Treatment And Prevention of Deep Vein Thrombosis

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Abstract. Deep vein thrombosis (DVT) is caused by abnormal deep vein coagulation, which is most common in the lower limbs, but sometimes it may also occur in other parts such as the subclavian vein. The main adverse consequence of DVT is pulmonary embolism (PE), which will seriously affect the quality of life of patients, and even endanger their lives. Although Paget-Schroetter syndrome (PSS) syndrome is rare, it also affects the physical and mental health of patients to a certain extent. Many factors may lead to the occurrence of this disease. Clinically, more attention should be paid to the risk factors to prevent the occurrence of the disease. At the same time, when the disease occurs, active treatment and intervention should be carried out to delay the progress of the disease. Anticoagulation is the basic treatment of DVT, which can inhibit the spread of thrombus, facilitate the autolysis of thrombus and recanalization of the lumen, and reduce the incidence and mortality of PE. At the same time, combined with other treatment programs, co-intervention.

Keywords: Deep Vein Thrombosis (DVT), Subclavian DVT, Paget-Schroetter Syndrome.

1. Introduction

Deep vein thrombosis, also called deep venous thrombosis (DVT), is a medical condition that occurs when blood clots form in the deep veins of human bodies. The condition typically happens in the lower legs and thighs, but sometimes a thrombus also occurs in the deep veins of other parts of the body.

When a DVT is developed, it is usually on one side of the body. Patients might experience symptoms such as throbbing pain in affected parts, which may be accompanied by swelling, changes in skin color of the pain area (redness), and warm skin around the site. The thrombus itself is not lethal, but it can become dangerous when the clot falls off the venous wall and travels through the bloodstream. When a clot travels to a narrow blood vessel that is too small for it to pass through, it would block the vessel and hinder blood flow. In this case, the situation is called an embolism. Embolism can damage organs and lead to loss of functions by limiting blood supply and lowering oxygen level. It can also lead to ischaemic stroke if blood flow to the brain is cut off.

Nowadays, a sizable portion of the population is affected by this illness. And the annual incidence rate is about 1-2 episodes per 1000 individuals. As suggested by scientific modeling, a number of 900,000 people suffer from DVT annually in the United States. Among them, 60,000-100,000 die of DVT or pulmonary embolism (PE), a condition in which the artery in the lung is blocked by a blood clot. Data also shows that 10% to 30% of patients pass away within a month after diagnosis. Additionally, about 1 in 3 of the 900,000 will experience post-thrombus problems like pain, edema, or discoloration. Within 10 years, 33% are likely to have another incident [1].

Subclavian vein thrombosis is a peripheral vascular disease with a relatively low incidence rate. PSS is the primary subclavian axillary vein thrombosis, also known as "frustrated" thrombosis. The incidence rate is relatively low, but it also has a greater impact on people's lives, especially the young women [2-4].

This paper will focus on the treatment and prevention of deep vein thrombosis, with a particular focus on the subclavian deep vein thrombosis. Multiple curing methods will be compiled and compared. Using experimental data from published papers, treatments will be compared on the basis of their effective rates.

2. Subclavian DVT

A subclavian deep vein thrombosis is a type of DVT that happens when blood clots form in the subclavian veins just below the clavicles. These paired subclavian veins are located on either side of the body and play a vital role in blood circulation. They help transport deoxygenated blood from extremities, such as the neck and the head, back to the heart. When a thrombus forms in subclavian veins, people might experience symptoms like neck or arm pain, fatigue or swelling in arms, and anomalous muscle bulks. If not treated in time, subclavian DVT could be life-threatening.

Certain risk factors may increase the likelihood of developing a blood clot: have been immobile or sedentary for a long period of time; family history of blood clots; obesity; pregnancy or giving birth within the past six months; surgery or fractures (most commonly in the hip or pelvic area); a long-term catheter in the vessel, which is the most common cause of upper extremity DVT. Moreover, cancer patients, smokers, women taking birth control pills or estrogens are at a higher risk of developing blood clots. The risk can be even higher when multiple above risk factors are combined. In recent years, a link between COVID-19 and thrombosis has been discovered. Research showed that severe Covid-19 is associated with increased risk of DVT as the chance of thrombus formation has been elevated on account of inflammatory reactions to the coronavirus causing coagulation abnormalities. Data indicates that patients with severe COVID-19 infection had a higher risk of DVT and PE than patients who do not have COVID-19 but have illnesses of a similar severity [5]. Some severe COVID-19 cases require hospitalization, and the resulted immobility adds to the risk factor of DVT.

Either a primary or a secondary etiology is responsible for subclavian DVT, which accounts for approximately 10% - 20% of all upper extremity DVT cases [6]. The primary subclavian DVT is often referred to as effort thrombosis or Paget-Schroetter syndrome (PSS), and it happens when the vein is being compressed at the tunnel formed by the first rib, subclavius muscle tender and the anterior scalene muscle tendon [7]. Patients with PSS are usually those who frequently participate in sports or in jobs that require repetitive arm motions. Injury in the upper extremity such as rib or collarbone fracture can also trigger subclavian vein thrombosis. Nevertheless, with an estimated annual incidence of only 2 per 100,000 people, PSS is rare.

Secondary subclavian vein thrombosis is more common and associated with catheters or lines in the vein. As a result of increasing use of sophisticated cardiac devices and long-term central venous catheters (CVC) insertion in cancer patients, secondary thrombosis is becoming more common and accounts for more than 10% of all DVT instances [8]. Accompanying consequences of secondary subclavian DVT are often fatal and frequently leads to a higher death rate than that of lower extremity deep vein thrombosis. Both primary and secondary thrombosis can lead to mortality or life-threatening complications if left untreated or failure to obtain timely treatment. Therefore, early diagnosis and treatment of subclavian DVT are crucial to the prevention of complications and PE.

3. Treatment

It has been a long battle against DVT in human history. The first well-documented case of DVT can be traced back to the Middle Ages, when a man developed unilateral swelling in his ankle that later spread to his leg. Following that, the frequency of reported DVT cases rapidly rose, with the highest frequency in pregnant and postpartum women. In order to treat this medical condition, many treatment techniques that were inspired by the prevalent ideas back at that time were invented and put in use. Complementary treatments, such as vena cava clips and surgical thrombectomy, were also invented to reduce DVT mortality, though nowadays, the majority of these treatments have been abandoned.

Currently, the standard treatment for curing acute DVT is through medications, inferior vena cava (IVC) filters, or DVT thrombolysis. The medications are also referred to as anticoagulation or blood thinning medications. In fact, the medications do not actually ‘thin’ the blood; instead, they prevent the expansion of existing blood clots and allow blood flow around the thrombi by controlling various

clotting factors. Right now, the most commonly-used blood thinning medications are Apixaban (Eliquis), Betrixaban (Bevyxxa), Dabigatran (Pradaxa), Edoxaban (Savaysa), Fondaparinux (Arixtra), Heparin, Rivaroxaban (Xarelto), Warfarin [9,10]. However, these medications will not clear any thrombi that have already formed in the vein, rather, they help limit the growth of thrombi and rely on the patients' own defense system to dissolve the clots. Sometimes, it may take several months for the body to dissolve a thrombus. However, when the defense system fails to dissolve the blood clots, the clots can remain inside the vein permanently.

Certain cases necessitate additional DVT treatment when medications alone are insufficient or are not recommended. Under these circumstances, a surgeon will insert a tiny filter in the inferior vena cava (IVC), the major vein that brings the blood back to the heart, to facilitate the blood flow around thrombi and avoid developing PE. Similarly, an IVC filter does not eradicate clots in the vein. For patients diagnosed with acute DVT or large clots, a process called DVT thrombolysis will be performed to relieve symptoms and remove clots. During DVT thrombolysis, a tiny catheter is inserted into the leg under ultrasound and x-ray supervision. Mechanical devices and clot-dissolving drugs can both be put into the catheter to remove or decrease the size of the clot. This method frequently reveals one or more confining venous sites that contributed to the blood clot formation. If needed, veins can be widened via angioplasty, or to use a mesh-like venous stent to keep the vein open. DVT thrombolysis may as well lessen the likelihood of getting Post Thrombotic Syndrome (PTS). The best results from DVT thrombolysis treatment are seen in patients with newly-appearing symptoms.

3.1. Treatment for Paget-Schroetter syndrome (PSS)

Evidence has proven that immediate thrombolysis, followed by a resection of the first rib or a scalenectomy is the most effective treatment for severe PSS cases. Anticoagulation alone is typically insufficient for treating PSS patients. Additionally, early surgical intervention often yields a better outcome than conservative therapy. Catheter-directed thrombolysis at an early stage is the most potent approach, with a success rate as high as 75% to 84%. For a thrombosis formed longer than 2 weeks, thrombolytic therapy success rate decreases to 29% [11].

In research published in The Journal of Cardiovascular Surgery, data shows that PSS patients who underwent surgical decompression of the thoracic outlet (SDTO) and subclavian vein recanalization early in the illness had better vein patency and long-term function outcomes [12]. In a cohort study of 33 PSS patients between January 1978 to January 2013, all patients, among which 16 women and 17 men aging 14 to 53, underwent SDTO procedure either through transaxillary or combined supra-infraclavicular approach. Patients with surgeries performed within 10 days were categorized as the early group, whereas those with surgeries performed between 30 to 120 days were categorized as the late group. There were 13 people in the early group and 20 in the late group. In the early group, subclavian vein recanalization was achieved through thrombolysis, thrombectomy, or endovenectomy followed by patch venoplasty. The late group was using chronic anticoagulation to prepare for subclavian vein recanalization. After a median duration of 240 months, a follow-up was conducted to inspect the outcomes of procedures. It has found that the majority (12 out of 14) patients have their subclavian vein remained patent, while multiple re-occlusions and chronic subclavian vein occlusions were discovered in the late group. The results are statistically significant (p-value equals 0.005) and suggested that interventions at an early stage yielded significantly better outcomes.

When handling acute PSS, preoperative thrombolysis is linked to better venous patency and functional results following first rib removal. In a study involving 100 PSS patients, half received treatment with both thrombolysis and anticoagulation, whereas the remaining half only received the latter. Following the first rib removal operation, venography showed that 92% of the combined treatment group had achieved vein patency, but only 74% of the anticoagulation group were able to reach the same result. The study concludes that thrombolysis, along with anticoagulation may lead to an enhanced final vein patency after first rib removal procedures.

To better understand the need and importance of first rib resection (FRR) in treating acute PSS, an analysis has been performed on postoperative outcomes of 684 patients, aged over 18 years old with symptoms appearing within the past 14 days. 448 of the patients in the study received FRR following thrombolysis, 68 had FRR with venoplasty, and 168 only underwent thrombolysis with no FRR. A clear improvement in both symptom relief and patency is supported by data as 98% of the FRR group, 86% of the FRR plus venoplasty group and 48% of the non-FRR group had higher vein patency. At the same time, 95%, 93%, 53% of the three groups respectively reported relief of PSS symptoms. Vein patency was considerably more probable in the FRR and FRR plus venoplasty groups compared to the non-FRR group, as was symptom alleviation, suggested by follow-up. The data also indicates with a p-value less than 0.0001 that patients who underwent FRR (with or without venoplasty) have a better outcome than those who received no other interventions after thrombolysis. Therefore, FRR is believed to be positively associated with improved vein patency and long-term symptom relief.

Despite the promising outcome of a surgical approach, not all patients are suitable for thrombolysis surgeries, and complementary therapeutic operations may be needed based on patients' health conditions and symptom severity. In general, surgery is recommended for all PSS patients except for those who are asymptomatic or are unable to undergo surgeries. For individuals with mild symptoms, decompression surgery along with anticoagulation is given. For those with more severe symptoms, a saphenous patch can serve as a treatment if the veins are reconstructible. However, the treatment should vary according to different vein conditions [13].

3.2. Treatment for secondary subclavian DVT

Treatment for this type of subclavian DVT varies according to patients' health status, and several factors should be taken into consideration before initiating therapy. Patients can be divided into two categories based on the condition of their catheters. In the first category, catheters are removable. If the risk of developing PE is low, then catheters should be removed and anticoagulation is not necessary after procedures. However, if the possibility of developing PE is high, then anticoagulation should be administered after removal of catheters. In the situation of non-removal catheters, usually due to catheters still in use, anticoagulation therapy should start immediately and continue for more than 3-6 months after catheter removal. Once the long-term catheters have served their purpose, they should be taken out right away. In general, among individuals diagnosed with a secondary subclavian DVT, the majority show clinical improvement after a catheter removal and a systematic anticoagulation for 3 months. Thrombolysis may be necessary if there is axillo-subclavian DVT extension and appearance of severe symptoms.

4. Prevention

DVT should be given enough attention as they may lead to life-threatening complications if blood clots break loose. Therefore, it is important to prevent DVT because it can strike anyone at any time and result in lethal disease, incapacity, and in extreme circumstances, even death. A simple way to prevent DVT is through changing unhealthy habits such as smoking, being sedentary, and eating unhealthy diets. Quitting smoking helps avoid DVT, because nicotine in cigarettes increases blood viscosity by raising the quantity of blood platelets. When prolonged immobility is inevitable due to occupations or traveling, intentional walking and stretching at regular intervals will inhibit blood clots from accumulating in your deep veins by making muscles contract. Moreover, regular exercise and a healthy diet can also lower the chance of developing DVT by preventing obesity, which is a large risk factor of DVT as it reduces the level of fibrinolysis, a process that impedes blood clots from growing.

With the help of technology, prevention of DVT can be further improved. Precise diagnostic screening on patients both before and after surgery can greatly reduce the risk. By discovering early, provision of treatment can be carried out in time to stop the deterioration of conditions and to prevent the morbidity and mortality that come with acute DVT. However, there are some downsides about diagnostic screening. Contrast venography is pricy, often uncomfortable, and impracticable to carry

out outside of clinical research. Venous ultrasonography is less sensitive in asymptomatic patients than in symptomatic patients [5].

5. Further thoughts

Although deep vein thrombosis and pulmonary embolism and their related complications, mortality, and hospitalization have become a tremendous public concern and burden in modern societies, public awareness of these diseases is still lagging. Only 28% of the respondents in a survey performed in six developed countries were aware of the signs of PE, while only 19% were aware of the symptoms of DVT [5]. Health education sectors and governments should seek to raise public awareness as an increased global awareness of DVT and PE is critical to the discovery of these medical conditions and, as a result, the prevention of fatal PE.

Besides, further research and analysis are still needed in order to discover the optimal treatments for PSS. Although the fundamental treatments for subclavian DVT are generally acknowledged, the database for studying PSS is too limited to make improvements on current medical approaches, given the incidence of PSS to be 2 out of 100,000 people.

Though severe COVID-19 has proven to increase risk of DVT, the association between mild COVID-19 and DVT is less clear. In a case-control study performed in 2020-2021 on 661 patients with mild COVID-19 infection, the results are statistically significant and suggest mild COVID-19 might be an independent risk factor of DVT [14]. However, the limitations of this study include its retrospective nature, which raises the possibility of reporting bias, and the fact that it has only sampled a small number of COVID-19 patients. In order to better understand the association between mild COVID-19 and thrombosis, a less biased and more comprehensive approach should be considered.

Aside from environmental factors, the risk of DVT is also influenced by genetics. Only lately, human understanding of genetic risk of this medical condition has improved, thanks to the high-throughput approaches. Nevertheless, DVT and PE are still complicated illnesses that are affected by interactions between environmental and genetic components. Although we are only just starting to comprehend this relation, future research is necessary and should concentrate on a comprehensive strategy that takes into account both genetic and environmental factors [15].

6. Conclusions

Deep vein thrombosis is caused by both environmental and genetic factors such as long-time immobility, obesity, unhealthy habits, and family history of blood clots. The subclavian DVT is a category of DVT and refers to blood clots forming in the subclavian veins below the clavicles. When thrombosis occurs, patients might experience pain, swelling, change of skin color around affected areas. If left untreated, the conditions can escalate into pulmonary embolism, which is a life-threatening situation when blood clots break loose and block the artery in the lung. Regular exercise, avoiding prolonged immobility, good health habits, and precise screening can all help reduce the risk of DVT. Currently, the standard treatment for DVT is through anticoagulation medications, inferior vena cava filters, or DVT thrombolysis. However, the best treatment should be tailored to the patients according to their unique health status. In general, it is widely acknowledged that early intervention produces better results than late treatment. In the treatment of subclavian DVT, catheters should be removed as soon as they serve their purpose, if possible.

References

[1] CDC. 2015. “Data and Statistics on Venous Thromboembolism.” Centers for Disease Control and Prevention. June 22, 2015.

[2] Muñoz Rodríguez FJ. Diagnosis of deep vein thrombosis. Rev Clin Esp. 2020 Jun 27: S0014-2565(20)30132-6.

[3] Cai TY, Rajendran S, Saha P, Dubenec S. Paget-Schroetter syndrome: A contemporary review of the controversies in management. Phlebology. 2020 Aug;35(7):461-471.

[4] Sangani V, Pokal M, Balla M, Gayam V, Konala VM. Paget-Schroetter Syndrome in a Young Female. J Investig Med High Impact Case Rep. 2021 Jan-Dec; 9:23247096211003263. Nicholson, Matthew, Noel Chan, Vinai Bhagirath, and Jeffrey Ginsberg. 2020. "Prevention of Venous Thromboembolism in 2020 and Beyond." Journal of Clinical Medicine 9 (8): 2467.

[5] Nicholson, Matthew, Noel Chan, Vinai Bhagirath, and Jeffrey Ginsberg. 2020. "Prevention of Venous Thromboembolism in 2020 and Beyond." Journal of Clinical Medicine 9 (8): 2467.

[6] "Axillo-Subclavian Vein Thrombosis: Causes, Symptoms & Treatment." n.d. Cleveland Clinic.

[7] Keir, Graham, and M. Blair Marshall. 2017. "Management Strategy for Patients with Chronic Subclavian Vein Thrombosis." The Annals of Thoracic Surgery 103 (2): 672–75.

[8] Noyes AM, Dickey J. The Arm is Not the Leg: Pathophysiology, Diagnosis, and Management of Upper Extremity Deep Vein Thrombosis. R I Med J (2013). 2017 May 1;100(5):33-36.

[9] Stuart, Annie. 2007. "Treatment for Deep Vein Thrombosis (DVT)." WebMD. WebMD. June 15, 2007.

[10] Li Xiaoqiang, Zhang Fuxian, Wang Shenming. Guidelines for diagnosis and treatment of deep vein thrombosis (third edition) [J]. Chinese Journal of Vascular Surgery (electronic edition), 2017,9 (04): 250-257.

[11] Hangge P, Rotellini-Coltvet L, Deipolyi AR, Albadawi H, Oklu R. Paget-Schroetter syndrome: treatment of venous thrombosis and outcomes. Cardiovasc Diagn Ther. 2017 Dec;7(Suppl 3): S285-S290.

[12] Peek J, Vos CG, Ünlü Ç, Schreve MA, van de Mortel RHW, de Vries JPM. Long-Term Functional Outcome of Surgical Treatment for Thoracic Outlet Syndrome. Diagnostics (Basel). 2018 Jan 12;8(1):7.

[13] Lugo J, Tanious A, Armstrong P, Back M, Johnson B, Shames M, Moudgill N, Nelson P, Illig KA. Acute Paget-Schroetter syndrome: does the first rib routinely need to be removed after thrombolysis? Ann Vasc Surg. 2015 Aug;29(6):1073-7.

[14] Clavijo MM, Vicente Reparaz MLA, Ruiz JI, Acuña MA, Casali CE, Aizpurua MF, Mahuad CV, Eciolaza S, Ventura A, Garate GM. Mild COVID-19 Illness as a Risk Factor for Venous Thromboembolism. Cureus. 2021 Sep 24;13(9): e18236.

[15] AlSheef M, Alshammari FT, Alhawish MK, Alghamdi AG, Alqudhybi AF, Abu-Shaheen A. Clinical epidemiology of venous thromboembolic disease: An institutional registry. Front Cardiovasc Med. 2022 Jul 22; 9:928094.