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Orjinal Araştırma / Original Article

Risk Factors for Venous Thromboembolism in Patients with Spinal Cord Injury: A Single-Center Turkish Study

Spinal Kord Yaralanmalı Hastalarda Venöz Tromboembolizm için Risk Faktörlerinin Ortaya Konması: Tek Merkezli Türkiye Verileri

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Abstract

Objective: Spinal cord injury (SCI) occurs due to trauma or non-traumatic conditions may be associated with comorbidities related to cardiovascular system and higher risk for venous thromboembolism (VTE). This study aimed to identify risk factors for VTE in patients with SCI who participated the inpatient rehabilitation program.

Material and Method: The study included 326 patients diagnosed as SCI that were admitted to the inpatient tertiary research hospital rehabilitation clinic and enrolled in a conventional rehabilitation program. The data were collected retrospectively. Risk factors for developing VTE were identified.

Results: There were no significant differences in age, comorbidities or SCI etiology between the patients with and without VTE. The groups differed significantly in gender, level of injury and duration of SCI. Risk factor for VTE were only level of injury.

Conclusions: The present findings show that paraplegic injury level may be considered risk factor for developing VTE in SCI patients. It should be considered when approaching the possibility of VTE in SCI patients.

Keywords: Spinal cord injury, venous thromboembolism, deep venous thromboembolism, pulmonary embolism

Öz

Amaç: Spinal kord yaralanması travmatik veya travmatik olmayan nedenlerle oluşur ve kardiyovasküler sistem hastalıkları ve yüksek venöz tromboembolizm (VT) riski ile ilişkilidir. Bu çalışmanın amacı yatarak rehabilitasyon programına dahil edilmiş spinal kord yaralanmalı hastalarda VT gelişimi için risk faktörlerini ortaya koymaktır.

Gereç ve Yöntem: Çalışma spinal kord yaralanması tanısı olan ve 3. Basamak araştırma hastanesi rehabilitasyon kliniğine başvurup konvansiyonel rehabilitasyon programına dahil edilen 326 hastadan oluşmaktadır. Veriler retrospektif olarak toplanmıştır. Venöz tromboembolizm için risk faktörleri ortaya konmuştur.

Bulgular: Yaş, ek sistemik hastalıklar veya spinal kord yaralanması etiyolojisi açısından VT olan ve olmayan gruplar arasında fark yoktur. Gruplar cinsiyet, yaralanma seviyesi ve yaralanma süresi açısından farklılık göstermektedir. Tek risk faktörü yaralanma seviyesidir.

Sonuç: Bu çalışmada spinal kord yaralanmalı hastalarda yaralanma seviyesi risk faktörü olarak bulunmuştur. Spinal kord yaralanmalı hastalara VT açısından yaklaşımda akılda bulundurulmalıdır.

Anahtar Kelimeler: Spinal kord yaralanması, venöz tromboembolizm, derin venöz tromboembolizm, pulmoner emboli

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INTRODUCTION

Spinal cord injury (SCI) occurs due to trauma or disease, resulting in impairment, including motor-sensory deficits, bladder and bowel dysfunction, and pulmonary complications. Disability varies with injury level and whether or not the injury is complete or incomplete.[1] SCI is also associated with comorbidities related to the cardiovascular system. Irregularities of cardiac rhythm, orthostatic hypotension, or absence of cardiac pain can occur. Additionally, the risk of venous thromboembolism (VTE) is higher in SCI patients than in general population.[2] VTE includes deep venous thromboembolism (DVT) and pulmonary embolism (PE). Hypercoagulability and stasis are the most common factors that lead to deep vein thrombosis in SCI patients.[3]

DVT and PE are associated with multiple factors during all phases of SCI. It was reported that patient age and the presence of another injury are independent risk factors for VTE during the acute phase of SCI,[4] whereas some studies reported that patient age, gender, race, completeness of injury, and neurosurgery were not associated with VTE.[5] One study on the factors related to VTE in acute SCI patients in Australia observed that weight, male gender, duration of hospitalization, and lower limb fractures are risk factors for VTE;[6] however, it was noted that the risk of VTE is higher during the acute phase of SCI[7] and a systematic review reported that risk of VTE is higher even during the subacute phase (3-6 months).[8] The present study aimed to identify the risk factors for VTE in SCI patients during all phases of SCI.

MATERIAL AND METHOD

Patients

This retrospective study included SCI patients that were hospitalized in the inpatient rehabilitation clinic of Başkent University Medical School, Ankara Hospital, Ankara, Turkey, between January 2005 and January 2021. The data were collected from the records of the patients kept by the health care professionals. Patients with paralysis due to rheumatologic diseases, those with SCI accompanying traumatic brain injury and those were using anticoagulant agents due to atrial fibrillation and valve replacement were excluded. In all, data for 358 SCI patients were retrospectively analyzed, but due to incomplete data, 32 patients were excluded from the study, leaving 326 patients. Only the first time hospitalizations of the patients were taken into consideration and only complications during hospitalizations and venous thromboembolism histories were recorded.

Patient age, co-morbidity, etiology of SCI (traumatic or non-traumatic), duration of SCI, completeness of injury, injury level, functional and ambulation level, complications of SCI, including spasticity, bladder-bowel incontinence and urinary tract infections, and the presence of other trauma or fracture, were recorded. Spinal cord injuries occurred by spinal cord compression, vascular disease, neoplasms, hemorrhage, syringomyelia and myelitis were classified as non-traumatic spinal cord injuries. Completeness of injury was based on the Asia Impairment Scale (AIS), as follows: AIS A: complete injury; AIS B, C, and D: incomplete injury. Participants with a paraplegia showed a lesion below Th1 and participants with a tetraplegia a lesion level between C1-7. Functional assessment and level of ambulation were determined according to the Functional Independence Measure (FIM) and the Functional Ambulation Classification (FAC), respectively.

FIM is an 18-item scale used to assess physical, cognitive, and social functioning, with a focus on disability.[9] The FIM motor subscale includes self-care, sphincter control, locomotion, and transfer information. The FIM cognitive subscale collects information about communication and social functioning. Additionally, FIM is used to objectively assess development. FAC is a 6-point Likert-type (0-5) scale used to evaluate walking ability and the need for human support during ambulation. In this study FAC ambulation was categorized as dependent (non-ambulatory or ambulatory with physical assistance) (FAC score: 0-2) and independent (FAC score: 3-5).[10]

Duration of SCI was defined as acute SCI (<3 months), subacute SCI (3-6 months), and chronic SCI (>6 months). The level of spasticity was determined according to the Modified Ashworth Scale (MAS). Patients were classified whether they had spasticity or not.[11] VTE was diagnosed according to establishment of the clinical probability of DVT or PE (pain, swelling, and/or dyspnea) based on an elevated D-dimer value, venous doppler ultrasonographic findings, and pulmonary imaging findings. If the venous doppler ultrasound finding was positive with clinical suspicion, the patients were diagnosed as deep vein thrombosis. If the venous Doppler ultrasound finding was negative, when the D-dimer result was found to be high, the patients were planned to have an ultrasound 6-8 days later. Despite clinical suspicion, deep vein thrombosis was excluded in patients with venous Doppler ultrasound findings negative and normal D-dimer level. For the diagnosis of PE, high-risk suspicion (patients with shock or/with hypotension) with positive immediate Computed tomography pulmonary angiography is diagnosed as pulmonary embolism. For the patients with non-high risk; elevated D-dimer and positive multi-detected spiral computed tomography is diagnosed also as pulmonary embolism.[12] All patients included in the study received thromboprophylaxis during their stay in our inpatient rehabilitation clinic (40 mg enoxaparin).[13] The study was performed in accordance with the Declaration of Helsinki. Ethics committee approval was received from Başkent University School of Medicine (Date: 24.05.2022, Decision No: KA22/203)

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows v.24.0 (IBM Corp., Armonk, NY, US). Continuous variables are shown as mean±SD, and categorical data

are shown as number and percentage. The Kolmogorov-Smirnov test was used to determine the normality of the distribution of continuous variables. Normally distributed data were compared with chi-square test, non-normally distributed data were compared using the Mann Whitney U test. For multivariate analysis estimating the risk of DVT/PE independent predictors of developing DVT/PE were tested using binary logistic regression analysis. The Hosmer-Lemeshow test was used for model concordance. The level of statistical significance was set at $p<0.05$.

RESULTS

Of the 326 SCI patients (mean age of 50.76 years) included in the study, 209 were male and 117 were female. In total, 238 of the patients were paraplegic and 88 were tetraplegic. Injuries were motor complete in 119 patients and incomplete in 207 patients. In all, 28 of the patients developed VTE, of which 7 had both DVT and PE.

Demographic and clinical characteristics of the patients are given in **Table 1**. There weren't any significant differences in age, co-morbidities (hypertension (HT), diabetes mellitus (DM), coronary artery disease (CAD), and malignancy) (p=0.574, p=0.858, p=0.477, p=0.096, respectively) or etiology between the SCI patients with and without VTE (p=0.695). There were significant difference between gender and level of injury (p=0.014). There weren't any significant differences in FIM, FAC, completeness of paralysis, urinary tract infection, presence of spasticity, presence of heterotopic ossification, bladder and bowel continence, decubitus ulcer or another injury or fracture between the patients with and without VTE.

Table 1. Demographic and clinical characteristics in the patients with and without VT

	Without VT (n=298)	With VT (n=28)	Total (n=326)	p
Age (Mean±SD)	50.65±19.47	51.85±19.79	50.76±19.47	0.748*
Gender (n, %)				
Female	101 (33.9%)	16 (57.1%)	117 (35.9%)	0.014**
Male	197 (66.1%)	12 (42.9%)	209 (64.1%)	
Etiology (n, %)				
Traumatic	192 (64.4%)	17 (60.7%)	209 (64.1%)	0.695**
Non-traumatic	106 (35.6%)	11 (39.3%)	117 (35.9%)	
Injury level (n, %)				
Tetraplegia	85 (28.5%)	3 (10.7%)	88 (27.0%)	0.045**
Paraplegia	213 (71.5%)	25 (89.3%)	238 (73.0%)	
DM (n, %)				
No	259 (86.9%)	24 (85.7%)	283 (86.8%)	0.858**
Yes	39 (13.1%)	4 (14.3%)	43 (13.2%)	
HT (n, %)				
No	217 (72.8%)	19 (67.9%)	236 (72.4%)	0.574**
Yes	81 (27.2%)	9 (32.1%)	90 (27.6%)	
Malignancy (n, %)				
No	280 (94.0%)	24 (85.7%)	283 (86.8%)	0.096**
Yes	18 (6.0%)	4 (14.3%)	22 (6.7%)	
CAD (n, %)				
No	277 (93.0%)	25 (89.3%)	302 (92.6%)	0.477**
Yes	21 (7.0%)	3 (10.7%)	24 (7.4%)	

* Chi-square testi, ** Mann Whitney U test

The SCI patients with and without VTE showed significant difference in duration of SCI (p=0.020) (**Tables 2** and **3**).

Based on the multivariate logistic regression analysis model, the higher odds of VTE were associated with level of injury (paraplegia/tetraplegia) (p=0.024). Accordingly, regarding the risk of developing VTE paraplegic patients had a 60-fold higher risk than tetraplegic patients (p=0.024, 95% CI: 1.7-2094.7) (**Table 4**).

Table 2. Clinical characteristics in the patients with and without VT

	Without VT (n=298)	With VT (n=28)	Total (n=326)	p
AIS (n,%)				
A	106 (35.6)	13 (46.4)	119 (36.5)	0.213**
B	39 (13.1)	6 (21.4)	45 (13.8)	
C	73 (24.5)	3 (10.7)	76 (23.3)	
D	80 (26.8)	6 (21.4)	86 (26.4)	
Duration of disease (n,%)				
Acute (<3 months)	149 (50.0)	19 (67.9)	168 (51.5)	0.020**
Subacute (3-6 months)	52 (17.4)	7 (25.0)	59 (18.1)	
Chronic (>6 months)	97 (32.6)	2 (7.1)	99 (30.4)	
Presence of another injury (n,%)				
Yes	27 (9.1)	24 (85.7)	295 (90.5)	0.323**
No	271 (90.9)	4 (14.3)	31 (9.5)	
FIM scores median (median±SD)				
FIM	60 (13-126)	52 (19-101)	59 (13-126)	0.061*
FAC level (n,%)				
FAC				
0-2	278 (93.3)	27 (96.4)	305 (93.6)	0.518**
3-5	20 (6.7)	1 (3.6)	21 (6.4)	

* Chi-square test ** Mann Whitney U test; FIM: Functional Indepence Measurement, FAC: Functional Ambulation Classification

Table 3. Comparison of the clinical characteristics in the patients with and without VT

	Without VT (n=298)	With VT (n=28)	Total (n=326)	p
Heterotopic ossification (n,%)				
Yes	10 (3.4)	1 (3.6)	11 (3.4)	0.777**
No	288 (90.9)	27 (96.4)	315 (96.6)	
Urinary tract infection (n,%)				
Yes	174 (58.4)	21 (75.0)	195 (59.8)	0.087**
No	124 (41.6)	7 (25.0)	131 (40.2)	
Bladder continence (n,%)				
Yes	129 (43.3)	8 (28.6)	137 (42.0)	0.131**
No	169 (56.7)	20 (71.4)	189 (58.0)	
Bowel continence (n,%)				
Yes	136 (58.4)	10 (35.7)	146 (44.8)	0.313**
No	162 (54.4)	18 (64.3)	180 (55.2)	
Spasticity (n,%)				
Yes	121 (40.6)	8 (28.6)	129 (39.6)	0.213**
No	177 (59.4)	20 (71.4)	197 (60.4)	
Decubitus ulcer (n,%)				
Yes	75 (25.1)	11 (39.2)	86 (26.4)	0.106**
No	223 (74.9)	17 (50.8)	240 (73.6)	

** Mann Whitney U test

Table 4. Determining estimated relative risks for developing VT with logistic regression analysis in patients with SCI

	Odds Ratio	95% Confidence interval (Lower-Upper)	p
Injury Level	60.0	1.7-2094.7	0.024

* The model included gender, injury level and duration of disease .

DISCUSSION

The present study aimed to identify risk factors for VTE in SCI patients. Since, one-third of our patients were related to the non-traumatic etiology, the mean age was 50.76. The findings show that only level of injury (paraplegia/tetraplegia) is an independent risk factor for developing VTE in SCI patients. Additionally, there was a significant difference in gender, level of injury and duration of SCI between the patients with and without VTE. Among the 16 female patients in the present study with VTE, 4 had both PE and DVT. Although, previously, male gender was identified as an independent risk factor for developing VTE in SCI patients, in the general population there isn't a significant difference between genders in incidence of VTE and that female gender is associated with recurrent VTE.[1,6,14-16]

Among the present study's 28 SCI patients with VTE, 16 did not have any co morbidities, but 2 patients had HT, 2 had DM, 2 had DM and HT, 1 had HT and CAD, 4 had HT and an undefined malignancy, and 1 had neurofibromatosis. According to the literature, both in the general population and SCI patients, such conditions as malignancy, congestive heart failure, obesity, and lower extremity fracture are risk factors for VTE; however, in the present study there wasn't a significant difference in these conditions or comorbidities between the patients with and without VTE.[6,14,17] It should be noted that the present study did not take into consideration patient body mass index. Maung et al.[1] reported that SCI patients with high-level thoracic injury had the highest risk for VTE, whereas those with high-level cervical injury had the lowest risk. Furthermore, earlier studies reported that SCI patients with thoracic-level injury have a higher risk for developing VTE.[7] Similarly, in the present study injury level was determined as an independent risk factor for developing VTE and a higher risk of thromboembolism was found in paraplegic patients compared to tetraplegic patients. The reason for this has not been determined in previous studies.[18]

Spasticity is known to protect against the development of VTE in SCI patients;[19] however, in the present study there wasn't an association between developing VTE and spasticity. Similarly, Green et al.[20] observed that SCI patients with flaccid paralysis had a higher risk of VTE than those with spasticity. In SCI patients immobilization can lead to VTE;[21,22] however, there wasn't a significant difference in FIM or FAC scores between the present study's SCI patients with and without VTE. In addition, both patient groups were similar in terms of independence and ambulation. It is well-known that immobilization is a risk factor for VTE due to stasis in immobilized extremities or paralyzed muscles, according to the Virchow triad.[21,22] In the present study low FIM and FAC scores were not observed to be risk factors for developing VTE, which was unexpected, but might have been due to the fact that all the SCI patients included study were inpatients undergoing conventional rehabilitation and were not considered fully immobile. Due to the same reason, completeness of injury was not observed to be a risk factor for developing VTE as well.[6,12,23,24]

In the present study there was a significant correlation between duration of SCI. It was reported earlier that VTE occurs most commonly in SCI patients within 3 months of injury,[7] the risk of VTE remains high in subacute SCI patients,[8] and that risk differs in acute- and subacute-phase SCI patients; however, according to the present study's multivariate analysis duration of SCI was not a risk factor.

CONCLUSION

The present study has some limitations, including lack of analysis of patient body mass index. In addition, only symptomatic VTE was considered, and lower extremity venous Doppler ultrasonography was not performed in all of the SCI patients. Based on the present findings, we conclude that the risk of developing VTE is high in paraplegic patients. Although, gender and duration of SCI differed significantly in patients with and without VTE, they were not found as risk factors for developing VTE in SCI patients. Clinician awareness of the risk factor might help yield optimal treatment outcomes in SCI patients undergoing rehabilitation.

ETHICAL DECLARATIONS

Ethics Committee Approval: Ethics committee approval was received from Başkent University School of Medicine (Date: 24.05.2022, Decision No: KA22/203)

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

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