

Deep vein thrombosis (DVT) and pulmonary embolism are the two main manifestations of venous thromboembolism (VTE). It is well established that anti coagulation with vitamin K antagonist (VKA) is the main stay of treatment for DVT, after initial treatment with unfractionated heparin [UFH] or low molecular weight heparin [LMWH]. However, in the light of emerging drugs like newer oral anti coagulants (NOACs) and new surgical options like catheter directed thrombolysis (CDT), the therapeutic options have broadened.

NOMENCLATURE — For the purposes of discussion in this topic, the following terms apply:

Unprovoked DVT – implies no identifiable provoking event for DVT is evident.

Provoked DVT – caused by a known event, ie; major surgery > 30 minutes, hospitalization or immobility ≥ 3 days, caesarian section), transient minor risk factors (minor surgery < 30 minutes, hospitalization < 3 days, pregnancy, estrogen therapy, reduced mobility ≥ 3 days) or persistent risk factors. Persistent risk factors include reversible conditions (eg, curable malignancy, inflammatory bowel disease that resolves) and irreversible conditions such as inheritable thrombophilias, chronic heart failure, and metastatic end-stage malignancy.

Proximal DVT – Located in the popliteal, femoral and iliac veins.

Distal DVT – No proximal component, is located below the knee and involves the calf veins.

INTRODUCTION

The earliest case of DVT was described by Sushruta in his book Sushruta Samhita around 600–900 BC. In 1856, German physician and pathologist Rudolf Virchow published what is referred to as Virchow's triad, the three major causes of thrombosis. The triad provides the theoretical framework for the current explanation of venous thrombosis.

The true incidence of VTE in India is underreported. In a retrospective study in CMC Vellore from (1996-2005) to determine the incidence of VTE among hospitalized patients and showed an overall incidence of confirmed DVTs to be 17.46 per 10,000 admissions with 64% being non surgical non trauma patients. PE was diagnosed in 14.9% of the study patients. Mortality in those with confirmed PE was 13.5%.

SIGNS, SYMPTOMS AND PHYSICAL EXAMINATION

Classic symptoms of DVT include swelling, pain, and erythema of the involved extremity. There may not necessarily be a correlation between the location of symptoms and the site of thrombosis. A complete history includes age, surgical procedures, hospitalization, trauma, pregnancy, heart failure, and immobility, use of oral contraceptives or hormone replacement therapy as well as their obstetric history in women. The presence of recurrent fetal loss in the second or third trimester suggests the possible presence of an inherited thrombophilia or antiphospholipid antibodies. Collagen-vascular disease, myeloproliferative disease, atherosclerotic disease, or nephrotic syndrome and the use of drugs which can induce antiphospholipid antibodies must be ruled out. The patient should also be questioned about a past history of cancer. Other findings that may suggest an underlying malignancy are constitutional symptoms such as loss of appetite, weight loss, fatigue, pain, hematochezia, hemoptysis, and hematuria. A positive family history of VTE is particularly important, since a well documented history of VTE in one or more first-degree relatives under age 50 suggests the presence of a hereditary defect and/or an increased susceptibility for venous thromboembolic disease.

The Wells criteria can be used for diagnosis of a DVT if the clinical suspicion is high.

Physical examination may reveal a palpable cord (reflecting a thrombosed vein), calf or thigh pain, unilateral edema or swelling with a difference in calf diameters, warmth, tenderness, erythema, and/or superficial venous dilation. The peripheral pulses must be documented to rule out venous gangrene and prevent compression related complications.

The initial laboratory evaluation in patients with venous thrombosis should include a complete blood count and platelet count, coagulation studies (eg, prothrombin time, activated partial thromboplastin time), renal and liver function tests, urinalysis, chest x-ray and ECG.

DIAGNOSIS OF DVT

A positive noninvasive study with a compression ultrasound in patients with a first episode of DVT usually establishes the diagnosis, with a positive predictive value for compression ultrasonography of 94%. If the initial study is negative and the clinical suspicion of DVT is high, a repeat study should be obtained on day 5 to 7.

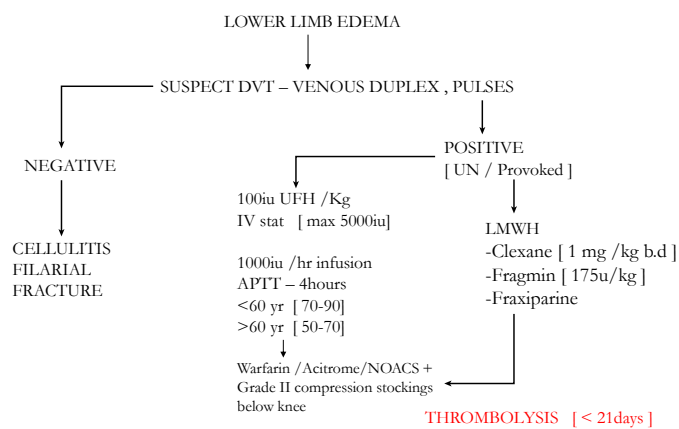


Fig. 1: DVT-Management

D-dimer level <500 ng/mL by ELISA or a negative SimpliRED assay in conjunction with a low clinical probability (ie, Wells score) or other negative noninvasive tests may be useful in excluding DVT, without the need for ultrasound testing

TREATMENT OF DVT (FIGURE 1)

The primary objectives for treatment of a DVT include

1. Prevent further clot extension
2. Prevent pulmonary embolism
3. Reduce the risk of the patient developing a chronic venous insufficiency
4. Reduce the risk of recurrence of DVT

Dosing requirements for LMWH are different for each LMWH product.

Treatment with LMW heparin, fondaparinux, or unfractionated heparin should be continued for at least 3 days and oral anticoagulation with a vitamin K antagonist should be overlapped with LMWH, fondaparinux, or UFH for at least 3 days.

Warfarin should be initiated simultaneously with the heparin, at an initial oral dose of approximately 5 mg/day. In elderly patients and in those at high risk of bleeding or who are undernourished, debilitated, or have heart failure or liver disease, the starting dose should be reduced. The heparin product can be discontinued on day 3 if the INR is therapeutic. Oral anticoagulation with a vitamin K antagonist should prolong the INR to a target range between 2.0 to 3.0.

For patients receiving UFH, ACCP guidelines suggest that platelet counts be obtained regularly to monitor for the development of thrombocytopenia. The heparin product should be stopped if any one of the following occurs: a precipitous or sustained fall in the platelet count, or a platelet count <100,000/microL.

Malignancy — For patients with malignancy and VTE, LMWH is the preferred anticoagulant for long-term use.

Pregnancy — LMWH is the preferred agent for long-term anticoagulation in pregnant women with acute VTE.

Renal failure — IV UFH is the preferred anticoagulant in those with severe renal failure.

Hemodynamic instability — IV UFH is the preferred anticoagulant in those who are hemodynamically unstable since thrombolysis, interventional procedure, or surgery may need to be considered in this population.

Extensive clot burden — IV UFH is the preferred anticoagulant for those patients with extensive DVT or with phlegmasia cerulea dolens, or those with massive or submassive PE which is based upon an anticipated need for a procedural or surgical intervention.

Obesity or poor subcutaneous absorption — There is no preferred agent in patients who are obese. However, therapeutic anticoagulation can be assured with IV UFH. IV UFH may also be an alternative to subcutaneous LMW heparin when subcutaneous absorption is potentially poor

Heparin-induced thrombocytopenia — For patients with VTE and a diagnosis of heparin-induced thrombocytopenia (HIT), anticoagulation with heparin, including UFH and LMW heparin, is contraindicated. Anticoagulation with a non-heparin anticoagulant (eg, Dabigatran, fondaparinux) should be administered.

The use of thrombolytic agents, surgical thrombectomy, or percutaneous mechanical thrombectomy in the treatment of DVT must be individualized. Patients with massive iliofemoral thrombosis (ie, phlegmasia cerulea dolens), and who are also at low risk to bleed, are the most appropriate candidates for such treatment.

Inferior vena caval filter placement is recommended when there is a contraindication to, or a failure of, anticoagulant therapy in an individual with, or at high risk for, proximal vein thrombosis or PE. It is also recommended in patients with recurrent thromboembolism despite adequate anticoagulation.

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.

Class 2 compression stockings should be started after anticoagulant therapy, within two weeks of the diagnosis, and continued for an year.

The minimal requirements for outpatient treatment for patients with DVT include

1. The patient is ambulatory, stable and with normal vital signs.
2. There is a low risk of bleeding.
3. Normal renal function.
4. There is a system in place for administration of heparin, appropriate monitoring and surveillance.

NEWER/NOVEL ORAL ANTI COAGULANTS

For most non-pregnant patients who do not have severe renal insufficiency (eg, creatinine clearance [CrCl <30mL/minute) or active cancer, we suggest the direct oral

878 anti coagulants, rivaroxaban, apixaban, edoxaban, or dabigatran, rather than warfarin and suggest warfarin rather than LMW heparin. While rivaroxaban and apixaban can be administered as monotherapy, edoxaban and dabigatran are preferably administered following a five day course of heparin. However treatment with newer anti coagulants is expensive and may place a large financial burden on the patient.

Typical initial doses in those with normal renal function are:

- Rivaroxaban - 15 mg by mouth twice daily for three weeks followed by 20 mg once daily
- Apixaban - 10 mg twice daily for seven days followed by 5 mg twice daily
- Edoxaban - 60 mg once daily
- Dabigatran - 150 mg twice daily

DURATION OF THERAPY

Most patients with a first episode of DVT (provoked or unprovoked) should receive anticoagulation for a minimum of three months.

Extending anticoagulation beyond three months is NOT routinely considered in patients who have a provoked DVT with the following: transient risk factors, assuming the risk factor is no longer present (eg, surgery, cessation of hormonal therapy), isolated distal DVT, sub segmental or incidental pulmonary embolism (PE), or those in whom the risk of bleeding is considered to be high.

Patients who should be considered as candidates for indefinite anticoagulation are recurrent VTE and diagnosed thrombophilia.

SUMMARY AND RECOMMENDATIONS

Anti - coagulation is the main stay of treatment of DVT. CDT is reserved for select patients in centres with the expertise to perform the procedure.