Prevalence of Acute Deep Vein Thrombosis in Patients with Ankle and Foot Fractures Treated with Nonoperative Management—A Pilot Study

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Abstract

The prevalence of deep vein thrombosis (DVT) among patients with ankle and foot fractures in Australia treated nonsurgically is unknown. Indications for thromboprophylaxis screening and management are unclear.

The primary outcome was the prevalence rate of DVT among nonsurgically managed ankle and foot fracture patients. Patients were enrolled into a prospective cross-sectional pilot study at an outpatient hospital fracture clinic. DVT risk factors and symptoms were recorded at time of recruitment followed by referral for compression duplex ultrasonography. Independent *t*-test and Fisher exact test were used to assess the significance of these variables with DVT.

A total of 72 patients were included in the final analysis. Overall, 11% (8/72) of patients had DVT—seven distal DVTs and one proximal DVT. Four were symptomatic including the patient with a proximal thrombus. In comparison, the majority of patients were asymptomatic of DVT (63/72). A significant risk factor found to be associated with DVT was age ≥ 45 ($p = 0.013$) years, and a lack of symptoms ($p = 0.006$) was associated with no DVT.

This pilot study is the first in Australia to investigate the prevalence of DVT in this specific subgroup of patients. We found a prevalence of 11% of DVT in a small group of patients with age ≥ 45 years, being the only significant associated risk factor. Future larger scale prospective studies are warranted to confirm these results.

Keywords
- deep vein thrombosis
- duplex
- ultrasound
- lower extremity
- proximal
- distal

Fractures damage adjacent blood vessel walls exposing collagen and tissue factor which activate the coagulation cascade and the resulting hypercoagulability increases the risk of thrombosis.[1] Deep vein thrombosis (DVT) causes significant mortality, morbidity, and financial burden on the community.[2–4] Immobilization, the mainstay of managing a fracture can increase the risk of thrombosis up to 19%[5] because of the loss of the calf muscle venous pump mechanism. Below knee cast immobilization for nonsurgical treatment of leg trauma is strongly associated with thrombosis (odds ratio, 12.7; confidence interval [CI] 95%, 6.6–24.6).[6] The high prevalence of lower limb DVT in hip, pelvic, and long bone fracture is well recognized but literature on ambulating patients with ankle and foot fractures is particularly sparse.[2,7–10] DVT in this subgroup has been reported to vary from 1.1 to 20%.[1,11–17] However, some of these studies report rates without differentiating DVT from pulmonary embolism and were confounded with nonbony injuries such as tendon ruptures, sprains, and dislocations. Accounting for studies that included only fractures, reported prevalence is from 0.6 up to 5%. Other risk factors for DVT have been well documented include high body mass index (BMI), old age, smoking, use of oral contraceptive pills (OCP), and hormone replacement therapy (HRT).[4,5,7–9,18]

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The variability in prevalence rates sets unclear indications for diagnosis and prophylaxis. In a UK survey, 84% of hospitals lacked routine prophylaxis for patients with ankle fractures requiring plaster casts and 64% did not perform DVT risk assessment.[19] The American College of Chest Physicians do not recommend prophylaxis for isolated injuries distal to the knee.[10] The aim of this pilot study is to evaluate the prevalence and risk factors of DVT in patients with ankle and foot fractures treated with nonoperative management.

Methods

This prospective cross-sectional pilot study was conducted in an outpatient orthopedic fracture clinic of a tertiary hospital in Sydney, Australia.

Between February and August 2014, consecutive patients $\geq$ 18 years of age with a radiologically confirmed ankle or foot fracture treated nonsurgically were identified at the clinic and recruited. An ankle fracture included lateral or medial malleoli and the distal tibiofibular, tibiotalar, or subtalar joint. A foot fracture included any bone distal to the subtalar joint. Exclusion criteria included the following: multitrauma, prior venous thromboembolism (VTE), current use of anticoagulant or antiplatelet agents, or presented to the clinic outside the 7 to 90 day postfracture period. All enrolled patients provided written informed consent.

Baseline demographic data, time to clinic follow-up, and ultrasound assessment since injury, DVT symptoms and specific DVT risk factors were recorded using a standardized questionnaire at the time of recruitment. Risk factors included age, gender, BMI, smoking status, use of OCP, use of HRT, history of active cancer, history of bleeding or clotting disorder, family history of DVT, method of immobilization, and weight-bearing status on discharge from the Department.[4,5,8,9,18] Patients were referred for compression duplex ultrasonography (CDUS) of the lower limb with the fracture. If a DVT was found, the contralateral leg was also scanned and the patient was referred to a vascular specialist for appropriate treatment. Distal DVT was defined as a thrombus in the deep veins of the calf including axial and muscular named deep veins. Thrombus in veins including or proximal to the popliteal vein was classified as proximal DVT. If CDUS was completed on a day after recruitment, time to CDUS was adjusted accordingly. Recruited patients were contacted by phone to confirm their participation if no result was available after 2 weeks.

The study was approved by the hospital's Human Ethics Research Committee (Approval number: LNR/13/SVH/397).

Statistical Analysis

Continuous and categorical variables were reported as medians, means, and proportions with 95% CIs. Nonparametric data underwent $\log_{10}$ transformation before testing significance. Patient characteristics and risk factors were assessed with independent t-test for continuous variables and Fisher exact test for categorical variables. Data were adjusted with bootstrapping (no. of resamples = 1,000) in all analyzes.

Table 1 Characteristics and risk factors of the study group[a]

Variables	*N* (%)	95% CI
DVT		
Nil	27 (37.5)	26.4–48.6
DVT detected	8 (11.1)	4.2–19.4
CDUS not completed	37 (51.4)	38.9–62.5
Age (y), median, range	38 (22–80)	
Gender		
Female	39 (54.2)	41.7–65.3
Male	33 (45.8)	34.7–58.3
BMI (kg/m^2), median, range	24 (14–43)	
Fracture		
Foot	40 (55.6)	44.4–66.7
Ankle	29 (40.3)	29.2–52.7
Ankle + foot	3 (4.2)	0.0–9.7
Ipsilateral	66 (91.7)	84.7–97.2
Bilateral	6 (8.3)	2.8–15.3
Immobilization		
Full cast	5 (6.9)	1.4–13.9
Backslab	11 (15.3)	6.9–23.6
CAMboot	50 (69.4)	58.3–80.6
Pressure bandage	3 (4.2)	0.0–9.7
None	3 (4.2)	0.0–9.7
Weight-bearing status		
NWB	34 (47.2)	36.1–58.3
PWB	13 (18.1)	9.7–27.8
WBAT	25 (34.7)	23.6–47.2
DVT symptoms		
None	63 (87.5)	
Calf pain	7 (9.7)	4.2–18.0
Edema	1 (1.4)	0.0–4.2
Combination	1 (1.4)	0.0–4.2
Time to fracture clinic (d), median, range	23 (7–90)	
Time to CDUS (d), median, range	32 (7–90)	
Smoking status		
Nonsmoker	28 (38.9)	26.4–50.0
Exsmoker	25 (34.7)	25.0–47.2
Current	19 (26.4)	16.7–100.0
History of current OCP use[b]	5/39 (12.8)	2.3–22.5
History of current HRT use[b]	7/39 (17.9)	5.9–29.9
Family history of VTE	2 (2.8)	0.0–6.9

Abbreviations: BMI, body mass index; CAMboot, controlled ankle movement boot; CDUS, compression duplex ultrasonography; CI, confidence interval; DVT, deep vein thrombosis; HRT, hormone replacement therapy; NWB, nonweight bearing; OCP, oral contraceptive pill; PWB, partial weight bearing; VTE, venous thromboembolism; WBAT, weight bearing as tolerated.
[a]$n = 72$.
[b]This data are for female patients ($n = 39$).
Note: No patients had history of active cancer or clotting/bleeding disorders.

A p value ≤ 0.05 was considered to be significant. All data were analyzed with SPSS v22.0 (Statiscal Package for Social Sciences; IBM, Armonk, NY).[20]

Results

During the study period, 116 patients treated with surgery presented to the clinic while 162 patients with nonsurgical ankle and foot fractures were identified. Overall, 90 patients were excluded (current anticoagulation or antiplatelet therapy, $n = 9$; multitrauma, $n = 7$; prior VTE, $n = 3$; presented outside the 7- to 90-day time period, $n = 35$; declined consent or did not attend the clinic, $n = 36$) leaving 72 patients for analysis. The characteristics and DVT risk-specific factors of the study cohort are shown in ►**Table 1**.

During the 6 months, there was significant loss to follow-up with 35 patients receiving a CDUS (CDUS-R) while the remaining patients were nonresponders ($n = 37$). These were patients who were recruited into the study, completed the questionnaire, referred for CDUS but did not attend and were lost to follow-up. In the CDUS-R group, 23% of patients (95% CI, 11.4–37.1; $n = 8$) were positive for DVT; seven distal DVT and one proximal DVT. Half of this group ($n = 4$) reported symptoms at the time of recruitment meaning the vast majority of the CDUS-R group were asymptomatic. Lack of symptoms was statistically significant for not developing a DVT ($p = 0.006$). The pertinent features of the eight patients with DVT are shown in ►**Table 2**.

Nonresponders were also mostly asymptomatic with only four patients reporting DVT symptoms—two had calf pain, one had calf swelling, and one had both pain and swelling. The characteristics of this group are outlined in ►**Table 3**.

Median follow-up time at the clinic postfracture was 23 days (range, 7–90 days) and the median time to CDUS from day of injury was 32 days (range, 7–90 days). Majority of patients (69%) and the CDUS-R group (71%) had their fracture immobilized with a controlled ankle movement walker (CAMboot). The characteristics and risk factors between CDUS-R patients with and without DVT are compared in ►**Table 4**. The mean age of patients with DVT was 53 ± 1.3 SD ($p = 0.011$) and age ≥ 45 was statistically significant ($p = 0.013$).

Discussion

The prevalence of DVT in patients recovering from an ankle or foot fracture with nonoperative management was 23% after undergoing CDUS. Suboptimal patient adherence to CDUS strongly suggests that our results must be interpreted with caution. However, as majority of the patients with CDUS-R without DVT were asymptomatic (96.3%), if we assume this was a consistent trend asymptomatic nonresponders (89.2%) would then likely have scanned negative for DVT. Applying this assumption to the whole sample, results in an extrapolated prevalence of 11% (8/72; 95% CI, 5.6–18.1). As a best conservative estimate, this still exceeds the highest reported

Table 2 Features of patients with deep vein thrombosis[a]

Patient	Age	Gender	BMI	Fracture	dDVT vs. pDVT	Time to CDUS	Other risk factors
1	34	Male	31	Combination[b]	Distal	63	Exsmoker, full cast, NWB, calf pain
2	45	Male	22	Calcaneus[c]	Distal	73	Smoker, CAMboot, NWB, calf pain
3	46	Male	23	Metatarsal	Distal	42	Smoker, full cast, PWB, nil symptoms
4	52	Female	25	Calcaneus	Distal	16	Smoker, CAMboot, WBAT, calf pain, HRT use
5	55	Male	23	Malleolus	Distal	23	Nonsmoker, CAMboot, NWB, nil symptoms
6	66	Female	14	Distal fibula	Proximal	21	Exsmoker, CAMboot, PWB, calf pain
7	80	Female	27	Distal fibula	Distal	37	Smoker, CAMboot, WBAT, nil symptoms
8	57	Female	19	Combination[d]	Distal	9	Nonsmoker, CAMboot, WBAT, nil symptoms, HRT use, family history of VTE

Abbreviations: BMI, body mass index; CAMboot, controlled ankle movement boot; CDUS, compression duplex ultrasonography; dDVT, distal deep vein thrombosis; HRT, hormone replacement therapy; NWB, nonweight bearing; pDVT, proximal deep vein thrombosis; PWB, partial weight bearing; VTE, venous thromboembolism; WBAT, weight bearing as tolerated.

[a] $n = 8$.

[b] Metatarsal, cuneiform and Lisfranc fractures.

[c] This patient had bilateral calcaneal fractures.

[d] Medial malleolus, distal tibial, and fibular fractures.

Table 3 Characteristics of nonresponders[a]

Variables	*N* (%)	95% CI
Age (y), median, range	33 (22–59)	
Gender		
Female	17 (45.9)	29.7–62.1
Male	20 (54.1)	37.9–70.3
BMI (kg/m^2), median, range	24 (19–32)	
Fracture		
Foot	21 (56.8)	40.5–73.0
Ankle	15 (40.5)	24.3–56.8
Ankle + foot	1 (2.7)	0.0–8.1
Ipsilateral	34 (91.1)	81.1–100.0
Bilateral	3 (8.1)	0.0–18.9
Immobilization		
Full cast	0	0
Backslab	9 (24.3)	10.8–37.8
CAMboot	25 (67.6)	51.4–81.1
Pressure bandage	1 (2.7)	0.0–8.1
None	2 (5.4)	0.0–13.5
Weight-bearing status		
NWB	20 (54.1)	37.8–70.3
PWB	5 (13.5)	2.7–24.3
WBAT	12 (32.4)	18.9–48.6
DVT symptoms		
None	33 (89.2)	78.4–97.3
Calf pain	2 (5.4)	0.0–13.5
Edema	1 (2.7)	0.0–8.1
Combination	1 (2.7)	0.0–8.1
Time to fracture clinic (d), median, range	17 (7–70)	
Smoking status		
Nonsmoker	17 (45.9)	29.7–62.2
Exsmoker	12 (32.4)	18.9–48.6
Current	8 (21.6)	8.1–35.1
History of current OCP use[b]	4/17 (23.5)	5.9–43.8
History of current HRT use[b]	1/17 (5.9)	0.0–20.0
Family history of VTE	1 (2.7)	0.0–8.1

Abbreviations: BMI, body mass index; CAMboot, controlled ankle movement boot; CI, confidence interval; DVT, deep vein thrombosis; HRT, hormone replacement therapy; NWB, nonweight bearing; OCP, oral contraceptive pill; PWB, partial weight bearing; VTE, venous thromboembolism; WBAT, weight bearing as tolerated.
[a]$n = 37$.
[b]This data are for female patients ($n = 17$).
Note: No patients had history of active cancer or clotting/bleeding disorders.

prevalence of 5% in comparable studies. Therefore, despite the low numbers in our study, the prevalence of DVT in this subgroup of orthopedic patients may be under recognized.

There are few published studies that specifically identify the prevalence of DVT in patients with ankle and foot fractures exclusively.[21] Patil et al identified DVT in 5% of patients with ankle fractures treated with below-knee plaster.[11] Manafi Rasi et al found a proportion of DVT at 3.1% in 95 patients with ankle sprains and stable foot and ankle fractures.[13] A similarly low occurrence of 3.5% was found by Solis and Saxby in a prospective study of 201 patients postsurgical repair of ankle and foot injuries.[22] In comparison, Lapidus et al observed DVT in 28% of patients 5 weeks after ankle fracture surgery without postoperative thromboprophylaxis.[23] In a prospective study of 2,761 patients with nonsurgical isolated lower limb injuries, DVT occurred at 6.4%.[15] Our study observed a prevalence of 11% in 72 patients with only ankle or foot fractures.

We found that age ≥ 45 years was the only statistically significant risk factor for DVT. In two other prospective studies, the mean age of patients with DVT after ankle or foot fracture was approximately 50 years.[11,13] Patients older than 50 years has been shown to be an independent significant risk factor for DVT in nonsurgical lower limb injuries[15] and after ankle or foot surgery.[22] Increasing age is a risk factor for DVT[4,8,9,18] which doubles with each decade beyond 40 years regardless of other risk factors.[24]

Nearly all our patients who had normal CDUS were asymptomatic (96.3%, 26/27) which reflects existing literature.[11,13,15,22,23,25] Ciuti et al observed a prevalence of 20.7% for asymptomatic DVT[26] while an observational study of 1,071 patients reported 1.8%.[27] In the blind prospective CALTHRO study, 85% of outpatients with symptoms of DVT and abnormal D-dimer levels did not have DVT on whole leg color Doppler ultrasound.[25]

Most of our patients had distal DVT and recent evidence has suggested that the risk factor profile for distal DVT is different for proximal DVT.[25] Distal DVT is associated with transient risk factors such as recent trauma, immobilization, long haul travel, and preexisting leg varicosities rather than advanced age, pregnancy, prior VTE, or active cancer.[25,26] Our patients presented 7 to 90 days postfracture with ankle or foot immobilization and distal DVT is known to develop and propagate within this time.[1,28–30] The CALTHRO study suggested only 3% of isolated distal DVT extend proximally and over 90% resolve by 3 months.[14,25] It is possible in our study that the patients who had later scans may have already underwent recanalization leading to an underestimated prevalence rate.

Aside from age, all other risk factors we assessed did not show statistical significance although numerous studies have shown otherwise. Riou et al demonstrated that rigid immobilization ($p < 0.0001$) was an independent significant risk factor for DVT along with age older than 50 years ($p < 0.0001$), severe injury (defined as fracture, dislocation, or tendon rupture; $p < 0.0002$), and nonweight bearing ($p < 0.0015$).[15] A combination of three or more risk factors ($p = 0.01$) significantly increases the incidence of DVT[13] as

Table 4 CDUS-R group[a]

Variables	No DVT ($n = 27$)	DVT detected ($n = 8$)	p Value
Age (y)[a]	39 ± 1.4 (34.8–43.7)	53 ± 1.3 (44.3–63.7)	**0.011**
Gender			0.433
Female	18 (66.7)	4 (50.0)	
Male	9 (33.3)	4 (50.0)	
BMI (kg/m^2)[a]	25 ± 7.3 (23.7–27.4)	23 ± 9.9 (19.2–26.1)	0.159
Fracture			0.820
Foot	15 (55.6)	4 (50.0)	
Ankle	10 (37.0)	4 (50.0)	
Ankle + foot	2 (7.4)	0	
Ipsilateral	25 (92.6)	7 (87.5)	0.553
Bilateral	2 (7.4)	1 (12.5)	
Immobilization			0.898
Full cast	3 (11.1)	2 (25.0)	
Backslab	2 (7.4)	0	
CAMboot	19 (70.4)	6 (75.0)	
Pressure bandage	2 (7.4)	0	
None	1 (3.7)	0	
Weight-bearing status			1.000
NWB	11 (40.7)	3 (37.5)	
PWB	6 (22.2)	2 (25.0)	
WBAT	10 (37.0)	3 (37.5)	
DVT symptoms			0.006
None	26 (96.3)	4 (50.0)	
Calf pain	1 (3.7)	4 (50.0)	
Time to fracture clinic (d)[b]	28 ± 2.1 (21.3–36.5)	29 ± 2.0 (17.5–47.1)	0.871
Time to CDUS (d)[b]	28 ± 2.1 (20.8–36.7)	29 ± 2.0 (17.4–45.7)	0.905
Smoking status			0.597
Nonsmoker	9 (33.3)	2 (25.0)	
Exsmoker	11 (40.7)	2 (25.0)	
Current	7 (25.9)	4 (50.0)	
History of current OCP use [b]	1/18 (5.6)	4/4 (100.0)	1.000
History of current HRT use [b]	3/18 (16.7)	2/5 (50.0)	0.210
Family history of VTE	0	1 (12.5)	0.229

Abbreviations: BMI, body mass index; CAMboot, controlled ankle movement boot; CDUS-R, compression duplex ultrasonography received; CDUS, compression duplex ultrasonography; DVT, deep vein thrombosis; HRT, hormone replacement therapy; NWB, nonweight bearing; OCP, oral contraceptive pill; PWB, partial weight bearing; VTE, venous thromboembolism; WBAT, weight bearing as tolerated.
[a]$n = 35$.
[b]Conversion from Log_{10} transformed data.
[c]Comparison between female patients with no DVT ($n = 18$) and with DVT ($n = 4$).
Note: Data expressed as means ± SD (95% CI) or number (percentage). No patients had active cancer of history of clotting/bleeding disorders. Bold value highlights the only significant risk factor found in this study.

the incidence increases proportionally with the number of risk factors.[18,24,27]

Most studies conclude thromboprophylaxis and ultrasound screening is not routinely indicated in patients with ankle and foot fractures. We observed a prevalence of 11% (8/72) with a modest data set and large loss to follow-up so our results must interpreted with caution. However, it casts light back onto the question that risk assessment and stratification for DVT should be considered for patients postfracture in the ankle or foot.[9,10,25,27,31] This may identify higher risk individuals and facilitate early DVT prophylaxis or monitoring.

This pilot study has unveiled limitations and logistical issues to be addressed in the future. Notably, the limitations include the small number of patients and the low adherence to attending ultrasound assessment. Logistically, it was not possible to perform ultrasonography for patients at enrolment. The lack of lower limb symptoms, impaired subject mobility, and understaffed ultrasound clinic may have contributed to low compliance with CDUS. As the study was conducted at only one site and with low subject numbers, generalization of the results is not reliable. A larger prospective study in the future is feasible utilizing multiple study sites to further explore our results with minimal loss to follow-up.

Conclusion

As far as we know, this pilot study is the first study in Australia to investigate the prevalence of this disease in this specific subgroup of patients. We found a prevalence of 11% of DVT, with age $\geq$ 45 years being a significant risk factor for DVT. Future larger scale prospective studies of higher power are warranted to confirm this prevalence of DVT and this may result in reevaluation of current VTE prophylaxis guidelines in this patient group.

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