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Clinical characteristics and risk factors of lower limb deep vein thrombosis in elderly patients: An 18-year retrospective study at a single center

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ABSTRACT

Background: Deep vein thrombosis (DVT) of the lower limbs in the elderly is a major health problem, despite improved prophylaxis and diagnostic advances. It must be managed rapidly and effectively. The aim was to determine the main features and risk factors (RFs) of DVT in elderly patients admitted to internal medicine.

Methods: This was a retrospective, descriptive study carried out in the internal medicine department of Hedi Chaker Hospital in Sfax, over a period of 18 years. Records of patients hospitalized in the department during this period were reviewed.

Results: There were 102 cases, divided into 64 men (62.8%) and 38 women (37.2%), with an average age of 75.2 years. DVTs in the veins of the lower limbs were most often proximal (75%). In addition to advanced age, considered an independent RF for DVT, at least one RF for VTE was found in 54.6% of cases. Bed rest was the most frequent RF, noted in 44 cases (43.7%). A thrombogenic pathology predisposing to thrombosis was retained in 25 patients, i.e., 24.5% of cases. These were SAPL (11 cases), neoplasia (12 cases), Behçet's disease (1 case), and hyper-homocysteinemia (2 cases).

Conclusion: DVT in the elderly, a frequent pathology, poses above all a problem of etiological diagnosis. Identifying the RFs for recurrence in this population is important, as it enables appropriate prescription of anticoagulants. Such treatment is not without risk in elderly patients who are frequently polythematic, with a high excess risk of bleeding.

Keywords: deep vein thrombosis, geriatrics, neoplasia

INTRODUCTION

The incidence of venous thromboembolism (VTE) increases with age. Deep vein thrombosis (DVT) increased by a factor of 4.7 and pulmonary embolism (PE) by a factor of 6.2 over the age of 65 [1].

DVT of the lower limbs is the most frequent manifestation. In addition to its frequency, it has a major impact on morbidity, mortality and healthcare costs.

Better risk stratification of the disease and its recurrences, and of the risk factors (RFs) for venous thrombosis in this terrain, is needed in order to adapt preventive and curative treatment in the event of constituted VTE [2].

The outcome can be potentially serious, with complications that can be life-threatening (death from PE) or functional (post-thrombotic syndrome [PTS] and thrombotic recurrence).

Given the frequency of this pathology in geriatric medicine, we wanted to determine the characteristics and RFs of DVT in the elderly.

PATIENTS AND METHODS

Patients

This is a retrospective study of patients over 65 years of age with imaging-confirmed DVT of the lower limbs. We reviewed all the records of patients hospitalized in the internal medicine department of the Hedi Chaker Hospital in Sfax for DVT over an 18-year period (January 2004-December 2022).

Methods

For each case selected, we collected and analyzed epidemiological data: age, sex, personal and family history, DVT site as determined by ultrasound data, and known RFs for DVT (advanced age, obesity [body mass index (BMI) > 30], bed rest, recent surgery, varicose veins in the lower limbs, and recent travel). The etiological investigation was based on patient history, physical examination, and complementary tests ordered according to the clinical context.

Thrombophilia screening was not systematic; it was performed in selected cases based on clinical suspicion–

Table 1. Topography and site of deep vein thrombosis in our series

DVT site	Number of cases	Frequency (%)
Inferior vena cava	2	1.9
The external iliac vein	42	41.0
The popliteal vein	69	68.0
The common femoral vein	56	54.0
The deep femoral vein	31	30.0
The superficial femoral vein	51	50.0
The anterior tibial vein	2	1.9
Posterior tibial vein	4	3.9

specifically in patients with unprovoked or recurrent thrombosis, a family history of thromboembolic disease, early-onset events, or atypical thrombosis locations. All patients underwent routine tests including complete blood count, renal function tests, and chest X-ray. Additional investigations (anticardiolipin [aCL] antibodies, lupus anticoagulant, tumor markers, and abdominopelvic ultrasound) were requested based on clinical judgment.

The diagnosis of antiphospholipid syndrome (APS) was established according to the 2023 ACR/EULAR [3].

Ethical considerations

This study was approved by the Ethics Committee of Hedi Chaker University Hospital. Given its retrospective nature, the requirement for written informed consent was waived.

Statistical analysis

We carried out a descriptive and analytical statistical study. Data entry and statistical analysis were performed using SPSS version 20 software.

RESULTS

In a series of 585 patients with DVT, 102 were over 65 years of age, a prevalence of 17.4%. There were 64 men (62.8%) and 38 women (37.2%), with a sex ratio (M/F) of 1.28. The mean age at diagnosis for all patients was 75.2 years(65-88 years), with a range of 5.9 years. There were no significant gender differences.

The location of DVTs in the veins of the lower limbs was distal in 16 cases (15%) and proximal in 77 cases (75%). Thrombotic location was unspecified in 5 cases. DVT was associated with thrombosis of the inferior vena cava in 2 cases.

Thrombosis was bilateral in 3 cases and unilateral in the rest. The different types and sites of DVT are summarized in **Table 1**.

Sixty-three patients had a history of chronic disease. Progressive neoplasia was found in 8 patients (7.8%). The mean diagnostic delay between DVT and neoplasia was 90 days (range 15 days to 1 year). These were multiple myeloma (1 case), digestive cancer (4 cases), prostate cancer (1 case), and bladder cancer (1 case).

Other pathologies found were arterial hypertension (37 cases), diabetes (25 cases), dyslipidemia (13 cases), obstructive lung disease (2 cases), and Behçet's disease in one patient.

A history of DVT was found in 11 patients (10.8%). These included a single episode of DVT in 9 cases (8.8%), two episodes of DVT in 2 cases (1%) and three episodes of DVT in one patient.

One patient had a family history of DVT. This was a first-degree family history of DVT (two sons had presented with DVT). Thrombophilia investigation was negative.

An RF for DVT was found in 56 patients (54.6%). A single RF was found in 38 patients (37%), two in 15 patients (14.7%), and three in 3 patients (2.9%).

Bed rest was the most frequent RF, noted in 44 cases (43.7%). Eleven patients were fat (BMI greater than 30 kg/m^2). Obesity was more frequent in women (8 women vs. 3 men), with a statistically significant correlation (p = 0.02).

Recent surgery in the 2 months preceding the DVT episode was noted in 6 patients (5%). The mean duration of postoperative venous thrombosis was 20 days (extremes: 3-50 days). The nature of the surgical intervention was abdominal surgery (4 cases), ophthalmologic surgery (one case) and ENT surgery in one patient.

Three patients were being treated for neoplasia with predisposing treatment to DVT: two for prostate neoplasia on Zoladex® and Androcur® hormone therapy, and one for multiple myeloma on Thalidomide®.

In our series, a thrombogenic factor or pathology predisposing to thrombosis was retained in 25 patients, i.e., 24.5% of cases. APS was identified in 11 patients (10.7% of the total series). These included 4 women and 7 men. The mean age was 75 years. Antiphospholipid antibodies were ACL in 7 cases and ACC (4 cases). DVT was a revelatory of SAPL in all cases. It was recurrent in 2 patients. APS was primary in 7 patients (63%). It was associated with neoplasia in 4 cases. In 2 cases, DVT was associated with arterial thrombosis: digital ischemia (1 case) and thrombosis of the sural artery in 1 case.

Neoplasia was diagnosed in 12 patients (11.7%). These included 8 men (66%) and 4 women (34%). The mean age was 76 years.

DVT occurred during the course of neoplasia in 8 patients (82%). The mean time to onset of DVT was 96 days (range 15 days to 2 years). The search for occult cancer was based on a systematic clinical examination of all patients, together with a chest X-ray and a blood count. Abdominopelvic ultrasound and tumor markers were performed in 25 cases. DVT was indicative of neoplasia in 4 patients (18%). In all cases, the etiological diagnosis was based on questioning and clinical examination.

Solid cancers were found in 10 cases: digestive cancer in 5 cases: colorectal (4 cases), gastric (1 case), prostate cancer (2 cases), skin cancer (2 cases), laryngeal cancer (1 case).

Hemopathy was involved in 2 cases: multiple myeloma in one patient and non-Hodgkin's lymphoma in another. In one patient, DVT was part of Behçet's disease diagnosed at the age of 40, who presented with 3 episodes of recurrent DVT complicated by PE. The diagnosis of Behçet's disease was based on the association of bipolar aphthosis and uveitis.

Hyper-homocysteinemia was noted in 2 cases. The first patient was 72 years old, who was hospitalized for popliteal and superficial femoral DVT. The haemogram revealed macrocytic anemia with a hemoglobin level of 7.4 g/dl. The diagnosis of Biermer's anemia was made in view of a decreased vitamin B12 level with positive anti-parietal cell and anti-intrinsic factor antibodies. There was major hyper-homocysteinemia at 166 umol/l.

The second patient, aged 75, was hospitalized for a left femoropopliteal DVT. As part of the pre-treatment work-up, a haemogram showed isolated macrocytosis with a hemoglobin

Table 2. Results of the etiological investigation of deep vein thrombosis in our patients

Etiologies	Number of cases	Frequency (%)
Factors leading to thrombosis		
Bed rest	44	43.7
Recent surgery	6	5.0
Taking medication	3	2.5
Tobacco	8	7.8
Obesity	11	10.7
Thrombogenic pathology		
Antiphospholipid syndrome	11	10.7
Neoplasia	12	11.7
Behçet's disease	1	0.9
Hyperhomocysteinemia	2	1.9
No identified risk factor	46	45.0

level of 13.4 g/L. Vitamin levels were normal. Plasma homocysteine was 37 umol/L.

Table 2 summarizes the results of the etiological investigation of DVT in our patients.

Therapeutic management was primarily based on sodium heparin, low molecular weight heparins, vitamin K antagonists (VKA), and supportive symptomatic treatment. VKAs were introduced as a relay therapy following heparin in 102 patients. The molecules used in all cases was acenocoumarol (Sintrom®).

In cases of recurrent DVT, long-term anticoagulant therapy was maintained in all patients, regardless of the underlying etiology.

For patients with a single episode of venous thrombosis, the duration of anticoagulation varies according to the etiology.

In cases of APS, long-term anticoagulant therapy was maintained in the majority of patients. In the remaining cases, treatment duration ranged from 3 to 24 months. Complications were observed in 20 patients (19.6%).

The main risk associated with DVT is embolic migration, which can be fatal. PE was diagnosed with 5 patients.

The medium- and long-term course of DVT may lead to significant functional impairment due to the risk of recurrence and PTS. Thirteen patients (7.4%) experienced a recurrence, and PTS was observed in 9 patients (8.4%). Death occurred in 5 patients.

DISCUSSION

The present study provides a comprehensive overview of the clinical characteristics and RFs associated with lower limb DVT in elderly patients over an 18-year period at a single tertiary care center. As the aging population continues to grow worldwide, understanding the epidemiology and underlying factors of DVT in this vulnerable group is essential for improving prevention, diagnosis, and management strategies.

Our findings confirm that advanced age is not only a non-modifiable RF but also a context in which multiple predisposing conditions often coexist, including malignancy, prolonged immobility, cardiovascular diseases, and previous thrombotic events. In our cohort, a substantial proportion of cases were unprovoked, emphasizing the importance of considering occult malignancy and thrombophilia, particularly APS, in the diagnostic approach.

VTE is a common pathology that has a significant impact on morbidity, mortality and healthcare costs [1, 2].

The incidence of DVT increases exponentially with age [1, 4, 5]. A large population-based study carried out in Norway, showed that 70% of patients with a diagnosis of DVT are over 60, and 25% of these are over 80 [4].

In our series, among 585 patients hospitalized for DVT during the same period, DVT in the elderly represented 17.4% of all cases of venous thrombosis, reflecting the frequency of this pathology in this age group. In another Tunisian series, DVT in the elderly represented 47% of the total [6].

In Tunisia, we currently have no national statistics on the incidence of DVT in the elderly. However, it is very likely that the frequency of this disease will increase in the years to come, due to the aging of the population.

This risk is all the greater because, with age, these patient had frequently others associated comorbidities (such as surgery, immobility, or cancer), favoring the development of venous thrombosis [7-10].

Several mechanisms have been suggested: limited physical mobility, increased blood stasis, comorbidity (cancer, chronic inflammation, etc.), increased factor VIII and fibrinogen levels [11] as well as physiological changes in the venous network favoring venous stasis [5]. Gender does not appear to influence the overall of DVT, although hormone replacement therapy in women is associated with an increased risk of VTE. Anderson et al found the same rate of DVT in both sexes [11, 12]. Male genre was predominant in our series (56%) with no statistically significant correlation.

DVT was most often proximal in our elderly patients (77%). This notion was also reported in the Mahe study, where DVT was proximal in 76% of cases [7]. The high rate of proximal DVT observed in our study also raises important considerations for treatment intensity and duration, given the elevated risk of complications such as PE in this subgroup.

Various cross-sectional and longitudinal studies have identified several RFs for VTE in elderly patients [7]. While some RFs, such as age, can be considered intrinsic, others result from potentially thrombogenic pathological conditions.

VTE is most often multifactorial. In most studies, DVT patients have a higher number of RFs than the control population [13, 14, 15]. In a French study looking at RFs in an outpatient medical population, 57% of patients with DVT had at least 2 RFs, compared with 18% of the age- and sex-matched control group [13, 16, 17].

The frequency of DVT history varies from 6 to 29% depending on the series [9, 18, 19]. In our series, 11 patients (10.4%) had at least one history of DVT.

Thrombosis may be triggered by transitory factors such as bed rest. Immobilization slows venous return due to lack of muscle contracture [20].

In our series, in addition to advanced age, at least one DVT RF was found in 56 patients (54.6%). These were: a single FDR in 38 patients (37%), two RFs in 15 patients (14.7%) and three RFs in 3 patients (2.9%). The value of the history of VTE depends on several factors: confirmation of the history, the type of history (embolism or peripheral thrombosis), and the context in which the thrombosis occurred [12, 21-24]. Several longitudinal studies have shown that the risk of recurrence was greater when the patient had cancer (OR = 2.8), while the surgical context was a protective factor (OR = 2.7). The

idiopathic context also acts as a recurrence factor (OR = 1.9), making therapeutic management difficult.

A descriptive study involving 1,932 patients showed that bed rest was by far the most frequent stasis factor observed in half the cases [9]. In our series, bed rest of more than 3 days was also the predominant RF in this geriatric population, observed in 44 cases (43%). Immobilization is an important RF for associated DVT, requiring preventive anticoagulant therapy in these situations.

Anti-angiogenic treatments: thalidomide and lenalidomide used in myeloma, especially when combined with dexamethasone or doxorubicin, can increase VTE rates by 20-40% [21]. Hormonal treatment of prostate cancer is associated with an increased risk of DVT [22]. In our series, two patients with prostate neoplasia treated with zoladex and androcur respectively, developed DVT. This DVT would probably be multifactorial, associating the drug cause, but also age, bed rest and the presence of progressive neoplasia.

Surgery is an important and frequent RF for VTE.The risk of VTE depends partly on the type and duration of surgery, and partly on factors inherent in the patient (age, obesity, previous DVT and/or other thrombogenic pathologies) [23, 24].

The postoperative context is highly thrombogenic, particularly in orthopedic surgery (total hip or knee replacement) [20], neurosurgery and gynecological surgery [23]. Prevention strategies are well validated, but the risk has not disappeared. In our series, 5% of patients had DVT after recent surgery. Visceral surgery was the most frequent cause.

Obesity is a RF for VTE, which, when the BMI exceeds 30, is associated with a relative risk multiplied by 2.3 to 3, depending on the series [12]. Obesity is responsible for reduced mobility and fibrinolytic activity [25]. This factor was found in 11 of our patients (18.2%), particularly women.

The association of venous or arterial thrombosis or repeated fetal loss with the long-term presence of antiphospholipid antibodies (ACL or ACC type or antiß2 GP1) defines the APS. It is an acquired thrombophilia characterized by an increased risk of thrombosis and obstetrical complications. The frequency of APS varies from 4% to 21% in patients with VTE, depending on the series [26-28]. The frequency in patients aged over 65 remains unknown. Anti-cardiolipin antibodies are common among the elderly. In the study by Manoussakis et al, among 64 healthy elderly patients, 50% had positive ACLs [29]. Several studies have shown that the presence of anti-cardiolipin antibodies is an independent RF for VTE [30]. In our series, APS was identified in 11 patients (10.7%). Venous thrombosis in APS is associated with a very high risk of recurrence [1] but also with the presence of an underlying neoplasia in 15% of cases. In our series, APS was associated with neoplasia in 4 cases (36%).

Cancer disease “naturally” combines the elements of Virchow’s triad:

(1) venous stasis (bed rest, dehydration, etc.),

(2) vascular parietal aggression (surgery, implantable chamber, chemotherapy, radiotherapy, etc.), and

(3) hyper coagulability [1].

Cancer patients are 4 to 20% more likely to develop VTE, and 4 to 7 times more likely than non-cancer patients [31]. This occurrence varies according to the nature and location of the cancer, its invasive potential, its stage (metastatic or non-metastatic), the treatments offered (surgical, chemotherapy, radiotherapy, adjuvant treatments), and the numerous co-morbidities of patients, irrespective of their neoplastic state.

Cancers with the highest thrombotic potential include hematological, pulmonary, gastrointestinal and pancreatic neoplasia, lymphoma, leukemia, ovarian and renal cancers [32, 33]. Recognized RFs also include the various therapies offered to patients. Chemotherapy plays an undeniable role in the occurrence of VTE [33], , especially when administered during metastatic stages. The frequency of neoplasia in our study was 11.4%. DVT occurred during the course of neoplasia in 8 patients (82%). In 10-20% cases of preliminary VTE, cancer (often metastatic) is discovered (especially within six to 12 months), particularly in cases of recurrent, bilateral, idiopathic DVT, or DVT on VKA [34]. Most authors recommend that the search for occult neoplasia in the presence of a first episode of unprovoked DVT should be followed by a careful clinical examination and clinically-oriented investigations. In our series, DVT was indicative of neoplasia in 4 patients, representing 18% of patients with neoplasia. These were digestive cancer in 2 cases, skin cancer (1 case) and non-Hodjkin’s lymphoma (1 case). In all cases, neoplasia was suspected on the basis of questioning and clinical examination and confirmed by further investigations.

Obstructive or restrictive respiratory insufficiency, dehydration and cardiac rhythm disorders may predispose to the occurrence of DVT [35].

Pathologies that cause an inflammatory syndrome, such as severe infectious and systemic diseases, multiply the risk of DVT by 5.7 [12]. Ischemic stroke, cardiac pathologies, and chronic respiratory diseases also predipose to VTE.

VTE is a multifactorial, chronic and recurrent disease. Cohort studies indicate that in 50% of cases, the etiology remains unknown [1].

Compared to existing literature, the distribution of RFs and DVT characteristics in our elderly cohort aligns with previous reports, though regional differences may influence certain patterns, such as the prevalence of inherited thrombophilia or cancer types.

Etiological evaluation, which is systematic from a clinical point of view, must be all the more complete in the case of an event occurring without triggering circumstances. In the absence of clinical clues, the cost-effectiveness of routine investigations is poor, and investigations should be limited. Age is a major RF for VTE, with an exponential increase in thromboembolic events. In the elderly, the first step is to determine whether DVT is provoked or unprovoked.

The origin of thrombosis in the elderly is often multifactorial: several RFs are most often combined to cause venous thrombosis.

Approximately 50% of events occur after a triggering event (induced VTE), which is important to recognize. In fact, knowledge of a transient factor makes it possible to identify a population with a low risk of annual recurrence (< 3%, i.e., three to four times lower than VTE in the presence of a persistent factor or idiopathic VTE) [35], and thus to set the duration of treatment [36] and avoid the multiplication of complementary examinations aimed at etiology.

Knowledge of a patient’s permanent FDR, prior to the onset of VTE, helps to understand the condition, and also helps to determine the duration of treatment. A thorough clinical

examination looks for signs specific to certain pathologies in the elderly, in particular signs pointing to neoplasia.

According to the latest ACCP recommendations, a minimum workup should be performed on all patients [36]. It includes the following:

- an analysis of FDRs, antecedents, the context of occurrence and associated pathologies,
- a complete clinical examination including pelvic touch,
- a biological work-up including a blood count, prothrombin time, activated partial thromboplastin time and creatinemia, which also serves as a pre-therapeutic work-up, and
- a chest X-ray.

A more thorough assessment is carried out in patients with:

- venous thrombosis without cause,
- unusual thrombosis (isolated proximal, upper limb, visceral, neurological, etc.),
- bilateral thrombosis or tilted thrombosis,
- recurrent thrombosis, history of arterial thrombosis, and
- clinical or biological manifestations pointing to a secondary cause

This study has several limitations that should be acknowledged. First, its retrospective design inherently limits the ability to establish causal relationships and is subject to information and selection biases. Second, some patient records were incomplete, leading to missing data on certain clinical or laboratory variables, which may have influenced the comprehensiveness of the analysis. Third, the etiological workup, including thrombophilia and cancer screening, was not systematically performed for all patients but rather guided by clinical judgment or available resources, which may have introduced variability in the assessment of underlying RFs. These limitations should be considered when interpreting our findings, and future prospective studies are needed to confirm and expand upon these results.

CONCLUSION

In this 18-year retrospective study conducted at a single center, we identified key clinical characteristics and RFs associated with lower limb DVT in elderly patients. Our findings highlight the predominance of proximal DVT, the significant presence of comorbidities such as cancer and cardiovascular disease, and the relatively frequent occurrence of unprovoked thrombotic events in this population.

These results underscore the importance of thorough clinical assessment in elderly patients presenting with DVT, including targeted screening for underlying malignancies and APS when appropriate. Given the variability in etiological workup and limitations inherent to retrospective data, our findings should be interpreted with caution.

Future prospective studies with standardized diagnostic protocols are needed to better define optimal screening strategies and management approaches for DVT in the aging population, particularly in low-resource settings.

Author contributions: RBS: conceptualization, methodology, writing – original draft, writing – review & editing; **IC:** formal analysis, data curation; **FF:** methodology; **SM:** writing – review & editing; **ZB:** writing – review & editing, supervision. All authors have agreed with the results and conclusions.

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Ethical statement: The authors stated that the study was carried out in accordance with the Declaration of Helsinki. Ethical approval was waived by the local Ethics Committee of HedichakerHospital, Sfax, Tunisia in view of the retrospective nature of the study and all the procedures being performed were part of the routine care. All data (biological, clinical, and imaging) were obtained only for standard diagnostic following physicians' prescriptions (no specific sampling and no modification of the sampling protocol). The authors further stated that all patients from the authors' institution (the Hedi Chaker Hospital (Sfax, Tunisia) are informed that their clinical data can be used for research and give their consent for the use of their data unless they provide an opposition to it. None of the patients of the present study provided an opposition. Data analyses were carried out using an anonymized database.

Declaration of interest: No conflict of interest is declared by the authors.

Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

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