Management Of Deep Vein Thrombosis

Barnoyev Saidjon Sharifovich Bukhara State Medical Institute
Xayitov Dilshod Xayotovich Bukhara State Medical Institute

ABSTRACT

The term "deep vein thrombosis" (DVT) describes thrombosis that forms in the deep veins, usually in the lower limbs or pelvis. Due to the potentially lethal nature of pulmonary embolization, a consequence of DVT, this clinical condition has drawn attention. Consequently, in clinical practice, early detection and methodical management of DVT and associated consequences are crucial. In this review, we seek to provide an overview of recent research published within the last few years, given the recent improvements in clinical understanding of disorders related to deep vein thrombosis (DVT).

Keywords: Deep venous thrombosis, homeostasis, antithrombotic therapy, hyperfibrinolysis

Introduction: The development of thrombosis within the deep veins of the pelvis or lower limbs is known as deep vein thrombosis (DVT) [1]. Damage to the vessel endothelium results in reduced venous blood flow, slow blood flow, and, in extreme situations, the potential for pulmonary embolism (PE) as thrombi travel from deep veins to the lungs through the circulatory system. These symptoms all contribute to the formation of blood clots [2]. Early detection of DVT and prompt anticoagulant treatment are crucial from a therapeutic standpoint, as PE can be lethal in specific situations [3]. However, early detection of DVT is clinically hard due to its non-specific clinical symptoms, which can even be asymptomatic. In the last ten years, new techniques have been created to identify DVT in individuals who are at high risk early on. Through a methodical summary of the data published between 2010 and 2016, this review seeks to give clinical practitioners an update on the state of research on DVT and accompanying complications like PE.

Epidemiology

DVT contributes significantly to the global healthcare burden. According to reports, the annual prevalence of DVT is around 100 cases per 100,000 persons [4]. However, incidence rises with age, and males are more likely than women to experience DVT and its recurrence [5-7]. In addition, Black and Hispanic individuals are more likely than Caucasians to get DVT [1]. One significant risk factor for the onset of DVT is vascular aging. Additionally, it is believed that children have a lower capacity for thrombin synthesis, a higher capacity for anti-thrombin in the vessel walls, and a higher capability for alpha-2-macrogolobulin to inhibit thrombin [8]. Nonetheless, there is also evidence linking the use of contraceptives, puerperium, cesarean sections, and pregnancy to an increased risk of DVT [9].

Risk factors

Certain inherited or acquired risk factors, most frequently the following, enhance the likelihood of developing DVT [10]:

1) Age. DVT is extremely uncommon in children and increases in incidence with age [11].
2) Orthopedic Medicine. Patients who have had significant orthopedic surgery or have lower limb fractures are more likely to develop DVT. It has been proposed that DVT in these patients is linked to arterial wall damage, immobility, and active coagulation pathways [12].
3) Injuries. Patients with lower extremity fractures 1552 Int J Clin Exp Med 2018;11(3):1551-1561 have a much higher incidence of DVT than patients with injuries to other regions, like the belly, face, or thorax. Trauma patients may experience complications from DVT, such as early coagulopathy that could compromise anticoagulant therapy later on [13], hypoperfusion, acidosis, and resuscitation techniques [14, 15]. Therefore, early after traumatic damage, the coagulation system's homeostasis changes towards a pro-thrombotic state, emphasizing the need for early thromboembolism prophylaxis [16]. In fact, compared to individuals with little trauma, those with serious trauma have a roughly six-fold higher chance of developing DVT [17].
4) Cancer. Patients with cancer have a greater frequency of DVT, and the specific incidence of DVT varies according on the biological features of the tumor. Furthermore, individuals receiving active cancer treatment, such as chemotherapy, have been linked to a higher risk of developing DVT, possibly as a result of protein C and S's plasma activities being inhibited [18, 19].
5) Other common risk factors for DVT include: immobility, surgery, hospitalization, pregnancy and puberty, hormonal therapy, obesity, inherited and acquired hypercoagulable states, myocardial infarction, anesthesia, infections, inflammatory bowel disease, and renal impairment [20, 21]. On the other hand, it has been proposed that central lines, sickle cell disease, severe infections, and states of hypercoagulability may be risk factors for DVT in children [22].

Pathogenesis

Based on current understanding, thrombosis can be caused by aberrant changes in blood components, venous stagnation, and injury to the vascular wall. Major orthopedic surgery may result in these problems. Currently, the pathophysiology of deep vein thrombosis (DVT) is thought to involve down-regulated Von Willebrand factor (vWF) level and overexpression of thrombomodulin (TM) and endothelial protein C receptor (EPCR) in the endothelial cells of deep veins. This results in an overreaction to anticoagulation and inhibits procoagulant activities in the venous endothelium [23]. Slow vein flow may be a factor in DVT brought on by fractures or procedures involving the lower extremities. Endothelial damage can result from a convoluted femoral vein during hip arthroplasties that expose the acetabulum and femoral canal, obstructing blood flow. Additionally, coagulation factors aggregate when blood flow in veins is obstructed [24]. Endothelial damage can also result from anterior tibial subluxation and vibration from saws during knee arthroplasties. Furthermore, aberrant venous stasis is linked to the lower limbs' perioperative immobility. When it comes to the lower extremities, thrombosis can be classified as either distal (affecting the calf veins) or proximal (affecting the popliteal or thigh veins). Serious and perhaps fatal consequences have been linked to DVT in the proximal veins [25]. It's interesting to note that research suggests that DVT forms more frequently in the distal calf veins than in the pelvic or proximal thigh veins [26]. Larger thrombi that originate from proximal veins, however, were thought to be linked to a higher chance of developing severe PE.

Clinical manifestations

History

Although the clinical signs of DVT vary greatly amongst patients, they are typically localized discomfort, limb edema, and swelling. They can also be bilateral or unilateral, symptomatic, severe, or minor. One common particular sign of DVT is edema of the affected extremities. Many times, thrombi that do not totally block the venous outflow are asymptomatic. Both lower limb edema and thrombus involving the pelvic veins, iliac bifurcation, or vena cava are typically present. Mild bilateral edema of the limbs is frequently the result of proximal incomplete occlusion, which can be confused with edema brought on by systemic illnesses such hepatonephric insufficiency, congestive heart failure, and fluid overload. DVT is suggested by pain along the deep veins in the medial side of the thigh [27]. Pain and/or tenderness, as opposed to pain that is localized, usually does not point to DVT and instead points to a different diagnosis. The symptoms are nonspecific, yet DVT is associated with discomfort after the foot's dorsiflexion (the Humanzs sign) [28].

Physical examination

Once more, no single symptom or group of symptoms may reliably indicate the presence of DVT. Although Homans sign, or calfpain on dorsiflexion of the foot, is a suggestive symptom that may help identify DVT, only 50% of DVT patients exhibit it. It is possible to see discoloration in the lower limbs, with reddish-purple being the most prevalent color, which could be caused by venous blockage. Phlegmasia cerulea dolens, or "painful blue inflammation," is the word for the unusual condition in which there may be an ileofemoral large venous blockage and cyanotic leg.

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

In addition, edema may obstruct venous outflow, giving the leg a blanched appearance. Phlegmasia alba dolens, or "painful white inflammation," is the term used to describe the discomfort, edema, and discolouration [29].

Diagnosis

While thrombi left untreated can result in potentially fatal complications like PE, an accurate and timely diagnosis of DVT is essential. On the other hand, anticoagulation in the absence of thrombosis can be hazardous. The most widely accepted method based on evidence for diagnosing venous thrombus embolism (VTE) or DVT is a thorough evaluation that combines systematic clinical risk factors, symptoms, and indicators. Establishing the patient's risk of deep vein thrombosis (DVT) based on clinical factors, such as medical history and physical examination results, is a crucial initial step. Despite the promotion of other structured clinical probability scoring systems for patient stratification, the Wellscore is the most often suggested model due to its extensive research and widespread use [30]. The original Wells score model divided 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% based on medical presentation and risk variables. However, Wells et al. classified patients with DVT into two groups in a later study, further developing a simplified version for the diagnostic measures: 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

Table 1 [32] displayed the Wells scoring system components. Individuals with a Wells score of ≥ 2 are more likely to have DVT (28%), compared to 6% for those with a score of < 2. Alternatively, patients' individual Wells scores can be used to divide them into three groups: high-probability if Wells score > 2, moderate-probability if Wells score = 1-2, and low-probability if Wells score < 1, with respective likelihoods of developing DVT of 53%, 17%, and 5%.

D-dimer

D-dimer is a tiny protein that is released from the blood after fibrinolysis breaks down a blood clot. It is a byproduct of fibrin breakdown. It gets its name from the fact that it is made up of two fibrin protein D segments that are cross-linked. The widespread activation of fibrinolysis and blood coagulation is reflected in the presence of D-dimer [33]. In clinical situations when clots form, such as surgery, trauma, malignancy, sepsis, and hemorrhage, serum levels of D-dimer may rise, especially in hospitalized patients [34]. Interestingly, there is a correlation between these illnesses and a higher risk of DVT.

Patients with DVT continue to have elevated D-dimer levels for around seven days. Low levels of D-dimer may be found in patients who present later in the course of the disease, when the clots have formed and stuck. Similarly, patients who have a single case of DVT in the calf vein have smaller clot loads and lower D-dimer values, which may be below the assay's sensitivity cut-off. This could explain why, in the case of defined DVT, the D-dimer assay's sensitivity was reduced.

D-dimer can be very helpful in ruling out DVT even though it cannot confirm a DVT diagnosis. A normal D-dimer examination result can aid in ruling out DVT in patients whose Wells score indicates a low to moderate probability of the condition [35]. Diagnostic imaging tests, such as compression ultrasonography, are recommended in individuals with high Wells scores, and D-dimer may not be used to confirm the diagnosis in these cases [36]. In order to confirm or rule out DVT, another diagnostic technique, such as imaging, should be used if the D-dimer level is raised [37]. D-dimer has a high (almost 97%) sensitivity and a very poor (about 35%) specificity for DVT estimate [38]. D-dimer may be used as a rapid screening test for DVT if lower-extremity edema manifests with negative clinicoradiological signs, according to the findings of earlier DVT diagnostic research.

There are three ways to assess serum D-dimer levels: 1) Red blood cell whole blood agglutination assay (simpliRED); 2) latex agglutination assay; and 3) enzyme linked immunosorbent assay (ELISA).

The likelihood ratios, sensitivities, and specificities of these three assays vary. D-dimer assays for sensitivity and negative probability ratio are used by ELISAs to regulate the relative rating [3].

The American College of Chest Physicians recommends a compression ultrasound examination of the proximal veins or a D-dimer examination with moderate-to-high sensitivity for patients with low-probability DVT [37]. Nonetheless, prior to ultrasound imaging on proximal veins, the UK's National Institute for Health and Care Excellence (NICE) advises D-dimer assessment [39]. A high-sensitivity D-dimer test is favored over a whole-leg or compression vascular ultrasonography examination for patients with moderate-likelihood DVT [37]. The NICE recommendation does not go to a moderate-probability group and instead uses a 2-point Wells score [39].

Coagulation profile

It takes a coagulation profile analysis to identify general hypercoagulability. A low chance of DVT may not be indicated by an extended prothrombin time (PT) or an activated partial thromboplastin time (APTT). In 13% of patients, DVT might worsen after receiving full anticoagulant medication.

Seldom are DVT cases such that laboratory testing for these anomalies is basically conducted whenever a patient is diagnosed with DVT who is younger than 50 years old, or if there is a strong family history of coagulation

disease, or when DVT is found at uncommon places. Among these anomalies are:

- 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

The main imaging modality for DVT diagnosis is venous ultrasonography [40]. It is reasonably priced, non-invasive, and safe. Three popular modalities are as follows:

The initial and most popular imaging method for DVT diagnosis is compression ultrasound (CUS) [41]. B-mode imaging called CUS is frequently employed on the proximal deep veins, specifically the popliteal and common femoral veins [3]. In order to diagnose proximal DVT, the CUS has a 94% sensitivity and a 98% specificity [42]. On the other hand, asymptomatic proximal DVT diagnosis has lower sensitivity [43].

CUS has a relatively low sensitivity of 57% [42] to detect distal DVT and only 48% to diagnose asymptomatic calf vein thrombosis. While the negative predictive value for symptomatic events is 100% and for asymptomatic events is 94%, ultrasonography for proximal DVT has a certain predictive significance of 100% and 71% for symptomatic and asymptomatic instances, respectively [16]. Duplex Doppler ultrasonography is a tool for Doppler waveform analysis and B-mode imaging. Normal venous blood flow is seen in duplex Doppler ultrasonography as spontaneous, phasic with respiration, and augmentable by manual pressure [3]. Images are produced by a pulsed signal in color Doppler ultrasonography. For the purpose of identifying DVT in calf or iliac veins, the combination of duplex Doppler ultrasonography and color Doppler ultrasonography is useful [44].

Ultrasound imaging has many benefits, such as being safe, requiring no radiation exposure, non-invasive, low cost, and able to distinguish DVT from other conditions such as lymphadenopathy, superficial or intramuscular hematomas, femoral aneurysm, Baker's cysts, and superficial thrombophlebitis [3]. Ultrasound imaging has limitations, such as a reduced capacity to identify distal thrombus [45], and vein compression may be challenging in cases of edema, obesity, and discomfort. Furthermore, ultrasonic imaging is rendered impossible by mechanical restrictions like as immobilization by casts and splints.

Ultrasound imaging offers several benefits, such as safety, low radiation exposure, non-invasiveness, affordability, and the ability to distinguish DVT from other conditions such as lymphadenopathy, superficial or intramuscular hematomas, femoral aneurysm, Baker's cysts, and superficial thrombophlebitis [3]. Ultrasound imaging has limitations, such as a reduced capacity to identify distal thrombus [45], and vein compression may be challenging in cases of edema, obesity, and discomfort. Furthermore, ultrasonic imaging is rendered impossible by mechanical immobilization techniques like casts and splints.

Contrast venography

Contrast venography is the primary and traditional imaging technique used to diagnose DVT. An accurate diagnostic test for DVT entails cannulating and injecting noniodinated contrast medium (such as Omnipaque) into the affected extremity's peripheral veins. To ascertain whether venous blood flow obstruction has occurred, X-ray imaging is utilized [46]. Intraluminal filling flaws seen in two or more views, as well as the abrupt termination of a deep state, are the most reliable cardinal and crucial features for the diagnosis of phlebothrombosis [47]. It is highly specific and sensitive, especially when figuring out the location and size of DVT clots. But this test is rarely done because of its relatively high cost, invasiveness, availability, and other drawbacks such radiation exposure, allergic response risk, and renal insufficiency [48].

Computed tomography venography (CTV)

In order to evaluate DVT in lower extremities, CTV typically necessitates the injection of contrast medium into the forearm veins, which is subsequently scanned by helical computed tomography [48]. The pelvic veins, lower

extremities veins, and inferior vena cava can all be seen well with CTV. A single toll can reduce VTE work-up because DVT is a significant risk factor for PE. However, in order to adequately opacify the pelvic veins, lower limb veins, and pulmonary arteries, this one inclusive imaging modality for VTE requires a significant volume of iodinated contrast material [49].

Magnetic resonance imaging (MRI)

There are several applications for MRI. Certain methods (like phase-contrast venography and time-of-flight venography) rely on the inherent characteristics of blood flow and do not require contrast media. Nevertheless, the introduction of contrast agents, such as IV gadolinium, usually improves vascular imaging. To see the veins in the lower extremities, this contrast medium can be injected into the peripheral veins through the dorsalis pedis or forearm veins [50]. Because of the strong signal produced by the methemoglobin in the RBCs within the thrombus, MRI can also be used to directly image the thrombus and show DVT. MRI is typically not available for DVT evaluation at most institutions, despite the fact that this noninvasive approach does not involve the injection of contrast materials.

Guidance

A methodical evaluation is necessary to diagnose DVT.

The first step is to determine the test probability, which can be done by figuring out the Wells score. When the Wells score is less than 1 (DVT improbable), a D-dimer assay is called for. DVT is excluded in the event that the result is negative. Nonetheless, venous imaging ultrasound is recommended if the D-dimer test results are positive. DVT can be ruled out if the venous ultrasound scan returns negative results. A positive result allows for the diagnosis of DVT. It is recommended to perform an ultrasound venous scanning if the pretest likelihood assessment is above 2. DVT can be identified if the result is positive. However, if the result is negative, a D-dimer analysis needs to be done. A negative D-dimer test result can exclude DVT as a possible diagnosis. On the other hand, a D-dimer assay that is abnormal suggests venography or another ultrasound within a week.

When diagnosing DVT, MR venography and CT scans have the same sensitivity and specificity as CUS. However, those actions are recommended in cases where CUS assessment of the patient is not possible or where pelvic vein thrombosis or inferior vena cava thrombosis are suspected. When other tests are unable to conclusively confirm or rule out DVT, contrast venography serves as the reference pattern and prediction for DVT diagnosis [41].

Prevention

Clinical measures can be taken to prevent general risk factors for DVT. Particularly for patients admitted for urgent or elective surgery, a preoperative risk assessment is required. Surgeons and anesthetists generally agree with the safe and efficient DVT prevention approach that Warwick et al. proposed [51].

General procedures [51]

- Anesthesia: By increasing blood flow, spinal or epidural anesthesia can cut the risk of DVT by about 50%. Furthermore, it is best to avoid administering chemical prophylaxis and neuraxial anesthesia too soon after surgery in order to prevent spinal hematomas.
- Surgical technique: The release of thromboplastins can be efficiently reduced by precise manipulation of the surgical site. Long-term main vein twisting can harm the endothelium.
- Mobilization: In order to enhance vein blood flow, mobilization should be used as soon as possible after surgery.

Physical methods

- Graduated compression stockings: If the stockings are correctly woven and well-fitting, they can reduce the incidence of deep vein thrombosis (DVT) by half. Both the above-knee and below-knee varieties may be as effective [41].
- Intermittent plantar venous compression: This condition ensures that blood flows normally from the sole of the foot and improves venous blood flow in the leg by exerting intermittent

pressure on the venous plexus around the lateral plantar arteries. For patients who are bedridden, a mechanical foot pump can simulate this natural function by providing intermittent plantar venous compression. The thromboprophylactic efficacy of this device in individuals who have had hip fractures and hip or knee arthroplasty has been verified by prior research [41].

- Leg compression with intermittent pneumatic pressure - This device has been widely used to avoid deep vein thrombosis (DVT) and can help increase blood flow in the lower extremities' deep veins after surgery [52].
- Inferior vena cava filter: This filter is inserted subcutaneously into the inferior vena cava through the femoral vein. By capturing an embolus before it reaches the lungs, this apparatus can successfully stop PE. In individuals with a high risk of DVT, inferior vena cava filters should be the first option when anticoagulant treatment is contraindicated. Strict indications should be emphasized, and clinicians should be informed of any potential consequences, such as death from proximal coagulation. Patients with hemorrhagic stroke, those with recent or ongoing gastrointestinal bleeding, and those with hemostatic abnormalities like severe thrombocytopenia are among those who should get this mechanical prophylaxis for DVT [53]. Patients with peripheral vascular diseases causing lower extremities ischemia should not employ inferior vena cava filters because of the potential for fibrinolysis and clot dislodgement [54].

Chemical methods

The best chemical medicines for DVT prophylaxis are unfractionated heparin, low-molecular-weight heparins (LMWH), pentasaccharide (fondaparinux), and factor Xa inhibitors.

• Unfractionated heparin increases the frequency of heparin-induced thrombocytopenia, necessitates laboratory monitoring, and presents a risk of exacerbating bleeding after surgery [55]. As a result, it is not advised for elderly patients. • Because of its superior hematological and pharmacokinetic qualities, low molecular weight heparin (LMWH) is safer and more effective than unfractionated heparin; also, it doesn't require pharmacological monitoring when administered. Moreover, because LMWH may not have an impact on the quantity and activity of osteoclasts, it is linked to a decreased risk of heparin-induced osteoporosis in comparison to unfractionated heparin. Pharmacologically, it inhibits factor Xa more than unfractionated heparin and antithrombin III less than unfractionated heparin [56]. When taken at the right time before to surgery and at a reduced dosage in patients with poor renal function, LMWH is safe.

- With its indirect selective inhibitory effect on factor Xa, pentasaccharide is an anticoagulant [3]. It is as effective at preventing DVT as LMWH, but because it can cause hemorrhagic problems, it shouldn't be administered too soon after surgery (less than 6 to 8 hours). Since the liver metabolizes this drug while the kidney secretes it, the clinician should be aware of any potential hepatonephric dysfunctions.
- Rivaroxaban inhibits factor Xa directly. With a half-life of 4–12 hours and a high bioavailability of 80%, it works quickly [57]. Previous clinical phase III trials have demonstrated that rivaroxaban (recommended dose: 10 mg once daily) is superior to the LMWH for avoiding DVT in patients who underwent orthopedic procedures [58]. Oral rivaroxaban has been shown in another DVT trial to be just as successful as the current standard regimens (enoxaparin, fondaparinux, LMWH, or oral vitamin K antagonist) in preventing the recurrence of symptomatic VTE [59]. When administered appropriately, injectable or oral medicines can be useful in preventing DVT after hospitalization. Currently, some novel medications, including as apixaban and edoxaban, are undergoing clinical testing.
- With a 5-6% bioavailability, dabigatran is an oral direct competitive inhibitor of thrombin, which is immediately

absorbed from the gastrointestinal system. The half-lives of this drug are 8 hours for a single dosage and about 17 hours for successive doses; the plasma concentration peaks after 2 hours [57]. The kidney secretes it. It is possible that coagulation function monitoring is not required because of its limited bioavailability.

- A typical antagonist of vitamin K is warfarin. This drug is useful in avoiding DVT and can be taken at any stage of the perioperative period [60]. Notably, because it can cross the placenta and cause teratogenicity and bleeding in the fetus, it is not recommended as thromboprophylaxis in antepartum [61]. The international normalized ratio (INR) of 2-3 should be maintained while warfarin is being administered.
- Because of aspirin's relatively low efficacy and hemorrhagic risk, its use is contentious. Furthermore, aspirin has been shown to irritate the gastrointestinal tract [62].

It's still unclear how long thromboprophylaxis should be used for. Individual coagulation states and pertinent DVT hazards should be taken into consideration. Patients undergoing major lower-extremity surgeries should receive prolonged antithrombus treatment for 10–35 days, as recommended by prior studies. This is especially important for patients who have a high risk of DVT; even patients who are admitted with emergency disorders should receive antithrombus treatment until they are discharged [60].

Treatment

If DVT is not treated, PE may exacerbate the condition and there is a significant early recurrence risk [63]. Following the initial episode of DVT, there is a continuous increase in the incidence of recurrence and post-thrombotic syndrome (PTS) [64]. Effective pharmaceutical administration of unfractionated heparin, LMWH, or fondaparinux is initially necessary to prevent the progression or recurrence of DVT, emergent PE, and the progression of delayed consequences including pulmonary hypertension and PTS [3, 65]. When treating individuals with DVT, the basic pharmacological strategy is to begin with parenteral anticoagulants, such as LMWH or unfractionated heparin, and then move on to long-term vitamin K antagonists (VKAs). For individuals with moderate to high risk DVT, starting parenteral anticoagulation during the acute phase is advised prior to diagnostic testing [65].

A broad window of safety is offered by the hematological and pharmacokinetic benefits of LMWH over unfractionated heparin. Therefore, unless LMWH is contraindicated, LMWH is advised for patients with DVT rather than unfractionated heparin. When the INR falls between 2.0 and 3.0, which occurs after at least 4-5 days, heparin is usually administered in conjunction with warfarin [3]. The influence of low factor VII levels leads to extended INR.

Warfarin is the recommended drug for long-term treatment to avoid recurrence when strong anticoagulation is completed. LMWH is recommended throughout pregnancy [66].

Oral anticoagulants that do not include vitamin K (NOACs) have been developed to improve the management of VTE and get around the drawbacks and restrictions of traditional therapies. For the treatment of VTE, apixaban, dabigatran, edoxaban, and rivaroxaban have been approved in North America and Europe. In the context of prolonged VTE treatment, apixaban, dabigatran, and rivaroxaban have been compared with warfarin or a placebo [41].

Placement of inferior vena cava filters

The following indications were suggested by the American Heart Association (AHA) Guidelines for the implantation of inferior vena cava filters [67]:

Acute pulmonary edema or acute proximal deep vein thrombosis that completely precludes the use of anticoagulant medication.

- Failure to provide enough anticoagulation, as evidenced by recurrent occurrences of thromboembolism during anticoagulant therapy.
- Hemorrhage on anticoagulant therapy that could be fatal.
- In high-risk patients, a large, free-floating iliofemoral thrombus.
- Growing iliofemoral thrombus when taking anticoagulants.

• Patients with corpulmonale or pulmonary hypertension who experience chronic PE.

The advancement of inferior vena cava filters in arteries to trap emboli and reduce venous stasis can stop emboli larger than 4 mm from migrating.

Additionally, they can maintain regular blood flow.

The standard filter is the Greenfield filter, which has patency ratios of recurrent embolism rates greater than 95% and less than 5%, despite the availability of several other filters. Because to its conical form, emboli can be filled in the center without obstructing peripheral blood flow. Several novel filters, including detachable filters, are also being developed at the moment.

Thrombolysis

Because of the serious side effects associated with thrombolytic therapy, such as significant bleeding and cerebral hemorrhage, its indication is extremely rare. Patients with significant iliofemoral DVT should use it.

vascular impairment that could endanger limbs, acute or subacute symptoms, and a minimal risk of bleeding [68]. Patients with iliofemoral DVT have undergone testing for a range of endovascular treatments, such as thrombectomy and/or catheter-directed thrombolysis (CDT). Based on available data, CDT appears to be a more effective preventive measure against PTS and DVT recurrence than systemic anticoagulation [69]. Acute proximal (iliofemoral) DVT has recently been treated using pharmacomechanical CDT [70].

Conclusion

It is possible to prevent DVT, a dangerous and important clinical illness that has a significant morbidity and fatality rate. Identification of DVT provides a clinical challenge for medical professionals. Venous ultrasonography, D-dimer testing, and risk-factor evaluation using the Wells scoring system can help predict and identify DVT. While the main goals of treatment agents are to prevent problems after thrombus expansion, mechanical and pharmaceutical preventive approaches are advised for high-risk patients.

References

1. Caldeira D, Rodrigues FB, Barra M, Santos AT, de Abreu D, Gonçalves N, Pinto FJ, Ferreira JJ, Costa J. Non-vitamin K antagonist oral anticoagulants and major bleeding-related fatality in patient with atrial fibrillation and venous thromboembolism: a systematic review and meta-analysis. Heart 2015; 101: 1204-1211.
2. Yang SD, Ding WY, Yang DL, Shen Y, Zhang YZ, Feng SQ, Zhao FD. Prevalence and risk factors of deep vein thrombosis in patients undergoing lumbar interbody fusion surgery: a single-center cross-sectional study. Medicine 2015; 94: e2205.
3. Kesieme E, Kesieme C, Jebbin N, Irekpita E, Dongo A. Deep vein thrombosis: a clinical review. J Blood Med 2011; 2: 59-69.
4. Al-Hameed F, Al-Dorzi HM, Shamy A, Qadi A, Bakhsh E, Aboelnazar E, Abdelaal M, Al Khuwaitir T, Al-Moamary MS, Al-Hajjaj MS, Brozek J, Schünemann H, Mustafa R, Falavigna M. The Saudi clinical practice guideline for the diagnosis of the first deep venous thrombosis of the lower extremity. Ann Thorac Med 2015; 10: 3-15.
5. Musil D, Kaletová M, Herman J. Venous thromboembolism-prevalence and risk factors in chronic venous disease patients. Phlebology 2017; 32: 135-140.
6. Naess IA, Christiansen SC, Romundstad P, Cannegieter SC, Rosendaal FR, Hammerstrøm J. Incidence and mortality of venous thrombosis: a population-based study. J Thromb Haemost 2007;5: 692-699.
7. Kyrle PA, Minar E, Bialonczyk C, Hirschl M, Weltermann A, Eichinger S. The risk of recurrent venous thromboembolism in men and women. N Engl J Med 2004; 350: 2558-2563.
8. VAN Ommen CH, Heijboer H, Buller HR, Hirasing RA, Heijmans HS, Peters M. Venous thromboembolism in childhood: a prospective two-year registry in The

Netherlands. J Pediatr 2001; 139: 678-681.
9. Bates SM, Ginsberg JS. Pregnancy and deep vein thrombosis. Seminars in vascular medicine Copyright© 2001 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA. Tel.:+ 1 (212) 584-4662 2001:097-104.
10. Gran OV, Smith EN, Brækkan SK, Jensvoll H, Solomon T, Hindberg K, Wilsgaard T, Rosendaal FR, Frazer KA, Hansen JB. Joint effects of cancer and variants in the factor 5 gene on the risk of venous thromboembolism. Haematologica 2016; 101: 1046-1053.
11. Baker D, Sherrod B, McGwin G Jr, Ponce B, Gilbert S. Complications and 30-day outcomes associated with venous thromboembolism in the pediatric orthopaedic surgical population. J Am Acad Orthop Surg 2016; 24: 196-206.
12. Whiting PS, White-Dzuro GA, Greenberg SE, VanHouten JP, Avilucea FR, Obremskey WT, Sethi MK. Risk factors for deep venous thrombosis following orthopaedic trauma surgery: an analysis of 56,000 patients. Arch Trauma Res 2016; 5: e32915.
13. Brohi K, Cohen MJ, Ganter MT, Schultz MJ, Levi M, Mackersie RC, Pittet JF. Acute coagulopathy of trauma: hypoperfusion induces systemic anticoagulation and hyperfibrinolysis. J Trauma Acute Care Surg 2008; 64: 1211-1217.
14. [14] Pealing L, Perel P, Prieto-Merino D, Roberts I; CRASH-2 Trial Collaborators. Risk factors for vascular occlusive events and death due to bleeding in trauma patients; an analysis of the CRASH-2 cohort. PLoS One 2012; 7: e50603.
15. [15] Selby R, Geerts W, Ofosu FA, Craven S, Dewar L, Phillips A, Szalai JP. Hypercoagulability after trauma: hemostatic changes and relationship to venous thromboembolism. Thromb Res 2009; 124: 281-287.
16. [16] Modi S, Deisler R, Gozel K, Reicks P, Irwin, E, Brunsvold M, Banton K, Beilman GJ. Wells criteria for DVT is a reliable clinical tool to assess the risk of deep venous thrombosis in trauma patients. World J Emerg Surg 2016; 11: 1-6.
17. [17] Chu CC, Haga H. Venous thromboembolism associated with lower limb fractures after trauma: dilemma and management. J Orthop Sci 2015; 20: 364-372.
18. [18] Murayama Y, Sano I, Doi Y, Iwasaki R, Chatani T, Horiki M, Kitada M, Okuno M, Kondo S, Fukuda H, Kashihara T. A case of type 4 gastric cancer with peritoneal dissemination complicating venous thromboembolism treated effectively by combination of S-1 and warfarin. Gan To Kagaku Ryoh2010; 37: 311-314.
19. [19] Mukherjee SD, Swystun LL, Mackman N, Wang JG, Pond G, Levine MN, Liaw PC. Impact of chemotherapy on thrombin generation and on the protein C pathway in breast cancer patients. Pathophysiol Haemost Thromb 2010; 37: 88-97.
20. [20] Ren W, Li Z, Fu Z, Fu Q. Analysis of risk factors for recurrence of deep venous thrombosis in lower extremities. Med Sci Monit 2014; 20: 199-204.
21. [21] Topfer LA. Portable compression to prevent venous thromboembolism after hip and knee surgery: the activecare system. CADTH issues in emerging health technologies. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2016-.146. 2016 Mar 31.
22. [22] Biss TT. Venous thromboembolism in children: is it preventable? Semin Thromb Hemost 2016; 42: 603-611.
23. [23] Brooks EG, Trotman W, Wadsworth MP, Taatjes DJ, Evans MF, Ittleman FP, Callas PW, Esmon CT, Bovill EG. Valves of the deep venous system: an overlooked risk factor. Blood 2009; 114: 1276-1279.
24. [24] Karasu A, Baglin TP, Luddington R, Baglin CA, van Hylckama Vlieg A. Prolonged clot lysis time increases the risk of a first but not recurrent venous thrombosis. Br J Haematol 2016; 172: 947-953.

25. [25] Zaghlool D, Franz R, Jenkins J. EkoSonic thrombolysis as a therapeutic adjunct in venous occlusive disease. Int J Angiol 2016; 25: 203-209.
26. [26] Shackford SR, Sise CB. Venous thromboembolism. Trauma Induced Coagulopathy 2016; Part V: 421-434.
27. [27] Hull CM, Rajendran D, Barnes AF. Deep vein thrombosis and pulmonary embolism in a mountain guide: awareness, diagnostic challenges, and management considerations at altitude. Wilderness Environ Med 2016; 27: 100-106.
28. Verma V, Mohil RS, Kumar S, Gupta A. Comparing ultrasound guided foam sclerotherapy with surgical treatment in patients of varicose veins. Int Surg 2016; 3: 2239-2245.
29. Ligi D, Mosti G, Croce L, Raffetto JD, Mannello F. Chronic venous disease-part I: inflammatory biomarkers in wound healing. Biochim Biophys Acta 2016; 1862: 1964-1974.
30. Van der Pol LM, Mairuhu AT, Tromeur C, Couturaud F, Huisman MV, Klok FA. Use of clinical prediction rules and D-dimer tests in the diagnostic management of pregnant patients with suspected acute pulmonary embolism. Blood Rev 2017; 31: 31-36.
31. Wells PS, Anderson DR, Rodger M, Forgie M, Kearon C, Dreyer J, Kovacs G, Mitchell M, Lewandowski B, Kovacs MJ. Evaluation of D-dimer in the diagnosis of suspected deep-vein thrombosis. N Engl J Med 2003; 349: 1227-1235.
32. Hargett CW, Tapson VF. Clinical probability and D-dimer testing: how should we use them in clinical practice? Semin Respir Crit Care Med 2008; 29: 15-24.
33. Pabinger I, Ay C. Biomarkers and venous thromboembolism. Arterioscler Thromb Vasc Biol 2009; 29: 332-336.
34. Adam SS, Key NS, Greenberg CS. D-dimer antigen: current concepts and future prospects. Blood 2009; 113: 2878-2887.
35. Lee N, Hui D, Wu A, Chan P, Cameron P, Joynt GM, Ahuja A, Yung MY, Leung CB, To KF, Lui SF, Szeto CC, Chung S, Sung JJ. A major outbreak of severe acute respiratory syndrome in Hong Kong. N Engl J Med 2003; 348: 1986-1994.
36. Chong LY, Fenu E, Stansby G, Hodgkinson S. Management of venous thromboembolic diseases and the role of thrombophilia testing: summary of NICE guidance. BMJ 2012; 344: e3979.
37. Guyatt GH, Norris SL, Schulman S, Hirsh J, Eckman MH, Akl EA, Crowther M, Vandvik PO, Eikelboom JW, McDonagh MS, Lewis SZ, Gutterman DD, Cook DJ, Schünemann HJ. Methodology for the development of antithrombotic therapy and prevention of thrombosis guidelines antithrombotic therapy and prevention of thrombosis, 9th ed: American college of chest physicians evidence-based clinical practice guidelines. Chest 2012; 141 Suppl: 53S-70S.
38. Cosmi B, Palareti G. D-dimer, oral anticoagulation, and venous thromboembolism recurrence. Semin Vasc Med 2005; 5: 365-370.
39. Howard LS, Hughes RJ. NICE guideline: management of venous thromboembolic diseases and role of thrombophilia testing. Thorax 2013; 68: 391-393.
40. Hirsh J, Lee AY. How we diagnose and treat deep vein thrombosis. Blood 2002; 99: 3102-3110.
41. Wang KL, Chu PH, Lee CH, Pai PY, Lin PY, Shyu KG, Chang WT, Chiu KM, Huang CL, Lee CY, Lin YH, Wang CC, Yen HW, Yin WH, Yeh HI, Chiang CE, Lin SJ, Yeh SJ. Management of venous thromboembolisms: part I. The consensus for deep vein thrombosis. Acta Cardiol Sin 2016; 32: 1-22.
42. 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; 5: 6.
43. Mohtadi NG, Johnston K, Gaudelli C, Chan DS, Barber RS, Walker R, Patel C, Mackay E, Odd-one Paolucci E. The incidence of proximal deep vein thrombosis after

elective hip arthroscopy: a prospective cohort study in low risk patients. J Hip Preserv Surg 2016; 3: 295-303.
44. Zierler BK. Ultrasonography and diagnosis of venous thromboembolism. Circulation 2004; 109: I9-14.
45. Dronkers CE, Klok FA, Huisman MV. Current and future perspectives in imaging of venous thromboembolism. J Thromb Haemost 2016; 14: 1696-1710.
46. Hofmann LV, Kuo WT. Catheter-directed thrombolysis for acute DVT. Lancet 2012; 379: 3-4.
47. Song K, Yao Y, Rong Z, Shen Y, Zheng M, Jiang Q. The preoperative incidence of deep vein thrombosis (DVT) and its correlation with post-operative DVT in patients undergoing elective surgery for femoral neck fractures. Arch Orthop Trauma Surg 2016; 136: 1459-1464.
48. Bates SM, Jaeschke R, Stevens SM, Goodacre S, Wells PS, Stevenson MD, Kearon C, Schun-emann HJ, Crowther M, Pauker SG, Makdissi R, Guyatt GH. Diagnosis of DVT: antithrombotic therapy and prevention of thrombosis: American college of chest physicians evidence based clinical practice guidelines. Chest 2012; 141 Suppl: e351S-e418S.
49. English WJ, Williams DB, Soto FC. Thromboembolic disease in the bariatric patient: prevention, diagnosis, and management. Bariatric Surgery Complications and Emergencies 2016; 51-71.
50. Guyatt GH, Akl EA, Crowther M, Gutterman DD, Schuunemann HJ. Executive summary: anti-thrombotic therapy and prevention of thrombosis, 9th ed: American college of chest physicians evidence-based clinical practice guidelines. Chest 2012; 141 Suppl: 7S-47S.
51. Babanazarov, U. T., & Barnoyev, S. S. (2023). Clinical Characteristics of Patients with Chronic Diffuse Liver Disease Against the Background of Covid-19. Genius Repository, 26, 49-55.
52. Hague A, Pherwani A, Rajagopalan S. Role of compression therapy in pathophysiology of the venous system in lower limbs. Surgeon 2017; 15: 40-46.
53. Francis CW. Prophylaxis for thromboembolism in hospitalized medical patients. N Engl J Med 2007; 357: 304-306.
54. Pavon JM, Adam SS, Razouki ZA, McDuffie JR, Lachiewicz PF, Kosinski AS, Beadles CA, Ortel TL, Nagi A, Williams JW Jr. Effectiveness of intermittent pneumatic compression devices for venous thromboembolism prophylaxis in high-risk surgical patients: a systematic review. J Arthroplasty 2016; 31: 524-532.
55. Smythe MA, Priziola J, Dobesh PP. Guidance for the practical management of the heparin anticoagulants in the treatment of venous thromboembolism. J Thromb Thrombolysis 2016; 41: 165-186.
56. McDonnell BP, Glennon K, McTiernan A, O'Connor HD, Kirkham C, Kevane B, Donnelly JC, Ni Áinle F. Adjustment of therapeutic LMWH to achieve specific target anti-FXa activity does not affect outcomes in pregnant patients with venous thromboembolism. J Thromb Thrombolysis 2017; 43: 105-111.
57. Weitz JI, Hirsh J, Samama MM. New antithrombotic drugs: American college of chest physicians evidence-based clinical practice guidelines. Chest 2008; 133 Suppl: 234S-256S.
58. Chen T, Lam S. Rivaroxaban: an oral direct factor Xa inhibitor for the prevention of thrombo-embolism. Cardiol Rev 2009; 17: 192-197.
59. Turobkulovich, B. U., & Tuymurodovich, K. M. (2022). Coronavirus Infection-A Trigger Factor in Liver Damage. Eurasian Research Bulletin, 15, 52-58.
60. Geerts WH, Bergqvist D, Pineo GF, Heit JA, Samama CM, Lassen MR, Colwell CW. Prevention of venous thromboembolism: American college of chest physicians evidence-based clinical

practice guidelines. Chest 2008; 133 Suppl: 381S-453S.
61. Basu S, Aggarwal P, Kakani N, Kumar A. Low-dose maternal warfarin intake resulting in fetal warfarin syndrome: In search for a safe anticoagulant regimen during pregnancy. Birth Defects Res A Clin Mol Teratol 2016; 106: 142-147.
62. Montoro-García S, Schindewolf M, Stanford S, Larsen OH, Thiele T. The role of platelets in venous thromboembolism. Semin Thromb Hemost 2016; 42: 242-251.
63. Kearon C. Natural history of venous thromboembolism. Circulation 2003; 107: I22-30.
64. Prandoni P, Bernardi E, Marchiori A, Girolami A. The long term clinical course of acute deep vein thrombosis of the arm: prospective cohort study. BMJ 2004; 329: 484-485.
65. Kearon C, Akl EA, Comerota AJ, Prandoni P, Bounameaux H, Goldhaber SZ, Nelson ME, Wells PS, Gould MK, Dentali F, Crowther M, Kahn SR. Antithrombotic therapy for VTE disease: antithrombotic therapy and prevention of thrombosis: American college of chest physicians evidence-based clinical practice guidelines. Chest 2012; 141 Suppl: e419S-e494S.
66. Frere C, Farge D. Clinical practice guidelines for prophylaxis of venous thomboembolism in cancer patients. Thromb Haemost 2016; 116: 618-625.
67. Babanazarov, U. T., & Qayimov, M. T. (2023). Epidemiology, Etiology, Clinical Description, and Prevention of Postoperative Cognitive Dysfunction. Eurasian Research Bulletin, 19, 38-46.
68. Jaff MR, McMurtry MS, Archer SL, Cushman M, Goldenberg N, Goldhaber SZ, Jenkins JS, Kline JA, Michaels AD, Thistlethwaite P, Vedantham S, White RJ, Zierler BK. Management of massive andsubmassive pulmonary embolism, iliofemoral deep vein thrombosis, and chronic thromboembolic pulmonary hypertension a scientific statement from the American heart association. Circulation 2011; 123: 1788-1830.
69. Srinivas BC, Patra S, Nagesh CM, Reddy B, Manjunath CN. Catheter-directed thrombolysis along with mechanical thromboaspiration versus anticoagulation alone in the management of lower limb deep venous thrombosis-a comparative study. Int J Angiol 2014; 23: 247-254.
70. Popuri RK, Vedantham S. The role of thrombolysis in the clinical management of deep vein thrombosis. Arterioscler Thromb Vasc Biol 2011; 31: 479-484.