Review Article

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Deep Vein Thrombosis

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Abstract

Deep vein thrombosis (DVT) and Pulmonary embolism (PE) and are two symptoms of venous thromboembolism (VTE). Both in the community and in hospitals, VTE significantly increases morbidity and death. Anticoagulation is the cornerstone of DVT treatment, assuming there are no contraindications. Patients with DVT have further anticoagulation after initial anticoagulation in order to guard against subsequent recurrences, emboli, and thrombosis related mortality. This article provides an overview of the management of lower extremity DVT.

Keywords: Deep; Vein; Thrombosis; Lower; Extremity; Management.

INTRODUCTION

Deep vein thrombosis (DVT) and acute pulmonary embolism (PE) are two manifestations of venous thromboembolism (VTE). VTE contributes to significant morbidity and mortality both in the community and in hospital.[1] The mainstay of therapy for DVT is anticoagulation, provided there is no contraindication.[2] Following initial anticoagulation, patients with DVT are anticoagulated further to prevent future recurrences, embolism, and thrombosis related death. An overview of the treatment of lower extremity DVT (distal and proximal), including indications for anticoagulation, alternate therapies, and treatment of special populations of patients with DVT, are discussed in this article.[3]

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MATERIALS AND METHODS

This study was conducted in the Department of Plastic Surgery in a tertiary care institute. It is a review article based on 50 articles on the Deep vein thrombosis after going through literature available in Scopus, PubMed, Google scholar & internet.

RESULTS

Based on the inclusion criteria 50 articles were studied to discuss Deep vein thrombosis under

following headings:

1. Aetiology
2. Pathophysiology
3. Clinical presentation
4. Complications of DVT
5. Diagnosis
6. Medical management
7. Surgical management
8. Conclusion

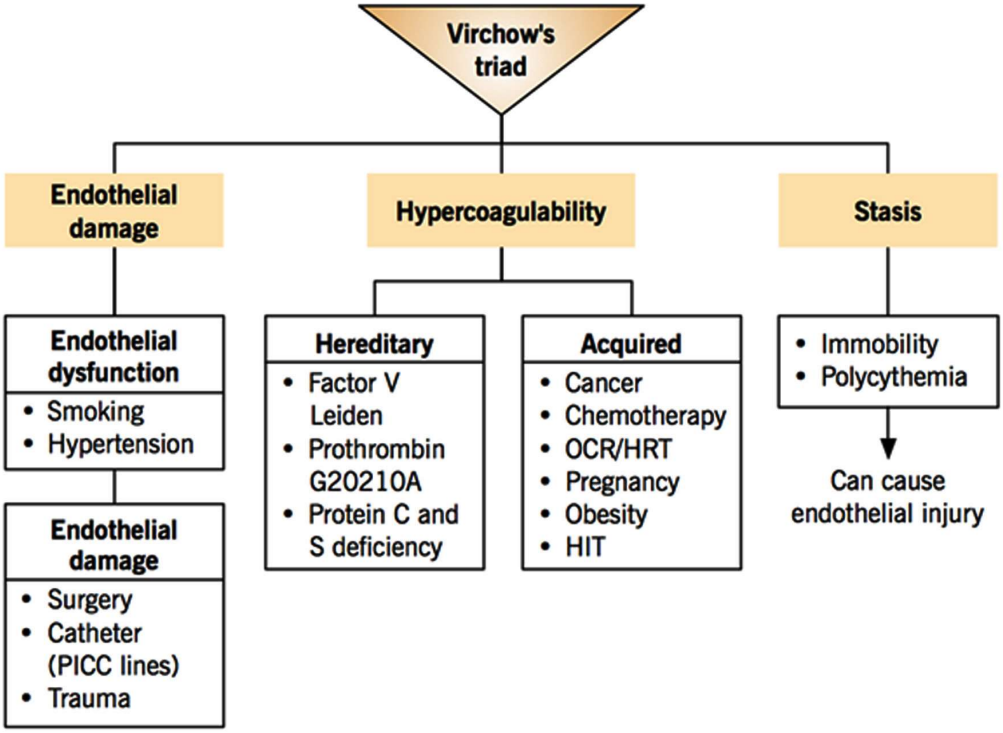

Fig. 1: Schematic representation of aetiology

Wells Clinical Prediction Rule for Deep Venous Thrombosis (DVT)

Clinical Feature	Points
Active cancer (treatment within 6 months, or palliation)	1
Paralysis, paresis, or immobilization of lower extremity	1
Bedridden for more than 3 days because of surgery (within 4 weeks)	1
Localized tenderness along distribution of deep veins	1
Entire leg swollen	1
Unilateral calf swelling of greater than 3 cm (below tibial tuberosity)	1
Unilateral pitting edema	1
Colateral superficial veins	1
Alternative diagnosis as likely as or more likely than DVT	-2
Total points	

DVT - deep venous thrombosis.

Risk score interpreatation (probability of DVT):

- 3 points: high risk (75%)
- 1 to 2 points: moderate risk (17%)
- 1 point: low risk (3%)

DISCUSSION

The Deep vein thrombosis of lower extremity are discussed under following headings.

Aetiology

Deep vein thrombosis (DVT) is referred to asunprovoked when there is no obvious environmental trigger for the condition.[4] The DVT that is typically triggered by a known event, such as surgery or hospitalisation, is known as Provoked DVT. Events of venous thromboembolism can be brought on by transient major risk factors, such as major surgery lasting more than 30 minutes, hospitalisation or immobility lasting less than three days, Caesarean section. Transient minor risk factors, such as minor surgery lasting less than 30 minutes, hospitalisation lasting less than three days, pregnancy, oestrogen therapy, or reduced mobility lasting less than three days.[5] Deep vein thrombosis can be brought on by risk factors including cancer, inflammatory bowel disease, inheritable thrombophilia, chronic heart failure, and metastatic end stage cancer.[6]

The most frequent triggering factor, which affects 20 to 40% of individuals, is malignancy. Other related risk factors for thrombosis include surgery, trauma, vena caval filter placement, pregnancy, and inheritable thrombophilia. Left-sided involvement is three to four times more frequent than right-sided involvement in the lower extremities.

Pathophysiology

The main causes of lower extremity DVT include decreased venous return in bedridden patients, endothelial damage or dysfunction following leg fractures, and other hypercoagulable conditions.[7] The most frequent cause of upper extremity DVT is endothelial injury brought on by central venous catheters, pacemakers, or medication injections. Upper extremity DVT can occasionally happen from subclavian vein compression at the thoracic outlet or superior vena cava syndrome, which can cause symptoms including facial oedema, dilated neck veins, and facial flushing.[8] It can also result from a hypercoagulable state. A normal or auxiliary first rib, a fibrous band, intense arm exercise (effort thrombosis), or Paget-Schroetter syndrome, which accounts for 1–4% of occurrences of upper extremity DVT, may be to blame for the compression.[9] Venous valve cusps are where deep venous thrombosis typically starts. Red blood cells, thrombin, fibrin, and a negligible number of platelets make up thrombi. Without therapy, red thrombi may spread locally initially and further go to the lungs. Deep vein thrombosis risk can be predicted using modified well criteria for the condition.[10]

TYPES OF LOWER EXTREMITY DEEP VEIN THROMBOSIS

Proximal DVT: Proximal lower extremity DVT is thrombus that is located in the popliteal, femoral, or iliac veins.

Distal DVT: Isolated distal DVT encompasses thromboses located below the knee in the calf veins. Most calf vein DVTs are located in the posterior tibial and peroneal veins while anterior tibial and muscular vein DVTs are uncommon.

Clinical Presentation

Patients typically have abrupt, excruciating pain, swelling, cyanosis, oedema, venous gangrene, and compartment syndrome, all of which compromise arterial supply and frequently result in circulatory collapse and shock.[12] A patient's limb or death could be lost if care is delayed. PCD falls under a clinical spectrum that also includes venous gangrene and phlegmasia alba dolens. PCD is caused by acute massive venous thrombosis, which is linked with a high level of morbidity and resulting in an obstruction of the venous drainage of an extremity (upper or lower).[13] PCD can happen at any age, although the fifth and sixth decades are the most prevalent. Females are more likely to experience it than guys are.

The manifestations can come on gradually or suddenly. Phlegmasia alba dolens, which causes symptoms of oedema, discomfort, and blanching (alba) without cyanosis, usually precedes occurrences of the disease. Massive fluid sequestration may cause the production of blebs and bullae as it worsens, and cyanosis (cerulea) and venous gangrene will finally follow. Constant, excruciating pain that typically begins at the femoral triangle and spreads to the entire extremity.[13-16] Cyanosis, which progresses from distal to proximal locations, is the pathognomonic sign of PCD.

COMPLICATIONS OF DVT

Acute pulmonary embolism (PE), substantial bleeding (from anticoagulation), additional clot extension, and death are the main early consequences of DVT. Recurrent clots, post-

thrombotic (post phlebitis) syndrome, and persistent thromboembolic pulmonary hypertension are examples of late consequences.[17] Proximal DVT has a greater fatality rate than distal DVT. Phlegmasia alba dolens and phlegmasia cerulea dolens are two much less frequent complications of acute DVT that, if left untreated, can end in venous gangrene.[18-20]

The leg turns milky white in phlegmasia alba dolens, a rare pregnancy related DVT event. It is unclear how oedema causes tissue ischemia and wet gangrene; however, it may raise soft tissue pressure above capillary perfusion pressures.[21]

Massive iliofemoral venous thrombosis in phlegmasia cerulea dolens results in nearly complete venous occlusion, causing the leg to become ischemic, excruciatingly painful, and cyanotic. Because venous return is blocked or severe oedema blocks arterial blood flow, pathophysiology may involve complete standstill of venous and arterial blood flow in the lower leg. Venous gangrene could happen.[22]

Venous clots seldom become infected. Following tonsillopharyngitis, jugular vein suppurative thrombophlebitis (Lemierre syndrome), an anaerobic bacterial infection of the internal jugular vein and adjacent soft tissues, may develop. Sepsis and bacteraemia are frequently complications.[23]

DIAGNOSIS

Ultrasonography

Since it is sufficient for detecting proximal DVT, where the need for anticoagulation is strong, we recommend proximal rather than whole leg compressive ultrasound for surveillance. Before testing, a history and physical examination can assist assess the likelihood of DVT. Doppler flow studies and ultrasonography are frequently used for diagnosis (duplex ultrasonography).[24]

D-Dimer

Increased levels of D-Dimer, a by product of fibrinolysis, indicate the recent presence and lysis of thrombi. While the sensitivity and specificity of D-Dimer assays might vary, the majority are sensitive and non-specific.[25] In patients with a normal D-dimer level on a sensitive test, DVT can be confidently excluded if the pretest probability of DVT is low. Therefore, a negative D-dimer test can help doctors identify individuals who have a minimal risk of developing DVT and do not need to undergo ultrasonography.[26] A positive test result is nonetheless non-specific because levels can also be raised by other illnesses such cancer, liver disease, recent surgery, trauma, pregnancy, positive rheumatoid factor, and inflammation.[27] Duplex ultrasonography can be performed concurrently with D-dimer testing if the pre-test risk of DVT is moderate or high. No of the D-dimer level, a positive ultrasound test supports the diagnosis. Having a normal D-dimer level can rule out DVT if ultrasonography does not show any signs of it. Depending on the clinical suspicion, patients with an elevated D-dimer level should undergo further imaging, such as venography, or repeat ultrasonography in a few days.[28]

Venography

Ultrasonography, which is non-invasive, more widely available, and nearly equally accurate for detecting DVT, has essentially supplanted contrast venography, which was the gold standard test for the diagnosis of DVT.[29,30] When ultrasonography results are normal but there is a significant pre-test suspicion of DVT, venography may be recommended. The main cause of the 2% complication rate is allergy to contrast agents. It is also possible to use MRI venography.[31,32] Additional imaging (such as CT pulmonary angiography or, less frequently, ventilation/perfusion [V/Q] scanning) is needed if the symptoms and indications point to PE. The yield of screening DVT patients for malignancy is minimal. A thorough history and physical examination, along with basic "standard" tests such a complete blood count, chest X-ray, urinalysis, liver enzymes, serum electrolytes, blood urea nitrogen (BUN), and creatinine, all aimed at finding cancer, should be enough to lead selective testing. Patients should also have any cancer screenings that are suitable for their age and gender (eg, mammography, colonoscopy).[34,35]

MEDICAL MANAGEMENT

Anticoagulation aims to avoid thrombosis and problems. Anticoagulation is appropriate for all individuals with proximal DVT, regardless of symptoms, unless contraindicated. Isolated distal DVT cannot be detected by routine proximal vein compression ultrasonography (proximal CUS), but it can be detected by whole leg ultrasonography, which is difficult to perform and interpret and institution dependent.[36,37] Serial proximal CUS can be used to detect thrombus that extends into the proximal veins. Isolated distal DVT is difficult to

treat and provides a therapeutic challenge.

Anticoagulation

Initial anticoagulation is anticoagulant medication given within 10 days of a DVT diagnosis. Long-term anticoagulant medication is normally given for three to six months, and sometimes a year.[38] Anticoagulation is given indefinitely. In most cases, anticoagulation should be started immediately to reduce the risk of life-threatening embolization. LMW heparin, fondaparinux, rivaroxaban or apixaban, or unfractionated heparin are options (UFH). Due to the delayed depletion of vitamin K-dependent coagulation components, warfarin cannot be used alone to treat DVT.

Outpatient treatment with LMW heparin suggests that home treatment is safe and beneficial in certain patients. Outpatient therapy is an option for hemodynamically stable patients with low bleeding risk and no renal impairment. Inpatient therapy for patients with significant DVT (eg, iliofemoral DVT, phlegmasia cerulea dolens) with concurrent symptomatic PE, high risk of bleeding on anticoagulant medication, and other reasons requiring hospitalisation.[39]

Oral or subcutaneous anticoagulation is available. Subcutaneous anticoagulants include LMW heparin and fondaparinux. Oral anticoagulants include factor Xa inhibitors (rivaroxaban, apixaban, or edoxaban), thrombin inhibitors (dabigatran), and vitamin K antagonists (warfarin). Decisions between factor Xa and thrombin inhibitors are dependent on physician experience, bleeding risks, patient comorbidities, preferences, cost, and convenience.[40]

The recommended period of anticoagulation depends on triggering events, recurrence and bleeding risk factors, and the patient's preferences and values. The ideal length of time to treat a patient with a first episode of DVT is unknown. Anticoagulants should be given for three months to most patients with a first DVT (provoked or unprovoked, proximal or distal) (eg, four or six weeks). The decision of anticoagulation of the DVT patients indefinitely should be based on the risk of recurrence and bleeding, as well as the patient's values and desires (eg, occupation, life expectancy, burden of therapy).

Absolute contraindications to anticoagulation include:

- Active bleeding
- Severe bleeding diathesis
- Recent, planned, or emergency high bleeding-risk surgery/procedure
- Major trauma
- Acute intracranial haemorrhage (ICH)

Relative contraindications to anticoagulation include:

- Recurrent bleeding from multiple gastrointestinal telangiectasias.
- Intracranial or spinal tumours.
- Large abdominal aortic aneurysm with concurrent severe hypertension.
- Stable aortic dissection.
- Recent, planned, or emergent low bleeding-risk surgery/procedure.

When possible, avoid anticoagulation in older individuals (>65) with multiple falls and various bleeding risk factors. Epistaxis or severe menstrual bleeding are not considered high risk for bleeding, and anticoagulation can usually be safely administered in this population. In cancer patients, DVT therapy is associated with greater morbidity from recurrent thrombosis and anticoagulant-related haemorrhage.[41] For early and long-term anticoagulation, LMW heparin is preferable. Initial and long-term anticoagulation in pregnant women with acute DVT is best with subcutaneous LMW heparin. This agent has a better safety profile than warfarin. When taken between weeks 6 and 9, Warfarin might cause embryopathy. LMW heparin alternatives include intravenous and subcutaneous UFH.[42]

Assessing Bleeding Risk

All patients should be assessed for bleeding risk assessed before and during anticoagulant medication. Patients' prothrombin, APTT, and INR are monitored. Those on direct factor Xa and thrombin inhibitors and those >75 should be examined for conditions that may influence anticoagulant half-life. Anticoagulation increases the risk of bleeding, which depends on the dose and pre-existing bleeding risks. Anticoagulated persons have bleeding risk estimation tools (eg, HAS-BLED score). VTE-Bleed was created utilising data from randomised studies of dabigatran as an anticoagulant for VTE. During the first three months of anticoagulation, the benefits are larger. Patients who want to avoid anticoagulant haemorrhage should get an IVC filter.[43]

Heparin-induced thrombocytopenia

For patients with a DVT and a diagnosis of heparin-induced thrombocytopenia (HIT), all forms of heparin should be discontinued. This includes UFH, LMW heparin, heparin flushes, heparin bonded catheters, and heparin containing medications. Immediate anticoagulation with a non-heparin anticoagulant (eg, argatroban, danaparoid, fondaparinux) is indicated, unless there is a strong contraindication to anticoagulation.[44]

Gradual compression stockings

Despite prior concerns regarding the potential for embolization, early ambulation is safe in patients with acute DVT and should be encouraged as soon as is feasible.Compression stockings may be useful for symptomatic relief and the promotion of ambulation. In general, we prefer to avoid the routine use of elastic graduated compression stockings (GCS) that provide 30 to 40 mmHg of ankle pressure for the prevention of PTS. The decision is made to use compression stockings, they should be started after anticoagulant therapy, within two weeks of the diagnosis, and continued for two years.Although GCS are not harmful, many patients also decline their use because they are uncomfortable, costly, inconvenient, and often require a healthcare giver for their application. However, a subset of patients with recurrent DVT or moderate to severe symptoms may consider the potential benefits of GCS to outweigh these inconveniences. When the decision is made to wear GCS, they should be started after anticoagulant therapy. This is to avoid the theoretical risk of promoting embolism to the lung from fresh clot in the lower extremity. GCS should be continued for two years, replaced every six months, and may require refitting once local swelling is reduced. Contraindications to GCS include skin ulceration, severe arterial insufficiency, allergy to the stocking material, and inability to apply stockings.

Surgical management

Thrombolysis and/or thrombectomy are reserved for patients with phlegmasia cerulea dolens, large iliofemoral DVT, or who fail therapeutic anticoagulation. Suitable patients for thrombolysis should have symptoms for 14 days, good functional status, and low bleeding risk. Thrombolysis causes faster and more complete lysis, although recurrent VTE and death remain unchanged. Most specialists deem systemic thrombolysis' risk of significant bleeding unacceptable.[45] Thrombolytics can be given systemically or by a catheter in a lower extremity vein (catheter directed thrombolysis). Catheter directed thrombolysis can lyse clots faster and with lower doses than systemic thrombolysis, minimising bleeding risk. Mechanical or surgical thrombectomy may be an alternative or adjuvant to thrombolysis.

Inferior vena cava filter

IVC filters are not typically implanted in patients with acute DVT. IVC filters are utilised in patients with acute proximal DVT and PE who cannot take anticoagulants due to surgery, haemorrhagic stroke, or current bleeding.[46,47] The insertion of an IVC filter is also explored as supplemental therapy in patients with recurrent embolism despite appropriate anticoagulation, as well as in hemodynamically unstable patients with inadequate cardiopulmonary reserve from large PE or underlying cardiopulmonary illness.[48] Retrievable filters are preferred, although compliance is low. Some cohort studies suggest lower short-term mortality rates in patients with IVC filters, but there is no evidence that IVC filters prevent PE-related death.In one of the largest trials to date (PREPIC1) that assessed the efficiency of IVC filters, an eight years follow-up of the same population of patients supported these findings that filter insertion reduced PE (15 versus 6 percent) but increased DVT (35 versus 28 percent). Infrarenal caval filter insertion won't prevent emboli from renal veins, heart chambers, or upper extremity veins. IVC filter implantation is associated with complications like guidewire entrapment, local haemorrhage, fracture, embolization, and death (0.12 to 0.3 percent), thus assessing these risks against recurrence is recommended.[49,50]

CONCLUSION

Timely investigation and treatment can prevent and treat DVT. Monitor patients for DVT and anticoagulation problems like Extension, recurrence, and embolization. Compressive lower extremity ultrasound is needed for diagnosis and monitoring. Post-thrombotic postphlebitic syndrome, persistent thromboembolic pulmonary hypertension, bleeding, thrombocytopenia, and thrombosisor bleeding-related mortality are also monitored. Prothrombin time (PT) ratio is the most used lab test to monitor warfarin (INR). INR 2 to 3 (target 2.5). Low molecular weight heparin, fondaparinux, and factor Xa and direct thrombin inhibitors don't need lab monitoring. IVC filters

and thrombectomy are done in special cases.

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