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Differences in Clinical Presentation, Rate of Pulmonary Embolism, and Risk Factors Among Patients With Deep Vein Thrombosis in Unusual Sites

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Abstract

Unusual site deep vein thrombosis (USDVT) is an uncommon form of venous thromboembolism with heterogeneous signs and symptoms, unknown rate of pulmonary embolism (PE), and poorly defined risk factors. We conducted a retrospective analysis of 107 consecutive cases of USDVTs, discharged from our University Hospital over a period of 2 years. Patients were classified based on the site of thrombosis and distinguished between patients with cerebral vein thrombosis, jugular vein thrombosis, thrombosis of the deep veins of the upper extremities, and abdominal vein thrombosis. We found statistically significant differences between groups in terms of age ($P < .0001$) and gender distribution ($P < .05$). We also found that the rate of symptomatic patients was significantly different between groups ($P < .0001$). Another interesting finding was the significant difference between groups in terms of rate of PE ($P < .01$). Finally, we found statistically significant differences between groups in terms of risk factors for thrombosis, in particular cancer ($P < .01$). Unprovoked cases were differently distributed among groups ($P < .0001$). This study highlights differences between patients with USDVT, which depend on the site of thrombosis, and provides data which might be useful in clinical practice.

Keywords

clinical epidemiology, deep venous thrombosis, unusual sites

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Introduction

Venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE), affects 1 to 3 per 1000 persons per year in Western countries and represents the third leading cause of cardiovascular mortality and the main cause of preventable mortality among hospitalized patients in the world.[1-4]

Although its most common clinical presentation involves the deep veins of the lower limbs, DVT may potentially occur in any section of the venous system. Indeed, DVT is also diagnosed, among others, in the veins of the arms, the jugular veins, the cerebral venous system, the abdominal veins.[5] The term "unusual site deep vein thrombosis" (USDVT) is used to refer to DVTs occurring in these relatively uncommon sites. Unusual site deep vein thrombosis represents a clinical challenge because of the heterogeneity of signs and symptoms, the potential severity of the clinical outcomes, and the lack of adequate evidence from clinical trials in terms of treatment strategies. Also, USDVTs have risk factors that may be different from

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Table 1. Baseline Characteristics and Clinical Presentation According to Thrombosis Site.

Characteristics	CVT, n = 25	JVT, n = 16	UEDVT, n = 33	AVT, n = 33	*P*
Age, years ± SD	47.1 ± 15.0	60 ± 21.6	56 ± 17.5	55.5 ± 15.8	<.0001
Men, n (%)	7 (28.0%)	8 (50.0%)	16 (48.4%)	22 (66.6%)	<.05
Symptomatic, n (%)	25 (100.0%)	12 (75.0%)	28 (84.8%)	15 (45.4%)	<.0001
Concomitant PE					
n/screened patients (%)	0/12 (0.0%)	0/12 (0.0%)	6/8 (75.0%)	9/28 (32.1%)	<.001
n/whole cohort	0/25 (0.0%)	0/16 (0.0%)	6/33 (18.2%)	9/33 (27.3%)	<.01

Abbreviations: AVT, abdominal vein thrombosis; CVT, cerebral vein thrombosis; JVT, jugular vein thrombosis; PE, pulmonary embolism; SD, standard deviation; UEDVT, upper extremities deep vein thrombosis.

those associated with DVT in canonical sites and are often specific of the anatomical site where the thrombosis occurs.

In this study, we have retrospectively analyzed cases of patients with cerebral vein thrombosis (CVT), jugular vein thrombosis (JVT), thrombosis of the deep veins of the upper extremities (UEDVT), and abdominal vein thrombosis (AVT), in order to detect differences between groups, in terms of age, gender, clinical features, rate of PE, risk factors for thrombosis, and treatment.

Methods

Ethical Approval

The study was approved by the Ethics Committee of the Fondazione Policlinico Universitario A. Gemelli IRCCS (Protocol number 49904/18).

Identification and Characterization of Patients With USDVT

We used the electronic database of the "Fondazione Policlinico Universitario A. Gemelli IRCCS," a University Hospital in Rome, Italy. The search included the period between January 01, 2015, and December 31, 2016. The *International Classification of Diseases, Ninth Revision* codes were used to identify consecutive patients discharged with a diagnosis of VTE. Next, the clinical charts of all identified patients were reviewed by 2 investigators, in order to confirm the diagnosis of DVT and distinguish between DVT of the lower limbs (which were considered DVT in usual sites) and DVT occurring in other anatomical sites (which were considered USDVT). Cases of isolated PE, without evidence of DVT, were excluded. For each patient with USDVT, the following parameters were determined by 2 investigators: age at onset of DVT, gender, signs and symptoms at hospital admission, concomitant presence of PE, risk factors for thrombosis (as recorded by anamnesis or assessed by laboratory and/or radiological examinations during hospital stay), and treatment during hospitalization and at discharge from the hospital.

Statistical Analyses

Comparisons were performed between patients with USDVT in different anatomical sites. Variables were age, gender, rate of symptomatic patients, rate of PE, and presence of risk factors. Differences between groups were analyzed by one-way analysis of variance for continuous variables and by bicategorical χ^2 for categorical variables. Differences were considered significant for $P < .05$.

Results

The search of our database led to the identification of 744 patients discharged with a diagnosis of VTE. Of these, 107 were consecutive cases of USDVT. They consisted of 25 cases of CVT, 16 cases of JVT, 33 cases of UEDVT, and 33 cases of AVT. In all cases, CVT was diagnosed by either contrast-enhance computed tomography (CT) scan and/or magnetic resonance angiography of the brain. All the diagnoses of UEDVT were done by upper extremities venous ultrasound (US) and/or contrast-enhanced CT scan. All cases of JVT were diagnosed by either US and/or contrast-enhanced CT scan of the neck. All cases of AVT were diagnosed by either abdominal US and/or abdominal contrast-enhanced CT scan.

Age and Gender

All USDVTs were new diagnoses, thus age at onset corresponded in all cases to age at the time of hospital admission. The mean age in the CVT group was 47.1 ± 15.0 years, while in the JVT, UEDVT, and AVT groups was 60.0 ± 21.6, 56.0 ± 17.5, and 55.5 ± 15.8 years, respectively. Age differences between groups were statistically significant ($P < .0001$). The female sex was more frequent among patients with CVT (72.0%), while the male sex was more common in the group of patients with AVT (67.0%). Men represented the 50.0% and the 48.4% of the patients in the JVT and UEDVT groups, respectively. Differences in gender distribution were statistically significant between groups ($P < .05$). None of the female patients was pregnant or in the postpartum period. These results are presented in Table 1.

Clinical Presentation and Rate of PE

Of the 107 patients with USDVT, 80 (74.7%) presented at least one sign or symptom of thrombosis at hospital admission. However, the percentage of symptomatic patients was significantly different among patients with CVT, JVT, UEDVT, and

AVT, as shown in Table 1 ($P < .0001$). In particular, the percentage of symptomatic patients was 100.0% in the CVT group, 75.0% in the JVT group, 84.8% in the UEDVT group, and 45.4% in the AVT group.

A total of 60 patients underwent CT scan of the chest (56.0% of the total population). In detail, they were 12 patients with CVT (on a total of 25), 8 patients with UEDVT (on a total of 33), 12 patients with JVT (on a total of 16), and 28 patients with AVT (on a total of 33). One reason that led to the execution of these CT scans was the presence of dyspnea. These patients underwent CT pulmonary angiography to rule out or confirm a suspicion of PE. Other reasons that, in the absence of dyspnea, led to execution of CT scans of the chest were a suspicion of cancer, or a known cancer that needed to be (re)staged. These patients underwent contrast-enhanced CT scan of the chest as part of a total body CT scan. Pulmonary embolism was relatively frequent among patients with UEDVT: 75.0% of the patients with UEDVT who underwent CT scan of the chest and 18.2% of the whole UEDVT population. Pulmonary embolism was frequent also among patients with AVT: 32.1% of the patients with AVT who underwent CT scan of the chest and 27.3% of the whole AVT cohort. On the other hand, no PE was detected in the CVT and JVT groups, although a total of 20 patients underwent CT scan of the chest in these 2 cohorts. Differences between groups were statistically significant ($P < .001$ among patients screened for PE and $P < .01$ among patients in the whole population). These results are reported in Table 1.

Signs and symptoms at admission, distinguished according to the thrombosis site, are presented in Table 2. Among patients with CVT, headache was the most common symptom (72.0%). Other frequent clinical manifestations of CVT were focal neurologic deficits (28.0%), seizures (24.0%), nausea and vomiting (24.0%), and aphasia (20.0%). Dyspnea was never present (0.0%).

The most frequent signs and symptoms among patients with JVT were pain and edema of the upper arm (25.0% and 25.0%, respectively), neck swelling (12.5%), headache (12.5%), and loss of consciousness (12.5%). Dyspnea was never present (0.0%). Edema of the arm (66.6%) and pain of the arm (39.4%) were the most common sign and symptom of UEDVTs. In this cohort, dyspnea was relatively common (5 patients, 15.1%). Of these 5 patients with dyspnea, 4 had PE and 1 did not have PE.

The symptoms found among patients with AVT were abdominal pain (33.3%) and dyspnea (12.1%). In particular, there were 4 patients with dyspnea. Of these, 3 had PE and 1 did not have PE.

Table 2. Signs and Symptoms According to Thrombosis Site.

Signs and symptoms in CVT patients, n = 25	
Headache, n (%)	18 (72.0%)
Focal neurologic deficits, n (%)	7 (28.0%)
Seizures, n (%)	6 (24.0%)
Nausea and vomiting, n (%)	6 (24.0%)
Aphasia, n (%)	5 (20.0%)
Loss of consciousness, n (%)	3 (12.0%)
Diplopia, n (%)	1 (4.0%)
Dizziness, n (%)	1 (4.0%)
Dyspnea, n (%)	0 (0.0%)
Signs and symptoms in JVT patients, n = 16	
Pain of the upper arm, n (%)	4 (25.0%)
Edema of the upper arm, n (%)	4 (25.0%)
Neck swelling, n (%)	2 (12.5%)
Headache, n (%)	2 (12.5%)
Loss of consciousness, n (%)	2 (12.5%)
Superior vena cava syndrome, n (%)	1 (6.2%)
Seizures, n (%)	1 (6.2%)
Dyspnea, n (%)	0 (0.0%)
Signs and symptoms in UEDVT patients, n = 33	
Edema of upper arm, n (%)	22 (66.6%)
Pain of the upper arm, n (%)	13 (39.4%)
Dyspnea, n (%)	5 (15.1%)
With PE, n (%)	4 (12.1%)
Without PE, n (%)	1 (3.0%)
Signs and symptoms in AVT patients, n = 33	
Abdominal pain, n (%)	11 (33.3%)
Dyspnea	4 (12.1%)
With PE, n (%)	3 (9.0%)
Without PE, n (%)	1 (3.0%)

Abbreviations: AVT, abdominal vein thrombosis; CVT, cerebral vein thrombosis; JVT, jugular vein thrombosis; PE, pulmonary embolism; UEDVT, upper extremities deep vein thrombosis.

Risk Factors for Thrombosis

The results of the analysis of risk factors for thrombosis are presented in Table 3.

Cancer. Cancer was the most common risk factor in the whole population. Indeed, 47 patients had cancer on a total of 107 individuals with USDVT (43.9%). Nonetheless, the frequency of cancer was significantly different between the various types of USDVT ($P < .01$). In particular, cancer was extremely frequent among patients with AVT (75.7%) and JVT (56.2%). It was less common among patients with CVT and UEDVT (24.0% and 21.2%, respectively). Solid cancers constituted 76.6% of all neoplasms (36/47). Among hematological cancers (n = 11), 7 (63.6%) were JAK2-positive myeloproliferative neoplasms (MPN). Of these, 3 were patients with CVT and 4 were patients with AVT.

Estrogen-containing oral contraceptives. A relevant percentage (27.7%) of female patients with CVT was taking estrogen-containing oral contraceptives. Of note, none of these women had additional risk factors (in particular they did not have cancer). The use of estrogen-containing oral contraceptives was instead never found among women with JVT, UEDVT, and AVT (36 women in total).

Other risk factors. The analysis of our database led to the identification of a number of risk factors and/or predisposing conditions for thrombosis, which were heterogeneously distributed among the various types of USDVT. For instance, the

Table 3. Risk Factors According to Thrombosis Site.

Risk Factor	CVT, n = 25	JVT, n = 16	UEDVT, n = 33	AVT, n = 33	*P*
Cancer, n (%)	6 (24.0%)	9 (56.2%)	7 (21.2%)	25 (75.7%)	<.01
Solid cancer, n (%)	3 (12.0%)	8 (50.0%)	6 (18.2%)	19 (57.6%)	
Hematological cancer, n (%)	3 (12.0%)	1 (6.2%)	1 (3.0%)	6 (18.1%)	
−JAK2+ MPN, n (%)	3 (12.0%)	0 (0.0%)	0 (0.0%)	4 (12.1%)	
Oral contraceptives, n/number of women (%)	5/18 (27.7%)	0/8, (0.0%)	0/17, (0.0%)	0/11, (0.0%)	
CVC, n (%)	0 (0.0%)	0 (0.0%)	16 (48.4%)	0 (0.0%)	
PM, n (%)	0 (0.0%)	0 (0.0%)	2 (1.8%)	0 (0.0%)	
Thoracic outlet syndrome, n (%)	0 (0.0%)	0 (0.0%)	6 (18.1%)	0 (0.0%)	
Liver cirrhosis, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (15.1%)	
Trauma, n (%)	0 (0.0%)	1 (6.2%)	0 (0.0%)	0 (0.0%)	
Sepsis, n (%)	0 (0.0%)	1 (6.2%)	0 (0.0%)	0 (0.0%)	
DIC, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.0%)	
Pancreatitis, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (3.0%)	
Surgery, n (%)	1 (4.0%)	0 (0.0%)	0 (0.0%)	1 (3.0%)	
None of the above-listed risk factors	13 (52.0%)	5 (31.2%)	2 (6.1%)	0 (0.0%)	<.0001

Abbreviations: AVT, abdominal vein thrombosis; CVC, central venous catheter; CVT, cerebral vein thrombosis; DIC, disseminated intravascular coagulation; JVT, jugular vein thrombosis; MPN, myeloproliferative neoplasm; PM, pacemaker; UEDVT, upper extremities deep vein thrombosis.

conditions most frequently associated with UEDVT were the presence of a central venous catheter (CVC), the presence of a pacemaker, and a diagnosis of thoracic outlet syndrome (48.4%, 1.8%, and 18.1%, respectively). Liver cirrhosis (with no cancer) was relatively frequent among patients with AVT (15.1%). Other less frequent conditions associated with various types of USDVT were sepsis, trauma, surgery, disseminated intravascular coagulation, and pancreatitis.

Unprovoked Cases

There were a total of 20 patients (18.7% of the whole population) who did not display any of the risk factors listed above. The percentage of such unprovoked cases was 52.0% among patients with CVT, 31.2% among patients with JVT, 6.1% among patients with UEDVT, and 0.0% among patients with AVT. These differences were statistically significant ($P < .0001$; Table 3).

Review of clinical charts demonstrated that in all these patients, a search for the following thrombophilic conditions was performed: protein C deficiency, protein S deficiency, Factor V Leiden (FV Leiden), G20210A prothrombin mutation, antithrombin deficiency, lupus anticoagulant (LAC), and antiphospholipid syndrome, elevated levels of Factor VIII (FVIII). The results of thrombophilia screening in this population are presented in Table 4. Among the 13 patients with unprovoked CVT, we identified 1 case of protein C deficiency, 1 case of protein S deficiency, and 1 case of heterozygous FV Leiden. One case of protein C deficiency was also identified among the 5 patients with unprovoked JVT, while the search for thrombophilia was negative in the 2 patients with unprovoked UEDVT. We also found 5 patients with a positive LAC test (4 in the CVT group and 1 in the JVT group). However, in none of these cases, LAC positivity was associated with the presence of antibodies against cardiolipin and/or β2 glycoprotein-1. In addition, in none of these cases, we could access medical data after hospital discharge to determine whether LAC positivity was confirmed 3 months later. This is an important limitation that significantly affects the interpretation of LAC positivity in our cohort. Finally, there were 4 patients in the CVT group who displayed elevated levels of FVIII (above the normal range of our hospital laboratory: 70%-140%). However, also in this case, we only had access to the medical records of the period of hospitalization, thus the elevated values that we report are those assessed at the time of acute thrombosis. This is a limitation, since FVIII may be transiently elevated in the acute inflammation phase response to thrombosis. Therefore, its role as possible thrombophilic condition in these patients remains uncertain.

Table 4. Thrombophilic Tests Among Patients With Unprovoked Thrombosis.

Test	CVT, n = 13	JVT, n = 5	UEDVT, n = 2
Protein C deficiency, n (%)	1 (7.1%)	1 (20.0%)	0 (0.0%)
Protein S deficiency, n (%)	1 (7.1%)	0 (0.0%)	0 (0.0%)
Factor V Leiden (heterozygous), n (%)	1 (7.1%)	0 (0.0%)	0 (0.0%)
Factor V Leiden (homozygous), n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
G20210 A prothrombin mutation, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Antithrombin deficiency, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lupus anticoagulant, n (%), (*only one determination during hospitalization*)	4 (28.5%)	1 (20.0%)	0 (0.0%)
Anti-cardiolipin antibodies, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Anti-β2 glycoprotein-1 antibodies, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Elevated factor VIII, n (%), (*only one determination during hospitalization*)	4 (28.5%)	0 (0.0%)	0 (0.0%)

We found that thrombophilia screening was performed also in 18 cases with provoked thrombosis. The reason why these patients were screened for thrombophilia was not always

Table 5. Treatment During Hospitalization and at Discharge According to Thrombosis Site.

Treatment	CVT, n = 25	JVT, n = 16	UEDVT, n = 33	AVT, n = 33
During hospitalization				
LMWH, n (%)	16 (64.0%)	11 (68.8%)	27 (81.8%)	28 (84.8%)
UFH, n (%)	5 (20.0%)	2 (12.5%)	1 (3.0%)	1 (3.0%)
No treatment, n (%)	4 (16.0%)	3 (18.8%)	5 (15.6%)	4 (12.1%)
At discharge				
LMWH, n (%)	14 (56.0%)	14 (87.5%)	26 (78.8%)	25 (75.8%)
AVK, n (%)	8 (32.0%)	1 (6.2%)	1 (3.0%)	3 (9.1%)
DOAC, n (%)	1 (4.0%)	0 (0.0%)	3 (9.1%)	3 (9.1%)
No treatment, n (%)	2 (8.0%)	1 (6.2%)	3 (9.1%)	2 (6.1%)

Abbreviations: AVK, antivitamin K; AVT, abdominal vein thrombosis; CVT, cerebral vein thrombosis; DOAC, direct oral anticoagulants; JVT, jugular vein thrombosis; LMWH, low-molecular-weight heparin; UEDVT, upper extremities deep vein thrombosis; UFH, unfractionated heparin.

clearly evident from the review of medical records, but in many cases, it was because the screening was ordered before the provoking factor for thrombosis was identified (as in cases of new cancer diagnosis).

According to our database, screening for paroxysmal nocturnal hemoglobinuria (PNH) was performed in 4 patients. No cases of PNH were found.

Treatment

We searched the database of our hospital to determine which anticoagulant treatment was prescribed to patients with USDVT during hospitalization and at the time of hospital discharge. The results are presented in Table 5.

During hospital stay, 82 patients (16 with CVT, 11 with JVT, 27 with UEDVT, and 28 with AVT) were treated with low-molecular-weight heparins (LMWH), while 9 patients (5 with CVT, 2 with JVT, 1 with UEDVT, and 1 with AVT) were treated with unfractionated heparin. There were 16 patients (4 with CVT, 3 JVT, 5 UEDVT, and 4 with AVT) who did not receive anticoagulant therapy while in the hospital.

At discharge from the hospital, 80 patients (14 with CVT, 14 with JVT, 26 with UEDVT, and 25 with AVT) were prescribed LMWH, while 20 patients (9 with CVT, 1 with JVT, 4 with UEDVT, and 6 with AVT) received prescription of an oral anticoagulant. According to the medical records, there were 7 patients (2 with CVT, 1 with JVT, 3 with UEDVT, and 2 with AVT) who did not receive any antithrombotic prescription upon discharge. Among patients discharged with oral anticoagulants, 13 (8 with CVT, 1 with JVT, 1 with UEDVT, and 3 AVT) received a vitamin K antagonist and 7 (1 with CVT, 3 with UEDVT, and 3 AVT) received a direct oral anticoagulant (DOAC). Among patients treated with DOAC, 3 received dabigatran, 3 received rivaroxaban, and 1 received apixaban.

Discussion

This is retrospective analysis of 107 consecutive cases of USDVT, with a focus on the demographic characteristics, clinical features, risk factors, and treatment, according to the thrombosis site.

Our results indicate that patients affected by CVT are more frequently young women, while patients with AVT are more commonly men. This is consistent with previous reports in the literature.[6-9] Second, it suggests that all cases of CVTs are symptomatic, while DVTs in other unusual sites may often be asymptomatic. Regarding PE, it is interesting to observe that its rate is 0.0% in our series of patients with CVT and JVT, while it is relatively common in the groups of patients with AVT. Pulmonary embolism is also frequent among patients with UEDVT, consistent with the results of a previous study that showed the presence of PE in 10% to 25% of patients with UEDVT.[10]

The analysis of risk factors revealed that cancer is largely the most common pathological condition associated with USDVT, especially AVT and JVT, consistent with other series in the literature.[11] Solid cancers are more common than hematological cancers. Nonetheless, hematological cancers—and especially JAK2-positive MPN—have a relevant role in patients with CVT and AVT in our population. Among women with CVT, in addition to cancer, a common risk factor is the use of estrogen-containing oral contraceptives. This finding is consistent with previously published data.[9] A significant risk factor for JVT reported in the literature is the presence of a CVC.[12] However, none of our patients had CVC-related thrombosis of the jugular vein. In our study, the presence of a CVC is instead the main risk factor for UEDVT. When these cases are added to those with thrombosis associated with an implantable cardiac device, they account for more than 50% of all UEDVTs. Thus, these patients need to be distinguished by those with thrombosis not associated with a device. In the latter case, cancer is again the most frequent risk factor. These findings are consistent with the results of a recent study that has reported that about 70% of UEDVTs are CVC-related and 30% to 40% occur in patients with cancer, with the risk of UEDVT being almost doubled in patients with an active cancer that also carry a CVC.[13]

An interesting finding of this study is the significantly different number of unprovoked thromboses between patients with CVT, JVT, UEDVT, and AVT. In particular, more than half of patients with CVT did not display any convincing risk factor for thrombosis. On the contrary, there were no case of unprovoked thrombosis among patients with AVT. According to our analysis, hereditary coagulopathies and thrombophilic conditions may explain only a portion of these unprovoked USDVT. Indeed, we only found 2 cases of protein C and protein S deficiency in the group of unprovoked CVT and 1 case of protein C deficiency in the group of unprovoked JVT. In addition to that, there was 1 patient with heterozygous FV Leiden in the CVT group. Regarding LAC positivity that was found during hospitalization in 4 cases of unprovoked CVT and 1 case of

unprovoked JVT, it is important to mention that we could not evaluate whether it was confirmed 3 months after the first determination, therefore its actual role in the pathogenesis of these thromboses remains uncertain. Similarly, there were 4 patients with elevated levels of FVIII during the acute phase of unprovoked CVT, but it is unknown whether these data were confirmed at later time points, making impossible to establish whether high FVIII was a transient phenomenon or an actual prothrombotic condition.

Regarding treatment, most patients were treated with LMWH during hospitalization. Low-molecular-weight heparins were the most prescribed anticoagulant drugs at the moment of hospital discharge as well. It is interesting to note that only a small portion of patients were discharged from the hospital with the prescription of an oral anticoagulant (20 on a total of 107 patients). This might depend on the fact that the vast majority of patients were affected by cancer, and LMWH still represents the first treatment option for cancer-associated VTE. We also found 7 patients who were discharged from the hospital with DOAC prescription. This indicates that DOACs are being used in clinical practice for the treatment of USDVTs, although convincing evidence on efficacy and safety of these medications in patients with thromboses in unusual sites are still lacking.

This study has some limitations. It is a retrospective analysis of medical records and data might be missing, especially regarding risk factors for thrombosis. Therefore, it is possible that the actual number of unprovoked cases might be lower than observed. Another limitation, as mentioned above, is the fact that some possible thrombophilic conditions, such as LAC positivity, elevated levels of FVIII, and PNH, were not fully investigated. Regarding the relatively small sample size, this might be a limitation, although it is worth mentioning that our cohort of 107 patients with USDVT is comparable with the most recent series available in the literature.[6] Finally, even if USDVTs are relatively rare, in our study, they accounted for more than 14% of all cases of VTE discharged from our hospital over a 2-year period. This high percentage might be due to the fact that our study only focused on inpatients, while many DVTs in usual site are often managed in an outpatient setting.

Conclusion

In conclusion, this study highlights demographical, epidemiological, clinical, and therapeutic differences between patients with USDVT, which mainly depend on the site of thrombosis, and provides potentially useful information for correct identification and management of patients with USDVTs in clinical practice.

Declaration of Conflicting Interests

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