

ORIGINAL RESEARCH

Association between Anatomic Configuration of Thrombosis with Clinical Symptoms and Risk factors in Admitted Patients with Deep Vein Thrombosis

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Abstract: Introduction: Deep vein thrombosis (DVT) is prevalent and challenging for physicians. Previously, the clinical symptoms of DVT are different based on the location of the thrombosis. In this study, the anatomic location of thrombosis and its relation with clinical symptoms and DVT risk factors were investigated. Methods: In this retrospective study, the hospital documents of 204 patients with acute lower extremity DVTs in Shohada-e-Tajrish hospital were reviewed from April 2020 to February 2021. The diagnosis was confirmed using Doppler ultrasound. Based on the location of the thrombosis, the patients were divided into four groups: unilateral proximal group (UPG), bilateral proximal group (BPG), unilateral distal group (UDG), and ipsilateral proximal and distal group (IPDG). Finally, the frequency of risk factors and symptoms were compared between the groups. Results: In this retrospective study, 204 patients with the diagnosis of acute lower extremity DVTs at the time of hospitalization or during hospitalization were studied. The mean \pm SD age of the patients was 57.1 \pm 19.2 years (range: 12-98 years). Of these, 114 (55.9%) were men and 90 (44.1%) were women. There were 174 patients in UPG, 16 in BPG, 5 in UDG and 9 in IPDG. In total, 97.5% of the patients had proximal thrombosis while only 6.9% of them had distal thrombosis. The incidence of different limb circumferences was significantly higher in UPG and IPDG compared to BPG and UDG ($P<0.05$). There was no statistically significant difference between groups in terms of other symptoms and risk factors. Conclusion: Most of the DVTs were found in the proximal veins of the lower extremities. It seems that these DVTs are more likely to create edema compared to others and in unilateral cases may result in different circumferences of the lower limbs. But there was no significant association between other clinical signs of DVT including limb pain, edema, erythema, palpitations, and shortness of breath with thrombosis location. Also not significant association between DVT risk factors and the location of thrombosis were found.

Keywords: Deep vein thrombosis; Anatomic location; Risk factor; Symptoms

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1. Introduction

Deep venous thrombosis (DVT) or the formation of blood clots in the deep veins of the pelvis or lower extremities (1) is one of the most important problems in various fields of medical sciences that can be very challenging to diagnose and treat. The incidence of DVT is reported to be about 100 per

100,000 (2). However, the incidence increases at older ages and its prevalence is affected by sex and race (1,3,4,5).

Approximately one-third of DVT cases lead to pulmonary embolism, which is the leading cause of death from DVT (6). It is also possible that 50% of people with DVT develop post-thrombotic syndrome within two years, with symptoms including limb pain, edema, and in severe cases, venous ulcers (7, 8). So far, various risk factors for DVT have been introduced, including female sex, pregnancy, obesity, major surgeries especially orthopedic surgery, cancer, hormone therapy, long-term immobility, old age, and trauma (9). Despite

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all the studies that have been done on DVT, its diagnosis and treatment are still very difficult and challenging. Therefore, there has always been an effort to prevent its occurrence or to detect DVT in the early stages. In fact, anticoagulation is a major part of DVT treatment and aims to prevent pulmonary embolism (PE) and thrombotic recurrence (10). The 30-day mortality rate of DVT in people with anticoagulation is about 3% and the risk of death is 10 times higher if PE develops (11). Various methods have been proposed for the diagnosis of DVT. Venography is considered as the standard method of DVT diagnosis but is less used because of its invasive nature. Doppler ultrasound is also one of the methods used to diagnose DVT, which has been used in several studies and its diagnostic efficiency has been confirmed. However, despite all the progress that has been made, the diagnosis of DVT is still delayed in many cases, which can cause many problems for the patient and the doctor. Therefore, knowing more about the symptoms and clinical features of DVT can be very helpful in its timely and effective diagnosis.

The clinical signs of DVT have been shown to vary with the extent and location of thrombosis (10). However, our knowledge of the different symptoms of DVTs that form in different veins is still not enough. Moreover, unlike previous treatments based on anticoagulation, today the extent and anatomic configuration of thrombosis is very important and the use of catheter-directed methods for mechanical removal of thrombosis is also developing, the use of which requires knowledge of the site of thrombosis (12). Considering that few studies have been done in this field, their contradictory results, and most of them did not consider the clinical signs, in this study, we assessed the relationship between DVT risk factors and its clinical signs and the location of DVT based on Doppler ultrasound examinations.

2. Materials and Methods

In this retrospective study, the records of patients who were admitted to Shohada-e-Tajrish Hospital during 2019-2020 for various reasons and developed acute lower extremity DVT were reviewed. The study was approved by the Ethics Committee and the information of all patients remained confidential.

DVT was diagnosed in all cases using color Doppler ultrasound (DUS). The ultrasound was performed by an expert radiologist with the same device (Toshiba Nemio XG). DUS was either performed after initial clinical signs or was part of the postoperative screening. Ultrasounds examined proximal veins including common iliac vein, external iliac vein, common femoral vein, deep femoral vein, superficial femoral vein, and popliteal vein, also distal veins including anterior tibial vein, posterior tibial vein, and peroneal vein. Patients were divided into four groups based on the location of

thrombosis, as follows: Unilateral Proximal Group (UPG), Bilateral Proximal Group (BPG), Unilateral Distal Group (UDG), and Ipsilateral Proximal and Distal Group (IPDG).

Information collected from patient records included risk factors such as smoking, history of hormone replacement therapy (HRT), pregnancy, body mass index (BMI), history of cancer, history of ischemic heart disease, prolonged hospitalization or immobility (more than three days), long travel, hyperlipidemia, diabetes mellitus, hypertension, surgery, and trauma. Also, the clinical symptoms found in each patient including limb pain, edema, erythema, shortness of breath, tachycardia and size differences between the two limbs were recorded. Finally, the obtained data were compared between the four groups.

Quantitative data were presented as mean \pm SD and qualitative data were presented as frequency and percentage. Chi-square test or Fisher's exact test was used to compare the variables between the groups. All analyzes were performed using SPSS software, version 18. P<0.05 was considered statistically significant.

3. Results

In this retrospective study, 204 patients with the diagnosis of acute lower extremity DVTs diagnosed upon or during admission were studied. The mean \pm SD age of these patients was 57.1 \pm 19.2 years (range: 12-98 years). Of these, 114 (55.9%) were men and 90 (44.1%) were women. Symptoms included limb pain, edema, erythema, shortness of breath, palpitations, and differences in limb size. Table 1 shows the frequency of each of these cases among the studied patients. Limb edema, followed by differences in limb size, limb pain, and erythema, was the most common, respectively, and were important symptoms seen in most patients with DVT. The frequency of predisposing factors is shown in table 2. Pulmonary CT angiography was performed in 67 (32.8%) patients and ventilation/perfusion lung scan in 27 (13.2%) patients.

The frequency distribution of patients in terms of the location of DVT diagnosis is shown in figure 1. Most patients had proximal DVT (85.3%). However, considering the patients of IPDG and BPG groups, about 97.5% of patients had thrombosis in the proximal veins of the lower extremities. Thrombosis was formed in the distal veins in 6.9% of the patients.

Apart from the size difference between the two limbs (P<0.001), there was no statistically significant difference between the groups in terms of other symptoms and risk factors. Also, it was observed that the incidence of limb size differences in patients with UPG was significantly higher than patients in BPG (P<0.001) and UDG (P= 0.031) groups. Similar results were obtained for the difference between the IPDG group and BPG (P<0.001) and UDG (P= 0.027) groups (tables



3 and 4).

4. Discussion

DVT is a common and challenging problem for physicians. The onset and treatment of DVT is associated with high costs to society and deprives the individual of the ability to return to work and production early (12). Normal blood physiology allows blood clotting when needed, but in some diseases and unusual conditions this condition changes and the balance between pro-coagulant and anti-coagulant factors is disturbed, which can lead to the formation of pathological thrombosis (10). DVT is a critical condition and is associated with significant morbidity and mortality but is preventable (9). Despite the many studies that have been done on DVT, our information on the anatomical distribution of this complication is still not enough and few studies have addressed this issue. Moreover, the relationship between clinical signs and risk factors for DVT and the location of thrombosis is not yet known to us. Accordingly, and because of the need to find more information in this field, in this study we investigated the location of thrombosis in the veins of the lower extremities. Similar to previous studies, we found that 97.5% of patients had thrombosis in the proximal veins, while only 6.9% of the patients had thrombosis in the distal veins. Under-diagnosis of distal DVT can be considered as one of the possible causes, especially since Doppler study in obese patients with severe edema of the legs may have some false negative results.

Ouriel and colleagues examined the venograms of patients with suspected acute DVT. In this study, 2763 venograms belonging to 2541 patients that had been performed for 10 years were examined. They observed that 885 (34.8%) patients had DVT. Of these, 344 (39%) were idiopathic. 307 (35%) patients had DVT after surgery, 84 (10%) patients due to malignancy and 70 (8%) patients due to trauma. In this study, distal thrombi were more common than proximal thrombi, with DVT in the calf region in 734 (83%) patients, DVT in the femoropopliteal region in 470 (53%) patients, and DVT in the iliac region in 75 (9%) patients. The most common site was peroneal vein thrombosis (595 patients, 67%). The researchers stated that the anatomical configuration of DVT formation was significantly correlated with its cause, as post-operative DVTs were usually distal and DVTs following malignancy were mostly proximal to the right. Left proximal DVT was seen mainly in idiopathic subjects. Finally, the researchers stated that their study findings could be very useful in planning interventions that directly address the site of thrombosis and perform recanalization (12).

Another study in Norway on 94,194 people over the age of 20 found that the prevalence of venous thromboembolism was 1.43/1,000 people per year for the first time and the prevalence

of DVT was 0.93/1,000 people per year. The researchers found that proximal DVT was three times more prevalent than distal DVT and often to the left. The prevalence of DVT increased with age and was higher in patients with cancer. The ratio of idiopathic thrombosis to secondary DVT was 1:1. The risk of mortality in the first month was higher than at other times (4).

One study estimated the location of DVT formation based on two large cohort studies in Denmark. Approximately 160,000 people aged 50-64 were surveyed. 358 cases of DVT were diagnosed. Of these, 12.3% had distal DVT, 36% had proximal DVT, 7.1% had pelvic DVT, and 2.6% had upper extremity DVT. In this study, 50% of cases were idiopathic (13).

Another retrospective study in Sweden found that 43% of lower limb DVTs were in the iliac, 36% in the femoropopliteal, and 21% in the crural veins. Iliac DVT was more common at older ages, while femoropopliteal DVT was more common at younger ages (14).

De Maeseneer and colleagues in a retrospective study using ultrasound data in 1338 patients with unilateral DVT examined the site of DVT formation in five locations including calf, popliteal, femoral, common femoral, and iliac. The median age of patients was 62 years and 50% of them were men. Left DVT was higher in all segments (57%) (15), possibly because of left-sided iliac vein compression syndrome (16). In a study by De Maeseneer and co-workers, Calf-vein DVT (distal DVT) was observed in 28% of patients. There was also femoropopliteal DVT in 33% and iliofemoral DVT (proximal DVT) in 38%. It should be noted that femoropopliteal DVT included segments 2 or 3 and iliofemoral DVT segments 4 or 5 (15).

In the present study, we observed that none of the risk factors and clinical signs of DVT, except for the difference in size of the two lower limbs, had a statistically significant relationship with the anatomical location of thrombosis. Regarding the difference in size between the two limbs, it should be explained that according to our findings, proximal vein thrombosis causes edema in the lower extremities. Accordingly, the incidence of size differences in the UPG group was much higher than the UDG group. But there was no significant difference between the UPG group and the BPG group, because in this group both limbs had edema and therefore there was no obvious difference in size. On the other hand, in the IPDG group, where we had proximal DVT, the unilaterally edema caused a difference in size between the two limbs, and this issue caused the prevalence of this finding in the IPDG group to be significantly higher than the two groups UPG and UDG. To our knowledge, no other study has mentioned this finding. Of course, it should be noted that in general, similar studies are scarce, and this limits the possibility of comparing our data with the data of other studies.

The most important limitation of the present study was its



retrospective nature, which made it impossible for the researchers to determine the conditions. Also, in terms of risk factors, patients were not evaluated for varicose veins, May turner syndrome, and blood coagulation disorders. Moreover, although the total number of patients studied in this study was relatively sufficient, because very few were in the BPG, UDG and IPDG groups, the results are not completely reliable and generalizable and prospective studies with larger sample size are recommended.

5. Conclusion

DVT is a common problem that most often affects the proximal veins of the lower extremities. Also, if a thrombus forms in one of the proximal veins, edema develops. If a person has bilateral proximal DVT, both sides develop edema and limb size difference may not be seen. In our study, there was no significant association between other clinical signs of DVT including limb pain, edema, erythema, palpitations, and shortness of breath with thrombosis location. Also, no significant association between DVT risk factors and the location of thrombosis were found.

6. Appendix

6.1. Acknowledgment

None.

6.2. Conflict of interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

6.3. Funding support

None.

6.4. Author's contributions

All the authors have the same contribution.

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Table 1: Frequency of symptoms of deep vein thrombosis in patients studied in the study.

symptoms	Frequency	Percentage
Limb pain	144	70.6
Edema	197	96.6
Erythema	130	63.7
Shortness of breath	46	22.5
Tachycardia	11	5.4
Limb size difference	162	79.4

Table 2: Frequency of risk factors for deep vein thrombosis in the studied patients.

Risk factors	Frequency	Percentage
Prolonged immobility	69	33.8
Travel	8	3.9
Hospitalization	75	36.8
Surgery	58	28.4
Trauma	34	16.7
Tobacco use	39	19.1
Hormone replacement therapy	13	6.4
Diabetes	21	10.3
Hypertension	60	29.4
Hyperlipidemia	22	10.8
Ischemic heart disease	24	11.8
Cancer	33	16.2

Table 3: Frequency of deep vein thrombosis symptoms in the patients.

Symptoms	IPDG (n=9)	UDG (n=5)	BPG (n=16)	UPG (n=174)	P value
Limb pain	2	1	7	124	0.56
Edema	9	4	15	169	0.171
Erythema	6	3	7	114	0.381
Shortness of breath	8	3	4	39	0.659
Tachycardia	0	1	0	10	0.313
Limb size difference	9	2	3	148	<0.001

Table 4: Frequency of DVT risk factors in patients.

Risk factors	IPDG (n=9)	UDG (n=5)	BPG (n=16)	UPG (n=174)	P value
Prolonged immobility	6	1	6	55	0.083
Travel	1	0	0	7	0.553
Hospitalization	2	2	9	62	0.314
Surgery	1	1	3	53	0.459
Trauma	0	1	4	29	0.451
Tobacco use	4	1	3	31	0.269
Hormone replacement therapy	1	0	1	11	0.878
Diabetes	3	1	2	15	0.098
Hypertension	4	3	4	49	0.319
Hyperlipidemia	1	1	2	18	0.913
Ischemic heart disease	0	0	2	22	0.571
Cancer	0	0	2	31	0.361



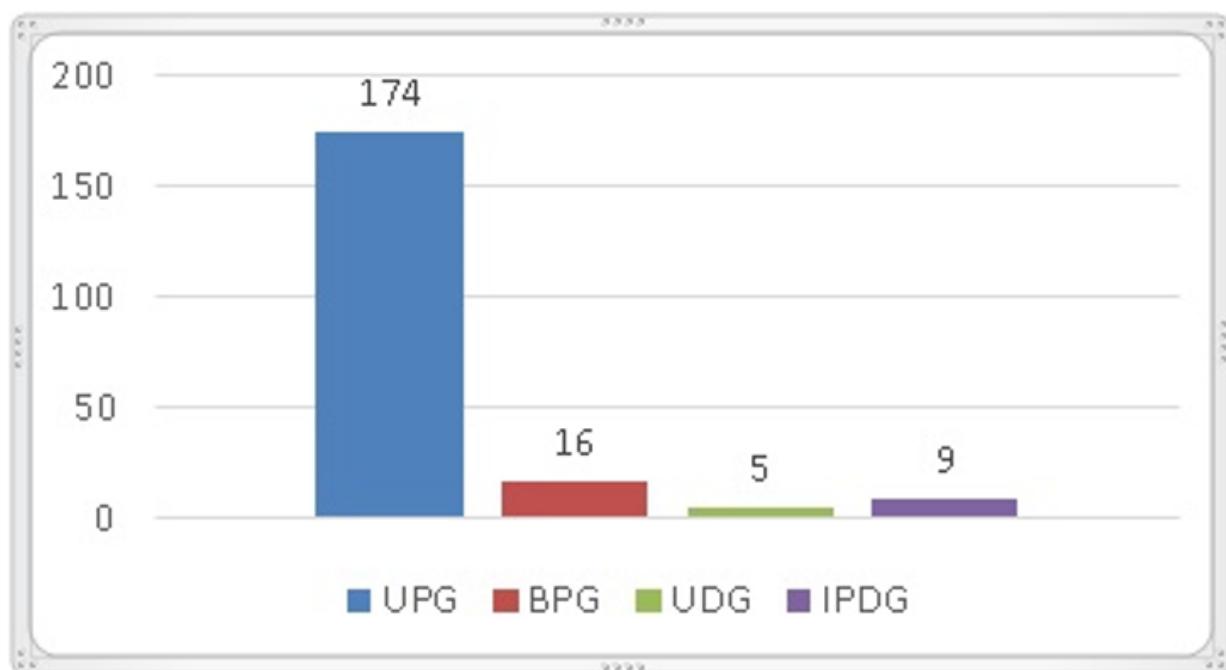


Figure 1: Frequency distribution of deep vein thrombosis diagnosis site in the studied patients.