



Venous thromboembolism prophylaxis in major orthopaedic surgery: A multicenter, prospective, observational study

Majör ortopedik cerrahilerde venöz tromboemboli profilaksisi: Çokmerkezli, prospektif, gözlem çalışması

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Amaç: Ülkemizde majör ortopedik cerrahi (MOC) için farmakolojik profilaksi uygulanan hastalarda venöz tromboembolizm (VTE) risk faktörleri, kullanılan profilaksi yöntemleri ve klinik bulgu veren derin ven trombozu (DVT) ve pulmoner emboli (PE) sıklığı araştırıldı.

Çalışma planı: Prospektif, çokmerkezli, açık, müdahalesiz bir gözlem çalışması planlanarak, 21 merkezden 899 hasta çalışmaya alındı. Olguların 316'sında (%35.2) total kalça protezi (TKP), 328'inde (%36.5) total diz protezi (TDP), 255'inde (%28.4) kalça kırığı (KK) cerrahisi uygulandı. Tüm hastalarda farmakolojik DVT profilaksisine başvuruldu.

Sonuçlar: Olguların %73.2'sinde VTE risk faktörleri vardı. En sık görülen risk faktörleri obezite (%72) ve uzamış immobilizasyon (%36.3) idi. Profilaksi için olguların %91.1'inde düşük molekül ağırlıklı heparin, %8.9'unda fondaparinux kullanıldı. Olguların 273'üne (%30.4) kısa dönem, 626'sına (%69.6) uzun dönem profilaksi uygulandı. Mekanik profilaksi 610 olguda (%67.9) elastik çorap ile, 67 olguda (%7.5) aralıklı hava basınç cihazı ile uygulandı. Üç aylık takip sonucunda sekiz olguda (%0.9) klinik bulgu veren DVT, dört olguda (%0.4) PE gelişti. Mortalite 10 olguda (%1.1) görüldü. Kanama komplikasyonu sekiz olguda (%0.9) majör, 40 olguda (%4.5) minör idi.

Çıkarımlar: Etkin VTE profilaksi yapıldığında MOC'de klinik bulgu veren DVT ve PE oranları düşük olmaktadır.

Anahtar sözcükler: Antikoagülan/terapötik kullanım; artroplasti, replasman, kalça; artroplasti, replasman, diz; ameliyat sonrası komplikasyonu; risk faktörü; tromboembolizm; venöz tromboz.

Objectives: We investigated risk factors for venous thromboembolism (VTE), prophylaxis measures employed, and incidence of symptomatic deep venous thrombosis (DVT) and pulmonary embolism (PE) in patients undergoing major orthopaedic surgery (MOS).

Methods: An open, multicenter, prospective, observational study was conducted in 21 medical centers, comprising 899 patients. Of these, 316 patients (35.2%) underwent total hip arthroplasty (THA), 328 patients (36.5%) underwent total knee arthroplasty (TKA), and 255 patients (28.4%) underwent surgery for hip fractures (HF). Pharmacologic prophylaxis was employed in all the patients.

Results: Risk factors for VTE were seen in 73.2% of the patients, the most common being obesity (72%) and prolonged immobilization (36.3%). Low-molecular-weight heparin (91.1%) and fondaparinux (8.9%) were used for prophylaxis, which was short-term in 273 patients (30.4%) and long-term in 626 patients (69.6%). Mechanical prophylaxis was performed with compression stockings in 610 patients (67.9%) and by intermittent pneumatic compression in 67 patients (7.5%). During three-months of follow-up, symptomatic DVT and PE were seen in eight (0.9%) and four patients (0.4%), respectively. Mortality occurred in 10 patients (1.1%). Complications of major and minor bleeding were seen in eight (0.9%) and 40 (4.5%) patients, respectively.

Conclusion: Effective VTE prophylaxis is associated with low risk of clinically apparent DVT and PE in MOS.

Key words: Anticoagulants/therapeutic use; arthroplasty, replacement, hip; arthroplasty, replacement, knee; postoperative complications; risk factors; thromboembolism; venous thrombosis.

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Total hip arthroplasty (THA), total knee arthroplasty (TKA), and hip fracture (HF) surgery, which are referred to as major orthopaedic surgery (MOS), are common interventions in the practice of orthopaedics and traumatology. Venous thromboembolism (VTE) is one of the complications which occurs in patients undergoing such procedures.^[1]

Postoperative deep venous thrombosis (DVT) and pulmonary embolism (PE) can be fatal. The rate of DVT is 45% to 57% after THA, 41% to 85% after TKA, and 46% to 60% after HF surgery if prophylaxis is not used.^[2, 3] As VTE prophylaxis, pharmacologic and mechanical prophylaxis methods can be used.

Although dextran, aspirin, and low-dose heparin were used in the past as pharmacologic methods, they are currently not preferred as first-line agents because of their controversial efficacies and the risks they bear.^[3, 4] In the last three decades, introduction of low-molecular weight heparin and the subsequent use of synthetic pentasaccharides in recent years enabled prophylaxis with effective and safe agents. Early mobilization, compression stockings, and intermittent pneumatic compression (IPC) can be used for mechanical prophylaxis. The rate of DVTs and PEs are between 2% and 24% following effective mechanical and pharmacologic thromboprophylaxis.^[5, 6]

The aim of the present study was to determine the VTE risk factors, prophylactic methods used, and the incidence of symptomatic DVTs and PEs in patients scheduled for MOS and who received pharmacologic prophylaxis in Turkey.

Patients and methods

A prospective, multicenter, open, non-interventional, observational study was planned and 21 centers in Turkey conducting more than 50 MOSs annually participated in the study. After obtaining approval from the local ethics committee of the coor-

inating center, a meeting with the investigators was conducted. A follow-up of 3 months was planned for each patient enrolled between March 2005 and March 2006, and the study commenced.

The inclusion criteria were determined as patients above 18 years of age who underwent MOS and were administered pharmacologic DVT prophylaxis. Exclusion criteria were not defined since the study was planned as a non-interventional, observational study. Five assessments were conducted for each patient: prior to the operation within the first 3 postoperative days, on discharge, on discontinuation of prophylaxis, and 3 months after surgery. Patients were assessed preoperatively in terms of sociodemographic characteristics, physical examinations, and VTE risk factors. After the surgery, operational data, vital findings, laboratory data, DVT prophylaxis and its complications, development of DVTs and PEs, and bleeding were evaluated. Nine hundred ninety-two patients from 21 centers were enrolled, each center contributing 4-50 patients. Ninety-three patients in whom the type of operation was not clearly defined or who were not assessed preoperatively were excluded from the study; therefore, 899 patients were evaluated.

Results

The MOSs performed and the distributions of the patients' mean age and gender are presented in Table 1. Three hundred sixteen patients (35.2%) underwent THA, 328 patients (36.5%) underwent TKA, and 255 patients (28.4%) underwent surgery for a HF. The primary diagnosis was osteoarthritis in 67.1% and 88.9% of the patients who underwent total hip and knee arthroplasties, respectively. Of the proximal femur fractures, 92.7% were caused by trauma, and 4.4% also had hip osteoarthritis.

Risk factors of venous thromboembolism

VTE risk factors existed in 73.2% of the patients. The observed frequencies for these risk factors in pa-

Table 1. Major orthopaedic surgeries and gender distribution

	General			Female		Male	
	Number	Percentage	Mean age	Number	Percentage	Number	Percentage
Total	899		64.2	665	74.0	234	26.0
Total hip arthroplasty	316	35.2	57.4	225	71.2	91	28.8
Total knee arthroplasty	328	36.5	65.6	279	85.1	49	14.9
Hip fracture	255	28.4	70.4	161	63.1	94	36.9

Table 2. Risk factors for venous thromboembolism

	Number	%
Obesity (body mass index >25 kg/m ²)	647	72.0
Prolonged immobilization (>72 hours)	326	36.3
Smoking	131	14.6
Venous insufficiency	110	12.2
Inflammatory disease	90	10.0
Congestive heart disease	86	9.6
History of surgery within the last 3 months	58	6.5
Chronic respiratory failure	55	6.1
Cancer	19	2.1
History of deep venous thrombosis or pulmonary embolism	13	1.5

tients undergoing THA, TKA, and HF surgery were 60.4%, 75.3%, and 86.3%, respectively. The most commonly encountered risk factors were obesity, prolonged immobilization, smoking, and venous insufficiency. Most patients had more than one risk factor (Table 2). Obesity was the most commonly observed risk factor in patients undergoing THA and TKA, and prolonged immobilization was most commonly observed in patients undergoing HF surgery.

When the threshold for obesity was accepted as 25 kg/m², 225 (71.2%) of the patients undergoing THA, 278 (84.8%) of the patients undergoing TKA, and 144 (56.5%) of the patients undergoing HF surgery were obese. When immobilization > 72 hours following surgery was considered as prolonged immobilization, 80 patients (25.3%) in the THA group, 77 patients (23.5%) in the TKA group, and 169 patients (66.3%) in the HF group had prolonged immobilization (Table 3).

Four hundred eighty-two patients (53.6%) general, 298 patients (33.2%) had spinal anesthesia, and 129 patients (14.4%) had epidural anesthesia.

For pharmacologic VTE prophylaxis, low-molecular-weight heparin (LMWH; enoxaparin, nad-

roparin, dalteparin, and tinzaparin) and fondaparinux were administered in 91.1% and 8.9% of the patients, respectively. As mechanical prophylaxis, compression stockings were used in 610 patients (67.9%), whereas IPC was used in only 67 patients (7.5%).

Prophylaxis was initiated in 449 patients (49.9%) before the surgery and in 450 patients (50.1%) after the surgery. Two hundred seventy-three patients (30.4%) were administered short-term prophylaxis and 626 patients (69.6%) were administered long-term prophylaxis; prophylaxis was terminated prematurely in 5.7% of the patients.

Eight patients (0.9%) developed DVTs and 4 patients (0.4%) developed PEs. Of the DVT cases, 6 in the TKA group and 2 in the HF group, 4 occurred within 10 days and the remaining 4 cases occurred after discharge. The diagnosis of DVT was based on a swollen thigh and limb. In three cases, the diagnosis was confirmed by Doppler ultrasonography. The risk factors for DVTs were obesity in three patients, obesity and prolonged immobilization in one patient, obesity and a history of a DVT in one patient, and prolonged immobilization in two patients. Obesity and prolonged immobilization were the most commonly encountered risk factors. Pharmacologic prophylaxis consisted of LMWH in seven patients and synthetic pentasaccharide in one patient who developed DVTs.

Two PEs occurred in the TKA group and two PEs occurred in the HF group. The diagnosis of PE was established by computerized tomography in three patients and by clinical findings in one patient. In all cases, PEs developed within the first 5 days and the patients had a positive response to treatment. Of the PE cases, one patient had obesity, one patient had prolonged immobilization and smoking, and one patient had a history of a malignancy. One patient did not have any risk factors for a VTE. Pharmacologic prophylaxis was administered to all the patients who

Table 3. Rates of obesity and prolonged immobilization as a risk factor of venous thromboembolism in major orthopaedic surgeries

	Number	Obesity		Immobilization	
		Number	Percentage	Number	Percentage
Total	899	647	72.0	326	36.3
Total hip arthroplasty	316	225	71.2	80	25.3
Total knee arthroplasty	328	278	84.8	77	23.5
Hip fracture	255	144	56.5	169	66.3

developed PEs with LMWH.

Death occurred in 10 patients (1.1%; 2 patients in the TKA group and 8 patients in the HF group). Sudden death occurred in two cases; nine deaths occurred in the hospital and one death occurred at home. The causes of deaths were reported to be cardiac causes in six cases, renal failure in one case, and the cause of death was not determined in three cases. An autopsy was not performed in any of the cases.

The number of cases requiring blood transfusion during surgery was 487 (54.2%). Wound site haematomas developed in 5 cases (0.6%), two of which required re-operation. In addition, intracerebral haemorrhage was observed in 3 cases (0.3%), minor bleeding was observed in 40 cases (4.5%), and thrombocytopenia was observed in 1 case (0.1%).

Discussion

DVT and PE are clinically significant, and even fatal complications commonly occurring in patients undergoing elective THAs and TKAs and urgently performed cases with HFs. Taking preventive measures are essential. Although the importance of preventing DVTs is well-known by orthopaedic surgeons, standardized prophylaxis is still lacking. This prospective study is the first and largest study performed in Turkey on this topic.

The present study was carried out in 21 centers conducting > 50 MOSs annually. In most of these centers, the target number was reached; however, one center contributed only four cases. Thirteen centers reached the target of 50 cases and the other centers contributed 31 or more cases. It was realized that efficient monitoring by the coordinator center and the controller company were important factors in reaching the specified target.

VTE risk factors, originally described by Virchow in 1956 and which are valid today, include stasis, endothelial damage, and hypercoagulability. Advanced age in the majority of the cases undergoing MOS, obstructed circulation, and endothelial damage in the vessels caused by the positioning of the leg during the operation are major risk factors for the development of a DVT. According to Beksac et al. [6], the risk of VTE is 11.7-fold higher in patients undergoing MOS. Therefore, studies of DVT prophylaxis are often focused on this group of patients [7-10]. We also selected patients

undergoing THA and TKA and those with HF as the study group.

The distribution of the 899 cases in the THA, TKA, and HF groups was comparable (35.2%, 36.5%, and 28.4%, respectively). The primary diagnosis was osteoarthritis in 67.1% and 88.9% of the patients in the THA and TKA groups, respectively; this finding is consistent with the literature. [11]

When the VTE risk factors were evaluated in patients undergoing MOS, 73.2% of the patients had a risk factor, and the most commonly encountered risk factors were found as obesity, prolonged immobilization, smoking, and venous insufficiency. Smoking and venous insufficiency, which are considered minor risk factors for VTE [6, 12], were found among the common risk factors in our study.

Obesity is a risk factor for VTE. Lowe et al. [12] reported that patients with a body mass index (BMI) > 30 kg/m² had a 2.04-fold higher risk of DVT, whereas White et al. [13] reported that the risk is 1.8-fold higher in patients with a BMI > 25 kg/m². Beksac et al. [6] reported that 379 of 1908 cases (19.8%) undergoing THA were obese; and 9 of 39 cases (23%) who developed DVTs and PEs were obese. In the present study, the rate of obesity was 71.2% and 84.8% in patients undergoing THAs and TKAs, respectively, and 56.5% in patients with HFs. Of 12 cases, who developed DVT and PE, 6 (50%) had obesity.

Immobilization is also an important risk factor. Heit et al. [14] demonstrated a 3.04-fold higher risk of DVTs in patients with paresis or paralysis. In another study, immobilization up to 14 days due to bed rest was associated with 5.6-fold higher risk of VTE, and patients confined to wheelchair or bed, depending on the duration, had 1.73 to 5.64-fold higher rates of DVTs [15]. In the present study, the mean age of patients in the HF group was 70.4 years; the rate of immobilization before and after the surgery was higher in this group (66.3%). Of 12 patients who developed DVTs and PEs, 5 (41.7%) had prolonged immobilization.

Varicose veins are known to be a risk factor for VTE. This risk is inversely related with varicose veins and age. The rate of VTE declines with increasing age. If varicose veins exist, the rate of DVT is 4.2-fold higher at 45 years of age, 1.9-fold higher at 60 years of age, and 0.9-fold higher at 70 years of age [6]. Heit et al. [14] reported smoking to be a minor risk factor for VTE

due to its negative effect on the vascular endothelium. In the present study, the presence of varicose veins and smoking were common risk factors of VTE during the pre-operative evaluation; however, of the patients who developed VTEs, only 1 patient (8.3%) had these risk factors.

As a pharmacologic prophylaxis, LMWH and fondaparinux were administered in 91.1% and 8.9% of the patients, respectively. This prophylaxis was short-term (7-10 days) in 30.4% of the patients and long-term (21-35 days) in 69.6% of the patients. Planes et al.^[16] indicated that long-term prophylaxis is required in patients undergoing THAs. Patients with HFs were reported to have a lower rate of DVTs with long-term prophylaxis due to their old age and late mobilization.^[2, 5, 10, 13] Based on the guidelines of the American College of Chest Physicians (ACCP)^[2] and the European consensus statement (ICS)^[17], LMWH, fondaparinux, and coumadin are recommended for VTE prophylaxis in THAs and TKAs and in patients with HFs.^[2] The pharmacologic prophylaxis method used in this study was in accordance with the international guidelines.

Among mechanical prophylaxis methods to prevent VTEs, compression stockings and IPC devices are adjuvant methods according to the guidelines of the ACCP and should not be used as a single method.^[2] In the present study, these methods were administered as an adjuvant to pharmacologic prophylaxis. Compression stockings were used in 67.9% of the patients and an IPC was used in 7.5% of the patients. The reason why compression stockings were not used in all patients was the higher number of obese patients, who are not suitable for compression stockings. Low rates of IPC use could be attributed to the absence of IPC devices in a center, refusal of administration by the patients, and physician discretion. In patients receiving enoxaparin after THA, the rate of DVT determined by venography or ultrasonography has been reported to range between 2.8% and 20%.^[5, 6, 18, 19] This rate is between 2.1% and 27.8% in patients undergoing TKA^[5, 20] who were administered LMWH and between 19.1 and 30.4% in patients with HFs who were administered LMWH.^[8, 10, 20] The patients undergoing THA in this study did not develop symptomatic DVTs; however, 1.8% of the patients undergoing TKAs and 0.8% of the patients with HFs developed DVTs. Absence of DVTs and PEs in patients undergoing THAs is thought to be related to the inability to establish a clinical diagnosis. The pati-

ents were followed clinically without performing routine venography or ultrasonography. The rate of symptomatic DVT is approximately 1% to 2% in MOSs.^[13] The rate in the current study was 0.9% when all of our cases were considered.

In patients receiving prophylaxis with vitamin K antagonists or standard heparin, monitoring for the risk of major bleeding is mandatory. However, monitoring is not necessary when LMWH or fondaparinux is administered. The rate of wound site or distant major bleeding following MOS is 1% to 3%.^[3, 21, 22] In the current study, 5 cases (0.6%) developed haematomas and 3 cases (0.3%) developed intracerebral haemorrhage. Re-operation was required in 2 cases (0.2%) due to wound site haematomas. The total rate of major bleeding in our cases was 0.9%. The rate of minor bleeding is reported to be 2% to 4% in the literature.^[3, 21] In the present study, the rate of minor bleeding was 4.5%, which is consistent with the literature.

Thrombocytopenia is observed with a rate of 2% to 4% in patients receiving long-term standard heparin, while the rate is < 2% in patients receiving LMWH.^[3] In the present study, only 1 patient (0.1%) with thrombocytopenia was observed. The lower than expected rate of thrombocytopenia was attributed to an inability to document the subclinical cases.

In THA procedures using VTE prophylaxis, the in-hospital mortality rate is 0.09%^[21] and the mortality rate within 90 days is 0.22% to 0.34%.^[5, 23] This rate is 0.1% to 0.15% in TKA procedures.^[20, 23] The overall mortality rate in MOS is 0.2% to 5%.^[2, 11] In the present study, the mortality rate was 0% in THAs, 0.6% in TKAs, and 3.1% in patients with HFs, and the overall mortality was 1.1%. The higher mortality rate observed in patients with HFs compared to elective THAs and TKAs is consistent with the literature.

As a result of this study, it was determined that in Turkey the most common risk factors for DVTs and PEs in patients undergoing MOSs are obesity and prolonged immobilization. Pharmacologic prophylaxis is in accordance with the literature, and LMWH is the most commonly used pharmacologic agent for VTE prophylaxis. Use of an IPC device as an adjuvant mechanical prophylaxis method was lower than reported in the literature. The rate of symptomatic DVTs and PEs following MOS was 1.3% and the rate of major bleeding was 0.9%.

References

- Anderson FA Jr, Spencer FA. Risk factors for venous thromboembolism. *Circulation* 2003;107(23 Suppl 1):19-16.
- Geerts WH, Pineo GF, Heit JA, Bergqvist D, Lassen MR, Colwell CW, et al. Prevention of venous thromboembolism: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest* 2004;126(3 Suppl):338S-400S.
- Altintas F. Thromboembolism in hip and knee arthroplasties. [Article in Turkish] *Acta Orthop Traumatol Turc* 2000;34:100-9.
- Ercan S, Altıntaş F. Tromboembolizmin deklanstran 70 ile profilaksisi. *Göztepe Tıp Dergisi* 1987;2:31-5.
- Warwick D, Friedman RJ, Agnelli G, Gil-Garay E, Johnson K, FitzGerald G, et al. Insufficient duration of venous thromboembolism prophylaxis after total hip or knee replacement when compared with the time course of thromboembolic events: findings from the Global Orthopaedic Registry. *J Bone Joint Surg [Br]* 2007;89:799-807.
- Beksac B, Gonzalez Della Valle A, Salvati EA. Thromboembolic disease after total hip arthroplasty: who is at risk? *Clin Orthop Relat Res* 2006;(453):211-24.
- Turpie AG, Levine MN, Hirsh J, Carter CJ, Jay RM, Powers PJ, et al. A randomized controlled trial of a low-molecular-weight heparin (enoxaparin) to prevent deep-vein thrombosis in patients undergoing elective hip surgery. *N Engl J Med* 1986;315:925-9.
- Esemenli T. Kalça cerrahisinde derin ven trombozu insidansı. *Acta Orthop Traumatol Turc* 1991;25:34-8.
- Tokgözoğlu AM. Ortopedik açıdan tromboembolik hastalıklar ve profilaksisi. *Hacettepe Ortopedi Dergisi* 1992;2:42-5.
- Altintas F, Ipekoglu C, Konal A, Kuru LI. Color Doppler ultrasonography and venography for the detection of deep venous thrombosis in patients who had a fracture of the hip. [Article in Turkish] *Acta Orthop Traumatol Turc* 1995;29:197-201.
- Leizorovicz A, Turpie AG, Cohen AT, Wong L, Yoo MC, Dans A, et al. Epidemiology of venous thromboembolism in Asian patients undergoing major orthopedic surgery without thromboprophylaxis. The SMART study. *J Thromb Haemost* 2005;3:28-34.
- Lowe GD, Haverkate F, Thompson SG, Turner RM, Bertina RM, Turpie AG, et al. Prediction of deep vein thrombosis after elective hip replacement surgery by preoperative clinical and haemostatic variables: the ECAT DVT Study. European Concerted Action on Thrombosis. *Thromb Haemost* 1999;81:879-86.
- White RH, Zhou H, Romano PS. Incidence of symptomatic venous thromboembolism after different elective or urgent surgical procedures. *Thromb Haemost* 2003;90:446-55.
- Heit JA, Silverstein MD, Mohr DN, Petterson TM, O'Fallon WM, Melton LJ 3rd. Risk factors for deep vein thrombosis and pulmonary embolism: a population-based case-control study. *Arch Intern Med* 2000;160:809-15.
- Weill-Engerer S, Meaume S, Lahlou A, Piette F, Saint-Jean O, Sachtel A, et al. Risk factors for deep vein thrombosis in inpatients aged 65 and older: a case-control multicenter study. *J Am Geriatr Soc* 2004;52:1299-304.
- Planes A, Vochelle N, Darmon JY, Fagola M, Bellaud M, Huet Y. Risk of deep-venous thrombosis after hospital discharge in patients having undergone total hip replacement: double-blind randomised comparison of enoxaparin versus placebo. *Lancet* 1996;348:224-8.
- Nicolaides AN, Fareed J, Kakkar AK, Breddin HK, Goldhaber SZ, Hull R, et al. Prevention and treatment of venous thromboembolism. International Consensus Statement (guidelines according to scientific evidence). *Int Angiol* 2006;25:101-61.
- Lassen MR, Borris LC, Christiansen HM, Boll KL, Eiskjaer SP, Nielsen BW, et al. Prevention of thromboembolism in 190 hip arthroplasties. Comparison of LMW heparin and placebo. *Acta Orthop Scand* 1991;62:33-8.
- Colwell CW Jr, Collis DK, Paulson R, McCutchen JW, Bigler GT, Lutz S, et al. Comparison of enoxaparin and warfarin for the prevention of venous thromboembolic disease after total hip arthroplasty. Evaluation during hospitalization and three months after discharge. *J Bone Joint Surg [Am]* 1999;81:932-40.
- Hirsh J. *Fondaparinux*. Hamilton: B. C. Decker; 2007.
- Hull RD, Pineo GF, Stein PD, Mah AF, MacIsaac SM, Dahl OE, et al. Extended out-of-hospital low-molecular-weight heparin prophylaxis against deep venous thrombosis in patients after elective hip arthroplasty: a systematic review. *Ann Intern Med* 2001;135:858-69.
- Patel VP, Walsh M, Sehgal B, Preston C, DeWal H, Di Cesare PE. Factors associated with prolonged wound drainage after primary total hip and knee arthroplasty. *J Bone Joint Surg [Am]* 2007;89:33-8.
- Howie C, Hughes H, Watts AC. Venous thromboembolism associated with hip and knee replacement over a ten-year period: a population-based study. *J Bone Joint Surg [Br]* 2005;87:1675-80.