vein thromboembolism (DVT) and PE simultaneously. We hypothesized that anticoagulant prophylaxis should be used selectively in THA cases, and that enhanced CT would be a useful screening method for asymptomatic VTE.

### Materials and Methods

Patients undergoing primary THA between May 2006 and December 2010 were divided into 4 groups after written informed consent was obtained. Based on the method of VTE prophylaxis, group A ( $n = 60$ ) received no anticoagulant prophylaxis between May 2006 and July 2007, group B ( $n = 100$ ) received a factor Xa inhibitor (fondaparinux; FPX) between July

2007 and December 2008, group C ( $n = 100$ ) received low molecular weight heparin (enoxaparin; LMWH) between January 2009 and December 2010, and group D ( $n = 62$ ) patients selectively received no anticoagulant prophylaxis—*i.e.*, neither LMWH nor FPX—between July 2007 and December 2010 (Table 1). The dose of FPX was 2.5 mg in patients with a creatinine clearance of  $> 30$  ml/min, and 1.5 mg in patients with a creatinine clearance of 20–30 ml/min. The dose of LMWH was 4,000 IU/day in patients with a creatinine clearance of  $> 50$  ml/min, and 2,000 IU/day in patients with a creatinine clearance of 30–50 ml/min. Patients who could not receive anticoagulants due to a volume of postoperative blood loss of  $> 600$  ml on postoperative days 0 to 2, weight  $< 50$  kg, and/or a hemoglobin level of  $< 9$  g/dl the day after surgery belonged to group D. We used a navigation system to position the acetabular cup prosthesis in all cases of cemented THA ( $n = 73$ ) and cementless THA ( $n = 249$ ). The transtrochanteric, anterolateral, or posterior approach was used with the patient placed in the supine or lateral decubitus position. All patients received 1,500 ml of Ringer's solution or hydroxyethyl starch daily for 3 days postoperatively. IPC was applied for 2 days postoperatively, with the application limited to nighttime hours for 1 week postoperatively, after ambulation was permitted. In groups B and C, prophylaxis began on postoperative day 2 and was continued for 10 days. Those receiving anticoagulants such as warfarin and heparin preoperatively, those not able to undergo examination for VTE by e-CT because of

**Table 1** Patient demographics, body mass index, and operative time for each group

Group	A No anticoagulants	B Fondaparinux	C LMWH	D No anticoagulants selectively
Hips	60	100	100	62
Disease (OA, RA, ION)	53 : 4 : 3	83 : 8 : 9	88 : 3 : 9	41 : 12 : 9
Gender (F/M)	53 : 4	78 : 22	91 : 9	59 : 3
Age	66 (41~84)	58 (35~82)	61 (40~86)	62 (25~80)
BMI	24 (14~34)	23 (16~40)	24 (17~45)	22 (14~30)
Operative time (min)	115 (60~220)	103 (59~185)	101 (60~180)	113 (60~180)

LMWH, low molecular weight heparin; OA, osteoarthritis; RA, rheumatoid arthritis; ION, idiopathic osteonecrosis; F/M, female/male; BMI, body mass index. The number of hips and gender distribution are different in group A, because group A included 3 bilateral cases.

allergy and renal dysfunction, and those not able to receive anticoagulants due to renal dysfunction were excluded from this study.

Enhanced 64-slice multidetector row computed tomography (MDCT) was performed in all 322 cases at 7 days postoperatively, and VTE was diagnosed by our in-hospital radiologists. Complications of anticoagulant prophylaxis including hepatic dysfunction, bleeding, persistent wound drainage, eruptions, and progression of anemia were assessed. Hepatic dysfunction was defined as an increase in aspartate aminotransferase (AST) or alanine aminotransferase (ALT) levels by two or more times the upper limit of normal (AST 70IU/l, ALT 84IU/l). Bleeding was defined as marked swelling and internal hemorrhaging at the wound site. Persistent wound drainage was defined as wound drainage that continued more than 2 weeks postoperatively. Eruptions that developed after administration of anticoagulants were diagnosed by dermatologists. Progression of anemia was defined as a decrease in the hemoglobin level of  $> 2\text{g/dl}$  at 3 days postoperatively; treatment with anticoagulant prophylaxis was stopped when this diagnosis was made. Plasma D-dimer levels were also assessed with a random access, high-volume coagulation analyzer (CS-5100; Sysmex Corporation, Kobe, Japan). The normal range was lower than  $0.9\mu\text{g/ml}$ . We also compared the hemoglobin values and D-dimer levels in each group on postoperative days 1, 3, 5, and 7.

Statistical analyses were carried out using SPSS version 19.0 (IBM, New York, NY, USA). The chi-squared test was used to compare the incidence of VTE, and the unpaired Student's *t*-test was employed to compare differences in hemoglobin and D-dimer levels between groups. A *p*-value of  $< 0.05$  was considered statistically significant.

This study was conducted in accordance with the Helsinki Declaration. Ethical approval was obtained from the institutional review board of Okayama University (approval number: 982).

## Results

A total of 9 cases of venous thromboembolism (VTE; 15%), including 4 cases of deep vein thromboembolism (DVT; 6.7%), 3 cases of pulmonary embolism (PE; 5.0%), and 2 cases of both DVT and PE (3.0%), were detected in group A. Nine cases of

VTE (9.0%), including 6 cases of DVT (6.0%), 1 case of PE (1.0%), and 2 cases (2.0%) of both DVT and PE, were detected in group B. Six cases of VTE (6.0%), including 4 cases (4.0%) of DVT and 2 cases (2.0%) of PE, were detected in group C. Four cases (6.4%) of VTE, including 3 cases (4.8%) of DVT and 1 case (1.6%) of both DVT and PE, were detected in group D (Fig. 1). Statistically significant differences were not found between groups. There were no cases of symptomatic VTE. After thrombolytic therapy, the thrombi disappeared or became smaller on e-CT re-examination.

Complications in group B (10 cases, 10.0%) included hepatic dysfunction in 4 cases (4.0%), minor bleeding in 2 cases (2.0%), persistent wound drainage in 3 cases (3.0%), and eruption in 1 case (1.0%). Complications in group C (2 cases, 2%) included persistent wound drainage in 1 case (1.0%) and progression of anemia in 1 case (1.0%). The prevalence of hepatic dysfunction in group B was significantly higher than that in group C. There were no cases of severe bleeding requiring blood transfusion.

Postoperative hemoglobin and D-dimer levels were compared. The mean hemoglobin level was significantly lower in group D compared with the other groups on postoperative day 1 (Fig. 2). The mean D-dimer level reached its nadir on postoperative day 3 in each group, then increased gradually, and was significantly lower

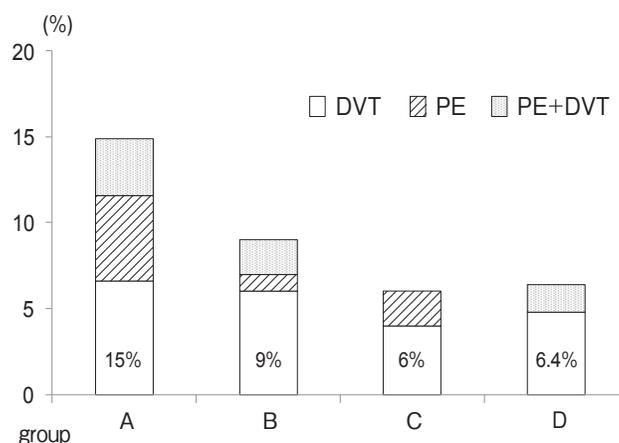


Fig. 1 The bar graph shows the VTE incidence in group A (receiving no anticoagulants), group B (receiving FDX), group C (receiving enoxaparin), and group D (selectively receiving no anticoagulants). The incidences of DVT, PE, and both PE and DVT are indicated by the white bar, striped bar, and dotted bar, respectively.

in groups B and C than in groups A and D on postoperative day 7 (Fig. 3). In patients with VTE on postoperative day 7, the mean D-dimer level was  $> 10 \mu\text{g/ml}$  in groups A and D and  $< 10 \mu\text{g/ml}$  in groups B and C (Fig. 4). If we set the cutoff value for the D-dimer level as  $10 \mu\text{g/ml}$ , the sensitivity in groups A, B, C, and D was 0.778, 0.556, 0.500, and 0.750, respectively. The specificity in groups A, B, C, and D was 0.412, 0.637, 0.628, and 0.414, respectively (Table 2).

**Case 1.** This patient was a 58-year-old Japanese woman who underwent a closed reduction for developmental dislocation of the hip. Her height, weight, and body mass index (BMI) were 155 cm, 55 kg, and 23,

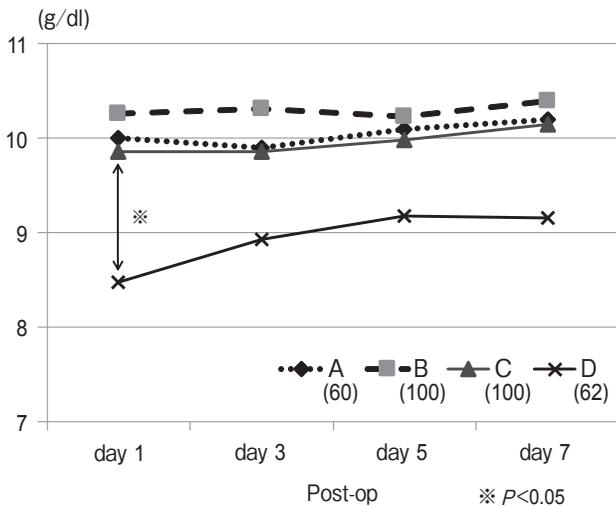


Fig. 2 The average hemoglobin level in each group. Values are shown for postoperative days 1, 3, 5 and 7, plotted for group A (receiving no anticoagulants), group B (receiving FDX), group C (receiving enoxaparin), and group D (selectively receiving no anticoagulants), and indicated by rhombuses, squares, triangles, and Xs, respectively. Values under the group are the cases in each group.

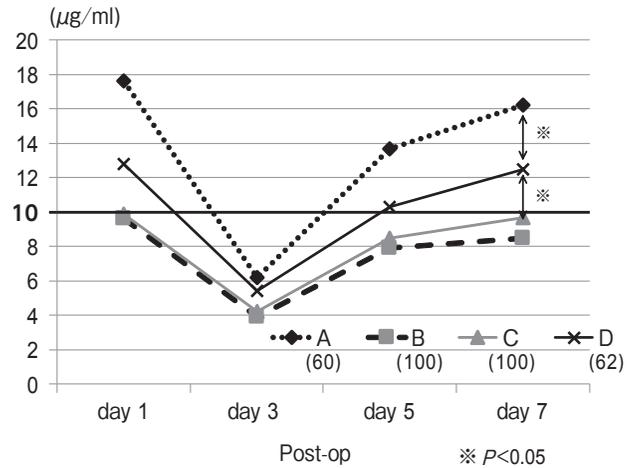


Fig. 3 The average D-dimer level in each group. Values are shown for postoperative days 1, 3, 5 and 7. Values under the group are the cases in each group.

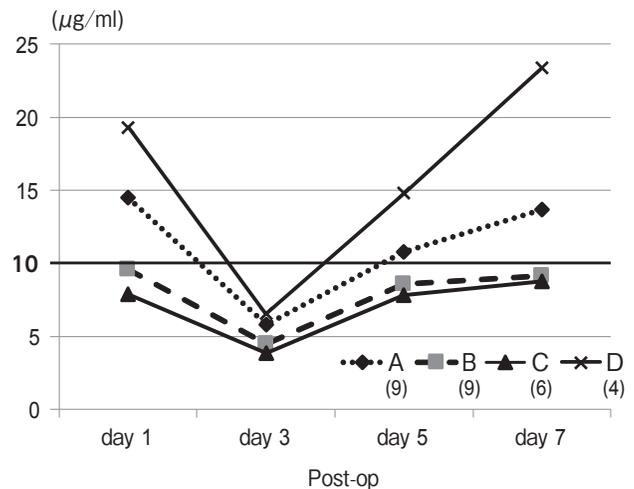


Fig. 4 The average D-dimer level in VTE patients of each group. D-dimer levels are shown on postoperative days 1, 3, 5 and 7. Values under the group are the cases in each group.

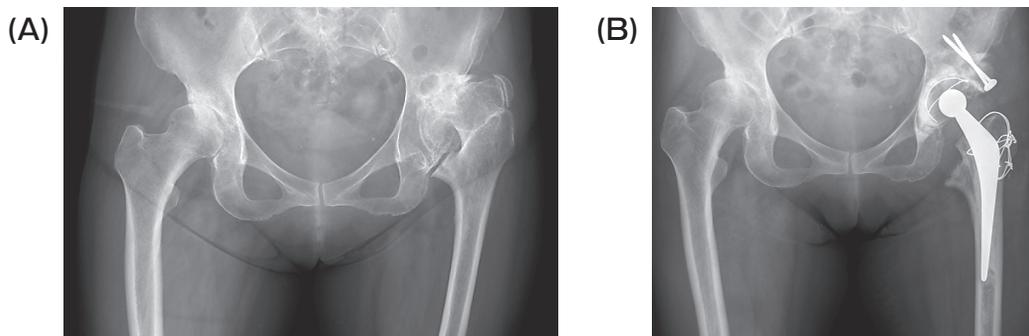
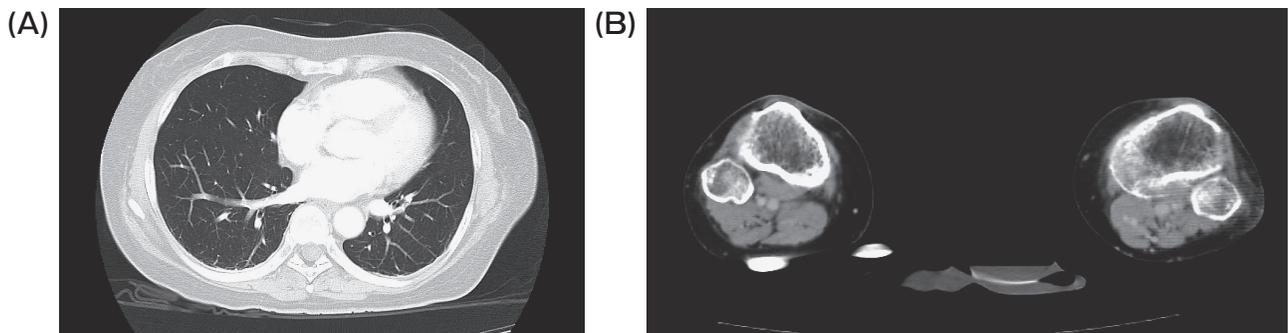


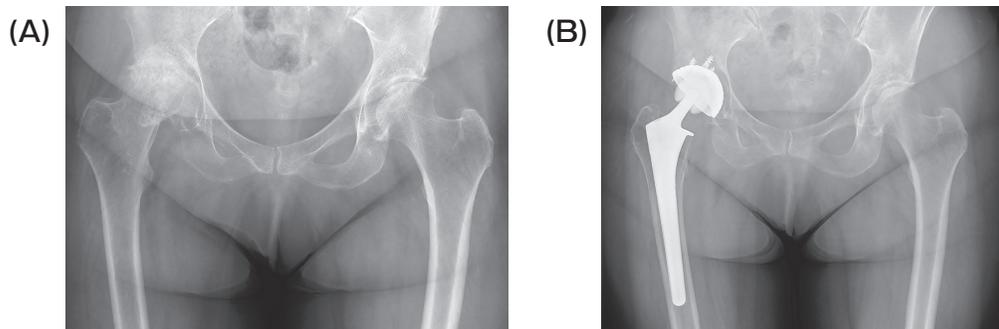
Fig. 5 The anteroposterior (AP) view of the hip joints in case 1. (A) Preoperative and (B) postoperative radiographs.

**Table 2** Diagnosis of VTE using a D-dimer level cutoff of  $10\mu\text{g}/\text{ml}$  on postoperative day 7 in each group

Group		A	B	C	D
		No anticoagulants	Fondaparinux	LMWH	No anticoagulants selectively
VTE(+)	$10 \geq$	7	5	3	3
	$10 <$	2	4	3	1
sensitivity		0.778	0.556	0.500	0.750
specificity		0.412	0.637	0.628	0.414



**Fig. 6** Enhanced CT scan of the lung and the lower leg in case 1. (A) PE was not detected in the entire lung. (B) DVT was not detected in the lower legs, neither.



**Fig. 7** Anteroposterior (AP) view of the hip joints in case 2. (A) Preoperative and (B) postoperative radiographs.

respectively. Cemented THA was performed. The operative time, intraoperative blood loss (Fig. 5A, B), and perioperative blood loss were 175 min, 500 ml, and  $> 600\text{ml}$ , respectively, so she did not require anticoagulant prophylaxis and could ambulate 2 days postoperatively. One week after surgery, her D-dimer level was  $22.3\mu\text{g}/\text{ml}$ , but no VTE was detectable on e-CT (Fig. 6).

**Case 2.** This patient was a 59-year-old American woman who lived in Japan. She had systemic lupus

erythematosus and osteonecrosis of the right femoral head. Her height, weight, and BMI were 168 cm, 88 kg, and 31, respectively. Ten years after the onset of right coxalgia, cementless THA was performed (Fig. 7A, B). The operative time and intraoperative blood loss were 90 min and 100 ml, and no blood transfusion, including auto-blood transfusion, was performed. She could ambulate with a walker 2 days after surgery, after which prophylactic LMWH was started. Seven days postoperatively, she had a hemo-

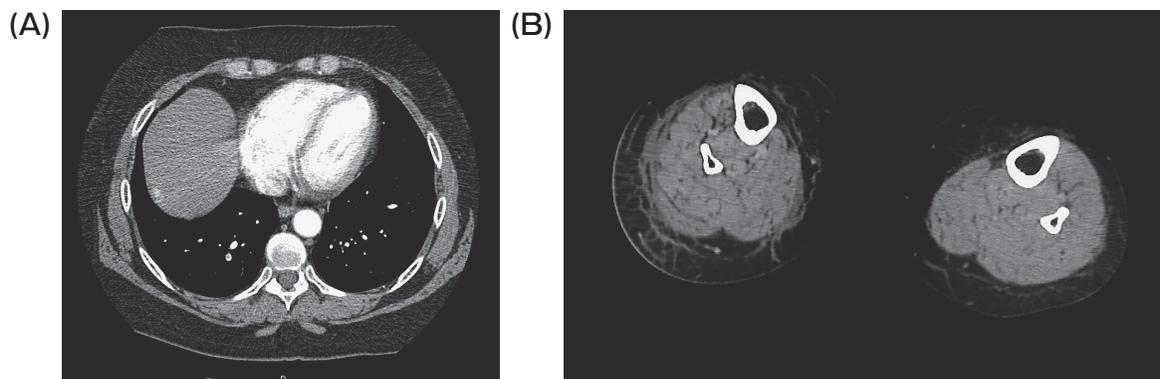


Fig. 8 Enhanced CT scan of the lung and the lower leg in case 2. (A) The axial image showed thrombus (arrow) in the A10 artery of the right lung. (B) The axial image revealed no DVT in the lower legs.

globin level of 6g/dl and did not complain of any symptoms. On e-CT, a PE alone was detected (Fig. 8). Thrombolytic treatment with heparin was started. Reevaluation by e-CT after treatment found no thrombi and no VTE recurrence.

### Discussion

In the United States and Europe, VTE has been recognized as a serious complication of orthopedic surgery since the 1960s. Screening for VTE and VTE prevention have been previously discussed [9]. Hume *et al.* [10] evaluated the incidence of lower leg DVT in 140 THA cases by impedance plethysmography and  $^{125}\text{I}$ -fibrinogen leg scanning; they found that one-quarter (35 patients) had VTE and mentioned the necessity of monitoring and routine prophylaxis. Harris *et al.* [11] screened for VTE by cuff-impedance phlebography and  $^{125}\text{I}$ -fibrinogen scanning. They found that the accuracy of DVT detection was 80% by cuff-impedance phlebography and 78% by  $^{125}\text{I}$  fibrinogen scanning; the effectiveness of cuff-impedance phlebography for detecting proximal thrombi was noted. Moskovitz *et al.* [12] administered low dose heparin for prevention of VTE in 67 patients undergoing THA. In their randomized double-blinded study, they used  $^{125}\text{I}$ -fibrinogen and venography to find VTE and radionuclide lung scanning to detect the onset of PE. VTE incidence was significantly lower in the prophylactic heparin group (23%) than in the placebo group (59%). However, the prophylactic heparin group required a significantly larger volume of transfused blood than the placebo group.

Two decades after these reports, VTE began to be recognized as a major complication of hip and knee arthroplasty in Japan. Using venograms to screen for VTE in 164 THA cases, Fujita *et al.* [13] found DVT in 22.6% and proximal DVT in 9.8%. At our institute, Shiota *et al.* [14] used bilateral venography to screen 54 patients with THA and found DVT in 22 of these cases (40.1%). As a result of their report, the use of IPC and early ambulation are now recommended in Japan. Recently, anticoagulant prophylaxis was also initiated for cases of TKA, THA, and hip fracture in Japan.

In a double-blinded, randomized study of the efficacy of fondaparinux (FDX; placebo, 0.75, 1.5, 2.5, and 3.0mg) in 74, 62, 65, 68, and 70 patients, respectively, Fuji *et al.* [15] reported that the incidence of VTE (detected by ascending venography 11–17 days postoperatively) was 33.8%, 24.2%, 4.6%, 7.4%, and 9.5%, respectively. Although there was a dose-response effect, there were no statistically significant inter-group differences in major events; it was concluded that FDX has a favorable benefit-to-risk profile in patients with VTE. Yamaguchi *et al.* [3] administered 2.5mg of FDX for 2 postoperative weeks to 71 patients undergoing THA and screened for VTE by ultrasonography on postoperative days 1, 4, and 14. DVT was detected in 27% of patients on postoperative day 4, but in only 11.9% of patients on postoperative day 14. Yukizawa *et al.* [16] investigated 170 THA cases, including 67 cases treated with IPC only and 103 cases treated with IPC and FDX. The incidence of VTE detected by MDCT and duplex ultrasonography was 25% in patients treated with IPC

only and 8% in patients treated with IPC and FDX. These recent reports indicate that anticoagulant prophylaxis is effective for the prevention of VTE in THA cases.

In our study, VTE was detected by 64-slice MDCT 7 days postoperatively, and the VTE incidence was 15% in group A (no anticoagulants), 9% in group B (FDX), and 6% in group C (LMWH). The difference between groups was not statistically significant. However, previous reports indicated a decrease in VTE incidence as a result of prophylaxis [3, 15, 17]. VTE incidence was lower in our report than in Shiota's report [14]; prophylaxis for VTE consisted of only IPC without anticoagulants and patients ambulated 1 week postoperatively. For this reason, we consider that anticoagulant prophylaxis and an early ambulation protocol will decrease VTE incidence.

Duplex ultrasonography is a common VTE screening method because of its low cost and convenience. On the other hand, e-CT has some disadvantages such as exposure to radiation, allergy to iodinated contrast media, and high cost. However, the e-CT scan covers the entire body and can detect sites of PE and DVT simultaneously. In the current study, 1.9%, 5.3%, 1.6%, and 8.7% of all 322 patients had PE, DVT, PE + DVT, and VTE 1 week postoperatively, respectively; PE completely resolved on reexamination. Thus, we consider that the PEs detected by e-CT were not fat emboli, so e-CT is needed for screening of asymptomatic VTE.

When using the D-dimer level as a screening test for VTE 1 week postoperatively, Shiota *et al.* [14] set the cutoff value at 10  $\mu\text{g}/\text{ml}$ . In our current study, the D-dimer level at 1 week postoperatively was significantly higher in groups A and D ( $> 10 \mu\text{g}/\text{ml}$ ) than in groups B and C, so we set the cutoff value at 10  $\mu\text{g}/\text{ml}$  to screen for VTE at 1 week postoperatively. Yukizawa *et al.* [16] defined the cutoff value as the increase in plasma soluble fibrin and plasminogen-activator inhibitor-1 levels from the preoperative to 1-day postoperative period, and found that the sensitivity and specificity were 100% and 67%, respectively, in the IPC group and 88% and 97%, respectively, in the FDX group. They also mentioned that it was inefficient to investigate the D-dimer level as a marker for VTE 1 week postoperatively, because the plasma D-dimer level increases following thrombus cleavage and activated plasmin is already formed. In

the current study, the average plasma D-dimer level in the groups with anticoagulant prophylaxis was lower than that in those receiving no anticoagulant prophylaxis (Fig. 3 and 4). It is useful to set a D-dimer cutoff value of 10  $\mu\text{g}/\text{ml}$  in the cases receiving no anticoagulant prophylaxis, but this does not apply in the anticoagulant prophylaxis cases (Table 2). Shimoyama *et al.* [17] reported that a preoperative D-dimer level of 0.85  $\mu\text{g}/\text{ml}$  is a useful screening tool for VTE. Although they concluded that the evaluation of VTE risk before surgery is useful, their study included a fairly small number of cases. In the current study, the preoperative D-dimer level was not determined for all cases, and thus further prospective research is needed.

Bleeding is an inevitable complication of anticoagulant prophylaxis, as previously reported [6, 12]. Although the ACCP recommends the use of enoxaparin sodium for VTE prophylaxis, Burnett *et al.* [6] reported that major complications such as bleeding occurred 3 times more often in patients receiving enoxaparin sodium prophylaxis than in those treated with prophylactic warfarin. In this study, the incidence of VTE was low in both the FDX and LMWH groups, but without a significant difference between the 2 groups. The complication rate was higher in the FDX group. VTE incidence was as low in the group selectively receiving no anticoagulant prophylaxis, as in the groups receiving anticoagulant prophylaxis. VTE was not symptomatic in this series, so we consider that it is sufficient to use anticoagulants selectively for VTE prophylaxis. Sugano *et al.* [18] reviewed 3016 patients undergoing elective hip surgery. Patients received intraoperative IPC, early ambulation, postoperative compression stockings, and prophylactic IPC. Although one patient with PE (0.003%) and 4 patients with DVT (0.013%) were symptomatic, no case of PE was fatal. In our study, all cases of VTE were detected by e-CT. In Sugano's study, no deaths had occurred within 6 months of treatment, even in symptomatic cases. They concluded that mechanical thromboprophylaxis without anticoagulant prophylaxis was effective enough. Although we agree with their opinion, not all their patients were screened. We consider that the incidence of asymptomatic VTE in THA cases is higher than previously reported and the risk of death in patients with asymptomatic PE remains high.

Our study was limited in that it had a retrospec-

tive design and was not a randomized controlled trial. In addition, there was a significant bias in gender and the cause of THA between the 4 groups. Finally, we did not continue to screen for VTE after discharge. In the future, a randomized controlled trial with a large number of patients, as well as more detailed pre- and postoperative assessments, will be needed.

In conclusion, we investigated the postoperative VTE incidence in THA cases for which anticoagulant prophylaxis was applied selectively based on e-CT. The results indicated that THA cases with perioperative blood loss > 600ml and a hemoglobin level < 9.0g/dl may not need anticoagulant prophylaxis to avoid the complication of bleeding.

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## References

1. Ando M, Fukuda I, Ito M, Kobayashi T, Masuda M, Miyahara Y, Nakanishi N, Niwa A, Ohgi S, Tajima H, Ishibashi H, Kanaoka Y, Nakamura M, Sakuma M, Satoh T, Tababe N, Yamada N, Yamashita M, Kuriyama T, Matsubara J, Nakao T, Ozaki Y, Sakata R and JCS Joint working group: Guidelines for the Diagnosis, Treatment and Prevention of Pulmonary Thromboembolism and Deep Vein Thrombosis. *Circ J* (2011) 75: 1258–1281.
2. Barrack RL: Current guidelines for total joint VTE prophylaxis. *J Bone Joint Surg Br* (2012) 94: 3–7.
3. Borris LC: Emerging antithrombotic agents for thromboprophylaxis, clinical potential and patient considerations. *J Blood Med* (2010) 1: 123–130.
4. Yamaguchi T, Hasegawa M, Niimi R and Sudo A: Incidence and time course of asymptomatic deep vein thrombosis with fondaparinux in patients undergoing total joint arthroplasty. *Thromb Res* (2010) 126: e323–326.
5. Lieberman JR and Pensak MJ: Prevention of venous thromboembolic disease after total hip and knee arthroplasty. *J Bone Joint Surg Am* (2013) 95: 1801–1811.
6. Burnett RS, Clohisey JC, Wright RW, McDonald DJ, Shively RA, Givens SA and Barrack RL: Failure of the American College of Chest Physicians—1A protocol for lovenox in clinical outcome for thromboembolic prophylaxis. *J Arthroplasty* (2007) 22: 317–324.
7. Jingushi S, Ohfuji S, Sofue M, Hirota Y, Itoman M, Matsumoto T, Hamada Y, Shindo H, Takatori Y, Yamada H, Yasunaga Y, Ito H, Mori S, Owan I, Fujii G, Ohashi H, Iwamoto Y, Miyanishi K, Iga T, Takahira N, Sugimori T, Sugiyama H, Okano K, Karita T, Ando K, Hamaki T, Hirayama T, Iwata K, Nakasone S, Matsuura M and Mawatari T: Osteoarthritis hip joints in Japan: involvement of acetabular dysplasia. *J Orthop Sci* (2011) 16: 156–164.
8. Dhupar S, Iorio R, Healy WL and Dhimitri K: A comparison of discharge and two-week duplex ultrasound screening protocols for deep venous thrombosis detection following primary total joint arthroplasty. *J Bone Joint Surg Am* (2006) 88: 2380–2385.
9. Tubiana R and Duparc J: Prevention of thrombo-embolic complications in orthopaedic and accident surgery. *J Bone Joint Surg Br* (1961) 43: 7–15.
10. Hume M, Turner RH, Kuriakose TX and Surprenant J: Venous thrombosis after total hip replacement. Combined monitoring as a guide for prophylaxis and treatment. *J Bone Joint Surg Am* (1976) 58: 933–939.
11. Harris WH, Athanasoulis C, Waltman AC and Salzman EW: Cuff-impedance phlebography and <sup>125</sup>I fibrinogen scanning versus roentgenographic phlebography for diagnosis of thrombophlebitis following hip surgery. *J Bone Joint Surg Am* (1976) 58: 939–944.
12. Moskovitz PA, Ellenberg SS, Feffer HL, Kenmore PI, Neviasser RJ, Rubin BE and Varma VM: Low dose heparin for prevention of venous thromboembolism in total hip arthroplasty and surgical repair of hip fractures. *J Bone Joint Surg Am* (1978) 8: 1067–1070.
13. Fujita S, Hirota S, Oda T, Kato Y, Tsukamoto Y and Fuji T: Deep venous thrombosis after total hip or total knee arthroplasty in patients in Japan. *Clin Orthop Relate Res* (2000) 375: 168–174.
14. Shiota N, Sato T, Nishida K, Matsuo M, Takahara Y, Mitani S, Murakami T and Inoue H: 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: 444–450.
15. Fuji T, Fujita S and Ochi T: Fondaparinux prevents venous thromboembolism after joint replacement in Japanese patients. *Int Orthop* (2008) 32: 443–451.
16. Yukizawa Y, Inaba Y, Watanabe S, Yajima S, Kobayashi N, Ishida T, Iwamoto N, Choe H and Saito T: Association between venous thromboembolism and plasma levels of both soluble fibrin and plasminogen-activator inhibitor 1 in 170 patients undergoing total hip arthroplasty. *Acta Orthopaedica* (2012) 83: 14–21.
17. Shimoyama Y, Sawai T, Tatsumi S, Nakahira J, Oka M, Nakajima M, Jotoku T and Minami T: Perioperative risk factors for deep vein thrombosis after total hip arthroplasty or total knee arthroplasty. *J Clin Anesth* (2012) 24: 531–536.
18. Sugano N, Miki H, Nakamura N, Aihara M, Yamamoto K and Ohzono K: Clinical efficacy of mechanical thromboprophylaxis without anticoagulant drugs for elective hip surgery in an Asian population. *J Arthroplasty* (2009) 24: 1254–1257.