Deep Vein Thrombosis is Not Uncommon in India

Edwin Stephen, Vimalin Samuel, Sunil Agarwal, Dheepak Selvaraj, Prabhu Premkumar
Department of Vascular Surgery, Christian Medical College, Vellore, Tamil Nadu, India

Abstract

Deep vein thrombosis (DVT) has for long been under-diagnosed and ignored as one of the major causes of morbidity worldwide. Knowledge of the pathology and treatment of DVT has progressed many fold over the years. Despite it being common, knowledge of diagnosis and treatment of this potentially fatal condition remains limited. In this review article, we look at the DVT and the available options for diagnosis and treatment.

Keywords: Deep vein thrombosis, pathophysiology, treatment

INTRODUCTION

The earliest case of deep vein thrombosis (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.

There have been studies published from India[1-10] proving that venous thromboembolism (VTE) is as common as it is in the West. The incidence is 17.46/10,000 admissions,[1] and is on the rise, attributed to an increased awareness amongst treating physicians. DVT is not uncommon in India.

By having a high index of suspicion and following a simple protocol we could make a difference in the lives of our patients by reducing the morbidity and mortality associated with DVT.

DVT and pulmonary embolism (PE) are the two main manifestations of 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 anticoagulants and new surgical options like catheter-directed thrombolysis (CDT), the therapeutic options have broadened.

TERMINOLOGY

• Unprovoked DVT: Implies no identifiable provoking event for DVT is evident
• Provoked DVT: Caused by a known event, i.e., (major surgery >30 min, hospitalization or immobility ≥3 days, cesarian section), transient minor risk factors (minor surgery <30 min, hospitalization <3 days, pregnancy, estrogen therapy, reduced mobility ≥3 days) or persistent risk factors. Persistent risk factors include reversible conditions (e.g., 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
• VTE: DVT, PE.

CLINICAL FEATURES

History

A complete history should include 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

Address for correspondence: Dr. Edwin Stephen,
E-mail: edwinserina@gmail.com

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Stephen E, Samuel V, Agarwal S, Selvaraj D, Premkumar P. Deep Vein Thrombosis is Not Uncommon in India. Indian J Vasc Endovasc Surg 2017;4:92-6.

Received: June, 2017. Accepted: June, 2017.
or antiphospholipid antibodies. Collagen-vascular disease, myeloproliferative disease, atherosclerotic disease, or nephrotic syndrome and the use of drugs which can induce antiphospholipid antibodies such as hydralazine, procainamide, and phenothiazines should be ruled out. The patient should also be questioned about a history of cancer. 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 fifty suggests the presence of a hereditary defect and/or an increased susceptibility for venous thromboembolic disease.

**Physical examination**

Unilateral edema or swelling with a difference in calf diameters, warmth, tenderness, erythema, and/or superficial venous dilation [Figure 1]. The examination may reveal a palpable cord (reflecting a thrombosed vein), calf, or thigh pain. The peripheral pulses must be documented to rule out venous gangrene and prevent compression-related complications. The two often quoted signs of DVT; Homan’s sign and Moses sign are considered of no diagnostic value as they are neither specific nor sensitive, hence unreliable.

**Predictive Scores: Well’s Score and Caprini Score**

Validated prediction scores help to reliably predict the pretest probability of DVT which guides further management. Of the available predictions score for outpatients, the modified Wells score [Table 1] seems to be most useful due to its reproducibility in predicting the pretest probability of DVT.

In patients undergoing general and abdominal-pelvic surgeries, the Caprini score [Table 2] is used to assess the risk of DVT.

**Interpretation of the Caprini risk score**

The Caprini score is calculated by adding the scores of all factors present in the patient. The Caprini score is interpreted in the following way:[11]

- Score 0–1: Low risk of VTE
- Score 2: Moderate of VTE
- Score 3–4: High risk of VTE
- Score ≥5: Highest risk for VTE.

**Diagnosis of Deep Vein Thrombosis**

A clinical suspicion of DVT is the first step toward establishing the diagnosis. A patient may be given a single dose of anticoagulation, if the clinical suspicion is high while waiting for further diagnostic studies. A positive noninvasive study with a compression ultrasound in patients with the 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 within 48 h.

**Table 1: Wells score**

| Clinical Characteristic                                                                 | Score |
|----------------------------------------------------------------------------------------|-------|
| Active cancer (patient either receiving treatment for cancer within the previous 6 months or currently receiving palliative treatment) | 1     |
| Paralysis, paresis, or recent cast immobilization of the lower extremities               | 1     |
| Recently bedridden for ≥3 days, or major surgery within the previous 12 weeks requiring general or regional anesthesia | 1     |
| Localized tenderness along the distribution of the deep venous system                   | 1     |
| Entire leg swelling                                                                     | 1     |
| Calf swelling at least 3 cm larger than that on the asymptomatic side (measured 10 cm below tibial tuberosity) | 1     |
| Pitting edema confined to the symptomatic leg                                           | 1     |
| Collateral superficial veins (non-varicose)                                             | 1     |
| Previously documented deep vein thrombosis                                             | 1     |
| Alternative diagnosis at least as likely as deep vein thrombosis                        | –2    |

Wells scoring system for DVT: –2:0: low probability, 1-2 points: Moderate probability, 3-8 points: high probability

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

**Treatment of Deep Vein Thrombosis**

The primary objectives for treatment of a DVT include:

1. Prevent further clot extension
2. Prevent PE
3. Reduce the risk of the patient developing a postthrombotic syndrome
4. Reduce the risk of recurrence of DVT.

We present our protocol used for management of patients with acute DVT [Figure 2].

Dosing requirements for LMWH are different for each LMWH product.

Treatment with LMWH, fondaparinux, or UFH should be continued for at least 3 days, and oral anti-coagulation with a VKA should be overlapped with LMWH, fondaparinux, or UFH for at least 3 days, till 2 consecutive INR values 2 days apart are between 2 and 3.

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.[12] Oral anti-coagulation with a VKA should prolong the INR to a target range between 2.0 and 3.0.

**A Word of Caution: Heparin-Induced Thrombocytopenia**

For patients receiving UFH, ACCP guidelines[10] 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/µL.

**Special Subset of Patients**

**Malignancy**
For patients with malignancy and VTE, LMWH is the preferred anti-coagulant for long-term use.\(^{[13]}\)

**Pregnancy**
LMWH is the preferred agent for long-term anti-coagulation in pregnant women with acute VTE, in the first trimester because of warfarin being associated with neural tube birth defects.

**Renal failure**
Intravenous (IV) UFH is the preferred anti-coagulant in those with severe renal failure and should be started at a lower dose as these patients are known to have platelet dysfunction.

**Heparin: Induced thrombocytopenia**
For patients with VTE and a diagnosis of HITS, anti-coagulation with heparin, including UFH and LMWH, is contraindicated. Anti-coagulation with a nonheparin
anti-coagulant (e.g., dabigatran, fondaparinux) should be administered.

**Catheter Directed Thrombolysis, Surgical Thrombectomy**

The use of thrombolytic agents, surgical thrombectomy, or percutaneous mechanical thrombectomy in the treatment of DVT must be individualized. ACCP 2016 places CDT for DVT as a Class 2b recommendation.[14] Centers in India with the expertise and availability of equipment needed have had good short-term outcomes. Long-term outcomes are awaited and need to be published.

Patients with massive ilio-femoral thrombosis (i.e., phlegmasia cerulea dolens), and who are also at low risk to bleed, are the most appropriate candidates for such treatment.

**Out-patient Treatment of Deep Vein Thrombosis**

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 the administration of heparin, appropriate monitoring and surveillance.

**Inferior Vena Caval Filter**

Inferior vena caval filter placement is recommended when there is a contraindication to, or a failure of, anti-coagulant 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 anti-coagulation. The use of temporary filters that can be retrieved once the patient can be anti-coagulated is encouraged.

**Newer/Novel Oral Anti-coagulants**

For most nonpregnant patients who do not have severe renal insufficiency (e.g., creatinine clearance <30 mL/min) or active cancer, we suggest the direct oral anti-coagulants-rivaroxaban, apixaban, edoxaban, or dabigatran, rather than warfarin and suggest warfarin rather than LMWH. While rivaroxaban and apixaban can be administered as monotherapy, edoxaban, and dabigatran are preferably administered following 5 days 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 3 weeks followed by 20 mg once daily
- Apixaban - 10 mg twice daily for 7 days followed by 5 mg twice daily
- Edoxaban - 60 mg once daily
- Dabigatran - 150 mg twice daily.

**Duration of Therapy for Provoked Deep Vein Thrombosis**

Most patients with a first episode of proximal DVT (provoked or unprovoked) should receive anti-coagulation for a minimum of 3 months.

Extending anti-coagulation beyond 3 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 (e.g., surgery, cessation of hormonal therapy), isolated distal DVT, subsegmental or incidental PE, or those in whom the risk of bleeding is considered to be high.

**Lifelong Anti-coagulation**

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

**Discharge Advice**

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. Adequate hydration and an active lifestyle including lifestyle modification to reduce modifiable risk factors of obesity is encouraged.

Class 2 compression stockings should be started after anti-coagulant therapy, within 2 weeks of the diagnosis, and continued for at least 1 year.

**Summary**

- A treating doctor should have a high index of suspicion when a patient presents with a recent onset swelling of the limb/s or develops breathlessness in the ward
- Anti-coagulation is the main-stay of treatment of VTE
- UFH or LMWH can be used based on treating doctor’s choice and keeping in mind the cost of LMWH versus the cost of regular activated partial thromboplastin time testing
- CDT should only be done in centres with the facilities and experience
- Increased awareness of prophylaxis for VTE will decrease the incidence of VTE and “sudden deaths” in hospitals.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Lee AD, Stephen E, Agarwal S, Premkumar P. Venous thrombo-embolism in India. Eur J Vasc Endovasc Surg 2009;37:482-5.
2. Agarwal S, Lee AD, Raju RS, Stephen E. Venous thromboembolism: A problem in the Indian/Asian population? Indian J Urol 2009;25:11-6.
3. Cohen AT, Tapson VF, Bergmann JF, Goldhaber SZ, Kakkar AK, Deslandes B, et al. Venous thromboembolism risk and prophylaxis...
Stephen, et al.: DVT is not uncommon in India

in the acute hospital care setting (ENDORSE study): A multinational cross-sectional study. Lancet 2008;371:387-94.

4. George AJ, Nair S, Karthic JC, Joseph M. The incidence of deep venous thrombosis in high-risk Indian neurosurgical patients: Need for early chemoprophylaxis? Indian J Crit Care Med 2016;20:412-6.

5. Kakkar N, Vasishtha RK. Pulmonary embolism in medical patients: An autopsy-based study. Clin Appl Thromb Hemost 2008;14:159-67.

6. Rajagopalan N. Thromboprophylaxis by dalteparin sodium in elective major orthopaedic surgery – A multicentric Indian study. Indian Journal Orthopedics 2003;37:4.

7. Leizorovicz A, Turpie AG, Cohen AT, Wong L, Yoo MC, Dans A; SMART Study Group. Epidemiology of venous thromboembolism in Asian patients undergoing major orthopedic surgery without thromboprophylaxis. The SMART study. J Thromb Haemost 2005;3:28-34.

8. Piovella F, Wang CJ, Lu H, Lee K, Lee LH, Lee WC, et al. Deep-vein thrombosis rates after major orthopedic surgery in Asia. An epidemiological study based on postoperative screening with centrally adjudicated bilateral venography. J Thromb Haemost 2005;3:2664-70.

9. Parakh R, Kakkar VV, Kakkar AK; Venous Thromboembolism (VTE) Core Study Group. Management of venous thromboembolism. J Assoc Physicians India 2007;55:49-70.

10. Kearon C, Akl EA, Ornelas J, Blaivas A, Jimenez D, Bounamenteux H, et al. Antithrombotic therapy for VTE disease: CHEST guideline and expert panel report. Chest 2016;149:315-52.

11. Caprini JA, Arceius JJ, Hasty JH, Tamhane AC, Fabrega F. Clinical assessment of venous thromboembolic risk in surgical patients. Semin Thromb Hemost 1991;17 Suppl 3:304-12.

12. Indian Consensus on Management of VTE. Available from: http://www.japi.org/september_2016_special_issue_consensus/pdf/02_consensus_on_management.pdf. [Last accessed on 2017 Jun 7].

13. Stephen E, Sen I, Lees T. The swollen leg. In: Coomoraswamy A, Shafi M, Davila GW, Chan KK, editors. Gynecologic and Obstetric Surgery: Challenges and Management Options. Ch. 57. Oxford, UK: John Wiley & Sons, Ltd; 2016.

14. Society of Interventional Radiology-News Release; 2017. Available from: https://www.sirweb.org/advocacy-and-outreach/media/news-release-archive/news-release-ATTRACT-Trial. [Cited on 2017 May 19].