Research article

Deep venous thrombosis in patients with chronic spinal cord injury

Magdalena Mackiewicz-Milewska[1], Stanisław Jung[2], Andrzej C. Kroszczyński[3], Hanna Mackiewicz-Nartowicz[4], Zbigniew Serafin[5], Małgorzata Cisowska-Adamiak[1], Jerzy Pyskir[6], Iwona Szymkuć-Bukowska[1], Wojciech Hagner[1], Danuta Rość[7]

[1]Department of Rehabilitation Collegium, Medicum in Bydgoszcz Nicolaus Copernicus University, Poland, [2]University of Technology and Live Science Bydgoszcz, Poland, [3]Kroszczynski Medical Practice, Kalisz, Poland, [4]Department of Phoniatry and Audiology, Collegium Medicum in Bydgoszcz Nicolaus Copernicus University, Poland, [5]Department of Radiology and Diagnostic Imaging, Collegium Medicum in Bydgoszcz Nicolaus Copernicus University, Poland, [6]Department of Biophysic Collegium, Medicum in Bydgoszcz Nicolaus Copernicus University, Poland, [7]Department of Patophysiology Collegium, Medicum in Bydgoszcz Nicolaus Copernicus University, Poland

Context/Objective: Deep venous thrombosis (DVT) is a well-known complication of an acute spinal cord injury (SCI). However, the prevalence of DVT in patients with chronic SCI has only been reported in a limited number of studies. The aim of our study was to examine the prevalence of DVT in patients with SCI beyond three months after injury.
Design: Cross-sectional study.
Setting: Rehabilitation Department at the Bydgoszcz University Hospital in Poland.
Participants: Sixty-three patients with SCI that were more than 3 months post injury. The patients, ranging in age from 13 to 65 years, consisted of 15 women and 48 men; the mean age of the patients was 32.1 years. The time from injury varied from 4 to 124 months.
Outcome measures: Clinical assessment, D-dimer and venous duplex scan.
Results: The venous duplex scan revealed DVT in 5 of the 63 patients. The post-injury time in four of the patients varied between 4 and 5 months; one patient was 42 months post-injury.
Conclusion: DVT occurred in patients with chronic SCI, mainly by the 6th post injury month.

Keywords: Spinal cord injuries, Venous thrombosis, Paraplegia, Tetraplegia, Quadriplegia

Introduction

Deep venous thrombosis (DVT) and pulmonary embolism (PE) are severe early complications of spinal cord injury (SCI).[1–3] The high risk of venous thromboembolism (VTE) results from the presence of all elements of Virchow's triad: endothelial abnormality, stasis of blood flow, and hypercoagulability.[1–5]

According to various reports, the incidence of DVT among patients with SCI ranges from 5.3–64% when prophylaxis is implemented and from 47 to 100% when no prophylactic measures are applied.[2,3,5–8] Inpatient rehabilitation centers treat both acute and chronic SCI. In these patients, the risk of DVT remains permanently increased secondary to immobilization, which raises the subject of the appropriate duration of DVT prophylaxis. Not many clinical studies have been conducted regarding DVT prophylaxis in patients with chronic SCI. In Poland, there are no clear guidelines regarding the duration of DVT prophylaxis after SCI. This aspect is typically based on the experience of the clinical staff in the inpatient rehabilitation centers. The aim of our study was to examine the prevalence of DVT in patients with patients with SCI beyond three months after injury.

Methods

This cross-sectional study involved all inpatients with SCI beyond the time frame of three months after the

Correspondence to: Magdalena Mackiewicz-Milewska, Department of Rehabilitation Collegium, Medicum, in Bydgoszcz Nicolaus Copernicus University, St Curie-Skłodowskiej 9, 85-094 Bydgoszcz, Poland.
Email: magmami@onet.eu

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injury admitted for inpatient rehabilitation at the Rehabilitation Department of the Bydgoszcz University Hospital, Poland, during the years of 2007–2009 and 2011–2013, who gave informed consent. Initially the study was planned to last for 2 years (2007–2009) however during this time frame there were not enough patients meeting the study entry criteria so the study was restarted in 2011. The time frame of the study is disjointed as in 2010 there were no SCI admissions. The study was approved by the Local Bioethical Committee. There were 63 patients (15 females and 48 males), mean age 32 years (13–65). Among the sample, 33 patients (52.3%) had cervical spine injury, 24 (38.7%) thoracic spine injury, and 6 (9.5%) lumbar spine injury. The neurological status was assessed according to American Spinal Cord Injury Association (ASIA) Impairment Scale (AIS) guidelines. The mean time from injury to admission was 21 months (3.5 to 124 months).

The details of pre-admission DVT prophylaxis and comorbidities were obtained from the medical documentation from previous institutions or from the patients' primary medical doctors' reports. Clinical examination was used to detect typical DVT symptoms like swelling of the lower limbs, redness, warmth, pain, and tenderness. All patients had a venous ultrasound duplex scan (US scan) between 5th and 7th day after admission performed by the same examiner. D-dimer was also measured. The diagnosis was based on the detection of acute deep vein thrombus through US scan. The D-dimer values were analyzed with Wilcoxon test. Standard protocol of venous ultrasound of lower extremities consisted of examination of deep veins from the groin to the ankle. The examination consisted of a compression B-scan, evaluation of the presence of an intravascular thrombus and color Doppler flow imaging.

The study assessed the relationship between occurrence of lower extremity DVT and comorbidities, patients' age, the time of the injury, utilization of DVT prophylaxis, and neurological status assessed using the AIS scale.

Results

In the analyzed group, 17 patients were 3–6 months post-injury, 14 patients 6–12 months post-injury, and 26 patients more than 12 months post-injury.

Lower limb swelling was present in 35 patients (55.5%) and redness in 3 (4.7%). The characteristic of the studied group is shown in Table 1. As a result of US exam, DVT was diagnosed in 5 individuals (Table 2). The mean age of these patients was 40

Table 1 SCI patients more than 3 months post injury

Level of spine injury	Number of patients	Average age (years)	DVT	Edema	Redness	Tenderness	AIS A	AIS B	AIS C	DVT in the past	HO*	DM*	Average time from injury (months)
Cervical	33	28 (13–55)	2	16	0	0	6	16	11	2	4	13	11 (3–124)
Thoracic	24	37 (13–65)	3	15	3	0	14	7	3	1	3	14	18 (3–84)
Lumbal	6	29 (20–46)	0	3	0	0	4	1	1	1	1	4	29 (4–87)

AIS = ASIA Impairment Scale; HO = Heterotopic ossification; DM = Diabetes mellitus.

Table 2 Patients with deep venous thrombosis

Injury level	Age	DVT in venous duplex scan	Female	Male	Redness	Edema	Time from injury (months)	Low molecular heparin prior to admission	Co- morbidities	AIS Grade	D-dimer (normal value 55–228 ug/l)
Cervical spine	30	1	1	0	0	0	48	0	Urinary tract infection	B	531
Cervical spine	23	1	0	1	0	1	4	1	None	C	88
Thoracic spine	41*	1	0	1	1	1	4	1	Urinary tract infection	A	1201
Thoracic spine	55	1	0	1	1	1	5	1	Hypertension	C	1000
Thoracic spine	49	1	0	1	0	1	4	1	Urinary tract infection + pressure sore	A	800

AIS = ASIA Impairment Scale; * thrombosis in another lower extremity and pulmonary embolism prior to admission.

years, while of the remaining individuals, the mean was 32 years. All of the diagnosed cases of DVT involved either deep veins of the lower leg or popliteal vein. In all of the patients, the DVT was limited to one extremity. Four of the DVT patients had swelling in the limbs and two had limb redness; none of them reported pain. One individual showed no symptoms of DVT.

One of the four DVT patients had a very high risk of thrombosis secondary to the history of DVT in contralateral lower extremity and PE. This patient also had a urinary tract infection during hospitalization. Another patient had a large sacral decubitus, urinary tract infection. He also had a history of septicemia during the acute post injury period. The decubitus certainly interfered with patient's rehabilitation what might have resulted in an increased risk of thrombosis. The subject who developed DVT 42 months post injury suffered from a urinary tract infection. Infections of the urinary tract are common in SCI and temporarily disrupt rehabilitation, which may result in an increased immobilization which leads to a higher risk of DVT.

The mean value of D-dimer in DVT patients was 724 μg/l (88–1201), whereas in the group without DVT, this value was 702 μg/l (35–7200); laboratory normal value: 55–228 μg/l. Only one individual in the DVT group had a normal D-dimer value (88 μg/l). Among the patients without acute DVT, 16 individuals had elevated D-dimer up to 7200 μg/l. In the patients with markedly elevated D-dimer, PE was also ruled out. There were no statistically significant relationships between elevated D-dimer in non-DVT patients and ongoing infections (mainly urinary tract infections). There were no statistically significant differences in D-dimer level among DVT and non-DVT patient groups. Secondary to the small number of DVT patients, the study did not reveal statistical relationships between the presence of acute DVT and the post injury time, the level of injury, AIS scale, comorbidities, and prophylaxis with low molecular weight heparin (LMWH). At admission, 21 patients (33.3%) were on LMWH, and 1 person was taking acenocoumarol. Patients receiving LMWH were studied from 3 to 10 months post injury. The duration of DVT prophylaxis with LMWH is presented in Table 3.

Table 3 DVT prophylaxis on admission to the inpatient rehabilitation unit

Level of inury	Number of patients on DVT prophylaxis	Mean duration of DVT prophylaxis (months)
Cervical spine	10	6
Thoracic spine	9	4.8
Lumbar spine	2	5.5

Despite such prolonged prophylaxis, DVT was diagnosed in four of them. DVT was also diagnosed in one patient with no prior prophylaxis 42 months after injury. Moreover, the US study revealed features of lower extremity venous insufficiency in five patients, three of whom had DVT diagnosed earlier, acutely post injury. Two others had no history of DVT. No cases of PE were diagnosed.

Non-pharmacologic DVT prophylaxis consisted on physical therapy, mobilization with passive and active exercises aimed to improve circulation in lower extremities. The scope of these exercises depended on the level and completeness of the injury. The patients were also sat upright and the wheelchair trained. No other non-pharmacologic interventions such as thigh high compression stockings, pneumatic calf compression boots were utilized.

Discussion

The most severe form of VTE is PE.[9,10] In patients with diagnosed DVT, its rate may be as high as 24%.[2] Apart from the recurrence (7–20% of DVT cases), late DVT complications include post-thrombotic syndrome, trophic skin changes, and ulcerations (20–50%). In patients with SCI, DVT may also increase spasticity and trigger autonomic dysreflexia.[8] Spinal cord injury is considered one of the major risk factors of DVT.[11] The majority of DVT cases in patients with SCI (up to 88%) are seen within the first three months (acute stage)—from the 3rd day[12] to the end of the 3rd month,[1,3,7,10,13,14] with its peak occurrence between the 7th and the 14th day post injury.[8] Following the acute phase, DVT frequency decreases, though it is still reported, as the risk factors of immobilization and stasis of blood flow are present.[2,3,7,10]

The problem of DVT in chronic SCI is rarely discussed. Jones surveyed patients from the 3rd to the 12th month after trauma and found DVT in 12% of the surveyed patients[2]; in our surveys, this value was 8%. Similar results were reported by others.[3,7,14,15] In our study, the time from the injury ranged from 3.5 to 124 months. Four patients were diagnosed with DVT between the 4th and the 5th month post injury, although one patient was diagnosed 42 months post injury. This confirms the results of others[3,7] that DVT does occur past the 3rd month, usually up to the 6th month. Age is a well-known risk factor of DVT.[11] In our study, the mean age of DVT patients was higher than in other surveyed patients with SCI.

Some authors[2,8,9] report that DVT occurs in paraplegic patients more frequently than in tetraplegic ones, and we also found this in our group, whereas in our study, most DVT patients demonstrated thoracic spine injury; however, the small number of DVT diagnosed patients makes it difficult to draw a conclusion. Green *et al.*[16] found contradictory results, while Yelnik *et al.*[17] reported no difference between patients with paraplegia and tetraplegia.

It is interesting to note that all of our patients with paraplegia with DVT had spastic paralysis. Deep vein thrombosis after SCI may be clinically asymptomatic.[2,3,18] Aito *et al.*[1] reported that it may be clinically mute in 65% of cases.

In our study, the typical clinical symptoms (swelling, redness, and tenderness) were present only in two patients. The significance of tenderness as a clinical symptom of DVT in patients with SCI is controversial, as pain sensation is absent or impaired in these individuals.

Swelling also seems to be an uncertain sign. Swelling in the lower limbs occurred in 34 individuals (54%) in our group, and among them, as many as 30 had no DVT.

D-dimer level can also be helpful in the diagnostic process. This test is highly sensitive; however, it lacks specificity.[5] Boudaoud *et al.* found that most of the patients with SCI without DVT had elevated D-dimer levels.[7] Our study also revealed elevated D-dimer levels in 16 patients without DVT or PE. Some of those patients had urinary tract infections; however, no statistically significant correlation was found between the infections and DVT levels. Presumably patients with SCI develop thrombosis in very small blood vessels which cannot be visualized on US scan. Elevated D-dimer levels may be present after major surgery, trauma, neoplasms, and infections and in individuals above 80 years old or with pressure sores.[13,19] In our study, one patient had normal D-dimer, despite being diagnosed with DVT by US scan.

The diagnostic process of DVT consists of clinical examination and imaging studies like contrast venography and US scan. Venography is considered a gold standard in the diagnosis of DVT, although US scan is the most commonly utilized test secondary to being non invasive and relatively cheap.[3,5,9,12,20] Specificity of US scan in detecting symptomatic DVT of proximal veins (femoral and popliteal) is 96.8–99% while sensitivity is 96.1–100%. However, detection of DVT in distal veins has lower specificity and sensitivity, respectively 50–70% and 60%.[21,22] According to various authors, the percentage of detected distal DVT ranges from 5 to 76.5%.[23,24]

DVT pharmacological prophylaxis with LMWH decreases its rate of what has been reported through multiple studies.[5,14,25,26] Most of the authors recommend the aforementioned level of prophylaxis until the end of the 2nd[1,25] or 3rd month post-injury.[3,5,14] Among our patients admitted from various institutions or from home only, 21 (33.3%) had been on prophylactic dose of LMWH. Their mean post-injury time was 5.3 months. The long duration of prophylaxis may be related to the fact that, in Poland, there are no guidelines on the duration of anti-thrombotic prophylaxis in patients with SCI with paraplegia or tetraplegia. Despite such prolonged prophylaxis, DVT was diagnosed in four patients in this group. DVT was also diagnosed in one patient who was 42 months post-injury and without prophylaxis. More frequent occurrence of DVT in the subgroup of patients on anti-thrombotic prophylaxis is likely related to the relatively short time post injury—5.3 months, while in the subgroup off prophylaxis this time longer—25.6 months.

Our study confirms that DVT occurs mostly in "early" chronic SCI (i.e. up to the end of the 6th month). In the literature, the DVT prophylaxis in chronic SCI has been rarely discussed. Bravo *et al.*[10] assert that prophylaxis should be prolonged throughout the whole year if the platelet rate is increased, while Mc Kinney *et al.*[20] recommend reinstitution of prophylactic measures in patients with chronic SCI who have acute medical illnesses or undergo surgical procedures if they are immobilized with a bed rest regime for prolonged periods of time. This might be in concordance with our findings, as four of five patients with DVT presented with co-morbidities.

A limitation of this study was admission of the patients at disparate times to the rehabilitation department. The patients were admitted in these disparate times for various reasons. First of all, patients with SCI in Poland besides outpatient rehabilitation have an option of so called chronic inpatient rehabilitation, which may be granted even several years after the injury. This is why they were admitted long after the initial trauma. The patients were selected according to the post-injury time and only those more than 3 months post-injury were enrolled in the study. For most of the patients it was a second admission to our facility as they had previously undergone an acute post-injury rehabilitation. Indeed, two of the patients with DVT had a history of a prolonged acute post-injury rehabilitation. One of them suffered from a decubitus and urinary tract infection while the other had a PE. The remaining three DVT patients were admitted to our center for so called late stage rehabilitation after having completed an acute rehabilitation.

Conclusion

In our opinion, the study should be continued, especially in patients between 3 and 6 months post injury. If further studies confirm our preliminary findings that the risk of DVT is relatively high, prolonged prophylaxis should be considered up to 6 months.

Disclaimer statements

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Conflicts of interest There are no conflicts of interest.

Ethics approval Collegium Medicum Bydgoszcz Nicolaus Copernicus University Bioethical Commitee.

References

1 Aito S, Pieri A, D'Andrea M, Marcelli F, Cominelli E. Primary prevention of deep venous thrombosis and pulmonary embolism in acute spinal cord injured patients. Spinal Cord 2002;40(6): 300–3.
2 Jones T, Ugalde V, Franks P, Zhou H, White RH. Venous thromboembolism after spinal cord injury: incidence, time course, and associated risk factors in 16,240 adults and children. Arch Phys Med Rehabil 2005;86(12):2240–7.
3 Furlan JC, Fehlings MG. Role of screening tests for deep venous thrombosis in asymptomatic adults with acute spinal cord injury: an evidence-based analysis. Spine 2007;32(17):1908–16.
4 Rouleau P, Guertin PA. Early changes in deep vein diameter and biochemical markers associated with thrombi formation after spinal cord injury in mice. J Neurotrauma 2007;24(8):1406–14.
5 Teasell RW, Hsieh JT, Aubut JA, Eng JJ, Krassioukov A, Tu L. Venous thromboembolism after spinal cord injury. Arch Phys Med Rehabil 2009;90(2):232–45.
6 Geerts WH, Code KI, Jay RM, Chen E, Szalai JP. A prospective study of venous thromboembolism after major trauma. New Engl J Med 1994;331(24):1601–6.
7 Boudaoud L, Roussi J, Lortat-Jacob S, Bussel B, Dizien O, Drouet L. Endothelial fibrinolytic reactivity and the risk of deep venous thrombosis after spinal cord injury. Spinal Cord 1997; 35(3):151–7.
8 Powell M, Kirshblum S, O'Connor CK. Duplex Ultrasound screening for deep vein thrombosis in spinal cord injured patients at rehabilitation admission. Arch Phys Med Rehabil 1999;80(9): 1044–6.
9 Chen D, Apple DF, Hudson LM, Bode R. Medical complications during acute rehabilitation following spinal cord injury—current experience of the model systems. Arch Phys Med Rehabil 1999; 80(11):1397–401.
10 Bravo G, Guizar-Sahagun G, Ibarra A, Centurión D, Villalón CM. Cardiovascular alterations after spinal cord injury: an overview. Curr Med Chem Cardiovasc Hematol Agents 2004; 2(2):133–48.
11 Caprini JA. Risk assessment as a guide to thrombosis prophylaxis. Curr Opin Pulm Med 2010;16(5):448–52.
12 Germing A, Schakrouf M, Lindstaedt M, Grewe P, Meindl R, Mügge A. Serial compression B-scan and Doppler sonography for the screening of deep venous thrombosis in patients with spinal cord injuries. J Clin Ultrasound 2010;38(1):17–20.
13 Roussi J, Bentolila S, Boudaoud L, Casadevall N, Vallee C, Carlier R, *et al.* Contribution of D-Dimer determination in the exclusion of deep venous thrombosis in spinal cord injury patients. Spinal Cord 1999;37(8):548–52.
14 Ploumis A, Ponnappan RK, Bessey JT, Patel R, Vaccaro ARO. Thromoprophylaxis in spinal trauna surgery; consensus among spine trauma surgery. Spine J 2009;9(7):530–36.
15 Lamb GC, Tomski MA, Kauffman J, Maiman DJ. Is chronic spinal cord injury associated with increased risk of venous thromboembolism?. J Am Paraplegia Soc 1993;16(3):153–6.
16 Green D, Chen D, Chmiel JS, Olsen NK, Berkowitz M, Novick A, *et al.* Prevention of thromboembolism in spinal cord injury; role of low molecular weight heparin. Arch Phys Med Rehabil 1994;75(3): 290–2.
17 Yelnik A, Dizien O, Bussel B, Schouman-Claeys E, Frija G, Pannier S, *et al.* Systematic lower limb phlebography in acute spinal cord injury in 147 patients. Paraplegia 1991;29(4): 253–60.
18 Sugimoto Y, Ito Y, Tomioka M, Tanaka M, Hasegawa Y, Nakago K, *et al.* Deep venous thrombosis in patients with acute cervical spinal cord injury in a Japanese population: assessment with Doppler ultrasonography. J Orthop Sci 2009;14(4):374–6.
19 Goodacre S, Sampson FC, Sutton AJ, Mason S, Morris F. Variation in the diagnostic performance of D-dimer for suspected deep vein thrombosis. QJM 2005;98(7):513–27.
20 McKinney D, Garstang SV. Prevention of thromboembolism in spinal cord injury: follow-up. E-Medicine, medscape.com updated 2009: Jan 13.
21 Crowhurst TD, Dunn RJ. Sensitivity and specificity of three-point compression ultrasonography performed by emergency physicians for proximal lower extremity deep venous thrombosis. Emerg Med Australas 2013;25(6):588–96.
22 Gaitini D. Current approaches and controversial issues in the diagnosis of deep vein thrombosis via duplex Doppler ultrasound. J Clin Ultrasound 2006;34(6):289–97.
23 Do JG, Kim du H, Sung DH. Incidence of deep vein thrombosis after spinal cord injury in Korean patients at acute rehabilitation unit. J Korean Med Sci 2013;28(9):1382–7.
24 Garcia ND, Morasch MD, Ebaugh JL, Shah S, Blackburn D, Astleford P, *et al.* Is bilateral ultrasound scanning of the legs necessary for patients with unilateral symptoms of deep vein thrombosis?. J Vasc Surg 2001;34(5):792–7.
25 Ageno W, Agnelli G, Checchia G, Cimminiello C, Paciaroni M, Palareti G, *et al.* Prevention of venous thromboembolism in immobilized neurological patients: guidelines of the Italian Society for Haemostasis and Thrombosis (SISET). Thromb Res 2009;124(5):26–31.
26 Spinal Cord Injury Thromboprophylaxis Investigators. Prevention of venous thromboembolism in the rehabilitation phase after spinal cord injury: prophylaxis with low dose heparin or enoxaparine. J Trauma 2003;54(6):1111–5.