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# Descriptive Data of Patients with Venous Thromboembolism

## Venöz Tromboemboli Tanısı Konulan Hastaların Tanımlayıcı Bulguları

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## ABSTRACT

**Purpose:** This study was designed for collecting descriptive data about diagnosis and treatment of patients with venous thromboembolism (VTE) in an university hospital and for reflecting approach to VTE in such a reference hospital in this way.

**Material and Methods:** We evaluated archive records of patients diagnosed with deep vein thrombosis (DVT) and pulmonary thromboembolism (PTE). Age average of patients was advanced and most of them were women. They had DVT, PTE, DVT and PTE respectively. Most common diagnostic method used for PTE was computed thomogrphy (CT), for DVT was ultrasonography (USG). VTE was diagnosed most frequently in emergency services and policlinics. Most common chronic risk factors for VTE were cancer, heart failure/romathismal cardiac disease, hyperlipidemia/atherosclerosis and obesity. Risk factors spesific to the attacks (or temporary) were immobilization, surgery, pregnancy, taking oral contraseptive drugs and trauma.

**Results:**In patients investigated for hemostatic risk factors, Factor V Leiden, Prothrombin 20210 A and MTHFR mutations were found respectively. Symptoms and findings of patients admitted with PTE were dyspnea-tachipnea, tachycardia, palpitation, pleural pain, caugh, fever, anginal pain, hemopthysis, diaphoresis and wheezing . Echocardiography gave positive results for the most of PTE cases. D-dimer test was found high sensitive. Treatments during accute attacks were low moleculer weight heparin (LMWH), standart heparin, thrombolytic therapy, surgery, aspirine and vena cava inferior filter placement. Acute term complications were death, bleeding and heparin induced thrombocytopenia.

**Conclusion:** This retrospective study reflects the approach of VTE diagnosis and treatment in a reference hospital and it may guide for prospective studies.

**Key Words:** Venous thromboembolism (VTE), Pulmonary thromboembolism (PTE), Deep vein thrombosis (DVT).

## ÖZET

**Amaç:** Bu çalışma; üniversite hastanesinde venöz tromboembolizmi (VTE) teşhisi ve tedavisi hakkında açıklayıcı veri toplanmasını ve böylece bir referans hastanesindeki VTE yaklaşımını yansıtmak için planlanmıştır.

**Materyal ve Metod:** Çalışmamızda derin ven trombozu (DVT) ve pulmoner tromboembolizmi (PTE) tanısı konulan hastaların arşiv kayıtlarını değerlendirdik. Hastaların birçoğunun yaşı ileri ve cinsiyeti kadındı. PTE için en sık kullanılan tanı yöntemi; bilgisayarlı tomografi (CT), DVT için ise ultrasondu. VTE acil servislerde ve polikliniklerde en yaygın tanısı konulan hastalıktır. Hastalara sırasıyla DVT, PTE, DVT ve PTE uygulandı. VTE için en sık rastlanan kronik risk faktörleri kanser, kalp yetmezliği/romatizmal kalp rahatsızlığı, hiperlipidemi/ateroskleroz ve obesitedir. Ataklara özgü risk faktörleri hareketsizlik, ameliyat, gebelik, oral kontraseptif ilaç ve travmaydı.

**Bulgular:** Hemostatik risk faktörlerinin araştırıldığı hastalarda; sırasıyla faktör V Leiden, protrombin 20210 ve MTHFR mutasyonları bulundu. PTE'li hastalarda bulunan bulgular ve semptomlar; dispne-takipne, taşikardi, palpitasyon, göğüs ağrısı, öksürük, ateş, boğaz ağrısı, hemoptiz, diyaforez ve hırıltılı solunumdu (vizing). Elektrokardiyografi, PTE

vakalarının çoğu için olumlu sonuçlar verdi. D-Dimer testi ise yüksek oranda duyarlı bulunmuştur. Akut ataklar sırasında uygulanan tedaviler; düşük molekül ağırlıklı heparin (LMWH), standart heparin, trombolitik tedavi, ameliyat, aspirin ve inferior vena kava filtresi yerleştirilmesidir.Akut dönem komplikasyonları ölüm, kanama ve heparin kaynaklı trombositopeniydi.

**Sonuç:** Bu retrospektif çalışma bir referans hastanesindeki VTE tanı ve tedavi yaklaşımlarını yansıtmakta olup ileriye dönük çalışmalar için yol gösterici olabilir.

**Anahtar Kelimeler:** Venöz tromboembolizm, pulmonar tromboembolizm, derin ven trombozu

## INTRODUCTION

VTE is a disease which has clinical reflections as deep vein thrombosis (DVT) and pulmonary thromboembolism (PTE) and can be cause death. It is important because it takes place in different locations, appears recurrent attaks, reduces life quality with late term complications and demages country economy. Preventİing VTE is possible. Venous thrombosis and its complications related to embolia are the most frequent cardiovasculer diseases coming after ischemic heart disease and stroke. Frequency of VTE is reported differently because there are some difficulties in diagnose. Only hospitalizated and only old patients are investigated, frequency of autopsy is low like in our country and cases determined at autopsies are not included in incidence numbers. Because DVT is found in certain groups of patients frequently and VTE may occur silently, it is possible to say that frequency of VTE is higher than estimated and patients diagnosed with VTE is top of the iceberg. Our aim in this study was to collect descriptive data related to diagnosis and treatment of patients diagnosed with VTE in an university hospital and to reflect approach of VTE in such a reference hospital.

## MATERIALS and METHODS

In this study, archive records of patients with VTE were evaluated and cases with splancnic vein thrombosis weren't included. Cases were selected among patients using ICD-10 (International Classification of Diseases and Related Health Problems) recording system. Deficient data in files were completed with records in hospital computer. Data were entered in a database program which had been developed at the Hematology Unit for hematological disorders including VTE. We presented numeral data by using mean value±standart deviation, categorical data by using percentage and ratio.

## RESULTS

Mean age of patients was 58±18, % 55,5 of them were women and % 45,5 were men. DVT was in % 42,8 of patients, PTE was in % 16,4. Diagnostic methods used for PTE were only computed thomography (% 88,69), only ventilation-perfusion sintigraphy (% 4,5), computed thomography and ventilation-perfusion sintigraphy (% 3,4), only magnetic resonance (% 1,1) and only pulmonary angiography (% 1,1). Diagnostic methods used for DVT were USG (% 98,9) and venography (% 1,1).

Most attacks (% 93,4) had been determined after admission to the emergency servise or policlinics (most frequently to policlinics of cardiovasculer surgery and chest disesaes departments). Other VTE attacks were in inpatients. They were seen in internal medicine service (% 2,6), neurology service (%1,3), urology service (%1,3), orthopedy service (% 0,7) and general surgery service (% 0,7).

Exept for 24 patients dead there were 89 patients whose mean following time was known. It was 230 days and there were recurrences in 7 patients. Median recurrence time was 69 days after the first attack. Recurrence ratio was found % 4,8 (% 6/146). Two of seven recurrent attacks had been occured in patients recieving no therapy, three of them had been in patients recieving warfarine and INR levels of these patients were

below therapeutic range. One patient had been using low molecular weight heparin irregularly.

Chronic risk factors for VTE were cancer (% 23,6), heart failure/romathismal heart disease (% 16,6), hyperlipidemia/atherosclerosis (% 24,6), obesity (% 11,5) and other diseases (Behçet Disease, Scleroderma, MGUS (Monoclonal Gammopathy of Undetermined Significance) (% 2,5). Temporary risk factors were immobilisation (% 38,5), surgery (% 19,2), pregnancy (% 5,1), using oral contraseptive drugs (% 1,3) and trauma (% 0,6). Other diseases not related to thrombosis were % 2,5 of all diseases. % 45,2 of patients had one, % 18,4 of them had more than one aquired risk factors.

Among the patients hemostatic risk factors investigated, there were heterozygote factor V Leiden mutation (% 50), homozygote factor V Leiden mutation (% 4,5), prothrombin 20210 A mutation (% 5,8) and MTHFR mutation (% 66,6).

Fibrinogen levels were elevated in 30 patients among the investigated 55 patients, Factor VIII level was elevated in 10 patients among the investigated 14 patients. Antiphospholipid anticores were negative in all of 46 investigated patients.

Symptoms and findings of patients with PTE were dyspnea and tachypnea (% 69,3), tachycardia (% 64,8), palpitation (%59,1), pleural pain (% 54,5), caugh (%21,6), fever (% 21,6), anginal pain (%11,3), hemopthysis (% 9,1), diaphoresis (% 4,6) and wheezing (%2,3).

Echocardigraphy was done for % 60,2 of patients with PTE and positive results (pulmonary hypertension and /or dilated right atrium and ventricule) were in % 81,1 of them.

Among patients admitted with VTE, D-dimer test was used in 51 attacks (% 33,3). In two of these patients (% 1,3) D-dimer level was under 0,5 µg /ml, in 49 of them (% 32) it was over 0,5 µg /ml. Minimum D-dimer level was 0,22 µg/ml, maximum level was 30 µg/ml, mean level was 8,37±8,96 µg/ml. Sensitivity of this test for VTE was found % 96 (% 49/51).

During acute attacks, LMWH especially enoxaparine and nadroparine had been used mostly (% 49,5). Other therapies were standart heparin (% 37,6), thrombolytic drugs (%6,9), surgery (%4,6) and vena cava inferior filter placement (% 1,4).

Acute term complications of VTE were death (in 20 patients) and bleeding (intracranial bleeding in 4 patients, gastrointestinal system in 3 patients, urinary system in 3 patients, nose in 2 patinets, intraabdominal in one patient, femoral in one patient). We couldn't get sufficient information about pulmonary hypertension and chronic venous failure because there were not available long term records of all patients. Pulmonary hypertension determined according to echocardiography findings at acute attacks was available %26 of patients. In most patients' file records (% 69,2), chronic complications were not present or were not mentioned about.

## DISCUSSION

In our study, mean age of patients were advanced and most of them were women. Especially over age of 40, VTE incidance increases because risk factors develop[1,2,3,4,5,6]. In a retrospective study related to VTE epidemiology, risk ratio of women versus man was found 1,2[1] and it was determined that risk of VTE was higher in women than men in early ages while it was higher in men than women in advanced ages[1,7,8]. In a study related to recurrence and gender in VTE, recurrent attacks were found more frequent in women than men[23]. In our study because we couldn't achieve all targeted records of VTE patients, making such a comparison for VTE risk among men and women was impossible.

There were PTE, DVT, PTE and DVT in patients respectively. Similarly in a study designed in an area with 100000 people for 25 years, there were PTE (%44), DVT (% 42), PTE and DVT (%42)[1].

In most patients PTE diagnoses was made by using BT while DVT by using USG. These results

are reflection of diagnostic methods preferred today. Although angiography and venography are the most sensitive methods, they were used rarely because of their invasiveness.

Most of the patients were outpatients. Their diagnosis were made in emergency service and policlinics. VTE was seen in patients rarely. It was seen in internal medicine service (% 2,6 of all patients), in neurology service (% 1,3), in urology service (% 1,3), in orthopedy service (% 0,7) and in general surgery service (% 0,7). This result suggests that VTE is not a disease related to only one department, it requires a multidiciplinary approach. Surgical processes and following immobilization are very important risk factors for VTE. It is known that there is a high risk especially after lower extremity surgery. Despite this condition, few patients had been diagnosed with VTE in surgery department services. This can be related to deficiency of effective prophylaxy for VTE or overlooking VTE. But it is possible that patients may have VTE attacks after leaving hospital. This possibility is supported by existence of surgery story recently (% 19,2) in temporary risk factors. There are some findings and ideas about necessity for maintaininig anticoagulant therapy after leaving hospital for 4-6 weeks in patients had orthopedic surgery.

As known before, VTE is a chronic and recurrent disease[10]. In our stuy there were recurrent attacks too. Several studies demonstrated that recurrent VTE is seen mostly in patients with cancer and recurrence ratio is higher in PTE than DVT in these patients[3,11,12]. In our study among patients with recurrence, 5 recurrent attacks were PTE, 2 attacks were DVT. There were 3 patients with cancer.

As chronic risk factors cancer was seen most frequently and followed by heart failure/romathismal heart disease, hyperlipidemia/atherosclerosis, obesity and other diseases such as Behçet's disease, Scleroderma, MGUS (Monoclonal Gammopathy of Undetermined Significance). As temporary risk factors immobilization was seen most frequently and followed by surgery, pregnancy, taking oral contraseptive drugs and trauma. Similarly with our results, some studies in literature reported that these factors increased risk of VTE[5,6,13,14]. When we investigated patients' aquired risk factors we found that % 45,2 of them had one, % 18,4 of them had more than one risk factor. In other words % 63,6 of patients had at least one aquired risk factor.

In patients invastigated hemostatic risk factors, Factor 5 Leiden, Prothrombin 20210 A and MTHFR gene mutations were found respectively. In a study designed with 126 VTE patients in our country, frequency ratios for Factor 5 Leiden heterozigoty was % 26,2, Factor 5 Leiden homozigoty was % 4,8 and prothrombin 20210 A mutation was % 7,1[15]. In our study low levels of protein C, Protein S, antithrombin III were not reliable because these tests were used during acute thrombosis attack. In addition whether homocysteine was detected in fasting blood sample couldn't be known. Therefore high homocysteine levels were not reliable either.

Most common symptom and finding of patients admitted with PTE was dyspnea-tachypnea. Others were tachycardia, palpitation, pleural pain, caugh, fever, anginal pain, hemoptysis, diaphoresis and wheezing. In literature, studies designed about this subject, dyspnea, pleural chest pain and tachypnea were reported as the most frequent symptoms and findings[16].

Echocardiography gave positive findings in the most of patients with PTE. In literature there are several studies reported that value of echocardiography was limited in diagnostic algoritm. And these studies suggest that echocardiography is a method supporting PTE diagnosis and it can't exclude PTE diagnosis[17,18,19]. Despite this, high positivity of echocardiography in our study suggests that it should be used as a complication screening method.

In our study sensitivity of D-dimer test is high. This was similar with results of studies about D-dimer sensitivity (6, 20). It was reported that when D-Dimer was used with clinical possibility, USG and CT, it is reliable for excluding VTE diagnosis[1,22,23,24]. There are studies suggesting this test has high negative predictive value[25,26]. PTE prevelance is only % 2 in patients for whom clinical possibility is low. For such patients normality of D-Dimer level is very useful for excluding PTE.

During acute attacks patients were given LMWH most frequently. Other therapies were standart heparin, thrombolytic drugs, thrombosis surgery, aspirine and vena cava inferior filter placement. Randomised studies demonstrated that LMWH was as effective as standart heparin in venous thrombosis as beginning therapy[27,28]. LMWH is more expensive but in point of developing heparin induced thrombocytopenia it is more advantageous than standart heparin.

Acute term complications were death, bleeding and heparin induced thrombocytopenia. We couldn't get sufficient data about chronic complications because of deficiencies of records. In literature most important complication of PTE was reported as severe chronic pulmonary hypertension which may result in right heart failure and death[29]. In patients these complications seen, pulmonary arterial pressure recovers after pulmonary thromboendarterectomy operation[30]. And patients not adequate for operation, lung transplantation can be thought about. Some patients may benefit from prostacyclin and epoprostenol therapy. In our study because patients' long term records couldn't be found in their files we were not able to get sufficient data about pulmonary hypertension and chronic venous insufficiency.

In conlusion, descriptive data about patients diagnosed with VTE were collected in this study. VTE can be seen in patients followed up by many departments in hospitals. Therefore VTE requires close cooperation between departments like neoplastic and infectious diseases. In hospitals, study groups can be formed for following up these patients. A fixed database network can be formed and recording of fixed format data can be provided. This retrospective study may be a guide for prospective studies will be designed about VTE.

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