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ORIGINAL ARTICLE

Differences in clinical presentation of deep vein thrombosis in men and women

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Summary. *Background:* As assessment of clinical pretest probability is the first step in the diagnostic evaluation of deep vein thrombosis (DVT), it is important to know if the clinical features of DVT are the same in men and women. *Objectives:* To compare the prevalence and clinical characteristics of DVT, and the accuracy of clinical pretest probability assessment, between men and women with suspected DVT. *Methods:* A retrospective analysis of individual patient data from three prospective studies by our group that evaluated diagnostic tests for a suspected first episode of DVT. Clinical characteristics, clinical pretest probability for DVT, and prevalence and extent of DVT was assessed in a total of 1838 outpatients. *Results:* The overall prevalence of DVT was higher in men than in women (14.4% vs. 9.4%) ($P = 0.001$). The prevalence of DVT was higher in men than in women who were categorized as having a clinical pretest probability that was low (6.9% vs. 3.5%; $P = 0.025$) or moderate (16.9% vs. 8.7%; $P = 0.04$), but similar in patients in the high category (40.2% vs. 44.0%; $P = 0.6$). In patients diagnosed with DVT, swelling of the entire leg occurred more often (41.5% vs. 15.7%; $P < 0.001$), and thrombosis was more extensive (involvement of both popliteal and common femoral veins in 47.9% vs. 21.6%), in women than in men. *Conclusions:* In outpatients with suspected DVT, the overall prevalence of thrombosis and the prevalence of thrombosis in those with a low or a moderate clinical pretest probability were higher in men than in women.

Keywords: clinical presentation, deep vein thrombosis, diagnosis, sex, pretest probability, Wells model.

Introduction

Venous thromboembolism constitutes a spectrum of disease that includes deep venous thrombosis (DVT) and pulmonary embolism. In the US over 200 000 new cases of venous thromboembolism are diagnosed each year, with an annual prevalence of about 1–2 per 1000 adults [1]. About half of these episodes are first episodes of DVT. Most studies have found a similar incidence of venous thromboembolism in men and women [2–5]. However, among patients younger than 40 years, in whom venous thromboembolism is generally uncommon, women may be affected more often than men [6]. Use of estrogen containing oral contraceptives and pregnancy may account for this difference [7]. Previous studies suggest that more women than men are investigated for DVT [8–17]. If DVT occurs with a similar prevalence in men and women, but more women are investigated for this condition, this suggests that the prevalence of DVT among investigated patients is lower in women than in men. Indirectly, a lower prevalence of DVT among women who are investigated would suggest that the clinical features of DVT differ between men and women. As clinical assessment of pretest probability is now considered the first step in the diagnostic evaluation of DVT, it is important to know if the clinical features of this condition are the same in men and women [18–20]. It is also important to know if patient sex influences the accuracy of clinical prediction rules that assess pretest probability for DVT.

We performed a retrospective analysis of individual patient data from three previously published studies by our group to evaluate the association between sex and clinical presentation of a first episode of DVT in the outpatient population [21–23]. We sought to answer four questions. (i) Is the prevalence of DVT the same in men and women who are referred for diagnostic testing? (ii) Is the side and extent of confirmed DVT the same in men and women? (iii) Are the clinical features of DVT the same in men and women? (iv) Is the accuracy of clinical pretest probability assessment similar in men and women?

Methods

Data sources

Patients participated in three prospective studies conducted in Hamilton, ON, Canada, that evaluated combinations of clinical assessment of probability of DVT, D-dimer testing,

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compression ultrasonography, impedance plethysmography and/or venography for the management of outpatients with a first suspected DVT [21–23]. All three studies were approved by the Research Ethics Board and participants provided written informed consent.

In the study by Kearon and colleagues published in 2001, all patients had the Wells clinical prediction rule performed but physicians were allowed to override this prediction rule when categorizing clinical pretest probability as low, moderate or high [21]. All patients also had a red blood cell agglutination D-dimer test. Patients with a low clinical pretest probability and a negative D-dimer test were considered to have had DVT excluded and underwent no further diagnostic testing. All other patients had compression ultrasonography of the proximal veins and impedance plethysmography, which were repeated after 1 and 2 weeks if the two tests were normal. Venography was performed if the results of impedance plethysmography and compression ultrasonography differed or if both tests were negative and patients had a high pretest probability and a positive D-dimer result [21].

In the study by Bates and colleagues published in 2003, all patients were categorized as having low, moderate or high clinical pretest probability of thrombosis using the Wells clinical prediction rule and had testing using a quantitative immunoturbidometric D-dimer test [22]. Patients with a low or moderate clinical pretest probability and a negative D-dimer test were considered to have had DVT excluded and had no further diagnostic testing (the side of suspected DVT was not available for this subset of patients). All other patients underwent compression ultrasonography of the proximal veins, which was repeated after 1 and 2 weeks if the initial test was negative [22].

In the study by Kearon and colleagues published in 2005, all patients had compression ultrasonography of the proximal deep veins [23]. If DVT was not diagnosed, patients were randomized to management based on D-dimer testing or to have repeat ultrasonography after 1 week. With D-dimer based management, patients with a negative D-dimer test had no further testing and patients with a positive test underwent venography to establish a definitive diagnosis. All patients underwent clinical pretest probability assessment using the Wells model; however, clinical pretest probability did not influence patient management in this study [23].

In all three studies, compression ultrasonography involved an assessment of compressibility of the deep veins from the common femoral vein down to and including the calf vein trifurcation. Patients not diagnosed with DVT by initial or follow-up compression ultrasound or by venography did not receive anticoagulant therapy and were followed prospectively for at least 3 months for development of venous thromboembolism. Pregnant women were excluded from all three studies.

Data abstraction and outcomes

To minimize bias, *a priori* criteria were used for data retrieval and analysis. In order to be included in the current analysis, there had to be documentation that patients had, or did not have, DVT diagnosed at initial presentation. Diagnosis of DVT required non-compressibility of the proximal deep veins or calf vein trifurcation on compression ultrasonography or an intraluminal filling defect of the proximal or distal veins on venography. Patients who were not diagnosed with deep venous thrombosis at presentation but who had deep venous thrombosis at follow-up were excluded from the analysis because it was uncertain if these patients had DVT at initial presentation.

When possible, the following information at the time of initial presentation was abstracted for each patient: age, sex, presence of cancer, components of the Wells clinical pretest probability model (presence or absence of: paralysis, paresis, or recent use of a plaster cast; bedridden for more than 3 days or major surgery within 4 weeks; tenderness of the deep veins; swelling of the entire leg; calf swelling of greater than 3 cm compared with the other leg; pitting edema; dilated superficial veins; an alternate diagnosis as likely as DVT), pretest probability category as assigned in the original study (low, moderate, high), presence of DVT, location of DVT (right, left, both), extent of DVT, and duration of symptoms. Extent of DVT was categorized as involvement of the common femoral vein, involvement of the popliteal or trifurcation veins, or involvement of both of these venous segments.

Statistical analysis

Statistical analysis is based on pooled individual subject data from the three previously noted studies [21–23]. Percentages were used to describe categorical variables, while means, standard deviations, medians and quartiles were used to describe continuous variables. Before analysis of pooled data, differences of proportions and means among the three studies were tested using chi-squared tests and analysis of variance; there were no statistically significant differences detected (Table 1).

Independent two-sample binomial tests for proportions and two-sample *t*-tests for means were used for comparisons of the characteristics of men and women with suspected DVT and of men and women diagnosed with DVT. To compare the demographic and clinical characteristics associated with deep vein thrombosis in men and women, univariate and multivariate logistic regression models were separately fitted for men and for women and odds ratios, with their corresponding 95% confidence intervals (95% CI), were calculated. A test for interaction was performed to compare odds ratios obtained in men and in women [24]. For all analyses, statistical significance was set at a two-sided 5% level ($P < 0.05$). Statistical analyses were performed using SAS version-9 for Windows (Cary, NC) and Minitab version-14 (State College, PA).

Results

Study population

A total of 1838 patients from the three studies were eligible for the current analysis. Baseline demographics and clinical

Table 1 Characteristics of subjects and prevalence of deep venous thrombosis in subjects with suspected deep vein thrombosis

Characteristic	Kearon *et al.* (2001)	Bates *et al.* (2003)	Kearon *et al.* (2005)	Three studies combined
Number of patients	429	550	859	1838
Age, mean (SD), years	61.5 (16.8)	62.0 (16.2)	60.2 (16.1)	61.0 (16.3)
Male	153 (35.7)	210 (38.2)	343 (39.9)	706 (38.4)
Duration of symptoms, days				
Mean (SD)	Not available	34.3 (238.8)	26.0 (96.2)	29.2 (167.0)
Median (lower, upper quartile)		8 (5, 21)	8 (4, 20)	8 (5, 21)
Cancer	47 (11.0)	50 (9.1)	75 (8.7)	172 (9.4)
Components of Wells model				
Paralysis/Plaster cast	12 (2.8)	12 (2.2)	32 (3.7)	56 (3.0)
Bedridden for 3 days	25 (5.8)	39 (7.1)	55 (6.4)	119 (6.5)
Tender veins	203 (47.3)	176 (32.0)	281 (32.7)	660 (35.9)
Entire leg swollen	30 (7.0)	83 (15.1)	98 (11.4)	211 (11.5)
Calf circumference increased >3 cm*	96 (22.4)	114 (20.7)	180 (20.9)	390 (21.2)
Pitting edema	87 (20.3)	251 (45.6)	227 (26.4)	565 (30.7)
Dilated superficial veins	33 (7.7)	28 (5.1)	37 (4.3)	98 (5.3)
Alternate diagnosis as likely	176 (41.0)	245 (44.6)	405 (47.2)	826 (44.9)
Clinical pretest probability				
Low	203 (47.3)	296 (53.8)	525 (61.1)	1024 (55.7)
Moderate	177 (41.3)	188 (34.2)	246 (28.6)	611 (33.2)
High	49 (11.4)	66 (12.0)	88 (10.2)	203 (11.0)
Prevalence of DVT according to clinical pretest probability				
All patients	61/429 (14.2)	55/550 (10.0)	92/859 (10.7)	208/1838 (11.3)
Low	13/203 (6.4)	17/296 (5.7)	19/525 (3.6)	49/1024 (4.8)
Moderate	23/177 (13.0)	17/188 (9.0)	33/246 (13.4)	73/611 (12.0)
High	25/49 (51.0)	21/66 (31.8)	40/88 (45.4)	86/203 (42.4)
Side of suspected DVT				
Right	194 (45.2)	115 (41.8)†	409 (47.6)	718 (45.9)
Left	225 (52.4)	118 (42.9)†	429 (49.9)	772 (49.4)
Both	10 (2.3)	42 (15.3)†	21 (2.4)	73 (4.7)
Extent of DVT				
Common femoral vein only	Not available	2 (0.4)	5 (0.6)	7 (0.5)
Popliteal/trifurcation veins only		36 (6.6)	37 (4.3)	73 (5.2)
Common femoral vein and popliteal/trifurcation veins		17 (3.1)	34 (4.0)	51 (3.6)
Isolated calf‡		Not tested	16 (1.9)	16 (1.1)

Data are presented as No. (%) unless otherwise indicated. DVT, deep vein thrombosis. *Compared with the opposite leg. †The side of the suspected DVT, which corresponds to the legs that were examined with ultrasonography, does not include the 275 patients who did not have ultrasonography because they had a low or moderate clinical pretest probability and a negative D-dimer test. ‡No study examined the deep veins of the calf with compression ultrasonography below the calf vein trifurcation. The study by Kearon *et al.* (2005) performed venography in patients randomized to receive D-dimer based management if there was no proximal deep vein thrombosis on ultrasound and the D-dimer test was positive.

characteristics of the patients included in each study were similar (Table 1).

Prevalence of DVT in men compared with women

Among patients who were referred for investigation, the prevalence of DVT was higher in men (14%) than in women (9%) ($P = 0.001$; Table 2).

Side and extent of DVT in men compared with women

DVT was located in the right leg only in 31% of men and in 41% of women ($P = 0.17$; Table 3), and was in the left leg only in 61% of men and 55% of women ($P = 0.19$; Table 3). DVT was bilateral in 8% of men and 8% of women ($P = 0.94$; Table 3). Therefore, DVT involved the left leg more often than the right leg in men (69% vs. 39%; $P < 0.001$) and in women (59% vs. 48%; $P = 0.10$), with no statistically significant difference between the sexes.

Of the confirmed episodes of DVT, both the common femoral vein and the popliteal or trifurcation veins were involved in 22% of men and 48% of women ($P < 0.001$; Table 3), the common femoral vein only was involved in 5% of men and 4% of women ($P = 0.71$; Table 3), and the popliteal or trifurcation veins only were involved in 65% of men and 34% of women ($P = 0.001$; Table 3). Therefore, women had more extensive DVT than men.

Clinical features of DVT at presentation in men compared with women

Among patients with confirmed DVT, clinical characteristics were similar in men and women except that 'entire leg swollen' was noted more often in women (41%) than in men (16%) ($P < 0.001$; Table 3). In order to try and explain why more

Table 2 Comparison of men and women with suspected deep venous thrombosis

Characteristic	Men (n = 706)	Women (n = 1132)	P value
Age, mean (SD), years	61.4 (15.7)	60.8 (16.6)	0.41
Duration of symptoms, days			
Mean (SD)	19.6 (49.1)	35.4 (210.4)	0.05
Median (lower, upper quartile)	8 (5, 16)	8 (4, 22)	
Side of suspected DVT			
Right	299/616 (48.5)	419/947 (44.2)	0.10
Left	291/616 (47.2)	481/947 (50.7)	0.17
Both	26/616 (4.2)	47/947 (5.0)	0.49
Cancer	66 (9.3)	106 (9.4)	0.99
Components of Wells model			
Paralysis/Plaster cast	28 (4.0)	28 (2.5)	0.09
Bedridden for 3 days	47 (6.7)	72 (6.4)	0.80
Tender veins	244 (34.6)	416 (36.7)	0.34
Entire leg swollen	80 (11.3)	131 (11.6)	0.87
Calf circumference increased >3 cm*	189 (26.8)	201 (17.7)	<0.001
Pitting edema	269 (38.1)	296 (26.1)	<0.001
Dilated superficial veins	34 (4.8)	64 (5.7)	0.43
Alternate diagnosis as likely	336 (47.6)	490 (43.3)	0.07
Clinical pretest probability			
Low	376 (53.3)	648 (57.2)	0.09
Moderate	243 (34.4)	368 (32.5)	0.4
High	87 (12.3)	116 (10.2)	0.18
Prevalence of DVT according to clinical probability			
All patients	102/706 (14.4)	106/1132 (9.4)	0.001
Low	26/376 (6.9)	23/648 (3.5)	0.025
Moderate	41/243 (16.8)	32/368 (8.7)	0.004
High	35/87 (40.2)	51/116 (44.0)	0.59

Data are presented as No. (%) unless otherwise indicated. DVT, deep vein thrombosis. *Compared with the opposite leg.

women than men with DVT were noted to have 'entire leg swollen', we compared the prevalence of this observation in patients who had DVT involving the femoral veins (common femoral vein only or common femoral vein and popliteal/trifurcation veins) with those who had DVT confined only to the more distal veins (popliteal/trifurcation veins or the calf veins). In men and women combined, there was a higher prevalence of 'entire leg swollen' among patients with femoral DVT (59%; 34/58) compared with those with more distal DVT (15%; 13/89) ($P < 0.001$). Among patients who had involvement of the femoral vein, the prevalence of 'entire leg swollen' was higher in women (71%; 27/38) than in men (35%; 7/20) ($P = 0.005$) Among patients who only had involvement of the more distal veins the prevalence of 'entire leg swollen' was also higher in women (23%; 8/35) than in men (9%; 5/54) ($P = 0.09$). Therefore, although a higher prevalence of entire leg swelling in women with DVT was partly accounted for by more extensive disease in women (i.e. involvement of the common femoral vein), swelling of the entire leg was more common in women even when the extent of thrombosis was similar in men and women.

Accuracy of pretest probability assessment in men compared with women

Among patients who were categorized as having a low clinical probability, the prevalence of confirmed DVT was higher in men (7%) than in women (4%) ($P = 0.025$; Table 2). Similarly, among those who were categorized as having a moderate clinical probability, the prevalence of confirmed DVT was higher in men (17%) than in women (9%) ($P = 0.004$, Table 2). However, the prevalence of DVT was similar in men (40%) and women (44%) who were categorized as having a high clinical pretest probability ($P = 0.59$; Table 2).

Predictors of the presence of DVT in men and women

Univariable and multivariable analyses were performed to determine if clinical characteristics and components of the Wells model discriminated between patients with, and without, DVT similarly in men and women. Univariable analysis suggested that age over 60 years, entire leg swollen, calf swelling, pitting edema, and having been bedridden, were more strongly associated with the presence of DVT in women than in men who were referred for diagnostic testing (Table 4). Conversely, swelling of the left leg was more strongly associated with DVT in men than in women (Table 4). In a multivariable model that included the nine elements of the Wells model (Table 4), age, duration of symptoms and sex, male sex was independently associated with a higher prevalence of DVT (odds ratio 1.5; 95% CI 1.1–2.1).

Discussion

We found that the overall prevalence of DVT was about 50% higher in men than in women who were referred for diagnostic

Table 3 Comparison of men and women with deep venous thrombosis

Characteristic	Men (n = 102)	Women (n = 106)	P value
Age, mean (SD), years	61.0 (13.7)	64.9 (16.1)	0.06
Duration of symptoms, days			
Mean (SD)	16.0 (35.7)	9.4 (11.0)	0.07
Median (lower, upper quartile)	6.50 (5, 14)	7.00 (4, 8)	
Cancer	25 (24.5)	39 (36.8)	0.05
Components of Wells model			
Paralysis/Plaster cast	7 (6.9)	6 (5.7)	0.72
Bedridden for 3 days	9 (8.8)	18 (17.0)	0.08
Tender veins	55 (53.9)	52 (49.1)	0.48
Entire leg swollen	16 (15.7)	44 (41.5)	< 0.001
Calf circumference increased 3 cm[†]	48 (47.1)	60 (56.6)	0.17
Pitting edema	52 (51.0)	60 (56.6)	0.42
Dilated superficial veins	9 (8.8)	12 (11.3)	0.55
Alternate diagnosis as likely	24 (23.5)	24 (22.6)	0.88
Clinical pretest probability			
Low	26 (25.5)	23 (21.7)	0.52
Moderate	41 (40.2)	32 (30.2)	0.13
High	35 (34.3)	51 (48.1)	0.04
Side of DVT			
Right	32 (31.4)	43 (40.6)	0.17
Left	62 (60.8)	55 (51.9)	0.19
Both	8 (7.8)	8 (7.6)	0.94
Extent of DVT			
Common femoral vein only	4/74 (5.4)	3/73 (4.1)	0.71
Popliteal/trifurcation veins only	48/74 (64.9)	25/73 (34.2)	< 0.001
Common femoral vein and popliteal/trifurcation veins	16/74 (21.6)	35/73 (48.0)	< 0.001
Isolated calf*	6/74 (8.1)	10/73 (13.7)	0.28

Data are presented as No. (%) unless otherwise indicated. DVT, deep vein thrombosis. [†]Compared with the opposite leg. *No study examined the deep veins of the calf with compression ultrasonography below the calf vein trifurcation. The study by Kearon *et al.* (2005) performed venography in patients randomized to receive D-dimer based management if there was no proximal deep vein thrombosis on ultrasound and the D-dimer test was positive.

Table 4 Predictors of the presence of deep venous thrombosis in men and women

	Men			Women			Interaction
Characteristic	DVT present (n = 102)	DVT absent (n = 604)	Odds ratio (95% CI)	DVT present (n = 106)	DVT absent (n = 1026)	Odds ratio (95% CI)	P value
Age > 60 years	54	340	0.87 (0.57–1.33)	72	556	1.79 (1.17–2.74)	0.02
Symptoms less than 8 days	26	237	1.89 (1.18–3.03)	18	393	3.03 (1.75–5.0)	0.19
Cancer	25	41	4.5 (2.57–7.74)	39	67	8.33 (5.23–13.28)	0.09
Components of Wells model							
Paralysis/Plaster	7	21	2.05 (0.85–4.94)	6	22	2.74 (1.08–6.91)	0.65
Bedridden	9	38	1.4 (0.67–3.08)	18	54	3.68 (2.07–6.55)	0.05
Tender veins	55	189	2.57 (1.68–3.93)	52	364	1.75 (1.17–2.62)	0.20
Entire leg swollen	16	64	1.57 (0.87–2.84)	44	87	7.66 (4.91–11.95)	< 0.001
Calf circumference increased 3 cm[†]	48	141	2.92 (1.89–4.50)	60	141	8.19 (5.36–12.50)	< 0.001
Pitting edema	52	217	1.85 (1.22–2.83)	60	236	4.36 (2.90–6.58)	0.004
Dilated superficial veins	9	25	2.24 (1.01–4.95)	12	52	2.39 (1.24–4.64)	0.90
Alternate diagnosis	24	312	0.29 (0.18–0.48)	24	466	0.35 (0.22–0.56)	0.56
Bilateral leg symptoms	8	18/514	2.35 (0.99–5.55)	8	39/841	1.68 (0.76–3.70)	0.57
Left leg symptoms	62	229/514	1.93 (1.25–2.98)	55	426/841	1.05 (0.70–1.57)	0.05

Univariable analyses are presented. Data are presented as No. (%) unless otherwise indicated. [†]Compared with the opposite leg.

testing. The clinical features of DVT also appeared to differ between men and women, with swelling of the entire leg occurring about three times as often in women with DVT compared with men. The higher frequency of entire leg swelling in women was partly explained by more extensive thrombosis in women than in men, with thrombosis involving the common femoral vein about twice as often in women. However, even among patients with a similar extent of thrombosis on

ultrasound, swelling of the entire leg occurred about twice as often in women. In keeping with the finding that clinical features differed between men and women with thrombosis, clinical assessment of pretest probability for DVT behaved differently between the sexes. The prevalence of DVT among patients who were categorized as having a low or moderate clinical pretest probability was about twice as high in men compared with women. If clinical pretest probability assessment had performed similarly in men and women, in parallel with the higher overall prevalence of DVT in men, a higher proportion of men would have had a high clinical pretest probability and a lower proportion would have had a low clinical pretest probability compared with women. This was not observed; the proportion of men and women with suspected DVT who were in each of the three categories was very similar. Consistent with our finding that clinical pretest probability assessment did not perform the same in men and women, the prevalence of DVT was still about 50% higher in males (OR 1.5; 95%CI 1.1–2.1) after adjusting for the nine components of the Wells model, age and duration of symptoms.

Few studies have compared the clinical characteristics of men and women with DVT. Consistent with our findings, Beebe and colleagues found that the prevalence of thrombosis was substantially higher in male than in female outpatients who were referred for diagnostic testing for DVT (14% vs. 9%; $P = 0.002$) [17] Among a mixture of outpatients and inpatients who were suspected of having DVT, Kahn and colleagues reported a higher prevalence of thrombosis among men than women and that this association was independent of other predictors in a multivariable regression model (odds ratio 2.8; 95% confidence interval 1.5–5.1) [25]. Among patients with suspected DVT seen by primary care physicians, Oudega and colleagues reported a higher prevalence of DVT in men than in women (37% vs. 25%; $P \leq 0.001$), and that male sex was a predictor of the presence of DVT (OR 1.9; 95% CI 1.2–2.7) independently of symptoms, signs and risk factors for venous thromboembolism [26]. This study, which was brought to our attention during peer-review of the current manuscript, reported that five clinical factors predicted the presence of DVT in both men and women, whereas age, surgery and pain when walking were only statistically significant in men, and malignancy, oral contraception and duration of symptoms were only significant in women (sex-specific odds ratios, and a comparison of such odds ratios between men and women, were not reported) [26]. Although it was not highlighted in the original publications, consistent with our findings, most studies that have evaluated diagnostic strategies for DVT in outpatients included many more women than men [8–11,13–16,27,28] and observed a substantially higher prevalence of thrombosis in the men than in women (only described in four studies) [10,11,14,26,27]. We know of no studies that have compared the anatomic extent, or the clinical features, of diagnosed DVT in men and women.

There is evidence that the natural history of venous thromboembolism may differ between men and women and, in particular, that men have a higher risk of recurrence after anticoagulant therapy is stopped [29]. Before we did this analysis, we speculated that men may experience more extensive DVT than women and that this difference might account for their higher rates of recurrence. As DVT was found to be less, rather than more, extensive in men our findings do not support this hypothesis. Similarly, our finding that DVT was more extensive in women than in men suggests that a lower threshold to perform diagnostic testing cannot explain the lower prevalence of thrombosis in women.

This study has a number of potentially important clinical implications. First, it raises the possibility that diagnostic strategies that use a low or a moderate clinical probability in combination with another negative test, such as D-dimer testing or negative compression ultrasound of the proximal veins, to exclude DVT may have a higher failure rate in men than in women. Second, this analysis suggests that the presence of entire leg swelling is more likely to predict the presence of DVT in women than in men.

Strengths of this analysis that reduce the potential for bias include that data were prospectively collected, DVT was objectively diagnosed using standardized criteria, and that study personnel were not aware that a comparison of findings between men and women would be performed when the studies were performed. Additional strengths are that we used individual data from a large number of patients, which allowed us to explore interrelationships between findings, and that analyses were performed according to a protocol that reduces the potential for overemphasis of chance findings.

Limitations of our study include that patients in this analysis may not be fully representative of consecutive patients suspected of having DVT as they were participants in clinical studies. In addition, only data that were collected as part of the original studies could be included in this analysis and, in one of the three studies [21], the anatomical extent of thrombosis was not available. As use of estrogen therapy was not consistently recorded, we are unable to assess if estrogen therapy influenced the findings in women. Lastly, this was a retrospective analysis and we cannot exclude that associations that occurred by chance in the original studies prompted some of the analyses that were performed.

In conclusion, our analysis suggests that there are differences in the clinical features of DVT in men and women and that the prevalence of DVT among those in whom thrombosis is suspected is substantially higher in men than in women. Although clinical pretest probability assessment stratifies the probability of DVT in both sexes, the prevalence of thrombosis was twice as high in men compared with women in the low or moderate categories. Swelling of the entire leg appears to be more common in women who develop DVT and this finding is also more predictive of thrombosis in women than in men.

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Disclosure of Conflict of Interests

The authors state that they have no conflict of interest.

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