

Evaluation of Deep Vein Thrombosis Diagnostic and Management Approach

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Abstract

Introduction: Deep Vein Thrombosis (DVT) is a common disease and is a subset of venous thromboembolism (VTE). It is a significant preventable cause of mortality and morbidity in the world. Anticoagulant therapeutic approaches such as heparin and also vitamin K antagonists were introduced during the early 20th century. The development of surgical thrombectomy and new vena cava clips treatments were promoted to reduce mortality and avoid unexpected complications. Moreover, new strategies have evolved to diagnose this condition. **Methodology:** PubMed published data was used for articles selection and using the following keys in the mesh ((“DVT”[Mesh])), ((“VTE”[Mesh])), ((“Deep Venous Thrombosis”[Mesh])), ((“Venous”[Mesh])). **Conclusion:** DVT is an annoying and prevalent problem for clinicians and it is important to promote diagnosis and treatment. Although the safety profile of DOACs has been quite favorable, dabigatran and rivaroxaban increase the risk of GI bleeding in patients, and further research is necessary.

Keywords: DVT, VTE, heparin, GI bleeding.

INTRODUCTION

Deep Vein Thrombosis (DVT) occurs when a blood clot forms in the deep veins of the lower extremities and is often associated with other more extensive conditions including Venous thromboembolism (VTE). The precise and reliable case was firstly reported in the medieval centuries. However, anticoagulant therapeutic approaches such as vitamin K antagonists and heparin were introduced in the early 20th century, and the development of surgical thrombectomy treatments and new vena cava clips decreased mortality or prevented late complications ^[1]. DVT has been a common problem in primary care, acute care, and inpatients. According to recent studies, DVT annually affects 1/1000 people and causes 60000-100000 deaths ^[2]. Post-thrombotic Syndrome rises in 50% of patients as a result of prolonged DVT in patients within two years. There are signs of chronic venous insufficiency in this disease, including dominant swelling, severe leg pain, and venous ulcers. Clinical features are imprecise; thus, advanced and new strategies have been monitored for diagnosing these conditions.

This review highlights updates in administrating and managing DVT and will assist physicians in better understanding of DVT and ultimately improving patient care.

METHODOLOGY:

PubMed was searched for journal articles containing the terms ‘Deep Vein Thrombosis’ ‘Venous thromboembolism’ within the title or abstract. After identifying relevant articles, their abstracts were read and eligible articles were retrieved. The function of related articles in PubMed was also used to identify articles not found in the original search. Only full-text English articles were interrogated for this review.

Review:

DVT is one of the common and leading preventable causes of mortality and morbidity in the world for most cases of pulmonary embolism. In the diagnosis of DVT, a

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multifaceted approach is required, which includes clinical impressions, work up evaluations, and diagnostic regimens.

Epidemiology:

The silent and fatal presentation of pulmonary embolism and DVT are missed in clinical examination and assessment but they are usually diagnosed on autopsy. Therefore, the incidence and prevalence of most cases are often miscalculated. Although, annual incidence proportion in 80 cases per 100,000, with a prevalence of lower limb DVT has a ratio of approximately 1:1000 [3-5]. Men develop eventful proximal DVT in the lower limbs more likely than women [6]. Furthermore, pregnant women have a much higher risk of developing VTE than nonpregnant women of the same age, with higher risk after the caesarian section than the vaginal delivery [7]. Certain conditions are associated with the high risk of pregnancy-related DVT, which include a previous history of thrombosis, acquired or inherited thrombophilias, sickle cell disease antiphospholipid syndrome, heart disease, and lupus [8].

Pathophysiology:

Virchow's triad was described in three major factors that are important in the pathophysiology of the DVT. The triad proposed that the activation of clotting cascade, as well as the aggregation of platelets and blood cells occur simultaneously to form a thrombus that might lead to serious thromboembolic complications [2, 4].

Diagnosis:

There are various ways in managing DVT. The first decision to be made is whether the patient needs to be hospitalized or can be discharged on anticoagulation. This is a complex decision that depends on many factors including patient adherence to medication, insurance issues, the reliability of follow-up, renal function, concomitant medications and comorbidities, the risk of falling, and how ill the patient appears [9].

The clinical presentation and physical examination impression of DVT modify and define the extent and site of a thrombus. Symptoms and signs of DVT are vital and include asymmetrical swelling of the extremities, heaviness or unbearable pain in thrombus site of the affected limb, and a high suspicion index. 40% of patients have a silent pulmonary embolism (PE) when they are diagnosed with symptomatic DVT. About 4% of patients treated for DVT develop symptomatic PE. Almost 1% of postoperative hospitalized patients develop PE. Wells' criteria are the most common criteria used to estimate the probability of DVT [2, 10].

Routine workup such as blood test helps clinicians in identifying patients with the risk for DVT and includes D-dimer assay; monitoring levels of antithrombin III (ATIII), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and N-terminal pro-brain natriuretic peptide (NT-proBNP). Increased D-dimer is related to thrombosis, nevertheless, it

can be elevated in various pathologic settings including malignancy, pregnancy, liver disease, and inflammatory conditions [3].

Diagnostic imaging is often utilized to confirm DVT. However, studies have suggested that the CEBI scoring system [Center for Evidence-Based Imaging] improves substantially on the Wells' Score, which is performed poorly in inpatients. Its strength is to precisely identify low-risk patients who do not need further imaging, potentially reducing overuse [11]. Diagnostic venographies used for DVT include magnetic resonance (MR), computed tomography (CT), and conventional contrast. Historically, the golden standard for DVT diagnosis is contrast venography, which assesses both proximal and distal deep veins of the lower limbs, but it is influenced by a number of settings including the availability of patient's information in the primary health care, user-dependence, patients satisfactory issues, inadequate visualization, and patient past medical history of clinical condition such as renal insufficiency and contrast allergy. Moreover, significant imaging modalities such as ultrasonography and venography are not suitable for most older patients with heart failure; there have been ongoing arguments about the D-dimer prognostic value in elderly as mentioned in many studies. Furthermore, most common disadvantages of venography include patient discomfort, incompatible hardware, and increased cost [12, 13].

The key points in the treatment of DVT are to prevent its complication to pulmonary embolism (PE), reduce mortality and morbidity, and to minimize the ultimate risk of post-thrombotic syndrome (PTS) [14]. Recent Ongoing ATTRACT trials have been done and few investigations have documented relationships among duplex ultrasonography (DUS) endovascular therapy, post-thrombotic syndrome (PTS), and its major effect on the quality of life (QOL).

Historically, the basic medical therapy in DVT has been heparin since it was introduced as an essential anticoagulant in 1935. Oral anticoagulants alone can treat DVT patients. Moreover, Mechanical- and catheter-directed thrombolysis (CDT) is recommended for 1 month in the acute phase of extensive cases and this modality rapidly induces clot lysis reducing Post Thrombotic Syndrome risks [15].

Currently, direct thrombin inhibitor (e.g. Dabigatran) and factor Xa inhibitors (e.g. apixaban, rivaroxaban, and edoxaban) have been approved to be used to prevent and treat the disease. But, treatment with thrombolytics increases the risk of major bleeding and has shown no benefit in preventing mortality in DVT patients. There are undeniable insufficient data forms that support models of integration for the bleeding risk during thrombolytic therapy. Despite the essential regimes in anticoagulation therapy that have proven its ability in inhibiting the thrombus proliferation, it was not able to remove the thrombus completely. Venous interventions certainly improve the outcomes of VTE patients, so further studies and trials should be done to fully determine their

advantages and disadvantages.^[16] Compression stockings and early mobility after surgery are essential. For those treated promptly, the outlook is good but the postphlebotic syndrome is known to occur in a significant number of patients.^[17]

CONCLUSION:

Although medical research focused on understanding DVT and developed new diagnostic strategies and modalities, and constant refinement in the use of venous thromboembolism, thrombolytic therapy remains under study. Despite progressions in anticoagulation therapy, there is undeniably insufficient data that supports bleeding risks during thrombolytic therapy. Finally, with all this in mind, physicians should feel confident in deferring ultrasound in truly low-risk patients and are not hesitant to pursue diagnostic imaging in most of the hospitalized patients.

REFERENCES

1. Galanaud JP, Laroche JP, Righini M. The history and historical treatments of deep vein thrombosis. *J Thromb Haemost.* 2013;11(3):402-411. doi:10.1111/jth.12127.
2. Stone J, Hangge P, Albadawi H, Wallace A, Shamoun F, Knuttien MG, Naidu S, Oklu R. Deep vein thrombosis: pathogenesis, diagnosis, and medical management. *Cardiovascular diagnosis and therapy.* 2017 Dec;7(Suppl 3):S276. doi:10.21037/cdt.2017.09.01.
3. Sharif S, Eventov M, Kearon C, Parpia S, Li M, Jiang R, Sneath P, Fuentes CO, Marriott C, de Wit K. Comparison of the age-adjusted and clinical probability-adjusted D-dimer to exclude pulmonary embolism in the ED. *Am J Emerg Med.* 2019 May;37(5):845-850.
4. Kruger PC, Eikelboom JW, Douketis JD, Hankey GJ. Deep vein thrombosis: update on diagnosis and management. *Med J Aust.* 2019;210(11):516-524. doi:10.5694/mja2.50201.
5. Hansen AT, Juul S, Knudsen UB, Hvas AM. Low risk of venous thromboembolism following early pregnancy loss in pregnancies conceived by IVF. *Hum. Reprod.* 2018 Oct 01;33(10):1968-1972.
6. Barco S, Klok FA, Mahé I, Marchena PJ, Ballaz A, Rubio CM, Adarraga MD, Mastroiacovo D, Konstantinides SV, Monreal M, RIETE Investigators. Impact of sex, age, and risk factors for venous thromboembolism on the initial presentation of first isolated symptomatic acute deep vein thrombosis. *Thrombosis Research.* 2019 Jan 1;173:166-71. doi:10.1016/j.thromres.2018.09.056.
7. Devis P, Knuttinen MG. Deep venous thrombosis in pregnancy: incidence, pathogenesis and endovascular management. *Cardiovascular diagnosis and therapy.* 2017 Dec;7(Suppl 3):S309. doi:10.21037/cdt.2017.10.08.
8. James AH, Jamison MG, Branciazio LR, Myers ER. Venous thromboembolism during pregnancy and the postpartum period: incidence, risk factors, and mortality. *Am J Obstet Gynecol.* 2006;194(5):1311-1315. doi:10.1016/j.ajog.2005.11.008.
9. Streiff MB, Agnelli G, Connors JM, Crowther M, Eichinger S, Lopes R, McBane RD, Moll S, Ansell J. Guidance for the treatment of deep vein thrombosis and pulmonary embolism. *Journal of thrombosis and thrombolysis.* 2016 Jan 1;41(1):32-67. doi:10.1007/s11239-015-1317-0.
10. Tran HA, Gibbs H, Merriman E, Curnow JL, Young L, Bennett A, Tan CW, Chunilal SD, Ward CM, Baker R, Nandurkar H. New guidelines from the Thrombosis and Haemostasis Society of Australia and New Zealand for the diagnosis and management of venous thromboembolism. *Medical Journal of Australia.* 2019 Mar;210(5):227-35. doi:10.5694/mja2.50004.
11. Parks AL, Kohlwes RJ. Refining Risk for Deep Vein Thrombosis in Hospitalized Patients. *J Gen Intern Med.* 2018;33(1):6. doi:10.1007/s11606-017-4194-8.
12. Xing F, Li L, Long Y, Xiang Z. Admission prevalence of deep vein thrombosis in elderly Chinese patients with hip fracture and a new predictor based on risk factors for thrombosis screening. *BMC Musculoskelet Disord.* 2018;19(1):444. Published 2018 Dec 20. doi:10.1186/s12891-018-2371-5.
13. Kraaijpoel N, Carrier M, Le Gal G, McInnes MD, Salameh JP, McGrath TA, van Es N, Moher D, Büller HR, Bossuyt PM, Leeflang MM. Diagnostic accuracy of three ultrasonography strategies for deep vein thrombosis of the lower extremity: A systematic review and meta-analysis. *PloS one.* 2020 Feb 11;15(2):e0228788. Published 2020 Feb 11. doi:10.1371/journal.pone.0228788.
14. Wood KE. A history of pulmonary embolism and deep venous thrombosis. *Crit Care Clin.* 2009;25(1):115-viii. doi:10.1016/j.ccc.2008.12.014.
15. Behraves S, Hoang P, Nanda A, Wallace A, Sheth RA, Deipolyi AR, Memic A, Naidu S, Oklu R. Pathogenesis of thromboembolism and endovascular management. *Thrombosis.* 2017;2017. https://doi.org/10.1155/2017/3039713.
16. Weinberg I, Vedantham S, Salter A, Hadley G, Al-Hammadi N, Kearon C, Julian JA, Razavi MK, Gornik HL, Goldhaber SZ, Comerota AJ. Relationships between the use of pharmacomechanical catheter-directed thrombolysis, sonographic findings, and clinical outcomes in patients with acute proximal DVT: Results from the ATTRACT Multicenter Randomized Trial. *Vascular Medicine.* 2019 Oct;24(5):442-51. doi:10.1177/1358863X19862043.
17. López-Núñez JJ, Trujillo-Santos J, Monreal M. Management of venous thromboembolism in patients with cancer. *J. Thromb. Haemost.* 2018 Dec;16(12):2391-2396.