DEEP VENOUS THROMBOSIS IN PATIENTS WITH ACUTE TRAUMATIC SPINAL CORD INJURY: PREVALENCE AND PATTERNS IN A MAJOR TEACHING HOSPITAL IN UGANDA

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ABSTRACT

Background: **Spinal cord injured patients are at high risk of developing Deep Venous Thrombosis (DVT). This is because spinal cord injury favours two of the Virchow's triad of factors for DVT; thus endothelial injury (trauma) and immobility (venous stasis). DVT and Pulmonary Embolism (PE) have long been known to be a major health problem in the West. However, the problem in Africa has been underestimated due to lack of data.**

Materials and methods: **A cross sectional descriptive study was carried out at the spine unit of Mulago National Referral and Teaching Hospital from September 2012 to February 2013. Traumatic spinal cord injured patients who met the inclusion criteria were assessed for DVT using the model developed by Wells and colleagues. This included clinical assessment, D-dimer assay and Doppler sonography. Thromboprophylaxis was not given to any patient at any stage; however, treatment was instituted in those showing the features of DVT on investigations.**

Results: **Out of 53 patients enrolled in the study, 48 were males and 5 were females. Most of the patients were in the age group of 21 to 40 years. DVT was found in 6 out of 53 patients representing 11.3%. All the patients who had DVT were in ASIA class A. There was bilateral involvement in one patient whereas two patients had thrombi in the left and three had thrombi in the right. A total of ten different thrombi were found, three proximal and seven distal. Clinical signs were found to be unreliable in the diagnosis of DVT in spinal cord injured patients. D-dimer test in combination with the Wells score was found to be a useful screening test and could reduce the need for further test if negative.**

Conclusion: **We found a prevalence of 11.3% in the spinal cord injured patients. This prevalence was comparable to studies done in Asia but within the lower border of studies done in Caucasians. Distal DVT was more common as opposed to Caucasians where proximal DVT is more common. Clinical features of DVT were found to be unreliable in spinal cord injured patients due to the neurological injury.**

Key words: **Deep vein thrombosis, Pulmonary embolism, Traumatic spinal cord injury, Wells score, D-dimer assays, Doppler sonography**

INTRODUCTION

Spinal cord injured patients are at high risk of developing Deep Venous Thrombosis (DVT). This is because spinal cord injury favours two of the Virchow's triad of factors for DVT; thus endothelial injury (trauma) and immobility (venous stasis). Thromboembolic events are a major cause of morbidity and mortality in patients with acute traumatic spinal cord injury (1). Hence one of the biggest challenge for clinicians managing spinal cord injured patients is decreasing their risk of developing DVT (2).

Thromboprophylaxis by means of chemical and mechanical methods significantly reduces the risk of DVT in patients with spinal cord injury and is widely practiced in the developed world. However, in Uganda and most developing countries, thromboprophylaxis in acute traumatic Spinal Cord Injuries (SCI) is still not widely practiced. This may be due to lack of knowledge of the gravity of the problem by the attending clinicians or the widely held view that DVT is a problem in the western populations hence the underestimation of the problem.

Complications of a DVT that may lead to significant morbidity include Pulmonary Embolism (PE), Post Thrombotic Syndrome (PTS), prolonged edema, pressure ulcers, spasticity and autonomic dysreflexia (3). Most serious of these is pulmonary embolism, which occurs in (8% to 14%) of patients with acute SCI, with a mortality rate of (2.5% to 4.7%) (4,5). Early recognition and appropriate treatment of DVT and its complications saves many lives.

Accurate and early diagnosis of deep vein thrombosis is critical to enable timely intervention and management. However, the diagnosis of DVT clinically is unreliable (4). Different methods have been developed for diagnosing Deep Venous Thrombosis (DVT). D-dimer, venous ultrasound and venous plethysmography have become more acceptable as noninvasive methods (6,7). Ascending venography is considered to be the best

diagnostic study but it is an invasive procedure and technically demanding so cannot be routinely applied. The prevalence of DVT in patients with a spinal cord injury ranges from 5% to 26% in several countries (1). However, there are very few studies highlighting the magnitude of the problem in the developing world. In Uganda the prevalence and presentation of DVT in acute traumatic SCI is not known. A review of mortality records in the spine unit of Mulago Hospital-Uganda's major teaching hospital has shown a rate as high as 10.7% of the acute traumatic SCI patients with majority being sudden deaths. Henriksen and Sejrsen (8) noted that the survival rate for patients with PE is low as sudden death is the initial clinical presentation in 25% of cases. Therefore, we hypothesized that PE complicating DVT could have contributed significantly to the high mortality rate in our hospital. In view of that, we undertook a cross sectional descriptive study of the prevalence and presentation of DVT in patients admitted with acute traumatic spinal cord injury.

MATERIALS AND METHODS

Study design: Following approval from the institutional research and ethics review committees, a cross sectional descriptive study was carried out from 1st September 2012 to 28th February 2013 at the spine unit of Mulago Hospital. In this hospital acute traumatic SCI patients are first resuscitated in the accident and emergency ward like any other trauma patient. From here they are admitted to the spine unit for definitive and specialized care. This may either be conservative or may involve a surgical intervention depending on the diagnosis. This is then followed by rehabilitation and discharge.

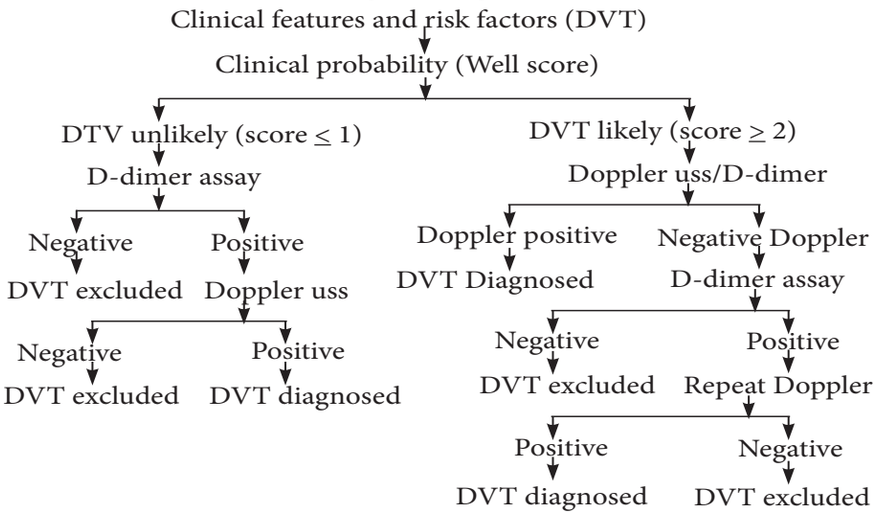
All patients with acute traumatic spinal cord injury admitted to spine unit were included in the study whereas patients on DVT prophylaxis for other conditions were excluded from the study.

Study procedure: After achieving an informed consent, patients presenting within four weeks of injury were purposively recruited into the study. They were then assessed for evidence of DVT using clinical assessment, D-dimer test and Doppler sonography. Patient demographics noted included sex and age. Additionally, date and cause of injury, severity of injury and associated musculoskeletal injury, presence of DVT, location and clinical features of DVT were noted. Skeletal injury was then classified according to the region of the spine injured and neurological status was assigned by the ASIA score (9). Clinical evidence of DVT in the lower limbs was assessed as follows: Measurement of thigh and calf circumferences. Reference point for measurement was 15 cm below and above the superior margin of the patella. (A 3 cm difference between limbs was considered significant); presence of pitting edema; a positive Homan's sign; (10) presence of collateral superficial veins (non varicose) and skin changes such as redness, warmth, and blisters. Screening for DVT was done based on the model developed by Wells and colleagues`. Patients were stratified into two risk categories: "DVT unlikely" if the clinical score was ≤ 1 and "DVT likely" if the clinical score was ≥ 2. Patients who were categorized as "DVT unlikely" had D-dimer assay done and a negative result excluded DVT. Those who had a positive D-dimer assay were examined by Doppler sonography; a positive test confirmed DVT, a negative test excluded DVT.

Patients falling into the "DVT likely" group were examined by Doppler sonography and D-dimer assays. A positive Doppler confirmed DVT. Those who had a negative Doppler test and a negative D-dimer test were excluded for DVT. Patients with negative Doppler and positive D-dimer test were examined with repeat Doppler in one week (Figure 1). Blood samples were taken for D-dimer assays between the first and second week. Based on the D-dimer results and/Wells score, Doppler sonography for the qualifying patients was done between the second and fourth week of admission.

Figure 1

Diagnostic algorism



Data was collected using a pre-tested questionnaire and entered into EpiData version 3.1, transferred with STATA transfer and analyzed using STATA version 10.1 (Copyright 1985-2011 Stata Corp LP, Texas, USA). A Chi Square was used as the measure of association and P -values of 0.05 or less were considered significant.

RESULTS

Diagnostic utility: Of the fifty three patients recruited into the study, seventeen patients were stratified as 'DVT unlikely' using the Wells criteria. D-dimer assays done were negative and DVT was excluded. Thirty six patients were stratified as 'DVT likely' based on the Wells score and had Doppler ultrasound and D-dimer test done. Based on the D-dimer and Doppler results, six patients were confirmed positive for DVT.

In this study, the sensitivity and specificity of the D-dimer test was found to be 83.3% and 70.2% respectively. The positive predictive value was 26% and the negative predictive value was 97%.

Socio demographics and injury characteristics

Age and sex distribution: Of the 53 patients recruited, 48 were males representing 90.57% and 5 were females representing 9.43%. The mean age of the respondents was 37 years (range 7-74 years) and the median age was 34 years (standard deviation 15.1).

Aetiology of injury: The main cause of injury was road traffic accidents (n=25) representing 47.17%. However, falls from height also accounted for a significant number of cases (n=17) representing 32.08%. Assault accounted for 1 case (1.89%). Other causes included industrial accidents, gunshots, collapsed buildings and sports injuries (n=10) representing 18.87% of cases.

Severity and spinal level of injury: The commonest injury was cervical spine injury which accounted for 28 (52.83%) patients. Thoracic spine injuries accounted for 8(15.09%), thoraco-lumbar injuries 4(7.55%) and lumbar spine injuries 12(22.64%) of the patients. The least reported injury was sacral/cauda equina (n=1) representing 1.89% of the patients.

According to the ASIA classification, 22(41.51%) were ASIA A, 12(22.64%) in ASIA B, 2(3.77%) were ASIA C, 7(13.21%) were ASIA D and 10(18.87%) were ASIA E.

Table 1

Patient demographics and injury characteristics

Characteristics	Distribution of study patients (n=53)	
	No.	(%)
Age in years		
<20	4	7.55
21-40	31	58.49
41-60	13	24.53
>60	5	9.43
Gender		
Female	5	9.43
Male	48	90.57
Cause of injury		
Road traffic accidents	25	47.17
Falls	17	32.08
Assault	1	1.89
Others	10	18.87
Spinal level injury		
Cervical	28	52.83
Thoracic	8	15.09
Thoraco-lumbar	4	7.55
Lumbar	12	22.64
Sacral/ Cauda equina	1	1.89
Asia impairment scale		
A	22	41.51
B	12	22.64
C	2	3.77
D	7	13.21
E	10	18.87

Prevalence of DVT: DVT was found in 6 out of 53 patients giving a prevalence of 11.3%. All the patients who had DVT were males with majority in the age group of 20 to 40 years (n=3), followed by those in the age group of 41 to 60 years (n=2).

DVT was diagnosed two to four weeks after injury with 66.7% diagnosed within the first three weeks and 33.3% within four weeks. The highest frequency was between the second and third week after injury.

Table 2
Location of DVT

Level	Unilateral, Total=5 patients		Bilateral, Total=1 patient			
	Right	Left	Right	Left		
Iliac	0	0	0	0	Proximal	3
Femoral	1	1	1	0		
Popliteal	3	1	1	1	Distal	7
Crural	1	0	0	0		
Total patients (%)	3/6(50.00)	2/6(33.33)	1/6(16.67)			

Table 3
Clinical features found in patients with DVT

Clinical features	Participants' DVT status DVT Present (n=6)	DVT Absent (n=47)	P value
Pedal edema			
Present	4(66.67)	4(8.51)	0.001
Absent	2(33.33)	43(91.49)	
Skin changes			
Present	1(16.67)	0	_
Absent	5(83.33)	47(100)	
Thigh difference			
Present	1(16.67)	0	_
Absent	5(83.33)	47(100)	
Calf difference			
Present	4(66.67)	0	_
Absent	2(33.33)	47(100)	

There was bilateral involvement in one patient accounting for 16.7% of the patients with DVT whereas two patients had thrombi in the left representing 33.3% and three had thrombi in the right accounting for 50.0% of the patients who had DVT. Of the six patients, two had multiple thrombi. A total of 10 different thrombi were observed in six patients, three were proximal DVT and seven were distal DVT.

Pedal edema was detected in four patients of the total number of patients with DVT. However some patients had pedal edema without DVT but the majority were still those with DVT and this difference was statistically significant (p=0.001).

Thigh circumference difference was detected in one patient and this patient had DVT. Four patients had unilateral increase in calf circumference. Two of the patients had increments of 1 and 2 cm and were thus considered insignificant. The other two had increments of 3 and 5cm and were considered to be significant. All four patients had DVT.

Skin changes (blisters) were seen in one patient representing 0.17% of the patients with DVT. Thirty three percent of the patients with DVT had no signs of DVT. Homan's sign and collateral superficial veins were not detected in any of the patients with DVT.

Table 4
Spinal level, ASIA class and associated injuries in patients with DVT

	Number (%) Total=6	Number (%) Total=47
Associated injuries		
Head injury	0	1(2.13)
Chest injury	1(16.67)	3(6.38)
Lower extremity	1(16.67)	2(4.26)
Injury	4(66.67)	41(87.23)
None		
Spinal level injury		
Cervical	2(33.33)	26(55.32)
Thoracic	3(50.00)	5(10.64)
Thoraco-lumbar	1(16.67)	3(6.38)
Lumbar	0	12(25.53)
Sacral/Cauda equina	0	1(2.13)
Asia Impairment scale		
A	6(100)	16(34.04)
B	0	12(25.53)
C	0	2(4.26)
D	0	7(14.89)
E	0	10(21.28)

Majority of the patients with DVT representing 66.6% (n=4) had no associated injuries. One patient each had associated chest injury and lower extremity injury.

DVT was found in patients with complete spinal cord lesions (ASIA class A). Overall, 50.0% of the patients with DVT had thoracic spine injury, 33.3% had cervical spine injury and 16.7% had thoraco-lumbar injury.

DISCUSSION

Socio demographics and injury characteristics of participants: Majority of the patients were young males between the second and fourth decade. This is due to the fact that Uganda has a relatively young population with average life expectancy of 48 years for males and 57 years for females (11). The active youth are involved in a number of risky activities in Uganda such as riding motor cycles and this puts them at risk of sustaining trauma based injuries. These findings have been reported in previous studies done in Uganda (12-14). Available literature from studies done in other countries was also consistent with these findings. In a study done in Turkey on deep vein thrombosis in spinal cord injured patients, majority of the patients were in the age group of 20 to 30 years which is the active youth (4). Another study in Pakistan reported similar findings (15). In United states, the average reported age was relatively higher at 53 years (2).

The main cause of injuries was road traffic accidents. This is consistent with other studies done in Uganda (12-14). However, falls from height also accounted for a significant number of cases representing 32.08%. Most of the falls were from trees, rooftops and electrical poles. In a study done in Pakistan involving 50 spinal cord injured patients, they found the opposite with falls from height been the main cause of injury representing 48% whilst road traffic accidents was the second cause of injury representing 22% of the patients with gunshot wounds accounting for 12% of the cases (15). In Uganda, the increased use of motor cycles as a means of transport has led to a rise in road traffic accidents.

Majority of the patients had cervical spine injury followed by thoracic spine injury. In a study done in Turkey involving 31 spinal cord injured patients, thoracic spine injuries were the commonest followed by cervical spine injuries (4). Similar findings were also reported in a study done in Pakistan (15). These differences could be due to the differences in aetiology of the injury. In our study, road traffic accident was the major cause of injury whilst in Pakistan, falls from height was the major cause of injury.

According to the ASIA classification, 64.1% of the patients had motor complete lesions (ASIA A 41.5% and ASIA B 22.6%) and 17.0% were classified as motor incomplete (ASIA C, D) as defined by the international standards for neurological and functional classification of spinal cord injury (16). Similar findings were reported according to studies done in the United States and Pakistan (2,15).

Prevalence of deep vein thrombosis: The prevalence of DVT in patients with acute traumatic spinal cord injury in Mulago Hospital was 11.3%. This prevalence is within the lower border compared to other studies done in different countries.

The prevalence of DVT in spinal cord injured patients range from 5% to 26% in several countries (1). Other investigators put the figure at 12% to as high as 100% depending upon the method of study (4). A study done in UK involving one hundred spinal cord injured patients found the prevalence of DVT to be 26% using clinical diagnosis (17). Another study involving fifty spinal cord injured patients found the prevalence to be 16% using venous plethysmography (18). The highest prevalence of 100% was found in a study involving twenty acute spinal cord injured patients using ^{125}I-fibrinogen uptake leg scanning (19).

There have been several studies done in Asia such as Japan, Malaysia, China, Thailand, and Pakistan on the prevalence of DVT in spinal cord injured patients; they found a prevalence of DVT of 2.6% to 17% (20). These figures are within the lower range of the prevalence in Caucasians. Studies done in Europe and UK put the figure at 12% to 53% (4,17,21,22).

Literature on studies done in Africa on DVT prevalence in spinal cord injured patients was lacking. Most of the studies cited were not focused on spinal cord injured patients. A study done at Mulago Hospital on patients with musculoskeletal trauma reported a prevalence of 14.3% (12) whilst in Sudan the prevalence was 9.6% following prostatectomy (23). Another study on postoperative deep vein thrombosis in a South African population found a prevalence of 50%, in the South African Bantu (24). The prevalence of post operative deep vein thrombosis in the series of Nigerians was found to be 30% (25).

Spinal cord injured patients are at high risk of DVT after sustaining injury. This is because spinal cord injured patients fulfilled two of the Virchow's triad of factors for DVT; thus endothelial injury (trauma) and immobility (venous stasis). However, the prevalence of DVT in spinal cord injury varies from place to place depending on genetic and predisposing acquired factors.

In this study, the reported prevalence of 11.3% was comparable to that reported in Asian studies, (26) but the prevalence was quite low compared to European studies (4). The factors responsible for the low prevalence probably include race, genetics, climate and diet. Race alone may not be a strong factor. Blacks (African Americans) who are living in the United States have the same or higher prevalence of DVT with the white Americans (27). Low dietary fat intake appears to be the most important factor for the low prevalence in Africans and Asians (20).

Climate may also have an effect on the prevalence of DVT. A study done in UK demonstrated a seasonal variation in prevalence of DVT with higher prevalence in the six cold months of the year than during the warmer months (28). This could be due to the fact that people are less active during the colder months and thus more prone to venous stasis. In addition, it has been shown that colder weather has a constrictor effect with reduction in blood flow. An increased blood flow and vaso-dilatation is produced by warmer weather (29). Other factors may include the practice of massage and passive exercises by attendants and the high prevalence of blood group 'O which has been known to decrease the risk of DVT (26, 30).

In this study the prevalence of 11.3% does not appear to offer a complete explanation to the cause of sudden deaths as hypothesized. However, a study done in 2012 on traumatic spinal cord injuries in Mulago Hospital: types, treatment and short term outcomes, identified pneumonia as the commonest complication at 7.8% (14). The mortality rate was also found to be 7.8% and all deaths were cervical spine injuries complicated with respiratory failure (14).

The mean age of the patients who developed DVT was 43 years (range 26 to 67 years) and are categorized as moderate risk group for DVT as recommended by the European Consensus Group (31). The prevalence of DVT is low in children due to decreased capacity to generate thrombin, increased capacity of alpha-2-macroglobulin to inhibit thrombin, and enhanced antithrombin potential of vessel walls (32). All the patients who developed DVT were males (n=6). This is probably due to the fact that 90% of the patients recruited into the study were males.

Most of the patients who had DVT were unskilled casual workers and this is reflective of the category of patients who are admitted into our general wards. In addition, these casual workers are more prone to road traffic accidents as they move around the city on foot and on motor cycles and risk been knocked by vehicles. DVT was diagnosed two to four weeks after injury. These findings are consistent with literature (1,12).

In this study, the sensitivity and specificity of the D-dimer test was found to be 83.3% and 70.2% respectively. The positive predictive value was 26% and the negative predictive value was 97%. A study done in Italy on the Wells rule and d-dimer for the diagnosis of isolated distal deep vein thrombosis reported the sensitivity and specificity of D-dimer test to be 84% and 50% respectively with a negative predictive value of 96% (33). A similar study conducted in the Netherlands found the negative predictive value of the D-dimer test to be 99% (34). These results are consistent with the findings in this study. Thus one can safely rule out DVT if the D-dimer is negative and is therefore a good screening test.

Location of DVT: Distal DVT was more common mainly in the calf. These findings are similar to studies done in Asia (1,35). However, it differs from studies done in Caucasians where proximal DVT was more common (4,36-38). The probability of PTE complicating DVT has been reported to be 46%, 67%, and 77% for the calf, thigh, and pelvic veins respectively (35). This probably explains why most of the patients were asymptomatic. No patient developed significant complications during the study and there was no death recorded. The reason for the differences in location of DVT in Africans and Asians as found in this study compared to that of Caucasians is not known. However, it has been shown clinically that proximal DVT is often associated with other chronic diseases and pre-existing risk factors whereas distal DVT is more often associated with recent risk factors such as trauma and immobilisation (32). Hence pre-existing risk factors such as smoking and obesity which are more common in the Caucasians could be the possible explanation for these differences. The right leg was the commonest site for DVT (50% of the patients) as compared with the left side (33% of the patients) with 17% been bilateral. In literature, the findings have been mixed (1,4,15). The reason for this is not known, but in pregnancy and in acute massive venous thrombosis, it has been shown that the left side is more commonly affected and it has been postulated to be due to compression of the left iliac vein by the right iliac artery (May-Thurner syndrome) (39). However, no literature was found as to whether patients with left sided DVT have a higher risk of PE than those with DVT on the right.

Presentation of DVT in spinal cord injury: The diagnosis of DVT in spinal cord injured patients can be difficult because of lack of subjective symptoms. Unilateral leg swelling, pedal edema and skin changes were some of the clinical signs found in this study. However not all patients with pedal edema had DVT and some patients with DVT did not have pedal edema, skin changes or unilateral leg swelling. Symptoms such as pain were mostly absent and no patient demonstrated a positive Homan's sign. The Homan's sign was therefore a very unreliable way of testing for DVT in spinal cord injured patients. Similar findings were reported in literature (40). Pedal edema was the only statistically significant finding (p value 0.001). Other findings include skin changes and unilateral leg swelling demonstrated by measuring the thigh/calf circumference difference between the two legs. Reference points for measurements were

15cm above and below the superior margin of the patella. A difference of 3cm or more was considered a significant finding. However, serial leg circumference measurements are not very sensitive as progressive wasting of muscles may affect the results. Similar findings have been reported in literature (26,41).

The clinical features of some of the complications of DVT can be missed as well. For example, pulmonary embolism in quadriplegics can be misinterpreted as weakness in the muscles of respiration or respiratory tract infection and thus the diagnosis of VTE can be missed (26).

Injury patterns associated with DVT

Relationship between spinal cord injury severity and DVT: DVT was found in patients with complete spinal cord lesions (ASIA class A). The findings in literature have been mixed. Several studies reported a significant association between spinal cord injury severity and the development of DVT (15,26,42) and other studies found no association between motor complete versus incomplete lesions (1,4). A study done on DVT among spinal cord injured patients using duplex sonography found no statistically significant relationship between motor complete (ASIA A, B) versus motor incomplete status (ASIA C, D) (25,43). We found a significant association between the injury severity and development of DVT. Patients in ASIA class A are significantly at a higher risk of DVT (p value 0.049).

Thoracic spine injury accounted for the majority of cases (50.0% of the patients with DVT). These findings are consistent with what has been reported in literature (42). Patients with high thoracic spine injury are at greater risk of DVT compared to lumbar and sacral spine injuries (26, 40).

CONCLUSIONS

The prevalence of DVT in patients with acute traumatic spinal cord injury at Mulago Hospital was 11.3%. This prevalence was comparable to studies done in Asia. However, the prevalence was quite low compared to European studies. Distal DVT was more common compared to European studies where proximal DVT was more common.

Patients with motor complete lesions are at a high risk of DVT compared to patients with incomplete lesions. Patients with high thoracic spine injuries are at relatively high risk of DVT.

The clinical features of DVT in spinal cord injured patients are unreliable due to the neurological injury. Pedal edema was however found to be a statistically significant finding. No patient had pulmonary embolism suggesting that most of the DVT were asymptomatic.

The Wells score combined with D-dimer test was a good screening tool for DVT in spinal cord injured patients. The negative predictive value of the D-dimer test was 97% and one could safely rule out DVT in patients categorized as low risk who had negative D-dimer results.

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