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Anatomic distribution of deep vein thrombosis in pregnancy

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Abstract

Background: Prospective studies of nonpregnant patients have demonstrated that most deep vein thromboses of the lower extremity originate in the calf veins and progress proximally, but the anatomic distribution of thromboses in pregnant patients is unclear. An understanding of the anatomic distribution of deep vein thrombosis in pregnancy has important implications for optimizing diagnostic imaging protocols. We undertook this study to determine the anatomic distribution of deep vein thrombosis of the lower extremity in symptomatic pregnant patients.

Methods: We systematically searched MEDLINE (1966 to January 2009), Embase (1980 to January 2009) and the Cochrane Library using prespecified criteria to identify articles providing objective diagnostic and anatomic information for unselected or consecutive symptomatic pregnant patients with deep vein thrombosis.

Results: Six articles from an initial list of 1098 titles met the inclusion criteria. These articles provided information for 124 pregnant women with a diagnosis of deep vein thrombosis. Overall, involvement of the left leg was reported in 84 (88%) of the 96 patients for which the side affected was known, and 87 (71%) of 122 thromboses were restricted to the proximal veins without involvement of the calf veins. Among these cases of proximal deep vein thrombosis, 64% (56/87) were restricted to the iliac and/or femoral vein.

Conclusion: Despite a paucity of studies in this area, the results of our review suggest that the anatomic distribution of deep vein thrombosis in pregnant women differs from that for nonpregnant patients. In addition to what was previously known — that left-sided deep vein thrombosis is more common in pregnancy — we also found that proximal deep vein thrombosis restricted to the femoral or iliac veins is also more common (> 60% of cases). If confirmed by larger studies, these findings could affect our understanding of the pathophysiology and derivation of diagnostic algorithms for examination of pregnant women with suspected deep vein thrombosis.

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The knowledge that deep vein thrombosis most commonly develops in the calf and then extends proximally[1–5] was critical in the development of diagnostic strategies for this condition using compression ultrasonography. Relative to venography (the reference standard), compression ultrasonography is highly sensitive (97%) for thrombosis of the proximal veins,[6] but it is less sensitive for thrombosis limited to the calf. To minimize the risk of missing isolated deep vein thromboses in the calf that subsequently propagate proximally, limited serial compression ultrasonography (over 7 days) has been advocated.[7,8] Knowing that thrombosis progresses proximally and that the thrombus is usually contiguous has allowed clinicians to limit compression ultrasonography examinations for patients with suspected deep vein thrombosis to two points along the venous system: the common femoral vein and the popliteal vein.[9,10]

The applicability and performance of diagnostic techniques involving compression ultrasonography for pregnant patients with deep vein thrombosis is less clear. Because of the risks associated with exposing the fetus to radiation and concerns related to administering contrast agent, few studies in pregnancy have used venography. In addition, there have been no prospective studies validating the use of compression ultrasonography for the diagnosis of deep vein thrombosis in pregnant patients.[11] Currently, diagnostic imaging algorithms for deep vein thrombosis in pregnant patients are often extrapolated from studies of the nonpregnant population.[12] This presumes that the pathophysiology, distribution and progression of deep vein thrombosis in pregnant patients are similar to those seen in nonpregnant patients.

Observational studies[13] have suggested that the anatomic distribution of deep vein thrombosis may in fact differ among pregnant patients. During pregnancy, deep vein thrombosis of the left leg is predominant,[13] and isolated thrombosis of the iliac vein is reported to occur.[14] The ideal study design to investigate the distribution of deep vein thrombosis among pregnant women might involve systematic leg venography for pregnant patients with acute deep vein thrombosis, but such a study is not feasible for ethical reasons, since it would involve exposing fetuses to contrast agent and ionizing radiation. Consequently, we undertook a systematic review of previously published studies of cohorts of pregnant women with deep vein thrombosis to build on our prior findings[12,13] and to better describe the anatomic distribution of deep vein thrombosis in pregnancy.

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Method

Literature review

Two of us (W.S.C., F.A.S.) performed a systematic search of MEDLINE (1966 to January 2009), Embase (1980 to January 2009) and the Cochrane Library with the search terms "deep vein thrombosis" and "venous thromboembolism"; the search was limited to English articles. We scanned the title and abstract of each article initially retrieved for content. We then studied articles that provided diagnostic information for unselected or consecutive women presenting with acute deep vein thrombosis of the lower extremity during pregnancy for suitability for data abstraction. Articles eligible for data abstraction were case series or observational cohorts of three or more participants (the minimum number of three being used to avoid reporting bias) in which deep vein thrombosis was diagnosed in unselected or consecutive pregnant women by means of objective techniques such as compression ultrasonography, magnetic resonance imaging, computed tomography or venography.

Data abstraction and analysis

Two of us (W.S.C., F.A.S.) abstracted data from eligible articles, including the side of the thrombosis (left, right or both) and the anatomic distribution of the thrombosis as revealed by diagnostic testing. We also specifically abstracted information on the involvement of each venous segment (iliac, femoral, popliteal and calf veins) at the time deep vein thrombosis was diagnosed. Any discrepancies were resolved by discussion. We used descriptive statistics to present our findings.

Results

We retrieved 933 articles from MEDLINE and 165 articles from Embase, but no articles from the Cochrane Library. After reviewing the abstracts, we retrieved 21 potentially eligible articles relating to unselected series of consecutive women with a diagnosis of deep vein thrombosis during pregnancy. Of these articles, three were excluded because impedance plethysmography was used to diagnose deep vein thrombosis,[15–17] nine were excluded because the anatomic description of the thrombi was inadequate,[18–26] one was excluded because of patient selection bias,[27] and two were excluded because of potential duplication of reporting.[28,29] We abstracted data from the remaining six articles[30–35] (Table 1).

Five of these articles[30–34] were retrospective case series, each from a single site, one of which reported results for both a retrospective cohort and a prospective cohort of patients.[33] The remaining article was a report from a registry of 183 medical centres.[35] The number of patients in each of the case series or cohorts was small (range 4 to 34 patients). The earlier studies, published more than 18 years ago,[30–33] reported primarily on the use of venography to diagnose deep vein thrombosis in pregnant

Table 1: Characteristics of studies reporting the anatomic distribution of deep vein thrombosis (DVT) in pregnant patients

Reference	Study design	Patient recruitment	Patient characteristics	Diagnostic modality
Bergqvist et al.[30]	Retrospective cohort	Consecutive patients diagnosed at one centre, 1974–1980	Mean age 26 (range 17–41) yr First trimester: 4 Second trimester : 7 Third trimester: 6	Venography
Bergqvist et al.[31]	Retrospective cohort	Consecutive patients referred to a thrombosis clinic at one centre, with diagnosis of DVT, 1970–1979	Mean age 26 (range 19–42) yr First trimester: 6 Second trimester: 11 Third trimester: 10 Unknown: 3	Venography
Greer et al.[32]	Retrospective cohort	Consecutive patients with suspected DVT, referred for compression ultrasonography of the leg over a two-year period	Mean age 31 (range 29–33) yr First trimester: 0 Second trimester: 1 Third trimester: 3	Compression ultrasonography, venography
Polak et al.[33]	(a) Retrospective cohort (b) Prospective cohort	(a) Consecutive patients referred to one centre from August 1984 to April 1987 with suspected DVT identified through medical records (b) Consecutive patients with suspected DVT referred to one centre from March 1988 to March 1989	Mean age 24.2 (range 18–41) yr First trimester: 4 Second trimester: 6 Third trimester: 8	Venography, compression ultrasonography
Aburahma et al.[34]	Retrospective cohort	Medical records of pregnant women treated for DVT at one centre, 1987–1994	Mean age 24 (range 17–39) yr First trimester: 1 Second trimester: 5 Third trimester: 18	Compression ultrasonography, venography
James et al.[35]	Prospective registry	Consecutive pregnant patients with DVT enrolled at 183 instituitions from October 2001 to March 2002	Data on age not reported First trimester: 15 Second trimester: 8 Third trimester: 9 Trimester unknown: 2	Compression ultrasonography

women, whereas studies published within the past 10 years[34,35] reported primarily on the use of compression ultrasonography. In all of these studies, the specific criteria for diagnosis of deep vein thrombosis with each diagnostic modality were not stated explicitly, but we assumed that they were similar to those used for nonpregnant patients. In all, deep vein thrombosis was diagnosed by venography in 55 patients, whereas compression ultrasonography was the primary mode of diagnosis for 69 patients.

Overall, involvement of the left leg was reported in 84 (88%) of the 96 cases for which the side affected was known, and there were no bilateral thromboses (Table 2). The most common site for acute deep vein thrombosis was proximal veins without involvement of calf veins (87/122; 71%). Among these 87 patients who had proximal thrombosis without calf vein involvement, 56 (64%) had thrombosis restricted to the iliac and/or femoral vein. The prevalence of isolated iliac vein thrombosis[29,31] was 17% (3/18), as derived from the two studies[30,32] that provided specific venographic anatomic detail. Isolated thrombosis of a calf vein was reported in 6% (7/124) of cases. Ninety-five per cent (36/38) of cases of iliofemoral deep vein thrombosis were reported in the left leg.

Discussion

The majority of nonpregnant patients with deep vein thrombosis have proximal thrombosis with involvement of the calf veins (58%–87%), whereas isolated proximal vein thrombi are uncommon (0%–13%).[1–5] However, in our review of deep vein thrombosis during pregnancy, 71% of the cases were restricted to the proximal veins, and 64% of these were in the iliofemoral region. These observations strongly suggest that the anatomic distribution of deep vein thrombosis in pregnant women, and perhaps the pathophysiology of the condition, may indeed differ from that reported in the general population.

The pathophysiology of iliofemoral deep vein thrombosis in both nonpregnant and pregnant patients requires further exploration. In a large retrospective study of venography performed in nonpregnant patients with deep vein thrombosis, Ouriel and colleagues[36] reported that the left to right ratio was 1.3:1 for infrainguinal deep vein thrombosis but 2.4:1 for iliac vein thrombosis. The authors speculated that in a substantial proportion of nonpregnant patients with iliac vein thrombosis, there may be undetected venous webs in the iliac vein (May–Thurner syndrome). In an observational study of the management of deep vein thrombosis in pregnant patients, Voke and associates[26] similarly reported that the more proximal the thrombosis, the more likely it was to be on the left side. In addition, iliofemoral thromboses were also more likely to be reported in the third trimester of pregnancy.

In our current study, iliofemoral deep vein thromboses were also predominantly in the left leg (95%). We might speculate that among pregnant women, a May–Thurner-like syndrome brought on by compression of the left iliac vein by the gravid uterus (at the point where it crosses the right iliac artery) plays a major role in the increased incidence of iliofemoral deep vein thrombosis in late pregnancy. However, given that deep vein thrombosis occurs with equal frequency in all three trimesters of pregnancy,[13] this hypothesis would presumably not apply to deep vein thrombosis observed in early pregnancy.

The higher prevalence of isolated deep vein thrombosis of the proximal veins seen in this study, relative to previous studies of nonpregnant patients, is clinically important. Patients with proximal deep vein thrombosis have a high risk of pulmonary embolism (40%–50%).[37] Untreated or unrecognized pulmonary embolism can result in maternal morbidity and mortality.[38] Commonly used protocols for compression ultrasonography to diagnose deep vein thrombosis in pregnant patients (e.g., two-point compression imaging) may be limited in their ability to detect isolated iliofemoral thrombi and may therefore be inadequate. Several authors have demonstrated the feasibility of using Valsalva manoeuvres and assessing flow changes with respiration throughout pregnancy to assess the patency of proximal veins.[39–41] However, the sensitivity of these manoeuvres for detecting isolated iliac vein thrombosis in pregnant women with suspected deep vein thrombosis is unknown.

Limitations

There are obvious limitations to a study of this nature. Our analy-

Table 2: Anatomic distribution of deep vein thrombosis (DVT) in 124 pregnant patients

Reference	No. of patients *n = 124*	Right side *n = 12*			Left side *n = 84*			Side unknown *n = 28*		
		Isolated calf DVT	Proximal with calf DVT	Proximal with no calf DVT	Isolated calf DVT	Proximal with calf DVT	Proximal with no calf DVT	Isolated calf DVT	Proximal with calf DVT	Proximal with no calf DVT
Bergqvist et al.[30]	14*	2	0	1	1	4	6			
Bergqvist et al.[31]	30	1	1	1	1	10	16			
Greer et al.[32]	4					1	3			
Polak et al.[33]	18		2†				16			
Aburahma et al.[34]	24								5	19
James et al.[35]	34	1		3	1	7	18			4

*This study also included three patients whose DVT was detected indirectly, by methods other than venography. As such, the anatomic distribution of the thrombosis could not be ascertained. These patients are not represented in this table.
†It was not possible to determine from the published article whether right-sided proximal thromboses in these patients involved the calf veins.

sis was derived from pooling small observational studies and excluded articles in languages other than English. As such, reporting bias and selection bias are possibilities. We tried to minimize reporting bias by selecting case series of three or more patients from one site. In all six studies (case series or cohorts), determining the anatomic distribution of deep vein thrombosis, the aim of the current study, was not the primary objective. Therefore, selective patient exclusion was unlikely. That said, deep vein thrombosis of the lower extremity was assessed with compression ultrasonography in more than half of the cases. Compared with venography, compression ultrasonography is relatively insensitive for the diagnosis of deep vein thrombosis of the calf and isolated iliac vein thrombosis.[6] Therefore, we might have underestimated the prevalence of isolated calf vein or iliac vein thrombosis. This might have affected our findings with respect to proximal and distal distribution of the thromboses.

Conclusion

Our primary objective in this study was to determine the anatomic distribution of deep vein thrombosis in pregnant patients. Our findings suggest that isolated proximal deep vein thrombosis, specifically iliofemoral thromboses, are common in pregnancy and that the anatomic distribution of these lesions in pregnant patients may differ significantly from that in nonpregnant women. Until prospective diagnostic studies are available for pregnant patients, it may be prudent to conduct a routine examination of the iliofemoral venous system when a pregnant patient presents with suspected deep vein thrombosis.

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