Bölüm 2

CLINICAL AND DIAGNOSTIC OVERVIEW OF DEEP VEIN THROMBOSIS

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INTRODUCTION

Deep vein thrombosis (DVT) is a term used to describe thrombosis that occurs in the deep veins of the lower or upper extremities, as well as in the visceral, cerebral veins, or vena cava. DVT can be asymptomatic or present with clinical manifestations of varying degrees up to pulmonary embolism. It is a part of venous thromboembolism, together with pulmonary embolism, which is the third most common cause of mortality from cardiovascular diseases after heart attack and stroke. Recurrent thrombosis and postthrombotic syndrome are the most important causes of morbidity in DVT (1,2).

DVT usually occurs in the deep veins of the lower extremities and proximal veins of the iliofemoral segment. Its incidence is approximately 10% in upper extremity deep veins, visceral, cerebral veins, or vena cava (3). Lower extremity DVTs are classified as proximal and distal, and this classification is important for treatment planning. Venous thrombosis in the anterior tibial vein, peroneal vein and posterior tibial vein distal to the popliteal vein is called distal DVT; Venous thrombosis in the popliteal vein and its proximal superficial femoral vein, deep femoral vein, common femoral vein and external iliac veins is called proximal DVT.

Epidemiology

Venous thromboembolism (VTE) is a clinical picture that includes deep vein thrombosis (DVT) and pulmonary embolism (PE). The mean annual incidence of venous thromboembolism is around 104-183 per 100,000 person/year (4,5). Its incidence rises to 68/1,000 in high-risk cases (6).

The incidence of DVT has been reported as 5 cases per 10000 people per year in the general population. Elderly patients are more likely to be seen. The incidence has been reported as 2-3 cases per 10000 people in the age range of 30-49, and 20 cases per 10000 people in the age range of 70-79 (3). It is more common in men than in women (1,2:1) (7). It is also very rare in those younger than 15 years old.

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DVT is more common in hospitalized patients, occurring in 25% of patients who do not receive prophylaxis. It is also shown in the 1st place in preventable hospital deaths. It has been reported that 25000 people die annually in the UK as a result of DVT and pulmonary embolism (8). In a 5-year retrospective study by Sandler et al., the cause of death was 10% in all autopsies performed in the hospital, and deep vein thrombosis was found in 83% of patients who died due to pulmonary embolism (9).

In studies conducted with hospitalized patients with the diagnosis of DVT, 80% of DVTs were found to be proximal DVT and 20% distal DVT (10,11).

Etiology

Knowing the etiology of DVT well is important in terms of preventing morbidity and mortality by providing effective treatment or prophylaxis. As a result of studies, many risk factors have been identified (Table 1) and it is thought that risk factors act cumulatively for the formation of DVT (12).

Table 1. DVT Risk Factors

Acquired Risk Factors	Inherited Risk Factors
• Advanced age	• Factor V Leiden mutation
• Immobilization	• Antithrombin III deficiency
• Obesity	• Protein C and S deficiency
• Surgery	• Prothrombin gene mutation (G20210A)
• Trauma	• Dysfibrinogenemia
• History of venous thromboembolism	• Hyperhomocysteinemia
• Inflammatory diseases	• Plasminogen and plasminogen activation disorder
• Oral contraceptive use	
• Hormone replacement therapy	
• Cancer	
• Varicose veins	
• Antiphospholipid syndrome	
• Nephrotic syndrome	
• Central venous catheters	
• Intravenous drug use	

Advanced age

Advanced age is an independent risk factor for DVT. The risk of venous thrombosis increases after the age of forty, and the risk approximately doubles every decade thereafter. It is reported that the risk is 15 times higher than the age of 40 if you are over the age of 85. DVT is very rare in the pediatric age group and most often the cause is venous catheters (13).

Immobilization

Immobilization is an important risk factor initiating DVT. The main mechanism in the development of DVT due to immobilization is the slowdown in venous blood flow and the loss of the pump effect due to the inactivity of the leg muscles. The risk increases especially in immobilization lasting more than three days. With the same mechanism, the risk of developing DVT increases during long-term car or airplane journeys. Accompanying immobilization with other risk factors increases the risk of developing DVT exponentially.

Obesity

Obesity increases the risk of DVT depending on the accompanying risk factors. It is known that the risk due to immobilization increases in obese patients. DVT risk is doubled in patients with a body mass index > 30 kg/m2 (8).

Surgical

Surgical interventions are one of the important risk factors for DVT. The risk may increase depending on the type and duration of the surgical intervention. The risk of DVT is increased especially in orthopedic surgeries, neurosurgery operations, abdominal and gynecological cancer surgeries, and cardiovascular surgeries (14). Advanced age, obesity, history of venous thromboembolism and cancer are additional risk factors for postoperative DVT in the surgical patient group. In addition, the anesthesia procedure applied also affects the risk of DVT. It has been reported that the risk of DVT is lower after regional and spinal anesthesia compared to general anesthesia (15,16).

Trauma

The risk of DVT is high in traumatized patients. The risk of DVT in patients with major trauma is around 50%. In a study by Geerts et al. evaluating 716 major trauma patients, DVT was detected in 53.8% of patients with head and neck injuries, 62% of patients with spinal injuries, and 80% of patients with femur fractures (17). It has been reported that the risk of DVT after minor traumas is 3-5 times higher than in the normal population (18).

Venous Thromboembolism History

A previous history of venous thromboembolism is a strong risk factor for the development of DVT. Having a history of venous thromboembolism, especially in high-risk surgical procedures, increases the risk of post-operative DVT development eightfold (19). The probability of recurrence of DVT in the following years after postoperative DVT is low. The probability of developing DVT again after

spontaneous DVT is high. In a study by Prandoni et al., the probability of recurrence within the first 1 year after spontaneous DVT was found to be 5-15%, and the probability of recurrence within 4 years was found to be 25% (20).

Oral Contraceptive and Hormone Use

Oral contraceptive drugs and drugs used in hormone replacement therapy increase the risk of DVT due to the estrogen they contain. Estrogen acts by increasing the plasma levels of some of the coagulation factors (Factor II, Factor VII and Factor X) and lowering the plasma levels of Antithrombin III. These effects are drug dose dependent and the risk increases within 4 months after starting the drug and continues for 3 months after the drug is stopped (21).

Malignancy

Malignancy significantly increases the risk of DVT. Causes of thrombosis in these patients; direct vein invasion or compression, abnormal production of procoagulant factors (fibrinogen, Factor VIII), increased plasma levels and decreased fibrinolytic activity. The type of malignancy determines the degree of DVT risk. The risk of DVT is doubled in tumors of the ovary, uterus, brain, pancreas, and leukemias (22).

Thrombophilia

Factor V Leiden mutation, antithrombin III deficiency, protein C and S deficiencies, prothrombin G20210A mutation are rare inherited disorders of the coagulation system and are risk factors for DVT. Thrombophilia is shown as the cause in approximately 50% of spontaneous DVTs. Especially in young DVT cases (under 50 years of age), these hereditary disorders should not be forgotten and should be investigated. Factor V Leiden mutation is found in 5% of the general population. Heterozygous patients increase the risk of DVT 3 times compared to the normal population, and homozygous ones increase the risk 50-80 times (23).

Pathophysiology

Three basic pathogenetic mechanisms were described by Rudolf Virchow in 1856. This mechanism, known as the Virchow triad, consists of vascular endothelial damage, decrease in venous blood flow (venous stasis) and hypercoagulopathy.

Endothelial Damage

Endothelial cells play an important role in maintaining vascular hemostasis. Due to their cell surface structure and the products they secrete, they create anticoagulant, antiplatelet and fibrinolytic effects; In case of damage to the cell structure, the

expression of cellular adhesion molecules increases, the anticoagulant property is lost and their procoagulant properties appear, causing local clot formation (24).

Endothelial damage may occur as a result of major surgery, central or peripheral venous catheter insertion, intravenous injections, traumas, burns, lower extremity orthopedic surgeries, septicemia, inflammatory and degenerative diseases and may cause venous thrombosis (25).

Decrease in Venous Blood Flow (Venous Stasis)

Venous return is normally achieved by contraction of the venous valves and calf muscles. Venous return is impaired due to long-term travel, immobilization in the postoperative period, venous compressions due to tumor, pregnancy or obesity, congestive heart failure, acute myocardial infarction and left heart failures due to cardiomyopathy. In case of prolonged contact of blood with the vascular endothelium, the release of coagulation factor inhibitors is prevented. Afterwards, with the release of adenosine diphosphate from the blood cells, thrombus formation begins, especially in the pockets formed by the venous valves (venous valve sinuses) where the blood flow is the slowest and the flow is reversed (25). The vasodilator and myorelaxant effects of anesthesia applied during the surgery cause the muscle pumping effect to decrease, the venous blood flow to slow down, and thus the predisposition to the formation of thrombosis (26). Temporary immobilization of the extremities, especially after orthopedic surgeries, can also cause venous stasis and DVT by the same mechanisms.

Hypercoagulopathy

With hereditary thrombophilic defects such as antithrombin III deficiency, Factor V Leiden mutation, Protein C and S deficiency, prothrombin gene mutation, activated protein C resistance; Coagulation may increase and DVT may develop due to acquired thrombophilic defects such as previous DVT, pregnancy, oral contraceptive drug use, malignancies, nephrotic syndrome, and systemic lupus erythematosus (27). The thrombus that causes DVT usually begins to form in the calf veins and venous valve sinuses. In cases that predispose to thrombosis such as venous stasis, these thrombi start to grow with the adhesion of fibrin and erythrocytes to the platelets in the venous valves and damaged endothelium, and they extend proximally, causing complete occlusion of the venous vessel in a short time. Thrombus increases the venous pressure and capillary pressure, increases the transcapillary filtration rate and causes edema in the extremities. The thrombus formed in approximately 50% of the patients dissolves in 3 months and is recanalized. While the thrombus is adhered to the wall in the vein segment where it formed in the acute period, its proximal end is free in the blood flow, and there is a risk that the soft

thrombus may rupture and cause embolism in this period. The most serious and feared complication of DVT in the acute phase is pulmonary embolism.

Clinical Features

The clinical features of DVT vary according to the localization of the thrombosis. Pain, tenderness, discoloration (redness, pallor or bruising), temperature increase, swelling and pitting edema in the extremities are the main clinical signs and symptoms. Extremity pain is usually in the gastrocnemius region, increases with ambulation, is cramping, and precedes swelling. However, more than half of lower extremity DVTs are asymptomatic. Isolated distal DVTs are usually asymptomatic, but have a low risk of pulmonary embolism. If a distal DVT patient has symptoms, the thrombus progresses proximally within a week at a rate of 25% (28). In proximal DVTs, different degrees of obstruction and venous valve damage may occur depending on the size and localization of the thrombus. Severe pain, swelling and pitting massive edema may occur secondary to increased venous pressure in the obstruction of the iliac vein and common femoral veins. Approximately 50% of patients with symptomatic proximal DVT have silent pulmonary embolism at diagnosis, and 10% have symptomatic pulmonary embolism (29). In massive iliofemoral thrombosis, edema, pallor and pain in the extremity (phlegmasia alba dolens) or severe edema may result in cyanosis due to arterial compression and spasm, as well as motor deficit, severe pain, bulla formation, tissue necrosis (phlegmasia cerulea dolens) due to neural compression and this clinical picture. may progress to venous gangrene.

In patients with DVT, pain in the calf caused by passive dorsiflexion of the foot during physical examination is called the 'Homans sign'. In addition, pain with calf squeezing is the 'Tschmarke sign'; pain in the calf ballotma 'Ducuing sign'; Pain caused by squeezing the Achilles tendon 'Payr's sign'; pain in the leg with coughing or cramping in the calf with walking 'Neageli-Natis sign'; The occurrence of pain in the calf by applying pressure above the systemic pressure in the thigh with a sphygmomanometer is called the 'Löwenberg sign' (30). DVT complications; pulmonary embolism, chronic pulmonary hypertension, chronic venous insufficiency, venous ulcers, postthrombotic syndrome and recurrent venous thromboembolism.

Diagnosis

Accurate diagnosis is very important in order to prevent complications that may occur by planning and applying treatment without delay in DVT. Clinical signs and symptoms are found in less than 50% of patients, and therefore it is unreliable to diagnose with clinical signs and symptoms. In addition, the diagnosis can be con-

firmed by tests in 25% of patients with DVT signs and symptoms (29). It should not be forgotten that there are diseases such as cellulitis, lymphangitis, lymphedema, leg trauma, abscess, hematoma, superficial vein thrombosis, and rupture of a Baker's cyst in the differential diagnosis. Imaging methods such as clinical risk scoring, laboratory tests (D-Dimer test) and ultrasonography are required to confirm the diagnosis. Table 2 shows the Wells scoring system, which is frequently used today in the diagnosis of DVT(30). Figure 2 shows the DVT diagnosis algorithm.

Table 2. Modified Wells Scoring System

Clinical features	Score
Active cancer (treatment ongoing, treated within the last 6 months, palliative treatment being done)	1
Paralysis, paresis or lower extremity immobilization	1
Bed rest for more than 3 days or major surgery within 12 weeks	1
Localized tenderness throughout the deep venous system distribution	1
Whole leg swelling	1
Leg swelling greater than 3 cm relative to the asymptomatic leg (10 cm below the tibial tuberosity)	1
Symptomatic leg pitting edema	1
Collateral non-varicose superficial veins	1
Prior DVT	1
Presence of differential diagnoses with higher probability than DVT	-2
Score < 2 DVT unlikely	
Score ≥ 2 DVT possible	

The Wells scoring system aims to calculate the probability of DVT with a score between -2 and 9 according to clinical features. It classifies patients as 'DVT unlikely' (score <2) and 'DVT probable' (score ≥ 2). While scoring, if the patient has symptoms in both extremities, the extremity with more symptoms is evaluated. As seen in Figure 2, D-Dimer test is recommended for patients with 'DVT unlikely' according to Wells score. A negative D-Dimer test means no DVT. If the D-Dimer level is high, that is, if the test is positive, ultrasonography should be performed. A negative ultrasonography excludes the diagnosis of DVT, while a positive one makes the diagnosis of DVT and treatment should be started. Ultrasonography is recommended for patients with 'probable DVT' according to the Wells score. If ultrasonography is positive, DVT is diagnosed and treatment is started; but if it is negative, the diagnosis of DVT cannot be excluded because the efficiency of ultrasonography in the diagnosis of distal DVT is low. In this case, D-Dimer testing is recommended (29,32).

Laboratory

D-Dimer is a fibrin degradation product formed as a result of the fibrinolytic response to thrombus formation in the body. The D-Dimer test is used in the diagnosis of DVT as a fast, inexpensive and highly sensitive (94-96%) test. Although its sensitivity is high, its specificity (42-52%) is low. It also increases in cases such as advanced age, malignancy, inflammation, sepsis, surgery, trauma, and pregnancy (34). Due to its low specificity, D-dimer testing may help rule out DVT in clinically low-risk patients, especially when combined with the Wells scoring system or ultrasonography.

Display Methods

Contrast Venography

It is considered the gold standard in the diagnosis of DVT. After placing the catheter in the vein on the dorsal aspect of the foot and applying the tourniquet for compression to the proximal thigh, contrast material is injected through the catheter and serial radiographic images are obtained. Proximal and distal thrombi appear as filling defects radiographically. Its sensitivity has been reported to be 97% in leg veins and 70% in iliac veins (35). The most important complication is that it can cause DVT at a rate of 3% due to the tourniquet procedure. Today, it is not used as a first-line imaging method because it is an invasive procedure, contrast material reaction, kidney failure, risk of DVT development, and developments in other methods.

Compression Ultrasonography

It is the first preferred imaging method in the diagnosis of DVT. It is the most commonly used imaging method because it is not an invasive examination, is reproducible, and is cheaper than other imaging methods. In a meta-analysis by Pomero et al, the sensitivity of compression ultrasonography in the diagnosis of DVT was 96.1% and the specificity was 96.8% (36). Its effectiveness in the diagnosis of distal DVT is low. In a meta-analysis by Goodacre et al., the sensitivity of ultrasonography in the diagnosis of proximal DVT was 94.2% and 63.5% in distal DVT (36).

Computed Tomography

In computed tomography (CT) venography, the deep venous structures of the lower extremities are visualized by injecting contrast material through the venous route from the upper extremity. It provides highly accurate cross-sectional imaging for DVT. It is especially used in the diagnosis of proximal DVT in patients

with suspected pulmonary embolism, and pulmonary CT angiography can be performed simultaneously in these patients, and both DVT and pulmonary embolism can be quickly diagnosed with a single examination. The sensitivity of CT venography has been reported as 100% and specificity as 96.6% (38). The risk of developing kidney failure with contrast material reaction due to radiation exposure and contrast agent injection are known side effects.

Magnetic Resonance

Magnetic resonance (MR) venography is a noninvasive imaging method. It is especially used in the diagnosis of iliac vein thrombosis. The sensitivity of MR venography has been reported as 95% and the specificity as 91%. Its disadvantages are high cost and patient intolerance (39).

REFERENCES

1. Di Nisio M, van Es N, Buller HR. Deep vein thrombosis and pulmonary embolism. Lancet. 2016 Dec 17;388(10063):3060-3073.
2. Falck-Ytter Y, Francis CW, Johanson NA, Curley C, Dahl OE, Schulman S, et al. Prevention of VTE in orthopedic surgery patients: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012;141(2 Suppl):e278S–325S.
3. Fowkes FJ, Price JF, Fowkes FG. Incidence of diagnosed deep vein thrombosis in the general population. Eur J Vasc Endovasc Surg 2003;25:1-5.
4. T.C. Sağlık Bakanlığı ve Türk Nefroloji Derneği Ortak Raporu 2019. Erişim adresi: http://www.nefroloji. org.tr/folders/file/registry_2019.pdf
5. Murad MH, Elamin MB, Sidawy AN, Malaga G, Rizvi AZ, Flynn DN, et al. Autogenous versus prosthetic vascular access for hemodialysis: A systematic review and meta-analysis. J Vasc Surg 2008;48(5 Suppl):34S-47S.
6. Almasri J, Alsawas M, Mainou M, Mustafa RA, Wang Z, Woo K, et al. Outcomes of vascular access for hemodialysis: A systematic review and meta-analysis. J Vasc Surg 2016;64:236-
7. Kniffin WD Jr, Baron JA, Barrett J, Birkmeyer JD, Anderson FA Jr. The epidemiology of diagnosed pulmonary embolism and deep venous thrombosis in the elderly. Arch Intern Med. 1994 25;154:861-6.
8. National Institute of Clinical Excellence (NICE). Venous thromboembolism in the over 16's: reducing the risk of hospital-acquired deep vein thrombosis and pulmonary embolism. NICE Guideline NG89. 2018. London: NICE.
9. Sandler DA, Martin JF. Autopsy proven pulmonary embolism in hospital patients: are we detecting enough deep vein thrombosis? J R Soc Med. 1989 Apr;82(4):203-5.
10. Cogo A, Lensing AW, Prandoni P, Hirsh J. Distribution of thrombosis in patients with symptomatic deep vein thrombosis. Implications for simplifying the diagnostic process with compression ultrasound. Arch Intern Med 1993;153:2777-80.
11. Robert-Ebadi H, Righini M. Management of distal deep vein thrombosis. Thromb Res. 2017 Jan;149:48-55.

12. Bozkurt AK. Periferik arter ve ven hastalıkları ulusal tedavi kılavuzu 2016. İstanbul: Baycınar Tıbbi Yayıncılık; 2016.
13. Raskob GE, Angchaisuksiri P, Blanco AN, Buller H, Gallus A, Hunt BJ, et al. Thrombosis: a major contributor to global disease burden. Seminars in thrombosis and hemostasis. 2014;40(7):724-735.
14. White RH, Zhou H, Romano PS. Incidence of symptomatic venous thromboembolism after different elective or urgent surgical procedures. Thromb Haemost. 2003 Sep;90(3):446-55.
15. Cook TM, Baylis RJ, Marjot R. Prophylaxis of venous thromboembolism. Regional anaesthesia reduces thromboembolic morbidity. BMJ. 1997 Apr 26;314(7089):1282.
16. Yentis SM. Anaesthetic technique and deep vein thrombosis. Br J Hosp Med. 1990 Jan;43(1):83.
17. Geerts WH, Code KI, Jay RM, Chen E, Szalai JP. A prospective study of venous thromboembolism after major trauma. N Engl J Med. 1994 Dec 15;331(24):1601-6.
18. van Stralen KJ, Rosendaal FR, Doggen CJ. Minor injuries as a risk factor for venous thrombosis. Archives of Internal Medicine. 2008;168(1):21-26.
19. Samama MM. Epidemiology of risk factors of deep venous thrombosis (DVT) of the lower limbs in community practice: the SIRIUS study. Thromb Haemost 1993;69:763.
20. Prandoni P, Lensing AW, Cogo A, Cuppini S, Villalta S, Carta M, et al. The long-term clinical course of acute deep venous thrombosis. Ann Intern Med. 1996 Jul 1;125(1):1-7. Venöz ve Lenfatik Sistem Hastalıkları
21. World Health Organization Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception: Venous thromboembolism disease. Lancet 1995;346(8990):1575–82.
22. Rocha AT, Paiva EF, Lichtenstein A, Milani R Jr, Cavalheiro CF, Maffei FH. Risk assessment algorithm and recommendations for venous thromboembolism prophylaxis in medical patients. Vasc Health Risk Manag. 2007;3(4):533-53.
23. Connors JM. Thrombophilia Testing and Venous Thrombosis. N Engl J Med. 2017;377(12):1177-1187.
24. Yang X, Chang Y, Wei W. Endothelial Dysfunction and Inflammation: Immunity in Rheumatoid Arthritis. Mediators Inflamm. 2016;2016:6813016.
25. Stone J, Hangge P, Albadawi H, Wallace A, Shamoun F, Knuttien MG, et al. Deep vein thrombosis: pathogenesis, diagnosis, and medical management. Cardiovasc Diagn Ther. 2017 Dec;7(-Suppl 3):S276-S284.
26. Sun ML, Wang XH, Huang J, Wang J, Wang Y. [Comparative study on deep venous thrombosis onset in hospitalized patients with different underlying diseases]. Zhonghua Nei Ke Za Zhi. 2018 Jun 01;57(6):429-434.
27. Carroll BJ, Piazza G. Hypercoagulable states in arterial and venous thrombosis: When, how, and who to test? Vasc Med. 2018 Aug;23(4):388-399.
28. Kearon C. Natural history of venous thromboembolism. Circulation. 2003 Jun 17;107(23 Suppl 1):I22-30.
29. Demir M, Erdemli B, Kurtoğlu M, Ongen G. Ulusal Venoz Tromboembolizm Profilaksi ve Tedavi Kılavuzu. İstanbul: Cortex; 2010.
30. Shafer N, Duboff S. Physical signs in the early diagnosis of thrombophlebitis. Angiology. 1971 Jan;22(1):18-30.
31. Wells PS, Owen C, Doucette S, Fergusson D, Tran H. Does this patient have deep vein thrombosis? JAMA 2006;295:199-207.
32. Kruger PC, Eikelboom JW, Douketis JD, Hankey GJ. Deep vein thrombosis: update on diagnosis and management. Med J Aust. 2019 Jun;210(11):516-524.

33. Wells P, Anderson D. The diagnosis and treatment of venous thromboembolism. Hematology Am Soc Hematol Educ Program. 2013;2013:457-63.

34. Di Nisio M, Squizzato A, Rutjes AW, Buller HR, Zwinderman AH, Bossuyt PM. Diagnostic accuracy of D-dimer test for exclusion of venous thromboembolism: a systematic review. J Thromb Haemost. 2007 Feb;5(2):296-304.

35. 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):338S–400S.

36. Pomero F, Dentali F, Borretta V, Bonzini M, Melchio R, Douketis JD, et al. Accuracy of emergency physician-performed ultrasonography in the diagnosis of deep-vein thrombosis: a systematic review and meta-analysis. Thromb Haemost 2013;109:137–145.

37. Goodacre S, Sampson F, Thomas S, van Beek E, Sutton A. Systematic review and meta- analysis of the diagnostic accuracy of ultrasonography for deep vein thrombosis. BMC Med Imaging. 2005 Oct 3;5:6.

38. Watanabe H, Sekiya H, Kariya Y, Hoshino Y, Sugimoto H, Hayasaka S. The incidence of venous thromboembolism before and after total knee arthroplasty using 16-row multidetector computed tomography. J Arthroplasty 2011;26(8):1488–93.

39. Fraser DG, Moody AR, Morgan PS, Martel AL, Davidson I. Diagnosis of lower-limb deep venous thrombosis: a prospective blinded study of magnetic resonance direct thrombus imaging. Ann Intern Med 2002;136(2):89–98.