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Research Article

Incidence of deep vein thrombosis in lower limb fractured patients

[1]Dan V. Pop, [2]Mara T. Dis, [3]Dragos Apostu, [3]Daniel Oltean-Dan, [3]Zsolt Gabri, [4]Ondine Lucaciu, [4]Alexandru Mester, [5]Andra Piciu, [3]Horea R. C. Benea

[1] Department of Anatomy and Embriology, "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania; [2] "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania; [3] Department of Orthopedics and Traumatology, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania; [4] Department of Oral Health, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania; [5] Department of Medical Oncology, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania.

Abstract. Objective: Deep vein thrombosis (DVT) is a common complication found in lower limb fractures, leading to an increased morbidity and mortality. Although multiple methods of thromboprophylaxis are currently used in practice, DVT is still present and its incidence is unknown. The aim of this study was to determine the incidence of deep vein thrombosis in our institution in the case of surgically treated patients and identify the patient specific or injury specific risk factors. Material and method: We have retrospectively reviewed inpatients who underwent surgical treatment in 2017 for lower limb fractures and Doppler ultrasound examination. Results: From the total of 1265 patients in our institution, we found 175 ultrasound examined patients and the incidence of DVT was 4.11% (n=52). We found statistically significant difference between DVT patients and no DVT patients in terms of hospitalization days until surgery ($p<0.001$) and history of stroke ($p=0.026$). Distal femur fractures (OR 1.68), history of stroke (OR 40.38) and gamma nail surgery (OR 3.92) have higher rates of DVT. Conclusion: Deep vein thrombosis remains a frequent complication of lower limb fractures. Distal femur fractures, gamma nail surgery and a history of stroke are related to higher rates of DVT.

Key Words: biomaterials, fracture, thrombosis, incidence, thromboprophylaxis

Corresponding Author: D. Oltean-Dan; e-mail: olteandandaniel@yahoo.com.

Introduction

Lower limb fractures are a frequent presentation in the emergency departments worldwide and can be treated either conservatively or surgically. Although lower limb fractures have a good prognosis overall, bone healing is a complex process and complications such as delayed union and nonunion can occur. These late complications can be treated using bone grafts or biomaterials (Cristescu et al 2015, Ionescu et al 2014). Biomaterials, due to their osteoconductive, osteoinductive and osteogenic properties, can reduce the fracture healing time and the risk of deep vein thrombosis due to a faster weight bearing (Winkler et al 2018). Deep vein thrombosis (DVT) is a complication found in lower limb fractures and can lead to pulmonary embolism (PE), thus increasing the morbidity and mortality of these patients (Auer & Riehl 2017). DVT occurs in both surgically and conservatively treated fractures, but the incidence remains relatively unknown, data ranging in the literature from 0.53% to 20% (Auer & Riehl 2017, Patil et al 2007). Deep vein thrombosis pathogenesis is related to the Virchow triad consisting in blood flow stasis, damage of vessels wall and hypercoagulability (Kumar et al 2010). Therefore, the risk of deep vein thrombosis depends on the type of injury (leading to vascular damage), patient comorbidities (leading to hypercoagulability) and type of treatment (immobilization leading to blood stasis) (Kumar et al 2010).

DVT is diagnosed using Doppler ultrasound (US) and can be prevented by an early patient mobilization, mechanical methods (e.g. Intermittent pneumatic compression devices, venous foot pump or graduated compression stockings), pharmacological prophylaxis (non-fractioned heparin, low-molecular-weight heparin, aspirin, fondaparinux, apixaban, dabigatran) or more rarely, inferior vena cava filter placement (Yang et al 2019, Kumar et al 2010). Recently, inferior vena cava filter has the ability to be biodegradable, due to new biomaterials (Kearon et al 2012, Lapidus et al 2013).

The indication of thromboprophylaxis in lower limb fractures is debatable. The American College of Chest Physicians Evidence-Based Clinical Practice Guidelines have been issued to recommend the type of thromboprophylaxis according to the fracture type (Yang et al 2019). In fractures of the hip treated surgically, pharmacological treatment is recommended, while in isolated lower leg injuries distal to the knee pharmacological treatment is not recommended (Yang et al 2019).

The aim of this study is to determine the incidence of deep vein thrombosis in the case of surgically treated orthopaedic patients and identify any patient specific or injury specific risk factors.

Materials and Methods

We performed a retrospective study at the Orthopedics and Traumatology Clinic in Cluj-Napoca, reviewing the data between 01.01.2017 and 31.12.2017. Our inclusion criteria were inpatients who underwent surgical treatment for lower limb fractures and the presence of a Doppler ultrasound examination. Exclusion criteria were represented by chronic treatment with oral anticoagulants and revision surgeries. All of the patients had signed an informed consent regarding the permission to use their medical data for reasearch purposes.

Doppler ultrasound examination was performed in patients with risk factors such as: diabetes, obesity, smokers, alcohol use, myocardial infarction, congestive heart failure, renal failure, cerebrovascular accident or cancer (Whiting et al 2016). The Doppler ultrasound examinations were performed by the same examiner in all cases. The patients were placed in supine position and the iliac veins, as well as the superficial and deep femoral veins were scanned bilaterally. A deep vein thrombosis was diagnosed if a complete compression of the vein was not possible and the thrombus was visible in B-mode. The examinations were performed using MyLab® Gold 25 mobile ultrasound system.

All patients underwent subcutaneous thromboprophylaxis with low molecular weight heparin (enoxaparine or nadroparine) at a dose of 0.4 ml if the patient had weight of less than 60 kg and 0.6 if the patient weighted 60 kg or more. The pharmacologic prophylaxis was initiated at 12 hours following the traumatic injury and was interrupted 12 hours prior to the surgery.

The collected data included age, gender, comorbidities, type of fracture, type of surgery, timing of surgery and Doppler ultrasound examination result.

Data regarding the total number of lower limb fractures that underwent surgical treatment in our institution between 01.01.2017 and 01.01.2018 was collected, in order to calculate the incidence of DVT in our hospitalized patients.

The statistical analysis was performed using GraphPad Prism 6.0. We have calculated means, standard deviations, Pearson correlation coefficient, odds ratio (Baptista-Pike method), realative risk (Koopman asyptomatic score) and Student test for unequal variances. The distribution was calculated using Shapiro-Wilk test. The results were considered statistically significant if p-value was less than 0.05.

Results

According to our inclusion and exclusion criteria, we found 175 lower limb fractured patients who had a Doppler ultrasound exam performed. The average age was 74.4 [±14,31] years. The distribution of fracture sites can be found in Table 1.

The average time from presentation to surgery in these patients was 5 [±3,7] days. The distribution of the surgery types and comorbidities are found in Table 2. Deep vein thrombosis was present in 52 cases (29.7% of Doppler-ultrasound examined patients), localized as follows: common femoral vein (35 cases), deep femoral vein (6 cases), superficial femoral vein (10 cases), iliac vein (2 cases), popliteal vein (5 cases), and posterior tibial vein (1 case). Seven cases had two sites of deep vein thrombosis. None of the patients had clinical manifestations of pulmonary embolism during hospitalization.

In the case of confirmed DVT, the surgical intervention was delayed until DVT resolution. Therefore, the average time of surgical intervention was 8.48 (±4.1) days in the confirmed DVT cases and 3.75 (±2.5) days in the non-DVT patients ($p<0.01$). No statistically significant difference was found between DVT patients and no DVT patients in terms of age ($p=0.4$). The risk factors are analyzed in Table 1 and Table 2.

Discussions

Deep vein thrombosis and pulmonary embolism are known complications after trauma, especially after lower limb fractures and some elective orthopedic procedures, with a significant rate of morbidity and mortality (Oltean-Dan et al 2018, Tomoaia et al 2006,14, Klok et al 2012, Geerts et al 2004). The real incidence of DVT in patients with isolated injury of the lower limb is not known and routine thromboprophylaxis for these patients in some European countries, including Romania, is considered to be standard treatment (Jorgensen et al 2002). However, previous studies showed that the incidence of DVT in various injuries of the lower limb treated in a plaster cast range between 1.1-20% (Geerts et al 2004, Jorgensen et al 2002).

The mean age of the patients was 74.4 years ranging between 21 to 96 years old. While in elderly patients the mechanism is usually low energy trauma, in young patients, the lower limb fractures result from high energy trauma and associate multiple lesions. Stannard et al in a prospective study on 312 patients with sustained high energy trauma, identified an 11.5% DVT rate despite thromboprophylaxis treatment (Geerts et al 2004). These results are comparable to ours that identified a 13.8% DVT rate in all fractures of the lower limb.

In our institution are admitted all trauma cases that occur on a very large geographical area, with 1265 cases of lower limb skeletal trauma in one year (61% cases of above the knee fractures and 39% cases below the knee fractures). There are currently controversies about distal femoral fractures that are categorized as fractures under the knee, so the recommendations for thromboprophylaxis are not very clear (Klok et al 2012). In a study on 253 patients with injuries of the lower limb immobilized in a plaster cast divided in two groups (group I received Fraxiparin injection daily and group II without thromboprophylaxis) showed a higher rate of DVT in no prophylaxis group (21 cases vs 6 cases, $p<0.01$). Regarding this results the recommendations was that all the patients with lower limb injury immobilized in a plaster cast, should be treated with a low-molecular-weight heparin to prevent thromboembolism events (Geerts et al 2004). On the other hand, in a prospective study on 93 patients with below the knee immobilization showed that DVT is not a common complication and thromboprophylaxis is not routinely necessary when the patients had less the three predisposing factors (Jorgensen et al 2002). In a systematic review from 2017 regarding the thromboprophylaxis with low molecular weight heparin for prevention of DVT in patients with lower-limb immobilization, including 3680 patients conclude that moderate-quality evidences showed that the use of prophylactic anticoagulants reduced DVT, while low-quality

Table 1. Cases of DVT according to fracture localization

	Hospitalized lower limb fracture patients which performed Doppler ultrasound			Total number of hospitalized lower limb fractures	
Fracture site	**Number of cases**	**Number of confirmed DVT cases**	**Percent of DVT**	**Number of cases**	**Percent of DVT**
Acetabulum	1	0	-	12	-
Proximal femur	139	45	32%	693	6.94%
Femoral diaphysis	10	3	30%	66	4.54%
Distal femur	3	1	33%	19	5.26%
Calf	18	3	17%	219	1.37%
Ankle	4	0	-	256	-

Table 2. Risk factors for DVT

Risk factors	Number of patients with DVT	Number of patients without DVT	p	Odds ratio (95% CI)	Relative risk (95% CI)
Patient characteristics					
Age	75.71 (±12.15) (Mean ± SD)	74.01 (±15.08) (Mean ± SD)	0.426	-	
		Fracture site			
Acetabulum	0	1		-	
Proximal femur	45	94		1.61 (1.00 to 2.58)	1.41 (1.00 to 1.98)
Femoral diaphysis	3	7		1.44 (0.36 to 5.77)	1.31 (0.49 to 3.47)
Distal femur	1	2		1.68 (0.14 to 18.94)	1.45 (0.28 to 7.34)
Calf	3	15		0.67 (0.18 to 2.41)	0.72 (0.25 to 2.10)
Ankle	0	4		-	
		Comorbidities			
History of stroke	12	1	0.026	40.38 (5.12 to 318.1)	4.03 (3.02 to 5.36
High blood pressure	64	23	0.698	9.36 (5.30 to 16.53)	3.21 (2.45 to 4.20)
Heart disease	54	18	0.496	10.1 (5.44 to 18.71)	3.27 (2.49 to 4.30)
Diabetes mellitus	20	5	0.314	13.46 (4.81 to 37.63)	3.49 (2.56 to 4.75)
Hypercholesterolemia	4	1	0.667	13.46 (1.47 to 123.2)	3.49 (2.12 to 5.75)
Chronic venous insufficiency	12	3	0.446	13.46 (3.65 to 49.53)	3.49 (2.46 to 4.94)
IMC > 35	2	1	-	6.73 (0.59 to 75.76)	2.91 (1.26 to 6.70)
Mental disorders	10	3	0.68	11.22 (2.97 to 42.29)	3.35 (2.29 to 4.91)
		Surgical intervention			
Total hip replacement	3	29		0.348 (0.10 to 1.18)	0.4 (0.13 to 1.23)
Partial hip replacement	1	19		0.177 (0.02 to 1.35)	0.21 (0.03 to 1.49)
Dynamic Hip Screw	6	23		0.877 (0.33 to 2.27)	0.9 (0.42 to 1.91)
Gamma nail	35	30		3.92 (2.20 to 6.99)	2.35 (1.69 to 3.26)
External fixator	0	3		-	
Plate and screws	5	22		0.76 (0.27 to 2.12)	0.8 (0.35 to 1.84)
Intramedullary nail	2	9		0.74 (0.15 to 3.57)	0.79 (0.22 to 2.84)

evidences showed less symptomatic venous thrombosis in anticoagulant group, but no clear differences in pulmonary embolism between the groups (Zee et al 2017). In our study the fractures of the femur and even of the distal femur are most prone to the occurrence of DVT (RR = 1.31-1.45) and as the fracture is more distal the relative risk decreases.

Furthermore, tibial plateau fractures have a tendency to increase the risk of DVT, and this risk decreases as the fracture is more distally (Goel et al 2009, Lapidus et al 2013]. According to the internal protocol of the clinic, thromboprophylaxis is administered to all patients with lower limb fractures at 12 hours after injury, adjusted according to the weight of the patient. However,

independent of prophylactic anticoagulant administration, there were 0.63% cases of DVT in patients with fractures below the knee. These findings are comparable with those in the literature that showed an incidence of DVT of 0.53% in below the knee fractures (Auer & Riehl 2017). Moreover, pharmacological prophylaxis has its risks such as bleeding, wound healing problems, thrombocytopenia and anemia. We didn't encounter any bleeding complications due to routinely use of prophylactic anticoagulants and there wasn't any case of thrombocytopenia. Regarding the treatment methods, there is a higher risk of developing DVT in patients with proximal femur fractures treated by internal fixation methods with a relative risk of 0.9 for DHS and 2.35 for Gamma Nail, compared with total or partial hip arthroplasty in which RR < 0.4. Moreover, in the cases of unstable trochanteric fractures treated with Gamma Nail, the patients are older, most often secondary to degenerative bone demineralization and associating multiple comorbidities, as well as a lower adherence of the patients to the rehabilitation treatment. Concerning the Doppler ultrasound examination, it is not routinely performed prior to surgery. We recommended it when we had suspected clinically a DVT or for patients with multiple comorbidities or risk factors. In the present study, there was no statistically significant difference between age, high blood pressure, heart disease, diabetes mellitus, hypercholesterolemia, chronic venous insufficiency and mental disordes and the presence of DVT. Contrary to our study, Anderson & Spencer (2003) showed that increasing age is a weak risk factor for deep vein thrombosis. Instead, association with risk factors such as older age, male gender, high BMI (body mass index) or ISS (injury society score) increase, pneumonia, prolonged immobilization, long duration of surgery and compartment syndrome may benefit from the pharmacological prophylaxis of DVT and clinical and imagistic follow-up. Also, DVT rate is increase by smoking and obesity, but it is uncertain if providing thromboprophylaxis to this subgroup of patients will prevent clinically-significant thromboembolism, and it would be cost-effective (Kapoor et al 2016). All the comorbidities evaluated in the current study showed a relative risk of 3 or greater of developing deep vein thrombosis with statistical significance only in patients with history of stroke. It is important to analyze these factors and initiate antithrombotic prophylaxis in their presence.

Total number of DVT cases is 175 (13.8%) out of 1265 patients admitted in our clinic, without a single case of PE. The results are significantly higher compared to the studies of Kapoor et al (2016) (4.8% DVT and 1 case of PE), Bagaria et al (2006) (6.12% DVT and 1 case of PE) and Mavalankar et al (2007) (7.2% DVT rate), but in all these studies the number of patients included were significantly lower. The DVT rate in patients with proximal femoral fractures is 5 times higher than in those with below the knee fractures, while for the femoral diaphysis and distal femoral fractures DVT is approximately 3 to 4 times more frequent.

In terms of ankle fractures, despite the large number of admissions (n=256), only 4 Doppler US examinations were performed, that excluded the diagnosis (0% DVT rate in ankle fractures). The rate of DVT in surgically treated ankle fractures is 0.28% in the literature (Jameson et al 2011). Although the use of thromboprophylaxis has increased in English surgeons after publication of 2007 NICE guidelines (Jameson et al 2011), these benefits had not been fully demonstrated and routine venous thromboembolism prophylaxis is not recommended. A case report from 2006 of death from pulmonary embolism in a 17-year-old girl following ankle fracture may prompt orthopedic surgeons to routinely administer thromboprophylaxis to all the patients (Chen & Soares 2006). However, in other study, the overall incidence of DVT after ankle fracture immobilized in plaster casts was 5% and the authors didn't recommend routine thromboprophylaxis in these cases (Patil et al 2007). Also, the guidelines issued by American College of Chest Physicians advised against routine thromboprophylaxis for patients with isolated lower limb injuries (Geerts et al 2004).

The limitations of the study include the relatively small number of patients that could not provide a statistically significant difference between comorbidities and DVT. Also, the use of routine thromboprophylaxis could not demonstrate any favorable results compared to the literature.

Conclusions

Deep vein thrombosis remains a frequent complication of lower limb fractures with increased risk of morbidity and mortality especially through pulmonary embolism. Routine administration of anticoagulants decreases the risk of deep venous thrombosis, but nevertheless there is a rate of patients who develop DVT independently. Distal femur fractures, gamma nail surgery and a history of stroke are related to higher rates of DVT.

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Authors

•Dan Vasile Pop, Department of Anatomy and Embryology, "Victor Babes" University of Medicine and Pharmacy, 2 Eftimie Murgu Street, 300041 Timisoara, Romania, email: popdan_68@yahoo.com

•Mara Teodora Dis, "Iuliu Hatieganu" University of Medicine and Pharmacy, 8 Victor Babes Street, 400012 Cluj-Napoca, Romania, e-mail: marateodora1995@yahoo.com

•Dragos Apostu, Department of Orthopaedics and Traumatology, "Iuliu Hatieganu" University of Medicine and Pharmacy, 47-49 Traian Mosoiu Street, 400132 Cluj-Napoca, Romania, e-mail: apostudragos@yahoo.com

•Daniel Oltean-Dan, Department of Orthopaedics and Traumatology, "Iuliu Hatieganu" University of Medicine and Pharmacy, 47-49 Traian Mosoiu Street, 400132 Cluj-Napoca, Romania, e-mail: olteandandaniel@yahoo.com

•Zsolt Gabri, Clinic of Orthopaedics and Traumatology, 7-49 Traian Mosoiu Street, 400132 Cluj-Napoca, Romania, e-mail: zsoltigabri@gmail.com

•Ondine Lucaciu, Department of Oral Health, "Iuliu Hatieganu" University of Medicine and Pharmacy, 8 Victor Babes Street, 400012 Cluj-Napoca, Romania, e-mail: ondineluc@yahoo.com

•Alexandru Mester, Department of Oral Health, "Iuliu Hatieganu" University of Medicine and Pharmacy, 8 Victor Babes Street, 400012 Cluj-Napoca, Romania, e-mail: alexandrumester@yahoo.com

•Andra Piciu, Department of Medical Oncology, "Iuliu Hatieganu" University of Medicine and Pharmacy, 34-36 Republicii Street, 400015 Cluj-Napoca, Romania, e-mail: piciuandra@gmail.com

•Horea Rares Ciprian Benea, Department of Orthopaedics and Traumatology, "Iuliu Hatieganu" University of Medicine and Pharmacy, 47-49 Traian Mosoiu Street, 400132 Cluj-Napoca, Romania, e-mail: apostudragos@yahoo.com

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