

Research Article | Araştırma Makalesi

EVALUATION OF UPPER EXTREMITY VENOUS THROMBOSIS WITH DOPPLER ULTRASONOGRAPHY IN PERIPHERAL VENOUS LINE APPLIED PATIENTS

PERİFERİK VENÖZ KATATER UYGULANAN HASTALARDA ÜST EKSTREMİTE VENÖZ TROMBOZUNUN DOPPLER ULTRASONOGRAFİ İLE DEĞERLENDİRİLMESİ

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Abstract

Objective: Peripherally inserted venous lines (PVL) may increase the risk of venous thrombosis due to vessel wall disarrangement. Aim of this study is to identify the cases of upper extremity venous thrombosis (UEVT) related to PVL since most of the PVLs applied to upper extremities.

Methods: Sixty-nine hospitalized patients with previous or present PVL insertions were included in this prospective study. Upper extremity Doppler compression ultrasonography (USG) examination were performed to on all patients. The cases with detected UEVTs were evaluated as group 1 and the remaining cases were evaluated as group 2. Demographic parameters, PVL applications, intravenous treatments were compared between the groups.

Results: UEVT was diagnosed by Doppler USG in 26 (37.7%) patients out of 69 patients. Lower extremity thrombosis was found in 10 (14.49%) patients. UEVT was observed in cephalic vein in 14 (53.8%) and in basilic vein in four (15.4%) out of 26 (37.7%) patients. Axillary and brachial deep UEVT was located in two (2.9%) cases. Superficial UEVT was found in 24 (34.8%) cases. Ceftriaxone, cefoperazone/sulbactam and esomeprazole were the mostly associated treatments with UEVT. UEVT was detected in five patients with PVL that were inserted only for drawing blood.

Conclusion: PVL is a risk factor for UEVT since almost 1/3 of the patients revealed UEVT. When PVL is no longer needed or the need for intravenous therapy decreases, oral therapy should be planned and PVL should be removed. Removal of PVL appears to be necessary to avoid UEVT.

Keywords: Peripheral venous line, upper extremity venous thrombosis, Doppler ultrasonography, intravenous therapy

Öz

Amaç: Periferik venöz kataterler (PVK), damar duvar hasarı nedeniyle venöz tromboz riskini artırabilir. Çalışmanın amacı, PVK'lerin çoğu üst ekstremitelere uygulandığı için, PVK'ya bağlı üst ekstremitte venöz tromboz (ÜEVT) vakalarını belirlemektir.

Yöntem: Bir aylık süreçte göğüs hastalıkları kliniğinde yatan hastalardan PVK'sı olan veya başvurusundan önce hastane yatışında PVK öyküsü olan 69 hasta bu prospektif çalışmaya dahil edildi. PVK'ya bağlı trombus oluşumunu değerlendirmek için tüm hastalara üst ekstremitte Doppler, kompresyon ultrasonografi (USG) tetkiki yapıldı. ÜEVT olan olgular grup 1, ÜEVT olmayan olgular ise grup 2 olarak değerlendirildi. Demografik parametreler ve intravenöz tedaviler (İV) gruplar arasında karşılaştırıldı.

Bulgular: Altmış dokuz hastanın 26'sında (%37,7) Doppler USG ile ÜEVT tanısı kondu. On hastada (%14,5) alt ekstremitte ven trombozu tespit edildi. Yirmi altı hastanın 14'ünde (%53,8) sefalik vende ve dört hastada (%15,4) bazilik vende ÜEVT görüldü. Derin ÜEVT iki olguda (%2,9) aksiller ve brakiyal venlerde; yüzeysel ÜEVT 24 olguda (%34,8) izlendi. Seftriakson, sefoperazon / sulbaktam ve esomeprazol, ÜEVT ile en çok ilişkili İV tedavilerdi. Sadece kan almak için PVK uygulanan beş hastada ÜEVT izlendi.

Sonuç: Çalışmamızın sonuçları, hastaların yaklaşık 1/3'ünde Doppler USG incelemesi ile ÜEVT tespit edildiği için PVK'nın ÜEVT için bir risk faktörü olduğunu göstermiştir. PVK'ya gereksinim kalmadığında veya intravenöz tedavi ihtiyacı azaldığında, oral tedavi planlanmalı ve PVK çıkarılmalıdır. ÜEVT'den kaçınmak için PVK'nın çıkarılması gerekli görünmektedir.

Anahtar Kelimeler: Periferik venöz katater, üst ekstremitte ven trombozu, Doppler ultrasonografi, intravenöz tedavi

Introduction

Peripheral venous line (PVL) is applied to most of the hospitalized patients in order to facilitate blood intake and intravenous (IV) therapy. Peripheral venous line is mostly applied to superficial upper extremity veins. Healthcare workers often witness visible complications of PVL such as pain and swelling on the trace of the vein. Many studies, especially that are in intensive care units, have shown that central venous catheters cause upper extremity venous thrombosis.^{1,2}

Superficial and deep vein thrombosis (DVT) can be seen in the upper extremities as well as in the lower extremities. Upper-extremity deep vein thrombosis (UEDVT) accounts for just about 10%-25% all DVT cases.³ Proximal UEDVT is defined as thrombosis involving the axillary or more proximal deep veins, and distal UEDVT is defined as thrombosis of the brachial veins. Axillary and subclavian veins are most frequently affected.³ Upper-extremity vein thrombosis (UEVT) is divided into two as primary and secondary. While primary UEVT does not have a defined underlying reason, secondary UEVT occurs on a ground of a preexisting cause such as malignancy, central venous catheter (CVC), surgery, and thrombophilia.^{3,4} The causes of upper extremity superficial thrombosis are mostly iatrogenic. Injury, stasis, and foreign material in the lumen of the vein itself lead to thrombosis. However, lower extremity superficial thromboses are mostly caused by varicose veins.⁵

We could not find any previous paper in literature that investigated venous thrombosis occurrence as a result of PVL and the location of the thrombosis with Doppler compression ultrasonography (USG). In our study, we aimed to investigate the rate of thrombus formation caused by PVL application in the upper extremities and the relationship of the thrombus with IV treatments or other applications.

Methods

Study Design and Patient Selections

This prospective, cross-sectional study was conducted in the Department of Pulmonary Diseases. Seventy-nine patients that were hospitalized in the pulmonary diseases inpatient clinic for 1 month were evaluated and 69 of them were included in the study. Patients hospitalized with pre-diagnosis of pneumonia, chronic obstructive pulmonary disease (COPD), asthma, respiratory failure, pulmonary embolism and malignancy, and who underwent PVL were included in the study. Pregnant women, patients who were immobile, hospitalized in intensive care unit and/or did not have previous or present PVL insertions were excluded from the study. Ethical approval was obtained from the local ethics committee (Clinical Research Ethics Committee decision number 2014/120; date: July 16, 2014). Informed consents were obtained from all participants. Ages, genders, comorbidities, and smoking habits of 69 patients were recorded. Complaints of the patients' on

admission were noted. History of venous thrombosis of the patients had been questioned and recorded. Previous admission to hospital of the patients and the history of venous line insertion were investigated. Diagnosis of patients and treatments were recorded. In order to determine the time of radiological examination, hospitalization times were recorded. The location of PVL and the given treatment were noted. Anticoagulant therapy was administered to patients with a diagnosis of pulmonary embolism (PE). Other patients were given prophylactic doses of anticoagulant treatment with low molecular weight heparin during their hospitalizations. Upper extremity Doppler USG examinations were performed to all patients by Logiq9 brand ultrasound machine to examine the thrombus formation. All of the Doppler USG examinations were conducted by the same radiologist. The number of Doppler USG examinations and the day of hospitalizations were noted when the thrombi were detected. Doppler USG was applied to both lower and upper extremities during the first five days of hospitalization if the pre-diagnosis of the patient was PE or DVT. It was also applied to both upper extremities 5 days after venous line insertion and hospitalization.

Statistical Analysis

The findings of the study were assessed for statistical analysis using SPSS 21.0 program (IBM, Armonk, New York, United States). Descriptive statistics were computed for each of the analyzed variables. Results are presented as mean \pm standard deviation (SD). The normal distribution of the data was tested by the Shaphiro Wilks test. In order to compare the different groups stratified by age and sex, the independent samples t-test and Chi-squared test were used. The Mann-Whitney U test was used for the parameters without normal distributions when comparing two independent groups. P-value < 0.05 was considered significant.

Results

Sixty-nine patients who were hospitalized in the pulmonary diseases inpatient clinic for 1 month were included in the study. The patients were divided into two subgroups: group 1 and 2. Group 1 consisted of 21 cases with sole UEVTs and 5 cases of UEVT and LEVTs. Cases without UEVTs formed group 2 and patients with sole LEVTs were included in this group. The mean age of the patients was 67.63 ± 17.25 (20-96) and 27 of them were female and 42 were male. Forty-one (59.4%) of the patients were smokers, 28 (40.6%) were non-smokers. Comparison of the demographic parameters between group 1 and group 2 is presented in Table 1.

Venous thrombosis was detected in total of 36 patients (52.2%). UEVT was observed in the 26 (37.7%) patients and 5 of them had both UEVT and LEVT. Pure LEVT was found in 10 patients. UEVT was observed in cephalic vein in 14 patients, in basilic vein in 4 patients and in antecubital vein in 1 patient. Brachial UEVT was detected in 2 cases (2.9%) (Table 2). Superficial UEVT was found in

92% of the UEVT patients. Only 8% of UEVT cases had deep UEVT. Doppler USG repetition was performed in only one patient after the 5th day and no thrombus was

detected. The patient was included in Group 2.

Table 1. Comparison of the demographic parameters according to the groups.

	Group 1 The patients with UEVT n = 26 (21+5) (37.7%)	Group 2 The patients without UEVT n = 43 (62.3%)	P value
Age (mean± sd)	65.73 ± 18.43	68.79 ± 16.62	0.472
Gender			0.550
Female	9 (34.6%)	18 (41.9%)	
Male	17 (65.4%)	25 (58.1%)	
Smoking			0.929
Smoker	16 (61.5%)	25 (58.1%)	
Non-smoker	10 (38.5%)	18 (41.9%)	

UEVT: upper extremity venous thrombosis, SD: standard deviation

Table 2. Results of Doppler USG of bilateral upper and lower extremities in the patients that participated in the study (n = 69)

Results of Doppler USG	n (%)
Upper extremity VT	21 (30.4%)
Superficial venous thrombosis	
Basilic vein	4 (5.8%)
Cefalic vein	14 (20.3%)
Antecubital vein	1 (1.4%)
Deep venous thrombosis	
Axillar vein	-
Brachial vein	2 (2.9%)
Upper + lower extremities VT	
Femoral vein+Cefalic vein	3 (4.3%)
Popliteal vein+Cefalic vein	1 (1.4%)
Vena saphena parva+Cefalic vein	1 (1.4%)
Lower extremity VT	10 (14.5%)
Superficial venous thrombosis	
Vena saphena magna	3 (4.3%)
Vena saphena parva	-
Deep venous thrombosis	
Femoral vein	2 (2.9%)
Popliteal vein	3 (4.3%)
Crural vein	2 (2.9%)
Total VT	36 (52.2%)

USG: ultrasonography, VT: venous thrombosis
USG: ultrasonography, VT: venous thrombosis

Thrombosis was detected in 13 patients who were diagnosed with PE or DVT during the first 5 days of their hospitalizations. Thrombosis was also found in 23 patients after 5 days of PVL insertions. 42 patients (60.9%) had previous hospital admissions and 28 of the 42 had been given intravenous therapy in their previous hospitalizations. PVLs were inserted in the right upper extremities in 36 patients (52.2%) and left upper extremities in 33 patients (47.8%) for their current treatments.

Diagnoses of the patients were noted according to the groups. Only 2 patients had PE in group 1. Since LEVT patients were in group 2, 10 patients were diagnosed with PE in this group. The most seen diagnosis was pneumonia in group 1 (Table 3). Intravenous esomeprazole was given to 34 patients, ceftriaxone to 25, cefoperazone/sulbactam to 16, furosemide to 10, methylprednisolone to 7, theophylline to 8, paracetamol and metoclopramide to 3 patients. Acetylcysteine,

hyosine butylbromide, piperacillin/tazobactam, and imipenem were prescribed to 1 patient.

Table 3. Diagnosis of 69 patients with and without UEVT

	Group 1 The patients with UEVT n = 26 (37.7%)	Group 2 The patients without UEVT n = 43 (62.3%)	Total n = 69
Diagnosis			
COPD	5 (19.2%)	5 (11.6)	10 (14.5%)
PE	2 (7.7%)	10 (23.2%)	12 (17.4%)
Pneumonia	15 (57.7%)	19 (44.2%)	34 (49.3%)
Lung Cancer	1 (3.8%)	2 (4.6%)	3 (4.3%)
Asthma	2 (7.7%)	4 (9.3%)	6 (8.7%)
NMD	1 (3.8%)	-	1 (1.4%)
OSAS	-	1 (2.3%)	1 (1.4%)
Heart Failure	-	1 (2.3%)	1 (1.4%)
ILD	-	1 (2.3%)	1 (1.4%)

UEVT: upper extremity venous thrombosis, COPD: chronic obstructive pulmonary disease, PE: pulmonary embolism, NMD: neuromuscular disease, OSAS: obstructive sleep apnea syndrome, ILD: interstitial lung disease.

Thrombus development was evaluated according to the treatments the patients were receiving. In the groups receiving cefaperazone/sulbactam, ceftriaxone, and esomeprazole patients developed UEVT more than other groups (Table 4).

Discussion

Hospitalization itself is a risk factor for numerous morbidities like infections and complications of several invasive procedures. As seen in our study as well, patients hospitalized in pulmonary inpatient clinics mostly require IV antibiotic treatment because of severe pneumonia and/or COPD attacks. Therefore, most of the hospitalized patients need PVL for their treatment or diagnosis. Placement of peripheral lines is shown to be the most commonly performed invasive procedure in acute healthcare settings with as many as 80% of hospital inpatients requiring intravenous access at some stage during their admission, and worldwide more than one billion lines are used annually.^{6,7} Generally, PVLs attached to peripheral arm veins are sufficient for these purposes. Once inserted, a well-functioning line can remain in use for several days if required.

Table 4. The relationship between the UEVT and PVL applications/treatments in 69 patients

Given therapy from the PVL	Total n (%) n = 69	Group 1	Group 2	P value
		The patients with UEVT n = 26 (37.7%)	The patients without UEVT n = 43 (62.3%)	
Ceftriaxone	25 (36.2%)	11	14	0.414
Cefoperazone/sulbactam	16 (23.2%)	6	10	0.986
Tazocin	1 (1.4%)	1	-	
Imipenem	1 (1.4%)	-	1	
Esomeprazole	34 (49.3%)	15	19	0.277
Paracetamol	3 (4.3%)	3	-	
Furosemide	10 (14.5%)	3	7	
Metoclopramide	3 (4.3)	-	3	
Theophylline	8 (11.6%)	3	5	
Methylprednisolone	7 (10.1%)	2	5	
Only serum	3 (4.3%)	1	3	
Only for blood taking	12 (17.4%)	5	7	0.754
PVL applied only in previous hospitalisation	3 (4.3%)	1	2	
PVL applied also in previous hospitalisation	28 (40.6%)	9	19	0.433

PVL: peripheral venous line, UEVT: upper extremity venous thrombosis.

Common side effects of PVL application are redness, pain, and edema on the applied arm. There are previous studies that have evaluated these symptoms and demonstrated the relationship between catheter applications and thrombus formation^{1,2,8} However, those studies were mostly related to intensive care settings and deep catheter procedures. Best of our knowledge, no study that conducted by using USG to examine PVL that is attached to the superficial veins in the upper extremities to show thrombus, was found in the English literature. UEVT was shown by Doppler USG in 37.7% of the patients in our study.

The major systemic risk factors for upper extremity thrombosis is the presence of malignancy.^{9,10} The mechanisms by which malignant tumors promote thrombosis were vary. In malignancies, pro-inflammatory cytokines released from the expression of tumor antigens increase the release of thrombotic substances in the blood, leading to hyper viscosity. Stasis develops secondary to compression of the veins in the thrombosed site and venous thrombosis progresses. Frequent hospitalizations, chemotherapy and additional aggressive supportive treatments are also defined as an important risk factor for the development of thrombosis in cancer patients. Although chemotherapeutic agents are frequently administered through the central venous catheter, other treatment is also delivered via with a peripheral catheter.¹¹ One of our three patients with lung cancer had upper extremity thrombosis.

Local factors may play a dominant role in UEVT compared with LEVT. Foreign material in the lumen of the arm veins is led to thrombosis. The highest reason of thrombosis is most frequently indwelling central venous catheters and pacemaker. The odds ratio in patient with UEVT by intravascular devices like central venous catheters eightfold increased risk of venous thrombosis of the arm.^{2,12} The specific features of central venous catheters which are the catheter type, technique, course and level of insertion may affect thrombosis occurrence. In addition, the duration of catheterization, recurrent PVL insertion, recurrent hospitalization, the fluid administered, number of punctures during catheter

insertion and catheter related infections may have an effect on the presence of thrombosis in patients with peripherally catheters. Less is known about the relation between peripherally catheters in patients with hospitalization and UEVT. The risk of arm vein thrombosis were significantly increased due to implanted port a catch systems and pacemaker.^{13,14} The major problem appears to be the thrombogenicity of the foreign material itself. Other potential risk factors include damage to the vascular wall and impaired blood flow due to hyper viscosity, according to Virchow triad.¹⁵ The presence of thrombophilia also increases the risk of UEVT. The previous investigations were found that the most common thrombophilia's, the factor V Leiden mutation and the prothrombin G21020A mutation, among patients related to UEVT.¹⁶⁻¹⁸ In our study, PVL was usually applied to the right cephalic vein. Upper extremity deep venous thrombosis was detected in two of 26 cases with UEVT, others were upper extremity superficial venous thrombosis. Superficial thrombi were mostly observed in the cephalic vein. Upper extremity deep venous thrombosis was seen in axillary and brachial veins.

Superficial UEVT sometimes may lead to deep UEVT so the cases that were found as superficial UEVT may have a risk of developing deep UEVT if the PVL duration time is prolonged and some drugs continue to be administered. Some studies showed that superficial LEVT patients have more risk of developing deep venous thrombosis.^{19,20} In European Society and Cardiology (ESC) Guideline of PE 2019; superficial venous thrombosis is considered as moderate risk factor which is two to nine fold increased risk of venous thromboembolism.²¹

In patients using ceftriaxone, cefoperazone/sulbactam as IV form antibiotics and esomeprazole, UEVT was significantly higher than other drugs in our study. Esomeprazole is a proton pump inhibitor and is widely used in the treatment of stomach ulcers and gastric protective treatment. The choice of IV treatment of this drug, instead of oral form, may increase the risk of UEVT. The limitations of our study were the relatively small sample size and the presentation of a single-centered

experience. In addition, a second Doppler USG could not be performed in patients with prolonged PVL duration. In conclusion, UEVT was detected by Doppler USG in 1/3 of the patients in our study. PVL appears to be a risk factor for the occurrence of UEVT. Although most of the UEVTs in our study were superficial, they also may pose a risk for pulmonary embolism. Therefore, to take off the PVL when the IV treatment and the need is over and to consider oral treatment form of the drugs, seems to be necessary to avoid from UEVT.

Compliance with Ethical Standards

Ankara Yildirim Beyazit University Faculty of Medicine Ethics Committee approved this study (decision number 2014/120; date: July 16, 2014). Informed consent was obtained from all participants.

Conflict of Interest

The authors declare no conflicts of interest.

Author Contribution

Authors contributed equally to this work.

Financial Disclosure

Financial disclosure none.

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