

The Risk of Venous Thromboembolism in Algerian Patients

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Abstract

Venous thromboembolism (VTE) including deep venous thrombosis and pulmonary embolism is a common disease associated with substantial morbidity and mortality. VTE is becoming increasingly common in Algeria but published data on its frequency and risk factors are lacking.

The purpose of our study was to determine the frequency, risk factors of this disease in Sidibel abbes region, Northwest Algeria.

A retrospective study of patients hospitalized for DVT and/or PE was carried out between January 1, 2006 and June 10, 2012 at the cardiology department of Sidibel abbes University Hospital Center.

183 VTE patients (71 men [38.7%, age 51.5 ± 17.7years] and 112 women [61.2%, age 46.4 ± 17.9 years]) were included. Deep venous thrombosis (DVT) occurred in 146 (79.7%), pulmonary embolism (PE) in 37 (20.2%) including 16 with concurrent DVT.

The most common risk factors among DVT patients were: immobility, hypertension, surgery and oral contraception whereas, immobility, surgery, hypertension and fractures were the most frequent risk factors among PE patients.

12.02% of patients had a previous VTE. 24.7% of patients had several risk factors. Lower extremity DVT accounted for 97.5% of cases and upper extremity DVT for only 2.5%.

In conclusion, although its frequency is not a cause for alarm, it will be important to adopt a suitable prophylactic strategy to combat the growing prevalence of VTE in the region of SidiBel Abbes.

Keywords: Venous thromboembolism; Frequency; Risk factors; Sidibel abbes

Introduction

Venous thromboembolism (VTE) is a disease that comprises two clinical entities: deep vein thrombosis and pulmonary embolism. This common disease with an annual incidence of 1-2 per 1000 in the general population can be fatal or result in serious functional disability [1,2]. The impact of VTE on morbidity and mortality together with the health care costs it engenders make this disease a major public health problem.

While rare in childhood - with a negligible yearly incidence of less than 5 per 100,000—the incidence of VTE rises sharply with age, reaching 450-600 per 100,000 per year, and is primarily a disease of the elderly [3].

The risk of thrombosis is probably potentiated by a synergistic combination of factors in the renowned triad described by Virchow in 1884: venous stasis, endothelial injury and hypercoagulability. The pathogenesis of VTE results from a complex interplay of genetic and environmental factors, both transient and acquired [4].

An ever more detailed set of decision rules for assessing thrombotic risk is the key to optimizing prophylactic intervention aimed at significantly lowering morbidity and mortality of venous thromboembolic disease.

In Algeria, the prevalence of this disease is on the rise but there are no published data on its frequency or on the thrombogenic potential of associated risk factors.

This retrospective study helps to shed some light on the true situation of venous thromboembolism in the SidiBel Abbes region (Northwest Algeria).

Patients and Methods

This was a retrospective study of patients hospitalized for DVT and/or PE in the cardiology department of the SidiBel Abbes University Hospital Center between January 1st 2006 and June 10th 2012.

The diagnosis of VTE was confirmed by Doppler ultrasonography or computed tomographic pulmonary angiography.

Data on age, risk factors and site of this disease were retrieved from medical records. Results are expressed as: Mean ± SD or n (%). Statistical analyses and calculations were performed using Stat view (version 5.0 for Windows; SAS Institute).

Variables	All VTE patients (n=183)	Men (n=71)	Women (n=112)
Age (years)	48.4 ± 17.9	51.5 ± 17.7	46.4 ± 17.9
DVT	146 (79.7)	52 (73.2)	94 (83.9)
PE	37 (20.2)	19 (26.7)	18 (16)

DVT=Deep vein thrombosis; PE=Pulmonary embolism

Table 1: Characteristics of patients with venous thromboembolism (VTE), Mean ± SD or n (%).

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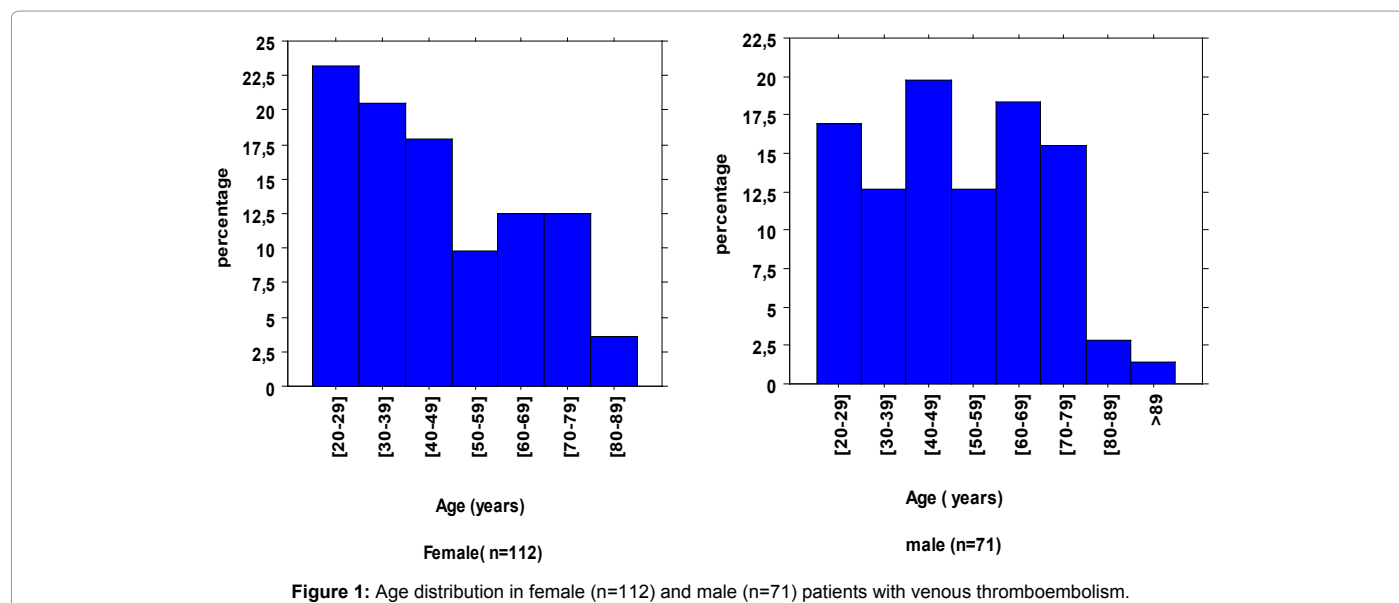


Figure 1: Age distribution in female (n=112) and male (n=71) patients with venous thromboembolism.

Results

During the study period, 183 patients were hospitalized with VTE, including 112 women (61.2%) with a mean age 46.4 ± 17.9 years and 71 men (38.7%) with a mean age of 51.5 ± 17.7 years (Table 1).

The proportion of women aged 20-39 years was higher than that aged 40-89, suggesting that women are more exposed to this type of pathology during their childbearing years, while in men, on the other hand, it is generally more common after age 40 (Figure 1).

There were 146 cases (79.7%) of isolated DVT and 37 cases (20.2%) of PE including 16 with concurrent DVT.

Among DVT patients, risk factors with a high thrombogenic potential were mainly immobility, hypertension, surgery and oral contraception. For PE patients, major risk factors were immobility, surgery, hypertension and fractures (Table 2). A previous VTE event was present in 12.02% of patients. 24.7% of patients had more than two risk factors, 43.5% had two and 31.6% had a single risk factor (Figure 2), whereas for 16 patients (8.7%: 14 DVT and 2 PE), no risk factors were identified.

Among 158 patients with lower limb DVT, the location was proximal in 97.5% and distal in 2.5%, and the majority affected the left leg (101 cases) versus 47 cases in the right leg and 10 with a bilateral location (Table 3).

In contrast, only 4 cases of upper limb DVT were observed, mainly on the left (Table 3), including a woman with breast cancer and one with malignant melanoma, and two men with no apparent underlying cause.

Analysis of administered treatment showed that (98%) of DVT patients received LMH, (96%) OAC, (2.7%) UFH whereas, Of PE patients, (97%) received LMH, (95%) OAC, (16.2%) UFH and (13.5%) thrombolysis. 34, 4% of patients received no prophylaxis.

Mortality rate is estimated at 3, 82% of patients including 5 patients with isolated PE and 2 patients with both PE and DVT.

Discussion

The incidence of venous thromboembolic events increases with

	DVT patients n=146	PE patients n=37
Age (years)	48 ± 18.1	50 ± 17.7
Smoking	11 (7.5)	3 (8.1)
Obesity	4 (2.7)	5 (13.5)
Immobility	39 (26.7)	14 (37.8)
Surgery	18 (12.3)	10 (27)
Fractures	11 (7.5)	8 (21.6)
Pregnancy	4 (2.7)	0 (0)
Postpartum	15 (10.2)	5 (13.5)
Post abortum	2 (1.3)	0 (0)
Oral contraceptives	16 (10.9)	2 (5.4)
Cancer	10 (6.8)	4 (10.8)
Diabetes	9 (6.1)	2 (5.4)
Hypertension	21 (14.3)	9 (24.3)
Behçet's disease	4 (2.7)	0 (0)
Nephrotic syndrome	9 (6.1)	0 (0)
Heart failure	8 (5.4)	0 (0)
Stroke	2 (1.3)	2 (5.4)
Myocardial infarction	1 (0.6)	3 (8.1)
Varicose veins	7 (4.7)	1 (2.7)
Pulmonary tuberculosis	6 (4.1)	0 (0)
Previous VTE	15 (10.2)	7 (18.9)
No obvious risk factor	14 (9.5)	2 (5.4)

DVT=Deep Vein Thrombosis; PE=Pulmonary Embolism

Table 2: Risk factors in 183 patients with deep venous thrombosis (DVT) or pulmonary embolism (PE), mean ± SD or n (%).

age, which is an independent thromboembolic risk factor. This risk is all the higher because age is also associated with a higher frequency of comorbidities such as surgery, immobility or cancer, which promote the development of venous thrombosis [5].

The incidence of first-time VTE rises exponentially with age, from a negligible rate (<5 per 100.000 per year) among children <15 years of age to values in the range of 450 to 600 per 100.000 per year ($\approx 0.5\%$ /year) among individuals over the age of 80 years [3]. According to Oger et al. [6], the incidence of VTE increases sharply with age, reaching 1% in individuals over 75, which is twice as high than in patients aged 60-74 [6].

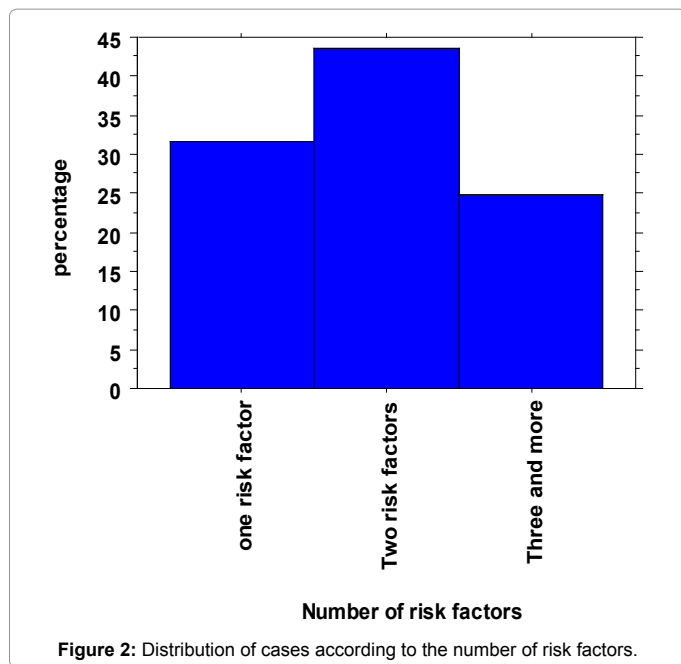


Figure 2: Distribution of cases according to the number of risk factors.

Lower extremity DVT (n=158)	Left DVT (n=101)	Right DVT (n=47)	Bilateral DVT (n=10)
Iliofemoral+IVC DVT	0 (0)	3 (6.3)	0 (0)
Iliofemoral DVT	17 (16.8)	5 (10.6)	2 (20)
Iliofemoro-popliteal DVT	34 (33.6)	10 (21.2)	3 (30)
Femoropopliteal DVT	37 (36.6)	18 (38.2)	5 (50)
Femoral DVT	2 (1.9)	8 (17)	0 (0)
Popliteal DVT	8 (7.9)	2 (4.2)	0 (0)
Tibial DVT	3 (2.9)	1 (2.1)	0 (0)
Upper extremity DVT (n =4)	Left DVT (n=3)	Right DVT (n=1)	Bilateral DVT (n=0)
Axillo-subclavian brachial DVT	3 (100)	0 (0)	0 (0)
Axillo-subclavian DVT	0 (0)	1 (100)	0 (0)

*Results are expressed as n (%), IVC: Inferior Vena Cava

Table 3: Distribution of cases according to the location of DVT.

Women of childbearing age are more frequently affected than men of the same age, a difference which is attributable to pregnancy and to the use of oral contraceptives. On the other hand, among the elderly, women are at considerably lower risk than men [7].

The physiological changes that occur in the elderly, together with concomitant risk factors, provide a favorable environment for the development of VTE. The significant reduction in the diameter and resting blood flow velocity of the femoral vein that occurs in people over the age of 60 is a predisposing factor for DVT resulting from stagnant blood flow in this vein [7]. Prolonged bed rest and immobility promote venous dilatation and blood stasis [7].

A reduction in venous return resulting from an age-related decrease in the venous pump function of the calf muscles was found in a plethysmographic study in subjects aged 23-40 years and 60-83 years. In addition, an increase in the levels of coagulation factors VIII, V, VII and IX and a variation in prothrombotic markers were found to be correlated with age [7]. In our study, some thrombogenic factors were more frequent than others: immobility, hypertension, surgery and oral contraception were the main risk factors found in DVT patients while

immobility, surgery, hypertension and fractures were found for PE.

Based on pathophysiological arguments, immobilization has been suspected of being a risk factor for venous thromboembolism (VTE). The supine position can lead to a muscular and diaphragm dysfunction which decreases the venous flow in the legs and causes “venous stasis” [8].

Venous stasis may in turn induce an hypercoagulability state, by activating the extrinsic pathway of coagulation via hypoxemia, and also by producing endothelial damage or by reducing the fibrinolytic activity [8].

Several studies have demonstrated that immobilization is a risk factor for VTE, as found in 17% of patients with DVT and 18% with PE in the study by Isma et al. and in 35% of patients with PE according to Ouldzein et al. [9,10].

Healy et al. [11] reported that prolonged work-related seated immobility was associated with a 2.8-fold increase in the risk of VTE [11]. Fletcher et al. [12] found an association between VTE and immobilization for 36.3% of the women in the study cohort [12].

A positive association between blood pressure and VTE was found only in the study by Tsai et al. which classified hypertension as >140/90 mm Hg. The other studies used higher cutoff values (>160/90 mm Hg) and found no effect [13].

Goldhaber et al. [14] identified hypertension as an independent predictor of PE in women [14].

Surgery increases the risk of VTE up to 20-fold, according to the type and duration of the procedure, the underlying pathology and the patient’s condition, which can exacerbate venous stasis, a major component of thrombus formation [15,16]

Without routine prophylaxis, DVT rates in general surgery range from 10-40% [17]. Abdominal, pelvic, orthopedic, neurosurgical, and oncologic surgeries place patients at the highest risk because of immobilization, secondary venous stenosis, and endothelial damage [18].

In addition to immobilization, stasis, and endothelial damage promoting DVT, surgery has been associated with activated coagulation and transient depression of fibrinolysis. An increase in thrombin activation as well as elevated levels of plasminogen activator inhibitor-1 (PAI-1) during the perioperative period have been described [18].

Women of childbearing age should always be asked if they are taking estrogen-progestin oral contraceptives, since combination birth control pills have long been associated with an increased risk of venous thromboembolism, which globally is multiplied by 4 [19,20]. The risk varies with different types of pills and with the dose. Thus, the risk is higher with increasing daily doses and with third generation versus second generation contraceptives [21-25].

The risk related to hormonal contraception is significantly modulated with age, especially beyond age 40, but also in the presence of other risk factors [20].

Hemostatic anomalies such as low levels of protein S and antithrombin and acquired activated protein C resistance have been observed in women taking oral contraceptives and provide a favorable biological environment for venous thrombosis [26-31].

Furthermore, the higher levels of SHBG (sex hormone binding

globulin) with third generation versus second generation progestogens are considered to be a marker of thrombotic risk [32-36].

Thromboembolic events are common after trauma, particularly in case of fractures, and the risk is increased by a factor of 13 after a recent trauma [37].

With respect to upper extremity DVT, the thrombotic risk is multiplied by four in the presence of malignant disease and is six times higher following chemotherapy. The MEGA study found that this risk is 18 times higher than in patients without cancer [37].

A Dutch study showed that in cancer patients without an indwelling catheter, the presence of distant metastases increased the risk of upper extremity DVT (OR=11; 95%CI: 2-80) as compared with non-metastatic tumors. The types of malignancies most commonly associated with upper extremity DVT in the absence of a catheter were lung cancer, breast cancer and lymphomas [38]. A state of hypercoagulability induced by direct activation of factors involved in clotting and fibrinolysis and cells that play a role in clotting promote a higher risk of thrombosis [39].

In a review of 1231 consecutive patients treated for VTE, 96% had at least one recognized risk factor. Furthermore, there is convincing evidence that the risk of VTE increases in proportion to the number of predisposing factors [40].

The risk of venous thromboembolism is considerably higher in patients who have had a previous VTE episode and the cumulative risk of recurrence after a previous episode is very high, which justifies considering VTE as a chronic disease. This risk is estimated at 5-10% per year [41-43]. Hansson found a 1-year recurrence rate of 7% and a 5-year cumulative incidence of 21.1% after a first DVT and 27.9% after a second DVT. The risk of recurrence was higher for proximal thromboses [44].

Conclusion

The findings from our study show that despite a frequency which is not cause for alarm, we must nonetheless adopt rigorous measures to deal with the growing prevalence of VTE in the region of SidiBel Abbes.

VTE is an insidious and terrible disease with high morbidity and mortality. This is why it is essential to institute strict prophylactic measures adapted to the level of thrombotic risk. This risk stratification takes into account not only the type of surgery or medical pathology, but also the risk factors specific to the patient.

In addition to physical methods and simple rules of venous hygiene, such as early mobilization, passive and active mobilization, elevation of the legs, degressive compression stockings and breathing exercises, which must be implemented at all risk levels to prevent blood stasis and accelerate venous return, antithrombotic treatments are prescribed in patients at moderate or high risk.

Furthermore, in the context of preventive medicine, lifestyle and dietary measures are a top priority to reinforce therapeutic intervention in the management of metabolic syndrome.

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