

Incidence and Clinical Characteristics of Deep Vein Thrombosis (DVT) after Total Knee Arthroplasty (TKA) with DVT Chemoprophylaxis

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Abstract

Objective: Deep vein thrombosis (DVT) after total knee arthroplasty (TKA) is very common and leading cause of death due to this procedure. The objective of this study was to investigate the incidence and clinical characteristics of DVT after TKA with DVT chemoprophylaxis. Methods: This is a prospective cohort study in single institution. The patients received postoperative DVT chemoprophylaxis (low molecular weight heparin (LMWH) or Fondaparinux), followed by duplex ultrasonography to check for DVT 1 - 2 weeks after TKA. The clinical characteristics were summarized and analysed by chi-square test and regression analysis. Results: Five hundred and thirty four patients were enrolled from January 2007 to December 2010. DVT chemoprophylaxis was administered in 524 (98.1%) of the 534 patients. DVT occurred in 9 subjects (1.69%); 8 subjects had DVT in the leg, and 1 subject had a pulmonary embolism. Among them, asymptomatic DVT was observed in 5 patients (0.94%). Univariate analysis showed that surgical methods (revision, P = 0.0007), body mass index (BMI) (>25, P = 0.0028), low platelet count (less than 150×10^3 , P = 0.0219), time in the intensive care unit (ICU) (P < 0.0001), no administration of prophylactic LMWH (P = 0.0392), and a history of DVT (P < 0.0001) were significant risk factors of DVT. Conclusions: The incidence of DVT was 1.69% after TKA with prophylactic antithrombotic therapy. Revision surgery, BMI, low platelet count, time in ICU, absence of prophylactic LMWH and history of DVT were significant risk factors of DVT.

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Keywords

Venous Thromboembolism, Thromboprophylaxis, Low Molecular Weight Heparin, Anticoagulation, Total Knee Arthroplasty

1. Introduction

In the United States and Europe, venous thromboembolism has gained attention due to the associated morbidity, mortality, and increased treatment costs. Guidelines for deep vein thrombosis (DVT) prophylaxis are being proposed [1]-[4]. For total hip replacement (THR) or total knee arthroplasty (TKA) in the orthopedic department, DVT prophylaxis is strongly recommended because, in its absence, the incidence of venous thromboembolism (VTE) is very high. Although the true incidence of venous thromboembolism in patients with injuries such as hip fractures is under dispute, DVT prophylaxis is still suggested [1]-[7]. In Asia, on the other hand, there is no consensus or agreement on the use of DVT prophylaxis, Furthermore, many orthopedic surgeons worry about postoperative bleeding with DVT chemoprophylaxis, and thus, it is administered arbitrarily. Recent studies performed in Asia reported that the observed incidences of venous thromboembolism were 50%, 9.8% - 64.3%, and 11.3% - 76.5% for pelvic fractures, THA, and TKA, respectively, when DVT prophylaxis was not administered. These results are similar to other studies performed in the United States and Europe [8]-[18]. Using the Asian Registry of Thrombosis [19], a study utilizing 2420 subjects who were not given a DVT prophylaxis found symptomatic venous thromboembolism in 2.3% of patients [55 patients, 99% confidence interval (CI): 1.6, 3.2]. In cases of TKA, symptomatic venous thromboembolism was exhibited in 1.4% of patients. Similarly, a high incidence of venous thromboembolism, especially in TKA cases (40.4%), was observed after major orthopedic surgery in a recent study [20] with 363 Korean patients. But, the incidence of DVT after TKA and DVT chemoprophylaxis in Asia were rarely reported so far. Here, we aimed to identify the incidence and clinical characteristics of DVT after total knee arthroplasty with DVT chemoprophylaxis.

2. Methods

This study was designed as prospective cohort study. The patient who received total knee arthroplasty de novo or as a follow-up surgery (revision) at Seoul St. Mary's Hospital from 2007 to 2010 was included in this study. The patient received DVT chemoprophylaxis and was followed by duplex scan 1 - 2 weeks after TKA. IRB (institutional review board) approval was obtained prior to the study. For DVT chemoprophylaxis, low molecular weight heparin (LMWH, Enoxaparin) or Fondaparinux (mg) was administered before and after surgery in patients who underwent TKA without leg edema. Duplex ultrasonography was carried out within 1 - 2 weeks (average 8.7 days) after the surgery to confirm the presence or absence of iliofemoral and below knee DVT. The registered vascular technician examined the iliac vein, femoral vein, popliteal vein, tibial veins, peroneal veins and calf muscle veins in both legs. The DVT in the iliofemoral vein was considered as proximal vein DVT and the DVT in below the knee vein was considered distal vein DVT. When pulmonary embolism (PE) was suspected, a diagnosis was conducted via pulmonary arterial computed tomography. The clinical characteristics of patients (Gender, age, surgery types, BMI clinical records, history of thrombotic vein thrombosis, and comorbid diseases, including malignant cancers) were investigated through medical and imaging records. Statistical analyses were performed by chi-square test and regression analysis using SAS software (version 9.3).

3. Results

Five hundred thirty four patients were enrolled from January 2007 to December 2010. **Table 1** represents the demographic information of the 534 patients. Most of the patients with TKA were females (90.45%), with a mean age of 68.7 years. DVT chemoprophylaxis (LMWH in 241 subjects (46%) and Fondaparinux in 283 subjects (56%)) was administered in 524 subjects (98.1%). Furthermore, 366 subjects (68.5%) concurrently wore compression stockings. Hypertension (60.86%) was the most common comorbid disease, followed by diabetes (19.5%), cardiovascular diseases (9.36%), and malignant cancers (5.81%). The mean length of stay was 13.2 days (0 - 733 days). DVT occurred in 9 subjects (1.69%); among them, 8 subjects had DVT in the leg and 1

Table 1. Baseline characteristics of the subjects $(n = 534)$.	Table 1	. Baseline	charac	teristics	of th	e subjects	(n = 1)	534)).
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		Average and standard deviation or rate (%)
Gender (M/F)		51(9.55)/483(90.45)
Age		68.72 ± 9.13
Duration of admission		11.93 ± 9.53(5 - 76)
The state of the s	Primary total knee replacement	479(89.70)
Types of operation	Revision surgery	55(10.30)
Body mass index (kg/m ²)		25.99 ± 3.89
	Hematocrit (%)	37.86 ± 4.02(14.10 - 49.30)
Laboratory findings	Platelet count (×10 ³)	$243.59 \pm 72.88 (34.4 - 664.0)$
	Serum creatinine level (mg/dl)	0.98 ± 1.81(0.34 - 24.40)
Compression stockings-wearing		366(68.54)
Administration of prophylactic anticoag	ulation	524(98.13)
	Enoxaparin	241(45.99)
Kinds of prophylactic anticoagulation	Fondaparinux	283(54.01)
	Diabetes	104(19.48)
	Hypertension	325(60.86)
	Past history of tuberculosis	6(1.12)
	Coronary artery disease	50(9.36)
Comorbidities	Cerebrovascular disease	19(3.56)
Comorbidities	Chronic renal failure	11(2.06)
	Chronic obstructive pulmonary diseases	8(1.50)
	Malignancies	31(5.81)
	Hyperlipidemia	9(1.69)
	Personal history of venous thromboembolism	1(0.19)

subject had a PE. Five patients (0.94%) showed asymptomatic DVT (**Table 2**). Proximal DVT occurred in 4 patients and distal DVT occurred in 4 patients. The patient with PE didn't have DVT in the legs during DVT evaluation. In univariate analysis of 9 patients with DVT and 525 patients without DVT, surgical methods (revision, P = 0.0007), BMI > 25 (P = 0.0028), low platelet count (less than 150×10^3 , P = 0.0219), length of admission in the intensive care unit(ICU) (P < 0.0001), administration of prophylactic anticoagulation (P = 0.0392), and history of DVT (P < 0.0001) were determined to be significant factors affecting the occurrence of DVT in the leg (**Table 3**).

4. Discussion

DVT is the leading cause of in-hospital death in the United States. However, it is a preventable disease, and its mortality rate can be lowered through prevention. As such, US surgeons have prepared guidelines to reduce the morbidity and mortality caused by venous thromboembolism [21]. The following references contain the current guidelines for the prevention of venous thromboembolism [1]-[5]; The ACCP recommendations are universally accepted and are actively updated [2] [3]. Following THA and TKA, administration of drugs such as LMWH, fondaparinux, apixaban, dabigatran, rivaroxaban, low-dose unfractionated heparin (LDUH), and adjusted-dose

hromboembolism (n = 534).				
Type of Embolism	No. of Patients (%)			
Symptomatic/Asymptomatic DVT	3/5(0.56/0.94)			
Distal DVT	4(0.75)			
Proximal DVT	4(0.75)			
Symptomatic PE	1(0.19)			
Total VTE	9(1.69)			

Table 2. Number and incidence of symptomatic or asymptomatic venous thromboembolism (n = 534).

Proximal DVT: iliofemoral DVT; Distal DVT: Below knee vein DVT.

Table 3. Characteristics of patients with and without deep venous thrombosis or pulmonary embolism.

Parameters		DVT or PE group $(n = 9)$	Control group ($n = 525$)	P value
Female gender		7(77.78)	476(90.67)	0.1291
Age ≥ 65 yr		8(88.89)	383(72.95)	0.2844
Hospital stay over 2 wks		3(33.33)	88(16.76)	0.1899
Revision Sugery		4(44.44)	51(9.71)	0.0007
$BMI \ge 25 \ (kg/m^2)$		1(11.11)	317(60.38)	0.0028
	Hematocrit < 38%	6(66.67)	250(47.62)	0.2567
Laboratory findings	Platelet count $< 150 \times 10^3$	3(33.33)	52(9.90)	0.0219
	Serum creatinine > 1.2 (mg/dl)	2(22.22)	94(17.90)	0.7380
ICU stay		3(33.33)	15(2.86)	< 0.0001
Use of compression stockings		6(66.67)	360(68.57)	0.9029
Administration of prophylactic anticoagulation		8(88.89)	516(98.29)	0.0392
Prophylactic anticoagulation (Enoxaparin/Fondaparinux)		6(66.67)	235(44.76)	0.1904
	Diabetes	2(22.22)	102(19.43)	0.8338
	Hypertension	5(55.56)	320(60.95)	0.7422
	Coronary artery disease	0(0.00)	50(9.52)	0.3308
	Cerebrovascular disease	0(0.00)	19(3.62)	0.5611
Comorbidities	Chronic renal failure	0(0.00)	11(2.10)	0.6608
	Chronic obstructive pulmonary diseases	0(0.00)	8(1.52)	0.7090
	Malignancies	1(11.11)	30(5.71)	0.4924
	Hyperlipidemia	0(0.00)	9(1.71)	0.6920
	Personal history of venous thromboembolism	1(11.11)	0(0.00)	< 0.0001
Local complication		1(11.11)	22(4.19)	0.3106

VKA is strongly recommended for at least 10 days for antithrombotic prophylaxis (Grade 1B). Furthermore, the recommendations suggest extending the administration of such drugs by more than 2 weeks, up to 5 weeks (35 days) (Grade 2B). Recently, recommendations have also been provided by Asia [22], including Japan [23] and Korea [24]. However, due to limited study results, they have used the ACCP recommendations as a base, with necessary modifications. To determine the effects of antithrombotic propylaxis, it is necessary to differentiate

not only symptomatic VTE but also asymptomatic VTE. In the present study, duplex ultrasonography was conducted within 8.7 days, on average, after the surgery, before discharge from the hospital. ACCP recommendations suggest ultrasound screening by Doppler after orthopedic surgery prior to hospital discharge (Grade 1B). However, ultrasonography immediately after surgery is not generally recommended [25]. Based on a study of 1435 patients in 2 trials, bilateral venography results, which were performed within 7 ± 2 days of surgery and followed by ultrasonography 1 day after surgery, showed that the specificity of ultrasonography was high (93%, 95% confidential interval 91.0% - 95.1%) while the sensitivity was very low (31.1%, CI 23.4% - 38.9%). In a study performed by Barnes et al. [26], the screening results of DVT using duplex ultrasonography were compared with the one by venography in asymptomatic patients after THA and TKA: The authors reported that the sensitivity and specificity of duplex ultrasonography were 86% and 97%, respectively. Antithrombotic prophylaxis after orthopedic surgery also seemed effective in the present study. As described in Table 2, the frequency of symptomatic and asymptomatic DVT patients was very low (0.56% and 0.94%, respectively). A past study found that the incidence of VTE was 1.69%; a lower incidence of 1.53% (8 subjects/524 subjects) was shown when excluding 10 patients without prophylaxis. Quinlan et al. [27] summarized 10 studies (5796 subjects) in which 30 mg b.i.d. or 40 mg o.d. enoxaparin was administered for 7 - 10 days prophylactically, followed by venography. The authors reported that the incidence of asymptomatic DVT in THA and TKA was 13.2% (proximal 3.0%, distal DVT 10.0%) and 38.1% (proximal 5.7%, distal DVT 32.2%), respectively. In this study, proximal DVT (0.75%) and distal DVT (0.75%) were similar to each other and the results were notably lower than that of the study by Quinlan et al. [27]. In a study by Xing et al. [28], who combined 4 large studies (4423 subjects), the occurrence of total DVT and proximal DVT after TKA surgery tended to decrease when the number of patients who received thromboprophylaxis increased; however, such a trend was not observed after THA surgery (r = -0.75, P = 0.031; r = -0.86, P = 0.007, respectively). Based on several meta-analyses, DVT and PE were lowered remarkably, by 40% - 69% and 46% - 61%, respectively, with LMWH antithrombotic prophylaxis after orthopedic surgery. In particular, TKA showed a more pronounced decrease in incidence [29] [30]. As prophylaxis was performed for most of the cases in the present study, it was difficult to quantify its impact on the incidence rate. Kannan et al. [31] found that administration of enoxaparin or utilization of IPC significantly reduced the incidence of DVT in Asian subjects. In the study, 440 patients with TKA were randomly classified into 4 groups of 110 subjects each, including (1) no prophylaxis, (2) graduated compression stockings (GCS), (3) intermittent pneumatic compression (IPC), and (4) LMWH (enoxaparin); DVT prevalence was investigated in these groups. Groups (1), (2), (3), and (4) showed 24%, 14%, 9%, and 6% DVT prevalence, respectively, indicating that the IPC and LMWH groups had significantly low DVT prevalence than that of the control group. Additionally, a greater than 2-fold difference in bleeding complication was exhibited in the LMWH group compared to the IPC group (4 subjects vs. 9 subjects), suggesting that utilization of IPC in Asian subjects was more reasonable. The ACCP recommendations also demonstrated that the VTE prophylactic effects of IPC utilization were equivalent to the prophylactic effects of drug administration after orthopedic surgery. However, IPC should be portable and be used more than 18 hours/day. Because of such reasons, compliance is low; in particular, as it is difficult to use continuously after hospital discharge, it is recommended to use as either in combination with prophylactic drug treatments during hospitalization or replacements for patients with bleeding risk [2] [3] [32]. In the present study, there was no difference in the utilization of LMWH when combined with additional GCS. Of that 524 patients who received LMWH, 361 subjects and 163 subjects either used or did not use a GCS in combination, respectively. The VTE incidence was 1.38% (5 subjects) in subjects using a GCS and 1.22% (2 subjects) in those that did not, although this was not a statistically significant difference. Even if the present study did not utilize the combined IPC, the utilization of LMWH combined with IPC would be effective, based on a previous study demonstrating that the prophylactic effects of VTE is more pronounced with LMWH+IPC than with LMWH LMWH+GCS [33], further supported by multiple recent recommendations. In this study, the incidence of VTE was significantly affected by length of stay at the intensive care unit (Table 2); the incidence of VTE during a short stay, 1 - 2 days, was 7.6% (1 of 13) while the incidence during a long stay, more than 3 days, was 40% (2 of 5).

Risk Factors

Based on a univariate analysis of this study, surgical types, BMI, platelet count, visit to the intensive care unit (ICU), and history of VTE were shown as risk factors.

Elective TKA and revision showed incidence rates of 1.3% and 14.2% in subjects who were placed in intensive care, respectively. In addition, there were differences in the mean length of ICU stay, 1.83 days in the group of Elective TKA vs. 3.5 days in the group of revision, indicating that the difference in VTE incidence is because of intensive care placement status as well as the duration of the stay based on the type of surgery. The factors that are most commonly reported as risk factors, including long-term hospitalization (more than 2 weeks), female, elderly (older than 65 years), cardiovascular disease, and malignant tumors were shown to be weakly associated based on the results of this study. Unexpectedly, BMI was smaller in the DVT group; this may be a statistical error due to the considerably low DVT incidence, unlike other studies, especially due to the relatively lower morbid obesity rate compared to the West. According to a SMART study [19] and Markovic-Denic et al. [34], chronic heart failure, varicose veins, and a history of VTE were independent risk factors. In an ENDORSE (Epidemiologic International Day for the Evaluation of Patients at Risk for Venous Thromboembolism in the Acute Hospital Care Setting) study [35], the primary risk factor for DVT in surgical patients prior to hospitalization was obesity (10%), followed by chronic heart failure (9%), chronic pulmonary disease (8%), and presence of varicose veins or venous insufficiency (7%); following hospitalization, the highest risk factors were complete immobilization (39%) followed by ICU stay (23%). Our results support that motor impairments and ICU stay after orthopedic surgery are the most significant risk factors for VTE.

5. Conclusion

The incidence of DVT was 1.69% after TKA surgery with DVT chemoprophylaxis in this study. Revision surgery, BMI, low platelet count, time in ICU, absence of prophylactic LMWH and history of DVT were significant risk factors of DVT. DVT chemoprophylaxis was effective to prevent DVT compared to previously reported incidence of DVT without DVT chemoprophylaxis. This rate is relatively low compared to studies conducted in the West. Therefore, prospective multicenter and randomized studies regarding VTE prophylactic treatments need to be performed in the future. In particular, detailed studies are warranted with regards to the length of ICU stay and the frequency of VTE to find effective treatments for patients who are expected to stay in an ICU.

References

- National Institute for Health and Clinical Excellence (NICE) (2007) Venous Thromboembolism: Reducing the Risk of Venous Thromboembolism (Deep Vein Thrombosis and Pulmonary Embolism) in Inpatients Undergoing Surgery. NIGE, London.
- [2] Geerts, W.H., Bergqvist, D., Pineo, G.F., et al. (2008) Prevention of Venous Thromboembolism: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest, 133, 381S-453S. http://dx.doi.org/10.1378/chest.08-0656
- [3] Guyatt, G.H., Akl, E.A., Crowther, M., et al. (2012) Executive Summary: Antithrombotic Therapy and Prevention of thrombosis. Chest, 141, 7S-47S. <u>http://dx.doi.org/10.1378/chest.1412S3</u>
- [4] (2007) American Academy of Orthopaedic Surgeons Clinical Guideline on Prevention of Symptomatic Pulmonary Embolism in Patients Undergoing Total Hip or Knee Arthroplasty. Adopted by the American Academy of Orthopedic Surgeons Board of Directors. www.aaos.org/research/guidelines/PE_guideline.pdf
- [5] Nicolaides, A.N. (2001) Prevention of Venous Thromboembolism. International Consensus Statement. Guidelines Compiled in Accordance with the Scientific Evidence. *International Angiology*, 20, 1-37. http://dx.doi.org/10.1177/000331970105200101
- [6] Goel, D.P., Buckley, R., de Vries, G., et al. (2009) Prophylaxis of Deep-Vein Thrombosis in Fractures below the Knee: A Prospective Randomized Controlled Trial. Journal of Bone and Joint Surgery—British Volume, 91, 388-394. http://dx.doi.org/10.1302/0301-620X.91B3.20820
- [7] Johnson, R., Carmichael, J.H., Almond, H.G., et al. (1978) Deep Venous Thrombosis Following Chamley Arthroplasty. Clinical Orthopaedics and Related Research, 132, 24-30.
- [8] Kim, Y.H. (1990) The Incidence of Deep Vein Thrombosis after Cementless and Cemented Knee Replacement. *Journal of Bone and Joint Surgery—British Volume*, 72B, 779-83.
- [9] Yoo, M.C., Kang, Y.H., Kim, Y.H., et al. (1997) A Prospective Study on the Use of Nadroparin Calcium in the Prophylaxis of Thromboembolism in Korean Patients Undergoing Total Hip Replacement. International Orthopaedics, 21, 399-402. <u>http://dx.doi.org/10.1007/s002640050194</u>
- [10] Kim, Y.H., Choi, I.Y., Park, M.R., et al. (1997) Deep Vein Thrombosis after Uncemented Total Hip Replacement.

Bulletin of the Hospital for Joint Diseases, 56, 133-139.

- [11] Moon, K.H., Kim, W.H. and Lee, J.Y. (1998) Deep Vein Thrombosis after Cementless Total Hip Replacement Arthropasty Using Doppler Ultrasound. *Journal of the Korean Orthopaedic Association*, **33**, 1553-1559.
- [12] Song, E.K., Kim, J.K., Lee, K.B. and Seon, J.K. (1998) Deep Vein Thrombosis after Total Knee Replacement. Incidence and Correlation with Clinical Risk Factors. *Journal of Korean Knee Society*, 10, 18-22.
- [13] Kim, Y.H. and Kim, J.S. (2002) Incidence and Natural History of Deep-Vein Thrombosis after Total Knee Arthroplasty: A Prospective, Randomized Study. *Journal of Bone and Joint Surgery*, 84B, 566-570. http://dx.doi.org/10.1302/0301-620X.84B4.12330
- [14] Dhillon, K.S., Askander, A. and Doraismay, S. (1996) Postoperative Deep-Vein Thrombosis in Asian Patients Is Not a Rarity. A Prospective Study of 88 Patients with No Prophylaxis. *Journal of Bone and Joint Surgery*, 78B, 427-430.
- [15] Fujita, S., Hirota, S., Oda, T., Kato, Y., Tsukamoto, Y. and Fuji, T. (2000) Deep Venous Thrombosis after Total Hip or Total Knee Replacement in Japan. *Clinical Orthopaedics and Related Research*, 375, 168-174.
- [16] Wang, C.J., Wang, J.W., Chen, L.M., Chen, H.S., Yang, B.Y. and Cheng, S.M. (2000) Deep Vein Thrombosis after Total Knee Arthroplasty. *Journal of the Formosan Medical Association*, 99, 848-853.
- [17] Fong, Y.K., Ruban, P., Yeo, S.J., Lee, B.P., Lo, N.N., Seow, K.H. and Ng, S.C. (2000) Use of Low Molecular Weight Heparin for Prevention of Deep Vein Thrombosis in Total Knee Arthroplasty. A Study of Its Efficacy in an Asian Population. *Annals of the Academy of Medicine, Singapore*, 29, 439-441.
- [18] Piovella, F., Wang, C.J., Lu, H., Lee, K., Lee, L.H., Lee, W.C., et al. (2005) Deep-Vein Thrombosis Rates after Major Orthopedic Surgery in Asia. An Epidemiological Study Based on Postoperative Screening with Centrally Adjudicated Bilateral Venography. *Journal of Thrombosis and Haemostasis*, **3**, 2664-2670. http://dx.doi.org/10.1111/j.1538-7836.2005.01621.x
- [19] Leizorovicz, A., Turpie, A.G.G., Cohen, A.T., Wong, L., Yoo, M.C., Dans, A., et al. (2005) Epidemiology of Venous Thromboembolism in Asian Patients Undergoing Major Orthopedic Surgery without Thromboprophylaxis. The SMART Study. Journal of Thrombosis and Haemostasis, 3, 28-34. <u>http://dx.doi.org/10.1111/j.1538-7836.2004.01094.x</u>
- [20] Cha, S.I., Lee, S.Y., Kim, C.H., Park, J.Y., Jung, T.H., Yi, J.H., et al. (2010) Venous Thromboembolism in Korean Patients Undergoing Major Orthopedic Surgery: A Prospective Observational Study Using Computed Tomographic (CT) Pulmonary Angiography and Indirect CT Venography. *Journal of Korean Medical Science*, 25, 28-34. http://dx.doi.org/10.3346/jkms.2010.25.1.28
- [21] US Department of Health and Human Services (2008) The Surgeon General's Call to Action to Prevent Deep Vein Thrombosis and Pulmonary Embolism. http://www.surgeongeneral.gov/topics/deepvein/calltoaction/call-to-action-on-dvt-2008.pdf
- [22] Cohen, A.T. (2010) Asia-Pacific Thrombosis Advisory Board Consensus Paper on Prevention of Venous Thromboembolism after Major Orthopaedic Surgery. *Thrombosis and Haemostasis*, **104**, 919-930. <u>http://dx.doi.org/10.1160/TH10-03-0190</u>
- [23] Mashio N. (2004) Japanese Guidelines for Prevention of Venous Thromboembolism. Journal of Japan Society for Clinical Anesthesia, 24, 480-487. <u>http://dx.doi.org/10.2199/jjsca.24.480</u>
- [24] Bang, S.M., Jang, M.J., Oh, D., Kim, Y.K., Kim, I.H., Yoon, S.S., et al. (2010) Korean Guidelines for the Prevention of Venous Thromboembolism. *Journal of Korean Medical Science*, 25, 1553-1559.
- [25] Schellong, S.M., Beyer, J., Kakkar, A.K., Halbritter, K., Eriksson, B.I., Turpie, A.G.G., et al. (2007) Ultrasound Screening for Asymptomatic Deep Vein Thrombosis after Major Orthopaedic Surgery: The VENUS Study. Journal of Thrombosis and Haemostasis, 5, 1431-1437. <u>http://dx.doi.org/10.1111/j.1538-7836.2007.02570.x</u>
- [26] Barnes, W.R., Nix, M.L., Barnes, C.L., Lavender, R.C., Golden, W.E., Harmon, B.H., et al. (1989) Perioperative Asymptomatic Venous Thrombosis: Role of Duplex Scanning versus Venography. Journal of Vascular Surgery, 9, 251-260. <u>http://dx.doi.org/10.1016/0741-5214(89)90044-X</u>
- [27] Quinlan, D.J., Eikelboom, J.W., Dahl, O.E., Eriksson, B.I., Sidhu, P.S. and Hirsh, J. (2007) Association between Asymptomatic Deep Vein Thrombosis Detected by Venography and Symptomatic Venous Thromboembolism in Patients Undergoing Elective Hip or Knee Surgery. *Journal of Thrombosis and Haemostasis*, 5, 1438-1443. http://dx.doi.org/10.1111/j.1538-7836.2007.02571.x
- [28] Xing, K.H., Morrison, G., Lim, W., Douketis, J., Odueyungbo, A. and Crowther, M. (2008) Has the Incidence of Deep Vein Thrombosis in Patients Undergoing Total Hip/Knee Arthroplasty Changed over Time? A Systematic Review of Randomized Controlled Trials. *Thrombosis Research*, **123**, 24-34. <u>http://dx.doi.org/10.1016/j.thromres.2008.05.005</u>
- [29] Leizorovicz, A., Haugh, M.C., Chapuis, F.R., Samama, M.M. and Boissel, J.P. (1992) Low Molecular Weight Heparin in Prevention of Perioperative Thrombosis. *British Medical Journal*, **305**, 913-920. <u>http://dx.doi.org/10.1136/bmj.305.6859.913</u>

- [30] Eikelboom, J.W., Quinlan, D.J. and Douketis, J.D. (2001) Extended-Duration Prophylaxis against Venous Thromboembolism after Total Hip or Knee Replacement: A Meta-Analysis of the Randomised Trials. *The Lancet*, 358, 9-15. <u>http://dx.doi.org/10.1016/S0140-6736(00)05249-1</u>
- [31] Kanaan, A.O., Silva, M.A., Donovan, J.L., Roy, T. and Al-Homsi, A.S. (2007) Meta-Analysis of Venous Thromboembolism Prophylaxis in Medically III Patients. *Clinical Therapeutics*, 29, 2395-2405. http://dx.doi.org/10.1016/j.clinthera.2007.11.015
- [32] Struijk-Mulder, M.C., Ettema, H.B., Verheye, C.C. and Büller, H.R. (2010) Comparing Consensus Guidelines on Thromboprophylaxis in Orthopedic Surgery. *Journal of Thrombosis and Haemostasis*, 8, 678-683. http://dx.doi.org/10.1111/j.1538-7836.2009.03728.x
- [33] Silbersack, Y., Taute, B.M., Hein, W. and Podhaisky, H. (2004) Prevention of Deep-Vein Thrombosis after Total Hip and Knee Replacement: Low Molecular-Weight Heparin in Combination with Intermittent Pneumatic Compression. *Journal of Bone and Joint Surgery*, 86, 809-812. <u>http://dx.doi.org/10.1302/0301-620X.86B6.13958</u>
- [34] Markovic-Denic, L., Zivkovic, K., Lesic, A., Bumbasirevic, V., Dubljanin-Raspopovic, E. and Bumbasirevic, M. (2012) Risk Factors and Distribution of Symptomatic Venous Thromboembolism in Total Hip and Knee Replacements: Prospective Study. *International Orthopaedics*, 36, 1299-1305. <u>http://dx.doi.org/10.1007/s00264-011-1466-5</u>
- [35] Cohen, A.T., Tapson, V.F., Bergmann, J.F., Goldhaber, S.Z., Kakkar, A.K. and Deslandes, B. (2008) Venous Thromboembolism Risk and Prophylaxis in the Acute Hospital Care Setting (ENDORSE Study): A Multinational Cross-Sectional Study. *The Lancet*, **371**, 387-394. <u>http://dx.doi.org/10.1016/S0140-6736(08)60202-0</u>



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