Review Article
Deep venous thrombosis: a literature review

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Abstract: Deep vein thrombosis (DVT) refers to the formation of thrombosis within the deep veins, dominantly occurring in the pelvis or lower limbs. This clinical syndrome has gained attention as one complication of DVT, pulmonary embolization, can be fatal. Therefore, early detection and systematic management of DVT and related complications are essential in clinical practice. As the clinical understanding of DVT-related diseases has improved over recent decades, in this review, we aim to summarize recent literature published within the past few years.

Keywords: Deep venous thrombosis

Introduction

Deep vein thrombosis (DVT) is defined as development of thrombosis within the deep veins of the pelvis or lower limbs [1]. Vessel endothelium injury causes sluggish blood flow, which promotes blood clot formation [2], and reduces venous blood flow, or in severe cases can induce pulmonary embolism (PE) as the thrombi move from the deep veins to the lungs via the vasculature. Since PE can be fatal in certain circumstances, early diagnosis of DVT and subsequent adequate treatment with anticoagulants is of great clinical significance [3]. However, because the clinical manifestations of DVT are unspecific, and it can be asymptomatic, early diagnosis is clinically challenging. During the past decade, new protocols for the early detection of DVT in patients at high risk have been developed. The aim of this review is to provide an update on the status of research into DVT and related complication such as PE for clinical professionals, by systematically summarizing evidence published between 2010 and 2016.

Epidemiology

DVT represents a significant healthcare burden worldwide. The prevalence of DVT is reported to be approximately 100 per 100,000 people per year [4], although incidence increases with age, and the incidence of both DVT and DVT recurrence is higher in men than women [5-7]. DVT is also more common in Black and Hispanic people than Caucasians [1].

Vascular aging is an important risk factor for the development of DVT. Moreover, children are considered to have insufficient thrombin formation capacity, higher anti-thrombin capacity in the vessel walls and higher alpha-2-macrogolobulin potential to inhibit thrombin [8]. However pregnancy, cesarean section, puerperium and the use of contraceptive agents are all also associated with higher incidence of DVT [9].

Risk factors

Development of DVT is increased by certain genetic or acquired risk factors [10], most commonly the following:

(1) Age. The incidence of DVT increases with age, and DVT is very rare in childhood [11].

(2) Orthopedic Surgery. DVT is more common in patients with lower limb fractures or after major orthopedic surgery. In these patients, DVT has been suggested to be associated with injury of vascular wall, immobility, and activated coagulation pathways [12].

(3) Trauma. Incidence of DVT is significantly higher in patients with lower extremity fractures

than those with trauma at other sites, such as the abdomen, face or thorax. DVT in trauma patients may be complicated, for example by the presence of early coagulopathy which may confound subsequent anticoagulation therapy [13], as well as by hypoperfusion and acidosis, in addition to resuscitative methods [14, 15]. Hence homeostasis of coagulation system shifts towards a pro-thrombotic state early after traumatic injury, highlighting the necessity of early thromboembolism prophylaxis [16]. Indeed, patients with major trauma are at an approximately six-fold increased risk of DVT in comparison to those with minor trauma [17].

(4) Cancer. Incidence of DVT is higher in patients with cancer, and the precise incidence of DVT varies according to the biological characteristics of the tumor. Moreover, patients undergoing active treatment for cancer, such as chemotherapy, have been associated with increased risk for DVT, perhaps due to inhibition of the plasma activities of protein C and S [18, 19].

(5) Other. Immobility, surgery, hospitalization, pregnancy and puerperium, hormonal therapy, obesity, inherited and acquired hypercoagulable states, anesthesia, myocardial infarction, past history of DVT, varicose veins, infections, inflammatory bowel disease, and renal impairment are common risk factors for DVT [20, 21]. However, central line, sickle cell disease, severe infections and hypercoagulability states were suggested to be potential risk factors for DVT in children [22].

Pathogenesis

As per the current knowledge, the causes of thrombosis include vessel wall injury, abnormal changes in blood constituents, and venous stagnation. These conditions can occur as a result of major orthopedic surgeries. The pathogenesis of DVT is currently considered to involve overexpression of thrombomodulin (TM) and endothelial protein C receptor (EPCR), and down-regulated Von Willebrand factor (vWF) level in the endothelial cells of deep veins, causing overreaction of anticoagulation and inhibiting the procoagulant activities in the venous endothelium [23]. For DVT induced by fracture or related surgeries of the lower-extremity, sluggish blood flow in the veins may contribute. In hip arthroplasties, for the exposure of femoral canal and acetabulum, the femoral vein may be tortuous and thus the blood

flow is obstructed, leading to endothelial injury. Moreover, the obstruction of blood flow in veins leads to aggregation of coagulation factors [24]. During knee arthroplasties, anterior subluxation of the tibia and the saw-related vibration may lead to endothelial injury as well. In addition, the perioperative immobility of the lower extremities is associated with abnormal venous stasis. Thrombosis occurring in the lower extremity can be categorized according to the veins affected proximal when the thigh veins or popliteal vein are concerned and distal when the calf veins are concerned. DVT in the proximal veins has been associated with serious and life threatening complications [25]. Interestingly, DVT was indicated to form most frequently in the distal calf veins instead of the proximal thigh or the pelvis veins [26]. However, larger thrombi generated from proximal veins were considered to be associated with higher risk of development of severe PE.

Clinical manifestations

History

Patients with DVT usually manifest as local pain, limb edema and swelling, although the clinical manifestations of DVT vary considerably between patients and can be symptomatic or asymptomatic, bilateral or unilateral, severe or mild. Edema of the effected extremities is a common specific symptom of DVT. Thrombus that do not completely obstruct the venous outflow are often asymptomatic. Thrombus involving the pelvic veins, the iliac bifurcation or the vena cava are usually associated with bilateral lower limb edema. Proximal incomplete occlusion often leads to mild bilateral edema of the extremities, and can be mistaken for edema caused by systematic diseases such as fluid overload, congestive cardiac failure, and hepatonephric deficiency. Pain along the deep veins in the medial aspect of the thigh suggest DVT [27]. Pain and/or tenderness, rather than pain confined to more specific areas does not usually indicate DVT and suggests another diagnosis. These symptoms are nonspecific, but pain following dorsiflexion of the foot (Homans sign) is observed in DVT [28].

Physical examination

Again, no specific symptom or collection of symptoms can accurately predict DVT. The suggestive symptom, Homans sign (namely calf

Table 1. The Wells scoring system for evaluating the probability of DVT (total score ranging from -2 to 9)

Variables	Point
Active cancer treated within last 6 months or in palliative care	+1
Paralysis, paresis, or recent immobilization of lower limbs with plaster	+1
Localized tenderness along the course of deep venous system	+1
Swelling of entire leg	+1
Calf swelling ≥ 3 cm increase in circumference over asymptomatic calf (measured 10 cm below tibial tuberosity)	+1
Unilateral pitting edema (in symptomatic leg)	+1
Dilated collateral superficial veins (non-varicose, in symptomatic leg)	+1
Previous history of diagnosed DVT	+1
Recently bedridden ≥ 3 days, or major surgery requiring regional or general anesthetic in the past 12 weeks	+1
Alternative diagnosis at least as likely as DVT	-2

pain on dorsiflexion of the foot), may facilitate the identification of DVT, nevertheless it is only seen in 50% of all DVT patients. Discoloration of the lower limbs may be observed, with reddish purple the most common, perhaps due to venous obstruction. In rare cases, there may be ileofemoral massive venous obstruction and the leg may become cyanotic, termed phlegmasia cerulea dolens ("painful blue inflammation"). Besides, edema can cause occlusion of venous outflow causing the leg to appear blanched. Pain, edema, and discoloration is described as phlegmasia alba dolens ("painful white inflammation") [29].

Diagnosis

Accurate and prompt diagnosis of DVT is necessary because thrombi left untreated can cause life threatening complication like PE; however conversely anticoagulation in the absence of thrombosis can be dangerous. The most well established evidence-based manner to diagnose DVT or venous thrombus embolism (VTE) is the comprehensive evaluation combining systematic clinical risk factors, symptoms and signs. The essential first step is to determine the patient's risk of DVT according to clinical features (including medical history and physical examinations). While many structured clinical probability scoring systems have been promoted to stratify patients, the most commonly recommended model that has been highly studied and widely applied is the Wells score [30]. Based on medical presentation and risk factors, the original Wells score model classified the patients with DVT into three groups (low-probability group, moderate-probability group, and high-probability group), with an estimated risk for DVT of 85%, 33% and 5%.

Nevertheless, in a subsequent study, Wells et al. further developed a simplified version for the diagnostic measures by categorizing patients with DVT into two groups: clinically unlikely to have DVT when the clinical score is ≤ 1, and clinically likely to have DVT when the clinical score is > 1 [31].

Wells scoring system

The items of Wells scoring system were shown in **Table 1** [32]. Patients with Wells scores of ≥ 2 have a 28% probability of developing DVT, while patients with Wells scores of < 2 have a 6% probability. Alternatively, patients can be categorized into three groups according to the individual Wells scores: high-probability group if Wells score > 2, moderate-probability group if Wells score = 1-2, and low-probability group if Wells score < 1, with likelihoods for developing DVT of 53%, 17%, and 5%, respectively.

D-dimer

As a degradation product of fibrin, D-dimer is a small protein present in the blood after a blood clot is degraded by fibrinolysis. It is so called because it consists of two cross-linked D segments of the fibrin protein. The presence of D-dimer reflects global activation of blood coagulation and fibrinolysis [33]. Serum levels of D-dimer may increase in clinical conditions where clots form, for instance surgery, trauma, cancer, sepsis, and hemorrhage, particularly in hospitalized patients [34]. Interestingly, these conditions are also correlated with greater risk of DVT.

The level of the D-dimer remains increased in patients with DVT for approximately 7 days. In patients that present late in the disease course,

when the clots formed and adhered, D-dimer may be detected at low levels. Likewise, patients with solitary DVT in the calf vein have a small clot load and lower levels of D-dimer, which may be below the sensitivity cut-off of the assay. This may account for the decreased sensitivity of the D-dimer assay in the context of defined DVT.

Although D-dimer cannot verify DVT diagnosis, it may be highly useful to rule out the DVT. For patients with a low to/or moderate probability of DVT according to Wells scoring, normal D-dimer examination results can help to exclude the diagnosis [35]. While in patients with high Wells scores, D-dimer may not applied to confirm the diagnosis, and diagnostic imaging examinations (compression ultrasound) is preferred [36]. Thus, if the D-dimer level is elevated, another diagnostic method, such as imaging, should be performed to confirm or exclude DVT [37]. The sensitivity of D-dimer for estimation of DVT is high (nearly 97%), with a relatively lower specificity (approximately 35%) [38]. Based on the results of previous diagnostic studies for DVT, D-dimer might be applied as a quick screening test for DVT if lower-extremity edema appears with negative clinicoradiological findings.

Serum D-dimer levels can be measured using three methods: 1) enzyme linked immunosorbent assay (ELISA); 2) latex agglutination assay; and 3) red blood cell whole blood agglutination assay (simpliRED).

These three assays have different specificities, sensitivities, and likelihood ratios. ELISAs control the relative rating through D-dimer assays for sensitivity and negative probability ratio [3]. For patients with low-probability DVT, the American College of Chest Physicians advices a D-dimer examination with moderate-to-high sensitivity or a compression ultrasound examination on the proximal veins [37]. However, the UK National Institute for Health and Care Excellence (NICE) recommends D-dimer measurement before ultrasound imaging on proximal veins [39]. For patients with moderate-likelihood DVT, a D-dimer testing with high sensitivity is preferred over whole-leg or compression vascular ultrasound examination [37]. The NICE guideline adopts a 2-point Wells score and does not switch to a moderate-probability group [39].

Coagulation profile

A coagulation profile study is needed to detect the overall hypercoagulability. A prolonged pro-thrombin time (PT) or activated partial thromboplastin time (APTT) may not indicate a low probability of DVT. DVT can progress regardless, with complete treatment of anticoagulation in 13% of patients.

There are seldom cases of DVT in which laboratory screening for these anomalies are essentially determined whenever DVT is diagnosed in patients < 50 years old, or in the presence of strong family history of coagulation disorder, or detection of DVT at unusual sites. These abnormalities include:

• Deficiency of protein S, protein C level.

• Decreased homocysteine level.

• Deficiency of antithrombin III (ATIII).

• Presence of prothrombin 20210A mutation, factor V Leiden and antiphospholipid antibodies [3].

Venous ultrasonography

Venous ultrasonography is the primary imaging modality for DVT diagnosis [40]. It is safe, non-invasive, and comparatively cheap. There are three mainstream modalities:

Compression ultrasound (CUS): Is the first and most commonly used imaging technique in DVT diagnosis [41]. CUS is a B-mode imaging and is widely used on the proximal deep veins, particularly the common femoral veins and the popliteal veins [3]. The sensitivity of the CUS in diagnosing proximal DVT is 94% and the specificity is 98% [42]. However the sensitivity is reduced in diagnosis of asymptomatic proximal DVT [43].

The sensitivity of CUS to identify distal DVT is comparatively low, at 57% [42], and is only 48% for diagnosing asymptomatic calf vein thrombosis. For proximal DVT, ultrasound has a certain predictive significance of 100% and 71% for symptomatic and asymptomatic cases, respectively, whereas the negative predictive value for symptomatic events is 100% and for asymptomatic events is 94% [16].

Duplex Doppler ultrasound: Is a B-mode imaging and Doppler waveform analysis tool. In duplex Doppler ultrasonography, normal venous blood flow is viewed as spontaneous, phasic with respiration, and can be enhanced by manual pressure [3]. In color Doppler ultrasonography, a pulsed signal is utilized to generate images. The unification of duplex Doppler ultrasonography and color Doppler ultrasonography is effective for identification of DVT in calf or iliac veins [44].

There are significant advantages of ultrasound imaging, including safety, no exposure to irradiation, non-invasive and inexpensive, and capable of differentiating DVT from other conditions like lymphadenopathy, superficial or intramuscular hematomas, femoral aneurysm, Baker's cysts, and superficial thrombophlebitis [3]. The limitations of ultrasound imaging include lower ability to diagnose distal thrombus [45], and edema, obesity, and tenderness can make compressing veins difficult. In addition, mechanical limitations like splinting and cast for immobilization make ultrasound imaging impossible.

Contrast venography

The primary and classic imaging method used for DVT diagnosis is contrast venography, a definitive diagnostic test for DVT involves cannulation and injection with noniodinated contrast medium (eg, Omnipaque) into the peripheral veins in the affected extremity. X-ray imaging is used to determine whether venous blood flow has been obstructed [46]. The most accurate cardinal and essential feature for the diagnosis of phlebothrombosis is intraluminal filling defects manifested in two or more views [47], and sudden cutoff of a deep status. It is very sensitive and specific, particularly for determining the DVT location and extent of clots. However, due to its relatively high cost, invasiveness, availability, and other limitations such as exposure to irradiation, potential risk of allergic reaction and renal deficiency, this test is rarely performed [48].

Computed tomography venography (CTV)

CTV routinely requires injection of contrast medium into the forearm veins, which is then imaged by helical computed tomography and allows the evaluation of DVT in lower extremities [48]. CTV can directly visualize the inferior vena cava, pelvic veins, and lower-extremity veins. As DVT is a major risk factor for PE, a single toll can minimize VTE work-up. However, this single inclusive imaging modality for VTE demands a considerable amount of iodinated contrast medium to produce adequate opacification of the pulmonary arteries, pelvic veins, and lower-extremity veins [49].

Magnetic resonance imaging (MRI)

MRI can be used in various ways. Some techniques (such as time-of-flight or phase-contrast venography) do not require contrast medium as they depend on the intrinsic possessions of blood flow. Nevertheless, vascular imaging is generally enhanced after the administration of contrast mediums (eg. IV gadolinium). This contrast mediums can be injected into the peripheral veins via the forearm veins or the dorsalis pedis veins for visualization of the lower-extremity veins [50]. MRI can also demonstrate DVT by directly imaging the thrombus due to the high signal generated by RBCs methemoglobin in the thrombus. While this noninvasive technique does not require injection of contrast mediums, nevertheless, MRI is not usually available for DVT evaluation in most institutions.

Guidance

Systematic assessment is required for DVT diagnosis.

Pretest probability is the first step, and can be achieved by calculating the Wells score. Where the Wells score $\leq$ 1 (DVT unlikely), then a D-dimer assay is requested. If the result is negative, DVT is excluded. However, if the D-dimer assay is positive, venous imaging ultrasound is indicated. If the venous ultrasound scan is negative, DVT can be excluded. If it is positive, DVT can be diagnosed.

If the assessment of pretest probability $\geq$ 2 then DVT is considered to be likely, venous scanning by ultrasound is indicated. If it is positive, DVT can be diagnosed. But if it is negative, D-dimer examination must be carried out. A negative D-dimer result can rule out the diagnosis of DVT. However, an abnormal D-dimer assay is an indication for repeated ultrasound in one week or venography.

CT scan and MR venograpghies have the same specificity and sensitivity as CUS in diagnosing

DVT. Nevertheless, those measures are indicated for situations wherever patients could not be assessed accurately by CUS or where thrombosis inside the pelvic veins, or inferior vena cava are suspected.

Contrast venography is the predication and reference pattern for diagnosing DVT and is confined for incidents where other tests are incapable of definitely confirming or excluding DVT [41].

Prevention

General risk factors for DVT can be clinically prevented. Especially, for patients admitted for elective or emergency surgery, a risk evaluation is necessary preoperatively. Warwick et al. proposed a safe and effective protocol for prevention of DVT which has been widely accepted by the surgeons and anesthetists [51].

General procedures [51]

• Anesthesia - Spinal or epidural anesthesia can enhance the blood flow and thus reduce the risk of DVT by approximately 50%. Additionally, for prevention of spinal hematomas, neuraxial anesthesia and chemical prophylaxis should be avoided to be given too close to surgery.

• Surgical technique - Meticulous operative manipulated skill can effectively reduce the release of thromboplastins. Prolonged torsion of main veins may cause endothelial injuries.

• Mobilization - Mobilization should be adopted in early stage postoperatively, which may improve the blood flow in veins.

Physical methods

• Graduated compression stockings - Graduated compression stockings can halve the incidence of DVT; the below-knee types and the above-knee types may have the similar effectivity, as long as the stockings are properly woven and well-fitted [41].

• Intermittent plantar venous compression - The weight bearing intermittently pressures on the venous plexus around the lateral plantar arteries, guaranteeing the normal flow of blood from the sole of the foot, and enhancing the venous blood flow in the leg. The mechanical foot-pump can mimic this physiological mecha-

nism providing intermittent plantar venous compression in bedridden patients. Previous studies have confirmed the thromboprophylaxis efficacy of this device in patients with hip fracture and patients who received hip arthroplasty or knee arthroplasty [41].

• Intermittent pneumatic compression of the leg - This device can facilitate the postoperative improvement of blood flow in the lower-extremity deep veins and prevent venous sluggish or stasis, and it has been widely used for prevention of DVT [52].

• Inferior vena cava filter - This filter is introduced percutaneously via the femoral vein and reach the inferior vena cava. This device can catch an embolus before the embolus travels to the lungs, effectively preventing PE. Especially in patients with high risk of DVT whereas anticoagulation therapy is contraindicated, inferior vena cava filters should be the preferred choice. However, clinicians should be aware of the potential complications, such as death from proximal coagulation, and strict indications should be highlighted. The indications of this mechanical prophylaxis for DVT include patients with hemorrhagic stroke, patients with recent or active gastrointestinal bleeding, and patients with hemostatic defects such as severe thrombocytopenia [53]. Inferior vena cava filters are contraindicated in patients with lower extremity ischemia caused by peripheral vascular disorders, as there may be risk of fibrinolysis and clot dislodgement [54].

Chemical methods

Unfractionated heparin, low-molecular-weight heparins (LMWH), Pentasaccharide (fondaparinux), and factor Xa inhibitors are the most effective chemical agents for prevention of DVT.

• Unfractionated heparin carries a risk of aggravated hemorrhage postoperatively, requires laboratory monitoring, and increases incidence of heparin-induced thrombocytopenia [55]. Therefore, it is not recommended in senile patients.

• Low molecular weight heparin (LMWH) is safer and more effective than unfractionated heparin due to its superior hematological and pharmacokinetic natures, and pharmaceutical monitoring is unnecessary during its adminis-

tration. Moreover, LMWH is associated with a lower risk of heparin-induced osteoporosis than unfractionated heparin as it might not affect the number and bioactivity of osteo-clasts. Pharmacologically, in comparison to unfractionated heparin, it inhibits factor Xa more substantially and antithrombin III less substantially [56]. LMWH is safe if used at the appropriate time before surgery, and at a lower dose in those with impaired renal function.

• Pentasaccharide is an anticoagulant with indirectly selective factor Xa inhibitory activity [3]. Its effectivity for preventing DVT is significant as LMWH, however it is associated with hemorrhagic complications and thus it should be avoided to be given too close to surgery (< 6-8 hours after surgery). This agent is secreted by kidney while metabolized by liver, the clinician should be aware of potential hepatonephric dysfunctions.

• Rivaroxaban is a direct inhibitor of factor Xa. It acts rapidly with a high bioavailability of 80% and a half-life period of 4-12 hours [57]. Rivaroxaban (recommended dose: 10 mg once daily) is superior to the LMWH for preventing DVT in patients who underwent orthopedic operations as shown in previous clinical phase III trials [58]. Another DVT trial has demonstrated that oral rivaroxaban is as effective for preventing recurrence of symptomatic VTE as the current standard regimens (such as LMWH, enoxaparin, fondaparinux, or oral vitamin K antagonist) [59]. For the post hospitalization prevention of DVT, injectable or oral medications can be effective and should be properly used. Some new agents (eg. apixaban and edoxaban) are still under clinical trials at present.

• Dabigatran is an oral direct competitive inhibitor of thrombin, which is directly absorbed from the gastrointestinal tract with a bioavailability of 5-6%. This agent has a half-life period of 8 hours following single dose and approximately 17 hours following multiple doses; the plasma concentration peaks at 2 hours [57]. It is secreted by kidney. Considering its low bioavailability, coagulation function monitoring may be unnecessary.

• Warfarin is representative Vitamin K antagonist. This agent can be used in any phase perioperatively and it is effective for preventing DVT [60]. Noteworthily, it is not advised as

thromboprophylaxis in antepartum as it can pass to the placenta and leads to teratogenicity and bleeding in the fetus [61]. During the administration of warfarin, it should be maintained at an international normalized ratio (INR) of 2-3.

• The usage of aspirin is controversial because of its relatively poor efficacy and the hemorrhagic risk. Additionally, aspirin can cause gastrointestinal irritation [62].

The optimal duration of thromboprophylaxis is still unknown. It should depend on individual coagulation state and relevant risks of DVT. As recommended in previous studies, patients who undergo major lower-extremity surgeries need prolonged antithrombus treatment of 10-35 days, particularly for those with high risks of DVT; even for the patients admitted with emergency disorders, antithrombus treatment should be continued until discharge [60].

Treatment

Left untreated, DVT can be complicated with PE and is associated with a high risk of recurrence at an early stage [63]. The risk of recurrence and post-thrombotic syndrome (PTS) constantly develop after the first incident of DVT [64]. The prevention of DVT progression or recurrence, emergent PE and progression of delayed complications like pulmonary hypertension and PTS initially depends on effective pharmacological application of unfractionated heparin, LMWH, or fondaparinux [3, 65]. The fundamental pharmacological approach in patients with DVT is to start with parenteral anticoagulants, either LMWH or unfractionated heparin, followed by long-term vitamin K antagonists (VKAs). Beginning parenteral anticoagulation in the acute phase is recommended before diagnostic tests for intermediate to high risk DVT patients [65].

The hematological and pharmacokinetic advantages of LMWH over unfractionated heparin provide a wide window of safety. Therefore, LMWH is recommended instead of unfractionated heparin for patients with DVT unless LMWH is contraindicated. Heparin is primarily given with warfarin, and aborted after at least 4-5 days, when the INR ranges from 2.0 to 3.0 [3]. Extended INR occurs due to the impact of depressed factor VII levels.

Once intense anticoagulation is accomplished, warfarin is the medication of choice for long-

term treatment to prevent recurrence. In pregnancy LMWH is preferred [66].

Non-vitamin K oral anticoagulants (NOACs) have been established to advance VTE management and overcome the restrictions and limitations of classical treatments. Rivaroxaban, dabigatran, apixaban, and edoxaban have been approved in North America and Europe for VTE treatment Rivaroxaban, dabigatran, and apixaban have been compared with placebo or warfarin in the setting of extended VTE treatment [41].

Placement of inferior vena cava filters

The American Heart Association (AHA) Guidelines for the placement of inferior vena cava filters proposed the following indications [67]:

• Acute proximal deep venous thrombosis or acute pulmonary edema with absolute contra-indication for anticoagulation therapy.

• Recurrent episodes of thromboembolism while the patient receives anticoagulation therapy (failure of adequate anticoagulation).

• Life-threatening hemorrhage on anticoagulation therapy.

• Large and free-floating iliofemoral thrombus in high-risk patients.

• Proliferating iliofemoral thrombus whilst on anticoagulant therapy.

• Chronic PE in patients with pulmonary hypertension or corpulmonale.

Inferior vena cava filters advanced in arteries to catch embolus and to lessen venous stasis can prevent the migration of embolus > 4 mm, and they can also preserve the normal blood flow. Although there are various available filters, the Greenfield filter is the mainstay, with patency rations of recurrent embolism rates greater than 95% and less than 5%. The conical shape permits central filling of emboli without restricting peripheral blood flow. Some new filters, including removable filters, are also under development currently.

Thrombolysis

Indication of thrombolytic therapy is very rare due to related severe side effects like intracra-

nial hemorrhage and major bleeding. It is indicated in patients with massive iliofemoral DVT, limb-threatening circulatory compromise, acute or subacute symptoms, and a low risk of bleeding [68]. A variety of endovascular interventions have been tested in patients with iliofemoral DVT, including catheter-directed thrombolysis (CDT) and/or thrombectomy. Current evidence suggests that CDT can minimize recurrence of DVT and prevents PTS better than systemic anticoagulation [69]. Pharmacomechanical CDT has recently been utilized for treating acute proximal (iliofemoral) DVT [70].

Conclusion

DVT is a serious and critical clinical condition that causes severe morbidity and mortality which could be prevented. Diagnosis of DVT presents a clinical challenge for physicians; risk-factor evaluation with Wells scoring system, D-dimer examination, and venous ultrasonography can facilitate the prediction and identification of DVT. Mechanical and pharmacological prevention methods are recommended in high risk patients, while the primary objectives of therapeutic agents are to prevent complications following expansion of thrombus.

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Disclosure of conflict of interest

None.

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