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Evaluation of deep vein thrombosis incidence with respect to age and gender in light of regional factors in central Anatolia: A population-based study

Bölgesel etmenlerin ışığında iç anadolu bölgesinde derin ven trombozu insidansı ile yaş ve cinsiyete açısından değerlendirilmesi: Nüfus bazlı çalışma

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Abstract

Aim: Deep vein thrombosis (DVT) is a prevailing cause of serious complications such as pulmonary thromboembolism, venous ulcer, chronic venous insufficiency, venous gangrene and post-thrombotic syndrome, and significantly increased hospitalization costs. The aim of this study is to determine the incidence of DVT and regional effects for its development as well as evaluate its distribution in terms of age and gender in Yozgat, a city with a population of more than 500.000 people, which is considered to fairly represent Central Anatolia with regards to geography, economy, industry, age distribution, morbidity and mortality.

Methods: For this cross-sectional study, we included all DVT cases aged 15 years and older from Yozgat diagnosed in Bozok University, Faculty of Medicine, Research and Application Hospital and Yozgat State Hospital between September 2012-September 2016. Patients and diagnostic characteristics were retrieved from medical records. The distribution of DVT cases were evaluated in terms of age and gender according to the data derived from address-based population registration system of Turkish Statistical Institute (TUSI) 2016.

Results: One thousand two hundred and eighty-seven patients were enrolled in this research. DVT incidence increased with age and substantially accelerated above the age of 40. The overall DVT incidence was 1:1000 persons per year and slightly higher among the female population (1:1000 persons/year vs 0.9:1000 persons/year) (P=0.924). According to TUSI 2016, the mean body mass index (BMI) of females was significantly higher than that of males (29.2 (5.3) kg/m² and 26.7 (3.6) kg/m², respectively, P<0.001). In the region comprising Yozgat, Sivas and Kayseri, labor-force participation rate of females and males were 28% and 49.6%, respectively, which was a significant regional risk factor for DVT development.

Conclusion: It would be possible to decrease the incidence of DVT and the high hospitalization costs of related complications, most of which can be avoided with suitable prophylaxis based on more reliable results obtained from further research. Appropriate precautions should be taken after considering regional socioeconomic and sociocultural values.

Keywords: Deep vein thrombosis, Incidence, Yozgat, Age, Gender, Body mass index

Öz

Amaç: Derin ven trombozu pulmoner tromboemboli, venöz ülser, kronik venöz yetmezlik, venöz gangren ve posttrombotik sendrom gibi ciddi komplikasyonların güncel bir sebebini oluşturmaktadır. Bu çalışmanın amacı 500.000'den fazla nüfusa sahip, gerek coğrafik, ekonomik, endüstriel ve yaş dağılımı gerekse morbidite ve mortalite oranları açısından İç Anadolu Bölgesi'nin temsil edebilecek özelliklere sahip Yozgat ilinde derin ve trombozu (DVT) insidansını tanımlamak ve DVT gelişim üzerinde etkisi olan bölgesel etmenler üzerine vurgu yapmaktır.

Yöntemler: Bu araştırma kesitsel bir çalışma olarak planlanmıştır. Yozgat ilinde ikamet eden Bozok Üniversitesi Tıp Fakültesi Araştırma ve Uygulama Hastanesi ile Yozgat Şehir Hastanesi'nde 2012 ve 2016 yılları arasında DVT tanısı almış 15 yaş ve üzeri bireyler çalışmaya dahil edildi. Hastalar ve hasta verileri medikal kayıtlardan elde edildi. DVT dağılımı, Türkiye İstatistik Kurumu'na (TUSI) ait adrese dayalı nüfus dağılımı verileri kullanılarak yaş ve cinsiyet açısından değerlendirildi.

Bulgular: Çalışmaya 1287 hasta dahil edilmiştir. DVT dağılımı yaşlanma ile artış göstermekte özellikle 40 yaş üzerinde ciddi bir ivmelenme göstermektedir. Genel DVT insidansı 1/1000 hasta/yıl olarak belirlendi ve kadın nüfusta 1/1000 hasta/yıl iken erkek nüfusta 0.9/1000 hasta/yıl olarak tespit edildi (P=0,924). TUSI 2016 verilerine göre Yozgat, Sivas ve Kayseri illerinde ortalama beden kitle indeksi (BKI) kadın popülasyonda erkeklere göre daha yüksek idi, kadın popülasyonsa 29,2 (5,3) kg/m² iken erkek popülasyonda 26,7 (3,6) kg/m² (P<0,001) ve işgücü katılım oranı kadınlarda %28 iken erkeklerde %49,6 olarak tespit edildi. Bu durum DVT gelişiminde bölgesel etmenlerin etkinliğini ortaya koymaktadır.

Sonuç: Bölgesel sosyoekonomik ve sosyokültürel realiteler göz önünde bulundurularak ve daha geniş çaplı çalışmalar ile elde edilecek veriler ışığında önceden alınacak önlemler ile DVT insidansını ve uygun profilaktik yaklaşımlar ile birçoğu önlenebilir olan ve yüksek sağlık giderlerine sebep olan ilgili komplikasyonların önüne geçmek mümkündür.

Anahtar kelimeler: Derin ven trombozu, İnsidans, Yozgat, Yaş, Cinsiyet, Beden kitle indeksi

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Introduction

Deep vein thrombosis (DVT) is the third most common cardiovascular disease, after ischemic cardiac diseases and stroke [1]. Despite many improvements in both medical and surgical management, DVT remains the cause of various serious complications, such as pulmonary thromboembolism, venous ulcer, chronic venous insufficiency, venous gangrene and post-thrombotic syndrome, along with significantly increased hospitalization costs [2,3].

DVT is rarely observed under the age of 20. However, its incidence gains significant acceleration after the age of 40 and peaks after the age of 70 [4-8]. The incidence of DVT is similar between males and females, although it remains slightly higher among the reproductive female population, which evens out after menopause [4,7,9,10].

To the best of our knowledge, no extensive research has been conducted in Turkey on DVT incidence to this date, however, it is possible to see many examples in the literature from different countries. In this article, we aimed to research the incidence of DVT and evaluate its distribution with respect to gender and age in Yozgat, a city with a population of more than 500,000 people, which is thought to represent Central Anatolia in terms of geography, economy, industry, age distribution, morbidity, and mortality.

Materials and methods

DVT cases were classified as idiopathic and secondary. Any DVT caused by malignancy, trauma, surgery, immobility (due to paresis, paralysis, prolonged bedrest) within the last 3 months, pregnancy or puerperium at the time of the event, or oral contraceptives used at the time of the event or up to 1 month before the event was regarded as secondary DVT. A DVT case was regarded as idiopathic DVT in case of the absence of precipitating factors for a secondary DVT.

This cross-sectional study was conducted in Bozok University, Faculty of Medicine, Research and Application Hospital and Yozgat State Hospital, the only centers of cardiovascular surgery in Yozgat city, with the approval obtained from Local Health Authority in Yozgat Governorship (no: 21143511-030.04.01). Ethics committee approval was not received due to the retrospective study design.

One thousand two hundred eighty-seven patients who were referred to Bozok University, Faculty of Medicine, Research and Application Hospital and Yozgat State Hospital between September 2012-September 2016, diagnosed with DVT based on physical examination and imaging (colored Doppler ultrasonography (CDUS) and venous computerized tomographic angiography) and treated either as an outpatient or inpatient, were enrolled in this research. The patients under the age of 15 and those who were not diagnosed in Yozgat were excluded. The medical records of the patients were reviewed retrospectively by getting the official permissions of related clinics.

Demographic data (age, gender, coexisting diseases and body mass index (BMI)) and the distribution of DVT cases were evaluated in terms of age and gender according to the data of address-based population registration system of Turkish Statistical Institute (TUSI) in 2016.

In both Cardiovascular Surgery Departments, the routine DVT treatment protocol was the same as that stated in "National Treatment Guide of Peripheral Artery and Vein Diseases, 2016" published by Turkish Cardiovascular Surgery Association and National Vascular and Endovascular Surgery Association. Each DVT patient was treated with subcutaneous low molecular weight heparin (LMWH) for at least five days and per oral vitamin K antagonist (VKA) starting at the time of diagnosis. International normalized ratio (INR) was monitored each day and when INR level reached 2-3 on two consecutive measurements, LMWH was stopped and treatment was continued with VKA alone. Each patient used compression socks with a pressure of 20-30 mmHg and frequent mobilization was advised. VKA treatment was stopped in patients whose INR level could not provide the set point on four consecutive measurements, and new oral anticoagulant (NOAC) therapy was ordered in the presence of normal values of liver and renal function tests.

Pharmacomechanic thrombectomy procedure was performed to two patients with iliac vein thrombosis following gastrointestinal carcinoma and a major abdominal surgery.

Statistical analysis

To calculate incidence rates of first DVT event, we used the observed number of cases of first DVT as the numerator and the sum of individuals per year as the total resident population as the denominator. This data was obtained from the data of address-based population registration system of Turkish Statistical Institute (TUSI) in 2016

Incidence rates for DVT were standardized by using the direct method, applying the age-specific rates in each 5-year age group to the world (Segi) standard population aged 15 years and above.

All analyses were performed using MINITAB™ Version 16. The Chi-square square test was used for the analysis of categorical data by creating crosstabs. Descriptive statistics were presented as frequency and percentages. For all tests, *P*-value <0.05 was considered statistically significant. Two samples test and t-test were used for demographic variables.

Results

The total sample comprised 1287 patients. Regarding the distribution of gender, 695 (54%) were female and 592 (46%) were male. The mean age of males and females were 54 (3.6) and 51 (2.3) years, respectively. Ninety-six (13.8%) females and 68 (11.4%) males were treated as in-patients (Table 1).

Accompanying diseases of the patients were shown in Table 1. There was not any statistically significant difference among the male and female patients in terms of diabetes mellitus (DM) (P=0.147), hypertension (HT) (P=0.074), cerebrovascular accident (CVA) (P=0.877), chronic renal failure (CRF) (P=0.162), peripheral arterial disease (PAD) (P=0.074), and left heart failure (LHF) (patients with left ventricle ejection fraction ≤30% in transthoracic echocardiography) (P=0.987). However, among those with chronic obstructive pulmonary disease (COPD), male patients had a significantly higher incidence of DVT compared to female patients (P=0.024). There was no

statistically significant difference between inpatient males and females (P=0.209).

The mean BMI of females and males were 29.2 (5.3) kg/m² and 26.7 (3.6) kg/m² respectively, (P<0.001) (Table 1).

Based on the data derived from TUSI, the overall incidence of DVT in Yozgat was one per 1000 persons-year, which was similar with the literature. DVT incidence increased with age and accelerated substantially especially above the age of 40 (Table 2).

DVT incidence was slightly higher among the female population (1:1000 persons/year vs 0.9:1000 persons/year) (P=0.924).

Table 1: Demographic data of DVT patients

	n (%)	*P*-value
Age		
Female	51 (2.3)	0.501
Male	54 (3.6)	
Gender		
Female	695 (54)	0.924
Male	592 (46)	
Inpatient		
Female	96 (7)	0.209
Male	68 (5)	
DM		
Female	184 (14)	0.147
Male	136 (11)	
HT		
Female	206 (16)	0.074
Male	203 (16)	
COPD		
Female	33 (3)	0.024
Male	46 (4)	
CVA		
Female	27 (2)	0.877
Male	24 (2)	
CRF		
Female	11 (1)	0.162
Male	16 (1)	
PAD		
Female	35 (3)	0.074
Male	44 (3)	
LHF		
Female	53 (4)	0.987
Male	45 (3)	
Major surgery history		
Female	61 (5)	0.749
Male	55 (4)	
Malignancy		
Female	86 (7)	0.812
Male	79 (6)	
Immobility		
Female	176 (14)	0.629
Male	154 (12)	
BMI		
Female	29.2 (5.3) kg/m²	0.001
Male	26,7 (3,6) kg/m²	
DVT incidence		
Female	1/1000	0.924
Male	0.9/1000	

DVT: Deep vein thrombosis, DM: Diabetes mellitus, HT: Hypertension, COPD: Chronic obstructive pulmonary disease, CVA: Cerebrovascular accident, CRF: Chronic renal failure, PAD: Peripheral arterial disease, LHF: Left heart failure, BMI: Body mass index

Table 2: The distribution of DVT patients above 15 years of age in terms of age and gender according to the data derived from address-based population registration system of TUSI 2016

	The distribution of population over the age of 15 according to the data derived from address-based population registration system of TUSI 2016 (n/%)	The distribution of DVT patients above the age of 15 in terms of age and gender (n) - 4 years	The distribution of DVT patients above the age of 15 in terms of age and gender (Mean person/year)
The age of 15-39	157.455 / 47.9%	131	2/10000
Male	80.838 / 51.3%	58	1.7/10000
Female	76.617 / 48.7%	73	2.2/10000
The age of 40-49	49.879/ 15.2%	296	1.4/1000
Male	25.254/ 50.6%	136	1.3/1000
Female	24.625/ 49.4%	163	1.6/1000
The age of 50-59	48.761/ 14.8%	302	1.5/1000
Male	24.255/ 49.7%	145	1.5/1000
Female	24.506/ 50.3%	157	1.6/1000
The age of 60-69	40.335/ 12.3%	293	1.8/1000
Male	19.326/ 47.9%	132	1.7/1000
Female	21.009/ 52.1%	161	1..9/1000
Above the age of 70	32.464/ 9.9%	265	2/1000
Male	13.843/ 42.6%	123	2.2/1000
Female	18.621/ 47.4%	142	1.9/1000
Summary	328.894/ 100%	1287	1/1000
Male	163.516/ 49.7%	592	0.9/1000
Female	165.378/ 50.3%	695	1/1000

TUSI: Turkish Statistical Institute, DVT: Deep vein thrombosis

Table 3: Characteristics of 1287 patients with DVT

	Idiopathic, n (%)	Secondary, n (%)	Total, n (%)
DVT	676 (53)	611 (47	1287 (100)
Female	372 (55)	323 (52)	695 (54)
Male	304 (45)	288 (48)	592 (46)
Median Age			
Female	52 (1.8)	50 (2.6)	51 (2.3)
Male	54 (2.6)	53 (3.7)	54 (3.6)
Location			
DVT Upper Extremity	6 (1)	11 (2)	17 (1)
DVT Abdominal	4 (1)	7 (1)	11 (1)
DVT Lower Extremity			
Proximal	452 (67)	421 (69)	873 (68)
Distal	214 (31)	172 (28)	386 (30)

Discussion

The annual cost of DVT and related complications in United States of America (USA) is about 7.5-39.5 billion American dollars and the preventable amount of this cost is about 2.5-19.5 billion American dollars [11-13]. It is possible to prevent one of every six-thromboembolic events with appropriate prophylactic treatment, which is administered to less than 55% of the patients eligible for prophylaxis [14-15].

The incidence of DVT is one per 1000 person-year [4,7,8,14]. In our study, the incidence of DVT in Yozgat was found to be the same with the literature.

There are various risk factors affecting the development of DVT. Advanced age is one of the most important independent risk factors of DVT. DVT is rarely observed under the age of 20 but the incidence starts increasing, particularly above the age of 40 [4-8]. The annual incidence of DVT in terms of age are 2-3 per 10000 persons-year (30-49 years of age), 5 per 10000 persons-year (50-59 years of age), 10 per 10000 persons-year (60-69 years of age) and 20 per 10000 persons-year (70-79 years of age) [4-6,8]. In an extended research of DVT patients conducted in 50 States and 400 hospitals in the USA between 1979 and 1999, Stein et al reported that the incidence of DVT above the age of 70 was 4 times higher than that under the age of 50 [16]. In our study, the incidence of DVT under the age of 40 was found to be two per 10000 persons-year, and showed an increase after the age of 40, reaching two per 1000 persons-year above the age of 70.

DVT incidence in reproductive females might be slightly higher than males but would even out after menopause. However, the overall DVT incidence in terms of gender is reported as 1.3 per 1000 persons-year among males and 1.1 per 1000 persons-year among females [4,7-10,17,18]. In this study, DVT incidence was found as 1 per 1000 persons-year among females and 0.9 per 1000 persons-year among males. Although it was not meaningful statistically, this result was different from the literature as being higher in female population.

Obesity is defined as BMI ≥30 kg/m² and morbid obesity, as BMI ≥40 kg/m². It is a major but preventable risk factor of DVT development. Obesity increases the risk of DVT development 2-3-fold, which is further escalated in morbid obese persons [19]. According to the data derived from TUSI 2014, in Turkey, the overall obesity rate among the general population above the age of 15 was 19.9%, 15.9% among males and 24.5% among females. In our study conducted in Yozgat, the mean BMI values of females and males were 29.2 (5.3) kg/m², and 26.7 (3.6) kg/m² respectively, the difference between which was statistically significant.

According to the data of TUSI 2016, in the region consisting of Yozgat, Sivas and Kayseri, the labor-force participation rates of females and males were 28% and 49.6%, respectively. The number of females participating the labor-force is nearly the half of the male population in Central Anatolia Region, bringing forth a sedentary lifestyle, which would inevitably contribute to obesity development. Due to both high obesity and low labor-force participation rates of female population living in Yozgat, DVT incidence is higher in females than in males.

Although the physiomechanism has not been described properly, geographic circumstances have a considerable effect on DVT incidence. DVT is observed less in the seaside in comparison with inland [20,21]. Due to the harder environmental conditions, DVT incidence is observed 10-15% times higher in winter [22]. Given these circumstances, Yozgat has additional risk factors of DVT development, since it is away from the seaside with compelling winter conditions and a high altitude. That is why further larger-scale and comparative studies would provide more reliable and beneficial results.

COPD is a disease with acute exacerbations, most of which are related to infections. COPD is usually observed in advanced ages and is due to the lack of adequate mobilization and a strong history of tobacco consumption [23,24]. In a research conducted by Chen CY et al, the overall incidence rate of DVT was higher in patients with COPD, with 18.78 events per 10,000 persons-years [25]. In our study, male patients with COPD showed a significantly higher rate of DVT incidence in comparison with female patients with COPD. The higher rates of tobacco consumption starting from the childhood years among the male population might have been effective on this result. There was no statistically meaningful difference between male and female DVT patients in terms of other concomitant diseases.

Limitations

The main limitation of our study is misdiagnosed or undiagnosed DVT cases. Sometimes DVT, especially those with an atypical clinical progress, can be misdiagnosed and treated as soft tissue injury, myalgia, or orthopedic problems, etc. The thrombosis of gastrocnemius and soleus deep veins are responsible of approximately 60% of mid-calf deep vein thrombosis cases, which are reported as normal venous anatomy with CDUS.

Conclusion

DVT is a multifactorial disease capable of serious morbid or mortal complications. However, with proper precautions it is possible to prevent a remarkable amount of DVT cases and related complications. Thus, studies that consider the sociocultural, socioeconomic, and geographic data would provide more realistic results in terms of prevention and treatment of DVT and related complications.

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