Comparison of the clinical history of symptomatic isolated muscular calf vein thrombosis versus deep calf vein thrombosis

Jean-Philippe Galanaud, MD,^{a,b} Marie-Antoinette Sevestre, MD,^{c,d} Céline Genty, MS,^{c,e} Jean-Pierre Laroche, MD,^f Violaine Zizka, MD,^g Isabelle Quéré, MD, PhD,^{a,b} Jean-Luc Bosson, MD, PhD,^{c,e} and the OPTIMEV SFMV investigators, *Montpellier*, *Grenoble*, *Amiens*, *Avignon*, *France*; and *Fort de France*, *Martinique*

Background: Half of all lower limb deep vein thromboses (DVT) are distal DVT that are equally distributed between muscular calf vein thromboses (MCVT) and deep calf vein thromboses (DCVT). Despite their high prevalence, MCVT and DCVT have never been compared so far, which prevents possible modulation of distal DVT management according to the kind of distal DVT (MCVT or DCVT).

Methods: Using data from the French, multicenter, prospective observational OPTimisation de l'Interrogatoire dans l'évaluation du risque throMbo-Embolique Veineux (OPTIMEV) study, we compared the clinical presentation and risk factors of 268 symptomatic isolated DCVT and 457 symptomatic isolated MCVT and the 3-month outcomes of the 222 DCVT and 390 MCVT that were followed-up.

Results: During the entire follow-up, 86.5% of DCVT patients and 76.7% of MCVT patients were treated with anticoagulant drugs (P = .003). MCVT was significantly more associated with localized pain than DCVT (30.4% vs 22.4%, P = .02) and less associated with swelling (47.9% vs 62.7%, P < .001). MCVT and DCVT patients exhibited the same risk factors profile, except that recent surgery was slightly more associated with DCVT (odds ratio, 1.70%; confidence interval, 1.06-2.75), and had equivalent comorbidities as evaluated by the Charlson index. At 3 months, no statistically significant difference was noted between MCVT and DCVT in death (3.8% vs 4.1%), venous thromboembolism recurrence (1.5% vs 1.4%), and major bleeding (0% vs 0.5%).

Conclusion: Isolated symptomatic MCVT and DCVT exhibit different clinical symptoms at presentation but affect the same patient population. Under anticoagulant treatment and in the short-term, isolated distal DVT constitutes a homogeneous entity. Therapeutic trials are needed to determine a consensual mode of care of MCVT and DCVT. (J Vasc Surg 2010;52:932-8.)

From the Vascular Medicine Unit, Department of Internal Medicine, Montpellier University Hospital, and Research Unit EA2992, Montpellier 1 University, Montpellier; Techniques de l'Ingénierie Médicale et de la Complexité (TIMC), Unité Mixte de Recherche 5525, Centre National de la Recherche Scientifique (CNRS), Université Joseph Fourier, Grenoble^c; Vascular Medicine Unit, Amiens University Hospital, Amiens^d; Clinical Investigation Centre, Centre Hospitalier Universitaire, Grenoble^e; vascular medicine physician, Avignon^f; and vascular medicine physician, Fort de France, Martinioue^g.

*A complete list of the OPTimisation de l'Interrogatoire dans l'évaluation du risque throMbo-Embolique Veineux (OPTIMEV) Société Française de Médecine Vasculaire (SFMV) investigators is given in the Appendix (online only).

This study was funded by a grant from the Hospital Clinical Research Program of the French Ministry of Health and a grant from Sanofi-Aventis. This study was supported by the French Society of Vascular Medicine (SFMV). All investigators are members of the Société Française de Médecine Vasculaire.

Competition of interest: Professor Bosson and Dr Sevestre received fees from Sanofi-Aventis Company.

Additional material for this article may be found online at www.jvascsurg.

Reprint requests: Jean-Philippe Galanaud, Service de médecine interne et maladies vasculaires, Hôpital Saint Eloi, Centre Hospitalier Universitaire de Montpellier, 80, avenue Augustin Fliche, 34295 Montpellier Cedex 05, France (e-mail: jp-galanaud@chu-montpellier.fr).

The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS policy that requires reviewers to decline review of any manuscript for which they may have a competition of interest.

0741-5214/\$36.00

Copyright © 2010 by the Society for Vascular Surgery. doi:10.1016/j.jvs.2010.05.019

Distal deep veins of the lower limb are made up of muscular (gastrocnemius and soleal) and deep calf—paired—(anterior and posterior tibial and peroneal) veins.

In venographic series, the proportion of distal DVT was of 20% of all DVT, notably because the exploration of muscle calf veins requires a special examination protocol and they were not systematically searched. With the possible modification of referral patterns, the use of color flow duplex ultrasound (US) imaging that has a sensitivity, a specificity, and an overall diagnostic accuracy >87% than contrast venography at the level of the calf, and a shorter time lag between the onset of symptoms and the realization of the diagnostic test, distal DVT now represents up to half of all lower limb DVT, roughly equally distributed between muscular calf DVT (MCVT) and deep calf DVT (DCVT).²⁻⁷

So far, international guidelines recommend treating isolated distal DVT for 3 months with full therapeutic doses of anticoagulants, without modulating the treatment according to the muscular or deep calf vein location of the thrombosis. ^{8,9} This is mainly explained by the fact that distal DVT management is itself still debated and by the absence of comparative data between MCVT and DCVT. ^{2,4}

However, if the natural rate of extension of distal DVT (MCVT and DCVT) to proximal deep veins was generally estimated to be about 10%, MCVT natural history—rate of extension to proximal deep veins and postthrombotic syndrome potentials—probably differs from that of DCVT. 4,10-14 This difference may be the consequence of the anatomy of mus-

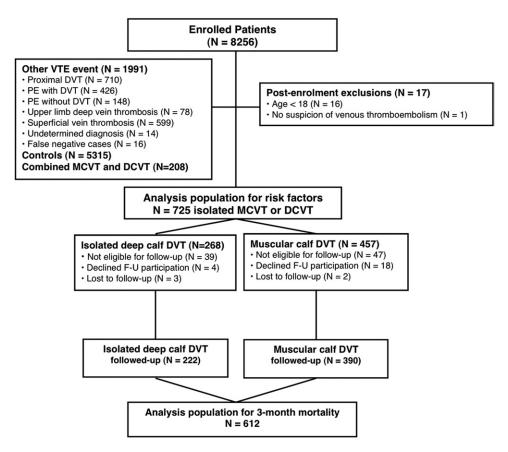


Fig. Patient enrollment and follow-up. DCVT, Deep calf vein thrombosis; DVT, deep vein thrombosis; F-U, follow-up; MCVT, muscular calf vein thrombosis; PE, pulmonary embolism.

cular vessels: their lower diameter and length result in a lower volume of thrombus and, for soleal veins, their higher distance from the proximal veins than deep calf veins. Another explanation may be a difference in patient profile as it has been previously described between distal and proximal DVT, for example.^{15,16}

Thus, distal DVT might be a heterogeneous entity affecting two different populations according to the kind of DVT (MCVT and DCVT). With this perspective, we analyzed the data of the prospective, multicenter, observational OPTimisation de l'Interrogatoire dans l'évaluation du risque throMbo-Embolique Veineux (OPTIMEV) study of inpatients and outpatients with objectively confirmed symptomatic venous thromboembolism (VTE). In this substudy, we focus on symptomatic isolated DVT, that is, without proximal extension or symptomatic pulmonary embolism (PE) at presentation and treated with conventional anticoagulant therapy. The objectives of this work were to compare the clinical characteristics at presentation, the risk factors profile, and the 3-month clinical history of symptomatic MCVT and DCVT to evidence possible different populations. These results may provide a basis to investigate whether distal DVT management should be modulated according to the kind of DVT.

MATERIAL AND METHODS

The study protocol has been extensively described elsewhere. It is available at Clinical Trials.gov (registration number: NCT00670540). The study was approved by the Ethics Committee (Comité Consultatif sur le Traitement de l'Information en matière de Recherche dans le domaine de la Santé) and the Comission Nationale de l'Informatique et des Libertés (CNIL). All participating patients received written information explaining the study objectives and could decline telephone follow-up and consult their data.

Patients. Briefly, between November 2004 and January 2006, the study enrolled 8256 patients aged ≥18 years, referred to the vascular medicine physicians of the 41 hospitals and 292 private practices participating in the study for clinically suspected VTE (DVT or PE; Fig).

All eligible patients underwent a comprehensive realtime B-mode and color Doppler US examination of both legs by a vascular medicine physician. The following veins were scanned transversally over their entire length: inferior vena cava, iliac veins, femoral veins, popliteal veins, anterior and posterior tibial veins, fibular veins, medial and lateral gastrocnemius veins, and soleal veins. ¹⁹ The diagnosis of DVT was confirmed if there was incompressibility of the vein. Only clots ≥5-mm in diameter on US were considered as distal DVT. ^{3,20} The diagnosis of PE was confirmed according to the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) criteria and after validation by an independent expert committee. ^{21,22} This study only took into account the 725 patients exhibiting a symptomatic isolated MCVT or a symptomatic isolated DCVT of lower limbs.

Study protocol. At inclusion, all demographic characteristics, clinical data, and diagnostic test results were prospectively collected by the vascular medicine physician. At 3 months, patients were asked by phone by clinical research associates to disclose all health-related events since inclusion. The general practitioner or the vascular medicine physician was contacted whenever a possible event was disclosed, and medical records were reviewed in case of hospitalization or a new visit to the vascular physician during this follow-up period. Routine follow-up US examinations were not performed. For practical reasons, patients enrolled in overseas territories, living outside of France, homeless, or for whom case report form completion was delayed were not eligible for follow-up.

Distal DVT. MCVT were classified in soleal or gastrocnemius DVT. DCVT were classified in tibial posterior (or anterior), peroneal, and calf trifurcation DVT. Because the reported rate of tibial anterior DVT is very low (<1% of all distal DVT), tibial anterior DVTs were classified among tibial posterior DVTs.^{3,5} To have the most homogeneous groups of distal DVTs as possible, the study excluded 208 combined MCVT and DCVT (22.3% of all isolated distal DVT).

Clinical symptoms at presentation. The clinical symptoms of screened DVT were swelling, dull or localized pain, and warmth of the lower limb. The Wells clinical pretest probability score was calculated for each patient.²³

Risk factors. The influence of the following potential risk factors for DVT was analyzed: age, sex, inpatient or outpatient status, and anticoagulant treatment at inclusion. Chronic risk factors for DVT studied were a personal or a family history of VTE of any kind, active cancer, varicose veins (CEAP ≥ 2), estrogen therapy within the last 2 months, and obesity (body mass index $\geq 30 \text{ kg/m}^2$). Transient risk factors analyzed were bed confinement, recent plaster immobilization of the lower extremities, recent travel (ie, travel > 3 hours in the last month), surgery within the previous 45 days, congestive heart failure (New York Heart Association class III or IV) or respiratory insufficiency (acute respiratory failure or exacerbation of chronic obstructive pulmonary disease), infectious disease, and pregnancy or recent childbirth (ie, early postpartum, <6 weeks). For each kind of DVT, comorbidities of the patients were estimated according to their Charlson index score.24

Study outcomes. The study outcomes were recurrent VTE (PE or DVT), major bleeding, and overall mortality at 3 months. If a recurrent DVT was suspected, a complete US examination of the lower limb was performed. The

diagnosis was confirmed in case of noncompressibility of a previously normal venous segment or of an enlargement of thrombus thickness ≥ 2 mm. Major bleeding episodes were fatal bleeding and overt bleeding within a critical organ (eg, intracranial, retroperitoneal, intraocular, pericardial, intraspinal, or in the adrenal glands) or associated with a fall in hemoglobin level ≥ 2 g/dL, or leading to a transfusion ≥ 2 units of packed red blood cells or whole blood. An independent expert committee adjudicated all the clinical outcomes.

Statistical analysis. Categoric variables are expressed as frequency and percentage; continuous variables are expressed as median and range. In univariate analyses, potential risk factors for VTE and 3-month outcomes were estimated using a χ^2 test for categoric variables or a Fisher test when the theoretic size of a group was <5, and the t test was used for continuous variables. A multivariate logistic regression was performed to estimate the adjusted odds ratios (OR) and corresponding 95% confidence interval (CI) associated with each risk factor for MCVT and DCVT. The independent covariates entered into the logistic regression models included age, sex, risk factors for VTE, inpatient vs outpatient status, and the use of anticoagulant therapies at the time of enrollment.

Cox models were performed to evaluate the influence of MCVT and DCVT on the occurrence of each 3-month clinical outcome. The independent covariates entered into the Cox models included age, sex, inpatient vs outpatient status, and anticoagulant therapy duration. In our multivariate analyses, we systematically assessed all first-order interactions involving the inpatient vs outpatient status. To account for patient clustering within enrolling physician practices, random intercept logistic regression models with the two levels defined by patient and physician were used. Two-sided values of $P \le 0.05$ were considered statistically significant. Statistical analyses were performed using Stata 10.0 software (Stata Corp, College Station, Texas).

RESULTS

Population characteristics. Of 725 patients with an isolated distal DVT of the lower limbs, 268 (37.0%) presented with a DCVT and 457 (63.0%) with a MCVT (Fig, Table I). Patients were a median age of 61 years (full range, 18-97), 42.2% were men, and 25.4% were inpatients.

Characteristics of isolated distal DVT at diagnosis. Among the 268 DCVT, 40 (14.9%) affected the calf trifurcation, 115 (42.9%) the posterior tibial veins, and 113 (42.2%) the peroneal veins. Ten (3.7%) affected both legs. Among the 457 patients with isolated MCVT, 250 (54.7%) presented a soleal DVT and 207 (45.3%) a gastrocnemius DVT. In 29 (6.3%), MCVT were bilateral. MCVT and DCVT exhibited a similar diameter of clot under compression on US (6.4 vs 6.1 mm, respectively; P = .16 respectively).

Clinical presentation at diagnosis. Localized pain was significantly more frequent in case of MCVT (30.4% vs 22.4%, P = .02), whereas in case of DCVT, higher frequency was found for swelling (62.7% vs 47.9%, P < .001)

Table I. Patient characteristics at baseline and risk factors for isolated muscular calf vein thrombosis (MCVT) vs isolated deep calf vein thrombosis (DCVT) by univariate and multivariate analyses

Characteristics	DCVT	MCVT	DCVT vs MCVT OR 95% [CI]
Patients, No.	268	457	
Age, median (IQR), y	61 (18-97)	62 (18-97)	
Age class, No. (%)	, ,	, ,	
≤50 years	83 (31.0)	137 (30.0)	Ref
51-75 years	130 (48.5)	210 (46.0)	1.20 [0.78-1.87]
>75 years	55 (20.5)	110 (24.1)	1.19 [0.69-2.04]
Men, No. (%)	115 (42.9)	191 (41.8)	1.11 [0.78-1.58]
Inpatients, No. (%)	70 (26.1)	114 (24.9)	1.13 [0.70-1.84]
Anticoagulant treatment, No. (%)	62 (23.1)	103 (22.5)	0.82 [0.51-1.31]
Risk factors for venous thromboembolism	, ,	, ,	
Transient risk factors, No. (%)			
Bed confinement	40 (14.9)	85 (18.6)	0.76 [0.46-1.24]
Recent plaster immobilization of lower limb(s)	28 (10.4)	$31(6.8)^{a}$	1.86 [0.98-3.53]
Recent travel	18 (6.7)	27 (5.9)	1.36 [0.67-2.73]
Recent surgery (≤45 days)	61 (22.8)	78 (17.1) ^a	1.70 [1.06-2.75]
CHF or respiratory insufficiency	8 (3.0)	21 (4.6)	0.70 [0.28-1.75]
Acute infectious disease, n (%)	2 (0.7)	6(1.3)	0.82 [0.14-4.75]
Pregnancy or postpartum <6 weeks	4 (1.5)	4 (0.9)	2.38 [0.48-11.74]
Chronic risk factors, No. (%)	, ,	, ,	
Personal history of DVT or PE	84 (31.3)	144 (31.5)	1.07 [0.73-1.57]
Family history of DVT or PE	55 (20.5)	86 (18.8)	1.13 [0.74-1.75]
Active cancer	32 (11.9)	49 (10.7)	1.16 [0.68-1.96]
Varicose veins	64 (23.9)	121 (26.5)	0.90 [0.60-1.36]
Oral contraception	18 (6.7)	26 (5.7)	1.13 [0.51-2.49]
Hormone replacement therapy	9 (3.4)	6 (1.3) ^a	2.82 [0.89-8.96]
Obesity (BMI $> 30 \text{ kg/m}^2$)	31 (11.6)	59 (12.9)	0.91 [0.54-1.52]

BMI, Body mass index; CHF, congestive heart failure; CI, confidence interval; DVT, deep vein thrombosis; IQR, interquartile; OR, odds ratio; PE, pulmonary embolism.

and a high pretest Wells probability score (ie, >2; (50.8% vs 41.2%, P = .01). There was no difference between MCVT and DCVT in warmth (16.2% vs 17.2%, P = .7) and dull pain (70.5% vs 67.9%, P = .47). There was no difference in time lag between the onset of symptoms and the realization of the complete US examination between MCVT and DCVT (5.8 vs 5.0 days, P = .09).

Risk factors for DVT at diagnosis. Risk factors are reported in Table I. Of the isolated DCVT, 7.5% were idiopathic, as were 11.2% of the isolated MCVT. Univariate analysis identified no significant difference in the risk factors profile between MCVT and DCVT. Multivariate analysis only evidenced that recent surgery was significantly more associated with DCVT (OR, 1.70; 95% CI, 1.06-2.75; P = .03). Compared to unilateral MCVT, bilateral MCVT were significantly and independently more associated with active cancer (OR, 4,6; 95% CI, 1.7-12.4) and age >75 years (OR, 25.3; 95% CI, 3.1-207.9). The number of bilateral DCVT was too small to perform a comparison of risk factor profile with unilateral DCVT.

Charlson index. There was no difference in comorbidities: 69.1% of MCVT patients and 70.5% of DCVT patients had no comorbidity (Charlson, 0), and 16% in both groups had two or more comorbidities.

Three-month outcomes. Among the 222 DCVT and 390 MCVT with follow-up data at 3 months, there was no

Table II. Clinical outcomes at 3 months in patients with isolated muscular calf deep vein thrombosis (MCVT) vs isolated deep calf vein thrombosis (DCVT) by univariate and multivariate analyses

Outcome	DCVT $(n = 222)$ $No. (%)$	MCVT $(n = 390)$ $No. (%)$	DCVT vs MCVT OR (95% CI)
Death Recurrent VTE Major bleeding	9 (4.1) 3 (1.4) 1 (0.5)	15 (3.8) 6 (1.5) 0 (0)	0.98 (0.24-4.11) 0.98 (0.24-4.11)

CI, Confidence interval; OR, odds ratio; VTE, venous thromboembolism.

difference in death, VTE recurrence, and major bleeding between MCVT and DCVT (Table II). Idiopathic MCVT and DCVT 3-month outcomes did not differ from that of MCVT and DCVT associated with a transient or a chronic risk factor for VTE (data not shown). The 29 bilateral MCVT patients exhibited a 17.4% risk of dying at 3 months vs 3.0% for unilateral MCVT patients (P = .008). The independent expert committee validated all declared deaths, 69% of declared VTE recurrence, and 33% of declared major bleedings.

Causes of death. The rate of death by PE, bleeding, and cancer was the same between MCVT and DCVT patients (Table III).

 $^{^{}a}P \le .10$ in patients with deep calf DVT vs muscular calf DVT (no $P \le .05$).

Table III. Causes of death at 3 months of patients with isolated distal deep vein thrombosis

Cause	DCVT (n = 222) No. (%)	MCVT (n = 390) No. (%)
Total death Pulmonary embolism Bleeding Cancer Other	9 (4.1) 2 (0.9) 0 (0) 4 (1.8) 3 (1.4)	15 (3.8) 2 (0.5) 0 (0) 7 (1.8) 6 (1.5)

DCVT, Deep calf vein thrombosis; MCVT, muscular calf deep vein thrombosis.

Table IV. Anticoagulant treatment received, according to the location of the distal deep vein thrombosis

Variable	DCVT No. (%)	MCVT No. (%)
No treatment	8 (3.6)	14 (3.6)
LMWH only	18 (8.4)	53 (14.1)
Prophylactic regimen	1 (5.6)	1 (1.9)
Full therapeutic dose	17 (94.4)	49 (92.5)
Unknown dose		3 (5.7)
LMWH + VKA	191 (89.3)	312 (83.0)
Unknown anticoagulant	5 (2.3)	11 (2.9)

DCVT, Deep calf vein thrombosis; LMWH, low-molecular-weight heparin; MCVT, muscular calf deep vein thrombosis; VKA, vitamin K antagonist.

Anticoagulant treatment. No anticoagulant therapy was administered to 3.6% of patients in both groups. DCVT patients were treated significantly longer, 86.5% of DCVT and 76.7% of MCVT were treated during the entire 3-month follow-up (P = .0031, Table IV).

DISCUSSION

This study's primary result is that MCVT and DCVT exhibit the same risk factors profile and Charlson index, suggesting that they affect the same patient population. Furthermore, under anticoagulant treatment, their prognosis was similar at 3 months.

In a previous analysis of the OPTIMEV study and in the Registro Informatizado de la Enfermedad Tromboembólica (RIETE) registry, we evidenced that according to their proximal or distal level, isolated symptomatic DVT of the lower limbs shared the same risk factors, but the weight of these risk factors was different. 15,16 Indeed, isolated distal DVT was more strongly associated with transient risk factors, whereas proximal DVT was more associated with chronic states. This could suggest that the population profile might vary according to the level of the symptomatic isolated DVT. This may at least partly explain why if one assumes that most DVTs originate in the muscle calf veins, only a limited number will extend at a more proximal level.²⁵ Our results, however, demonstrate that these two populations of isolated distal DVT are strictly comparable in risk factors and comorbidities. In contrast to McDonald et al, 13 who evidenced that active cancer was associated with a significant risk of extension of MCVT to DCVT, we could not determine any clinical characteristics more associated with DCVT and thus acting as a potential provider for proximal extension of MCVT. ¹³ Our short time lag of 5.3 days (equivalent between MCVT and DCVT) between the onset of symptoms and the realization of the CUS examination—and therefore the initiation of the anticoagulant treatment—may explain this absence of difference.

This similar population profile and the fact that most patients were treated with anticoagulant therapy probably explain why the 3-month clinical outcomes did not significantly differ between MCVT and DCVT, whatever the kind of outcome considered. The profile of causes of death was also equivalent, with similar rates of deaths by cancer (1.8% for both), PE (0.5% vs 0.9%, respectively), and bleeding (0% for both). However, 3 months is probably too short to evaluate difference in terms of mortality and VTE recurrence rates. Nevertheless, this time lag was sufficient to evidence a more severe prognosis for bilateral MCVT, with a 3-month patient fatality rate of 17.4% (relative risk, 5.8; 95% CI, 2.0-16.8), even greater than the 6.1% rate for unilateral proximal DVT (relative risk, 2.9; 95% CI, 1.1-7.4). 15 This suggests that those DVT should probably at least be diagnosed to evidence a population at high risk, as previously described for bilateral proximal and distal DVT. 15,26

Finally, MCVT and DCVT differ in terms of clinical presentation. Indeed, MCVTs that were more superficial were more associated with local symptoms (local pain), whereas DCVT were more associated with general symptoms, with swelling, and with positive pretest probability.

Our study presents a number of strengths and limitations. Among the strengths, the large number of DVT included (725 distal DVT) should be pointed out. The proportion of isolated distal DVT (56.3% of all DVT), 3,4,6,7,19 isolated MCVT (49% of all distal DVT), 3,5,7 and soleal DVT (54.7% of MCVT)^{5,27} is consistent with that of previous studies. Our DVT populations were homogeneous because we restricted our analysis to isolated symptomatic MCVT and DCVT, excluding asymptomatic DVT, joint MCVT and DCVT, distal DVT with proximal extension, and PE.

Among the limitations of our study, we cannot exclude that some distal DVT were misclassified. Indeed, Schwarz et al²⁸ demonstrated that the interobserver agreement decreases the further distal one goes. However, our CUS examinations were all performed by well-trained vascular medicine physicians according to a rigorous protocol and all regularly attended Société Française de Médecine Vasculaire (SFMV) continuous medical education programs.

In OPTIMEV, the 3-month thromboembolic risk in case of the first negative CUS examination was as low as 0.8% (15 of 1756), evidencing the safety of the procedure to exclude DVT. ^{17,18} Finally, as stated by Schellong et al,^{2,19} after 200 supervised CUS examinations, such an exploration is not more error prone than other vascular ultrasound procedures. Furthermore, the protocol stipulated that only clots with a diameter under compression on US of 5-mm or more were considered as significant, which reduces the risk of false-positive examination results and the risk of misclassification. However, in 55 cases, clots with a

diameter under compression of 4 mm were classified as distal DVT (31 DCVT, 24 MCVT) by the vascular medicine physician who performed the US examination (protocol violation). Because their management and outcomes were equivalent to that of clots >5 mm and they represented <10% of all distal DVT, we kept them in the analysis. We do not have the information on the management and outcomes of smaller clots because the diameter under compression was reported in the case report form only in the event of a positive US examination result.

The reliability of the outcome data may have been impaired by the lack of medical visits, although every event suspected by phone screening was confirmed by a medical record. We may also have missed a significant difference in terms of VTE recurrence or of PE between those DVT, because most patients were receiving anticoagulant treatment during the entire follow-up, DCVT being treated slightly but significantly longer than MCVT. MCVT and DCVT natural history are not assessable in this context. Two recent observational studies reported higher rates of VTE recurrence, but the context was different, with a longer follow-up and either a high proportion of lost to follow-up (>50%) or a significantly higher proportion of history of DVT among DVT patients. 27,29

CONCLUSIONS

The present results showed that isolated symptomatic MCVT and DCVT populations exhibit different clinical symptoms at presentation but affect the same population, with the same early outcome. In this context we can hypothesize, that under anticoagulant treatment and in the short term, isolated distal DVT constitute a homogeneous entity. If bilateral MCVT prognosis was found to be severe, probably justifying the detection of MCVT, this leaves open the key question of up to which level of distality it is necessary to treat lower limbs DVT with anticoagulant drugs. The ongoing Contention alone versus Anticoagulation for symptomatic Calf vein Thrombosis diagnosed by UltraSonography (CACTUS) study (NCT00539058) may therefore provide important elements of clarification thanks to subgroups analyses according to the muscular or deep calf vein location of the thrombus.

We are indebted to Carole Rolland for data management; Catherine Blanie, Maryline Blanc, Marion Proust, Sandrine Massicot, Ludovic Delhomme, Cathy Maillard, and Caroline Bonnet for data monitoring and patient follow-up, and Dominique Brisot, for his careful critical revision of the manuscript.

AUTHOR CONTRIBUTIONS

Conception and design: MS, JB, IQ Analysis and interpretation: JG, CG, JB, IQ Data collection: JG, MS, CG, JL, VZ, JB

Writing the article: JG

Critical revision of the article: JG, MS, CG, JL, VZ, JB, IQ Final approval of the article: JG, MS, CG, JL, VZ, JB, IQ

Statistical analysis: JG, CG, JB

Obtained funding: MS, JL, JB, IQ Overall responsibility: JG

REFERENCES

- Caggiati A, Bergan JJ, Gloviczki P, Eklof B, Allegra C, Partsch H; International Interdisciplinary Consensus Committee on Venous Anatomical Terminology. Nomenclature of the veins of the lower limb: extensions, refinements, and clinical application. J Vasc Surg 2005;41: 719-24.
- Schellong SM. Distal DVT: worth diagnosing? Yes. J Thromb Haemost 2007;5:S51-4.
- Righini M, Le Gal G, Aujesky D, Roy PM, Sanchez O, Verschuren F, et al. Complete venous ultrasound in outpatients with suspected pulmonary embolism. J Thromb Haemost 2009;7:406-12.
- Righini M. Is it worth diagnosing and treating distal deep vein thrombosis? No. J Thromb Haemost 2007;5:S55-9.
- Labropoulos N, Webb KM, Kang SS, Mansour MA, Filliung DR, Size GP, et al. Patterns and distribution of isolated calf deep vein thrombosis. J Vasc Surg 1999;30:787-91.
- Righini M, Paris S, Le Gal G, Laroche JP, Perrier A, Bounameaux H. Clinical relevance of distal deep vein thrombosis. Review of literature data. Thromb Haemost 2006;95:56-64.
- 7. Schellong SM, Schwarz T, Halbritter K, Beyer J, Siegert G, Oettler W, et al. Complete compression ultrasonography of the leg veins as a single test for the diagnosis of deep vein thrombosis. Thromb Haemost 2003;89:228-34.
- 8. Kearon C, Kahn SR, Agnelli G, Goldhaber S, Raskob GE, Comerota A. Antithrombotic therapy for venous thromboembolic disease: American College of Chest Physicians evidence-based clinical practice guidelines. 8th Ed. Chest 2008;133:454-545.
- Nicolaides AN, Fareed J, Kakkar AK. Prevention and treatment of venous thromboembolism. International Consensus Statement. (Guidelines according to scientific evidence). Int Angiol 2006;25:101-61.
- Masuda EM, Kessler DM, Kistner RL, Eklof B, Sato DT. The natural history of calf vein thrombosis: lysis of thrombi and development of reflux. J Vasc Surg 1998;28:67-73; discussion 73-4.
- Lohr JM, James KV, Deshmukh RM, Hasselfeld KA. Allastair B. Karmody Award. Calf vein thrombi are not a benign finding. Am J Surg 1995;170:86-90.
- Lohr JM, Kerr TM, Lutter KS, Cranley RD, Spirtoff K, Cranley JJ. Lower extremity calf thrombosis: to treat or not to treat? J Vasc Surg 1991;14:618-23.
- MacDonald PS, Kahn SR, Miller N, Obrand D. Short-term natural history of isolated gastrocnemius and soleal vein thrombosis. J Vasc Surg 2003;37:523-7.
- Schwarz T, Schmidt B, Beyer J, Schellong SM. Therapy of isolated calf muscle vein thrombosis with low-molecular-weight heparin. Blood Coagul Fibrinolysis 2001;12:597-9.
- 15. Galanaud JP, Sevestre MA, Bosson JL, Laroche JP, Righini M, Brisot D, et al. Comparative study on risk factors and early outcome of symptomatic distal versus proximal deep-vein thrombosis: results from the OPTIMEV study. Thromb Haemost 2009;102:493-500.
- Galanaud JP, Quenet S, Rivron-Guillot K, Quere I, Sanchez Muñoz-Torrero JF, Tolosa C, et al. Comparison of the clinical history of symptomatic isolated distal deep-vein thrombosis versus proximal deepvein thrombosis in 11086 patients (RIETE registry). J Thromb Haemost 2009;7:2028-34
- Sevestre MA, Labarère J, Casez P, Bressollette L, Taiar M, Pernod G, et al. Accuracy of complete compression ultrasound in ruling out suspected deep venous thrombosis in the ambulatory setting. A prospective cohort study. Thromb Haemost 2009;102:166-72.
- Sevestre MA, Labarère J, Casez P, Bressollette L, Haddouche M, Pernod G, et al. Outcomes for Inpatients with Normal Findings on Whole-Leg Ultrasonography. A Multicenter Prospective Cohort Study. Am J Med 2010;123:158-65.
- 19. Elias A, Mallard L, Elias M, Alquier C, Guidolin F, Gauthier B, et al. A single complete ultrasound investigation of the venous network for the diagnostic management of patients with a clinically suspected first

- episode of deep venous thrombosis of the lower limbs. Thromb Haemost 2003;89:221-7.
- Bosson JL, Riachi M, Pichot O, Michoud E, Carpentier PH, Franco A. Diameters of acute proximal and distal deep venous thrombosis of the lower limbs. Int Angiol 1998;17:260-7.
- Stein PD, Fowler SE, Goodman LR, Gottschalk A, Hales CA, Hull RD, et al. For the PIOPED II Investigators. Multidetector computed tomography for acute pulmonary embolism. N Engl J Med 2006;354:2317-27.
- The PIOPED Investigators. Value of the ventilation/perfusion scan in acute pulmonary embolism. Results of the prospective investigation of pulmonary embolism diagnosis (PIOPED). JAMA 1990;263:2753-9.
- 23. Wells PS, Anderson DR, Bormanis J, Guy F, Mitchell M, Gray L, et al. Value of assessment of pretest probability of deep-vein thrombosis in clinical management. Lancet 1997;350:1795-8.
- D'Hoore W, Sicotte C, Tilquin C. Risk adjustment in outcome assessment: the Charlson comorbidity index. Methods Inf Med 1993;32:382-7.
- Kakkar VV, Howe CT, Flanc C, Clarke MB. Natural history of postoperative deep-vein thrombosis. Lancet 1969;2:230-2.

- Seinturier C, Bosson JL, Colonna M, Imbert B, Carpentier PH. Site and clinical outcome of deep vein thrombosis of the lower limbs: an epidemiological study. J Thromb Haemost 2005;3:1362-7.
- Gillet JL, Perrin MR, Allaert FA. Short-term and mid-term outcome of isolated symptomatic muscular calf vein thrombosis. J Vasc Surg 2007; 46:513-9
- Schwarz T, Schmidt B, Schmidt B, Schellong SM. Interobserver agreement of complete compression ultrasound for clinically suspected deep vein thrombosis. Clin Appl Thromb Hemost 2002;8:45-9.
- Lautz TB, Abbas F, Walsh SJ, Chow C, Amaranto DJ, Wang E, et al. Isolated gastrocnemius and soleal vein thrombosis: should these patients receive therapeutic anticoagulation? Ann Surg 2010;251:735-42.

Submitted Jan 11, 2010; accepted May 12, 2010.

Additional material for this article may be found online at www.jvascsurg.org.

REQUEST FOR SUBMISSION OF SURGICAL ETHICS CHALLENGES ARTICLES

The Editors invite submission of original articles for the Surgical Ethics Challenges section, following the general format established by Dr. James Jones in 2001. Readers have benefitted greatly from Dr. Jones' monthly ethics contributions for more than 6 years. In order to encourage contributions, Dr. Jones will assist in editing them and will submit his own articles every other month, to provide opportunity for others. Please submit articles under the heading of "Ethics" using Editorial Manager, and follow the format established in previous issues.

APPENDIX (online only)

Expert Event Committee: Muriel Salvat, Christophe Seinturier, Gilles Pernod, José Labarère, Sandra David-Tchouda, Jacqueline Yver, Bernadette Satger, Anna Arslanian, Michele Fontaine, Olivier Pichot, Sophie Blaise, Mario Maufus, Marie-Agnès Ningres, Pierre Casez and Elodie Sellier.

Study Coordinating Center: Clinical Research Center, University Hospital, Grenoble, France.

OPTimisation de l'Interrogatoire dans l'évaluation du risque throMbo-Embolique Veineux (OPTIMEV) Société Française de Médecine Vasculaire (SFMV) investigators: BRESSOLLETTE Luc; DIARD Antoine; LA-ROCHE Jean-Pierre; PARADIS Hélène; TAMBOSCO Anne; PAILLARD Odile; GRANGE Claire; LENOIR Florence; BOSSON Jean-Luc; GAILLARD Catherine; PI-CHOT Olivier; DUPAS Stéphane; ESCOFFIER Christian; MORZOL Bernard; BOSSELUT Jean-Louis; KUNTZ Paul Hervé; CAYMAN Richard; LELIMOUZIN Yann-Valéry; BAUD Jean-Michel; NEAUME Nicolas; KUBINA Jean-Manuel; FLAMBART Michèle; BET-TAREL-BINON Catherine; HAROCHE Frederic; HUGON Vincent; BERREMILI Toufek; SEINTURIER Christophe; DEHANT Véronique; COGET Philippe; DIAMAND Jean-Marc; MISEREY Gilles; BARRELLIER Marie Therese; LE ROUX Philippe; LANOYE Patrick; GENRE Olivier; DEGEILH Maryse; CONSTANS Joel; ROSET-CACCIUTTOLO Marie-Anne; ELHARAR BERGO Corinne; LE FRANCQ Véronique; DUC-MAUGE Christophe; PETIT Alain; BEYSSIER WEBER Laurence; TRIBOUT Bruno; LAMOUROUX Jean-Philippe; SPRYNGER Muriel; BAZZI Carole; CHAMU Pascale; LEBRUN Didier; MASSON-CALVAYRAC Dorothée; SCHENONE-WITMEYER Agnes; PONCHAUX-CREPIN Francine; THIEL Hélène; CARLO Christian; DURERO Sabine; TRAN VAN Stéphanie; BEQUEREL Christine; BUISSON-BRALY Sylvie; DARGAUD Yesim; NINET Jacques; VAUDAINE Myriam; MONSALLIER Jean-Michel; AUDIN Jean Pierre; TOFFIN Luc; ROGER Benoit; MARTIN Myriam; GINESTET AUGE Marie Christine; MARTIN-POULET Marie-Laure; LAUSECKER Michel; RAPONSKY Janellie; COLSON Didier; POIRAULT François; GROGNET-LENNE Bénédicte; PARES Georges; DUBOIS-PACQUE Nicole; PEAN Marie Françoise; GOY Pierre-François; MADEC-BOUGEARD Geneviève; FILALI Mounir; BRISOT Dominique; CANAPLE Mathias; ELBHAR Chantal; ROUS-SIN Yann; QUASHIE Constant; COUPE Marlène; PENET Bertrand; DADON Michel; BARRIERE Jean Louis; DE HEREDIA Marie-Pierre; BUCCI François; DE HEREDIA François xavier; DUPREY Alain; VIARD Alain; DELTOMBE Bertrand; ROUYER Olivier; SAN-NIER Béatrice; RASTEL Didier; CUENOT Anne Marie; LAFFONT Joelle Yvette; COUZAN Serge; COLONNA Anne; COPPE Gérard; HECQUET Annie; DECAMPS LE CHEVOIR Joelle; VAVASSEUR Isabelle; CAPOU-LADE Philippe; CAZAILLON Sophie; ZECH-GELB Alexandra; DELHOUME LAJOIE Dominique; TOURVIE-

ILLE Isabelle; BAILLY Philippe; SOULIER-SOTTO Virginie: SAUVET OLIVIERO Michelle: GANICHOT Françoise; JURUS Christine; NEDEY Charles; TISSOT anne; GARNIER Florence; BARBE-ROTTIER Geneviève; THIOUB Cheikhou; GASPARINI Philippe; GASPA-RINI Géraldine; OUVRY Pierre; BOISSIER Christian; FEASSON Séverine; GOSSELIN Antoine; DEFOUIL-LOY Isabelle; KNAUER Vincent; TERRIAT Béatrice; SATGER Bernadette; YVER Jacqueline; FONTAINE Michelle; MAHOUX Delphine; BRYON Dominique; AVILES Christine; GERARD Jean Luc; HOGUIN Philippe; VAGLIO Jean-Pierre; LEFTHERIOTIS Georges; PERRIER Bruno; PETETIN Fabienne; MEXME Monique; PULCI Stéphane; NAZEYROLLAS LUPORSI Roselyne; BAUDOIN Patrice; BOUTAMI Caroline; TA-CHOT Yves; DE SEZE GODEFROY Isabelle; MARCH-AND Jean Marie; COUTURE-GERARDIN Dominique; CACAREIGT-BOURDENX Véronique; LECOCQ Jean Michel; DELATTRE Sylvie; QUERE Isabelle; BRAVETTI Gérard; GAGNIERE-MARSOIN Marie Christine; RACZKA MOREAU Véronique; CAZANAVE Alain; JEUFRAUX Anne; SABY Jean Claude; CAMUZAT Jean Patrice; DELHOUME Claudette; SASSIM-MAR-QUEZ Virginia; AIDANE Paul; FERAUD Brigitte; CHANTEREAU Philippe; HALLER Claude; THEBAUT Pascal; FESOLOWICZ Michel; GODILLON PRALO-RAN Odile; DESSIRIER Jean Bernard; TAIAR Mébarka; SADOUN Symon; MOLLET Sophie; MONNIN JAC-QUOT Anne; CHAMPION Olivier; DROUET Pascale; LEMOINE Jean François; VIARD Bertrand; RATTANI Samina; STIRNEMANN Christine; VINCENTI Marie Claude; PUGET Catherine; ZULTAK Bénédicte; DEU-DON Pascal; HALLIGON Jean; TERVER Isabelle; ZAP-PULLA Christine; CUMIN Marie Charlotte; ANTOINE Claude; BRACHET Agnes; BALOUL Fatsah; MARCY Laurent; ROCCA Daniel; PAVEC Eric; MOIRANT Cyrille; BUREAU DU COLOMBIER Pascale; BOYAD-JIAN Marie; BOUCHET Jacques; TONTI Franco; RIOM Hervé; HAIMOVICI Joseph; BOUCHER Martine; POU-MAREDE Dominique; LOUIS Patrick; LOUIS-VERG-ER-HIARD Stéphanie; RENAUT HOVASSE Hélène; LAMPEL Marion; DOUCHE Mostafa; MORIN Isabelle; RONCERAY Philippe; VERHULSEL Irene; BRUNEL Catherine; MATELOT Nicolas; GENAY Patrick; RICH-ARD Sylvie; BANNIER Annie; JEANTEUR GONZALEZ Laurence; AMARA Hamid; HANRION-DUVAL Jacqueline; MORET Laurence; RENAUDIN Jean Marc; BRI-ANT LEGER Christine; BRUN Monique; KISZELNIK Richard; BOIS JANICOT Dominique; STEINBACH Jean-Cristophe; MOLLARD Jean Marc; LEGARCON Patrice; MOUILLOT Eric; PORCENE Jean André; MUF-FET Muriel; LETURCQ Gérard; DEHAUT Saveria; VI-ONNET-FUASSET Michèle; LE GOFF Roger; LUREL Didier; CHANTREL Frédéric; JEANGEORGES Bernard; BOUTIN Jean Yves; BOSLER Frédéric; LAMAIZIERE Yves; WALTER Klaus; TARABAY Véronique; MERSEL Tahar; LUMINEAU GILBERT Valérie; QUEHE Philippe; LONG Anne; MEMETEAU Francois; CAILLARD

Philippe; LUCAS Joel; DANCHAUD Laurence; SCHMITT Cathie; LEGER Philippe; SICA Mario; LONDE Jean François; BALME Vincent; CAMINZULI Maryse; VILLEMUR Beatrice; IMBERT Bernard; CHEV-RIER Elisabeth; PAOLI-CAZANAVE Géraldine; CA-DENE Agnes; POGGI Jean Noël; DEFIVES Brigitte; REIGNIEZ Christel; SALAMA Corinne; GUILHEM CANTALA Nathalie; BALDASSINI-ESQUIS Anne laure; PHILIPPE Regis; ROULLET Jean-claude; LEGA-GNEUX Annie; LEGAGNEUX Michel; LE BESCOND Danièle; TRAN BARBIER Claudine; DELANNOY Raynald; PIERRU Marie Christine; CARRIERE Philippe; CHARREYRON Christine; GARBIT Christine; LEM-OUSSU Nicolas; VAUTARD VIGAN Danielle; DAUS-SIN Jean Luc; DE MIRMAN Christophe; DE LA LANCE Marie Noëlle; YVORRA Hubert; BRUCKERT Geneviève; CHASTAGNER Catherine; BLAISE Sophie; MA-ZLOUM Wassim; CAILLARD Philippe; SIMON MO-MEGE Béatrice; SEVESTRE Marie Antoinette; BEN-SOUSSAN Léon Claude; MARTINOT Pierre; PERRIN Anne Marie; INVERNIZZI Claudine; ALAN Claude; BE-NARD NUBER Alix; BAIETTO Marina; MEICLER Pascal; GILBERT Pascale; NGUYEN VAN Valérie; VALLE-CALLE SHINTU Annie; DEMIOT Bernard; PARPEIX Valérie; TOUCHARD Didier; HILTBRAND Bernard; JOUBIN Elisabeth; BAUVIN GOASGUEN Nathalie; GAUTIER Hubert; AGACHE Aude; POULAIN VEYRE Corinne; BENOIT Hervé; AUGUSTE Ingrid; GARCIA SERRANO Adeline; FRECHINOS Christian; DUTAR-TRE Thierry; GIORDANA Pascal; DUMESNIL Didier; ZIZKA Violaine; WEIBEL SHAH Stephan; DUFRESNE DE VIREL Claire; ISCOVICI Xavier; DAMOUR Jean François; HUSSON Catherine; DUMONT Gerard; JOUEN Eric; WALLON Paul; LEHODEY Yves; CHA-BOD Christiane; SANTACREU Manuela; SEILLER Christian; ROCCHI Jean Paul; CUSTOZA Emmanuel; CUEFF Christine; FAVA Paul; CHOQUENET Clarisse; HELEINE Patrick; SAINT CYR Charles; BOULANGER WEILL Jean Charles; MARIE Didier; BEAUGRAND Pascale; ROUSSIN PIGNEROL Isabelle; BRACON Jean Francois; TOUATI Natacha; BIRO Christine; AMRI Khalid; KELLER Anne; QUELLIER MOULIS Marianne; PURSER Christine; GILLET Jean Luc; FAïSSE Pascale; TAVEAU Jean François; SAADOUN Ange Marc; EID Antoine; KHARBOUTLI Laurence; SAÏDANI Sandrine; FERRE BONET David; ALLART Jean Dominique; MULLER Sebastien; MURAT Sandrine; VASSEUR Claire; HERCEK Muriel; OLIVE Karine; GADENNE Christine; CAMBOU Jean Pierre; DAVINROY Michel; DARIE Christian; STEIDEL Marie; POULAIN Caroline; and VESIN Claire.