Anatomic and physiologic changes in lower extremity venous hemodynamics associated with pregnancy

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Purpose: The purpose of this study was to describe the physiologic effects of pregnancy on lower extremity venous hemodynamics.
Methods: Eight pregnant women, six with no known venous disease (NVD) and two with documented deep venous obstruction (DVO), were identified in the first trimester (TM) and studied monthly until delivery and once postpartum (pp) by air plethysmography and duplex scan.
Results: None of six women in the NVD group (12 extremities) had obstruction or elevated ambulatory venous pressures as estimated by air plethysmography. In addition, despite significant increases in common femoral vein and saphenofemoral junction diameters, no woman in the NVD group had reflux by either test. Venous filling index increased significantly during pregnancy and decreased significantly pp, but all values remained within the normal range (0.55 ± 0.2 ml/sec first TM, 1.01 ± 0.38 ml/sec late third TM, 0.58 ± 0.08 ml/sec pp; $p < 0.03$ both comparisons). Common femoral vein diameters increased and decreased in similar fashion (0.99 ± 0.25 cm first TM, 1.21 ± 0.25 cm late third TM, 0.80 ± 0.11 cm pp; $p < 0.0005$ first vs late third TM, $p < 0.005$ late third TM vs pp). Saphenofemoral junction vein diameters similarly increased and decreased in size (0.46 ± 0.07 cm first TM, 0.68 ± 0.19 cm late third TM, 0.50 ± 0.10 cm pp; $p < 0.01$ first vs late third TM, $p < 0.03$ late third TM vs pp). Neither of the two women in the DVO group showed deterioration of outflow fraction or venous filling index as pregnancy progressed, and neither had thromboembolic complications despite moderate to severe preexisting obstruction. Both women in the DVO group delivered uneventfully. No woman in either group developed varicose veins.
Conclusion: Pregnancy-induced changes in lower extremity venous hemodynamics in the NVD and DVO groups were detected but were small. Hormonal or other systemic factors must play a significant role in the development of postpartum varicose veins. (J Vasc Surg 1996;24:763-7.)

The cause of primary varicose veins is probably multifactorial and includes valvular incompetence, vein wall alterations, and arteriovenous fistulae.[1] Many authors believe that heredity plays a major role as well (i.e., patients have a genetic or acquired predisposition to develop varicose veins).[2] But the degree to which each of these purported etiologic factors contributes to their development is difficult to ascertain. One commonly cited risk factor for the development of a variety of skin disorders including spider telangiectasias, purpura, and varicose veins is pregnancy.[3-6] Potential causes of pregnancy-induced "secondary" varicose veins include the mechanical effects of the gravid uterus and changes in vein wall distensibility mediated by high levels of estrogen, progesterone, and several other factors. The purpose of this study was to describe the anatomic and physiologic impact of pregnancy on lower extremity veins, focusing on the relative importance of obstruction and reflux in this disease process.

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METHODS

This study was approved by the Institutional Review Board at Tripler Army Medical Center, and

Table I. Mean APG and duplex parameters for six women in the NVD group (n = 12 exts)

Parameter	*First TM*	*Late 3rd TM*	*Postpartum*	p *Value**
OF (%)	58.6 ± 6.1	61.4 ± 3.2	59.4 ± 5.2	NS
VVol (ml)	90.9 ± 25.5	84.3 ± 12.1	88.9 ± 19.5	NS
VFI (ml/sec)	0.55 ± 0.20	1.01 ± 0.38	0.58 ± 0.08	<0.03 both
EF (%)	54.1 ± 9.5	59.3 ± 10.0	59.3 ± 17.7	NS
RVF (%)	19.2 ± 12.1	23.7 ± 18.9	21.5 ± 11.1	NS
CFVd (cm)	0.99 ± 0.25	1.21 ± 0.25	0.80 ± 0.11	<0.0005, <0.005
SFJd (cm)	0.46 ± 0.07	0.68 ± 0.19	0.50 ± 0.10	<0.01, <0.03
POPVd (cm)	0.61 ± 0.11	0.64 ± 0.15	0.52 ± 0.08	NS, <0.05
SPJd (cm)	0.33 ± 0.09	0.36 ± 0.04	0.30 ± 0.08	NS

No extremity exhibited reflux by duplex at any visit.
*Paired *t* tests: first TM versus late third TM; late 3rd TM vs postpartum; $p < 0.05$.
Vvol, Venous volume; *EF,* ejection fraction; *RVF,* residual volume fraction; *SPJd,* Saphenopopliteal junction diameter.

each woman gave informed consent. Women were identified in the first trimester and studied monthly until delivery and within 1 month after delivery by duplex scan (Biosound Phase II, Indianapolis, Ind.) and air plethysmography (ACI Medical, Sun Valley, Calif.). Each woman underwent seven to nine combined duplex and APG studies. First studies were performed at average 9.7 weeks of pregnancy (range 8.3 to 12.6 weeks). Final third-TM studies were performed an average of 15 days before delivery (range 4 to 30 days). Postpartum studies were performed an average of 2.5 weeks after delivery (range 4 days to 4 weeks).

Bilateral lower extremity duplex studies were performed at each visit with women in 20 degrees reverse Trendelenberg position. The greater saphenous (GSV), lesser saphenous (LSV), common femoral (CFV), superficial femoral (SFV), and popliteal veins (POPV) were interrogated. The profunda, perforating, and tibial veins were not studied. Methods to produce reflux included proximal compression maneuvers and the Valsalva maneuver. Spontaneous and phasic flow at the CFV level suggested proximal vein patency, whereas loss of respiratory variation or a continuous Doppler signal indicated proximal obstruction. In addition, maximum vein diameters were measured at four levels: CFV, GSV at the saphenofemoral junction (SFJ), POPV, and LSV at the saphenopopliteal junction (SPJ).

Bilateral APG maneuvers were conducted in standard fashion. No modifications were made to the Nicolaides protocol because of pregnancy. Calculated parameters included outflow fraction (OF), an estimate of proximal venous obstruction; venous volume, venous filling index (VFI), the rate of filling of calf veins; ejection fraction, an estimate of calf muscle pump efficiency, and residual volume fraction, an estimate of ambulatory venous pressure.

Statistical analysis consisted of paired *t* tests with results expressed as mean ± SD. Because intermediate duplex and APG parameter changes were small, this analysis compares the potentially most disparate time points (first TM vs late third TM; late third TM vs postpartum). Intermediate values are not reported. All tests were performed by the second author (T. G.) and were interpreted by the senior author (P. C.) in a blinded fashion.

RESULTS

Six women (12 lower extremities) with an average age of 26.6 years (range 21 to 35 years) and no history of deep venous thrombosis or varicose veins (NVD) were studied according to the previous protocol. Three of six women reported a family history of varicose veins; one woman had spider veins before pregnancy. Three of the six women were primagravida; the others were multiparous (G4P3, G5P2Ab2, and G6P2Ab3). Results at first TM, late third TM, and after delivery are summarized in Table I.

No woman in the NVD group developed obstruction as assessed by duplex scanning or APG. In addition, no woman in the NVD group developed reflux by either test despite significant increases in CFVd and SFJd. Statistically significant increases in VFI occurred, although VFI values did not exceed the normal range (<2 ml/sec) at any interval. VFI, CFVd, SFJd, and POPVd decreased significantly after delivery. APG parameters OF, venous volume, ejection fraction, and residual volume fraction and duplex parameter SPJd did not change significantly at any interval. No woman in the NVD group developed truncal or branch varicosities, although all had varying degrees of pedal edema.

Two women with preexisting unilateral deep venous obstruction (DVO) were studied as well. Patient 1, a primagravida who had had massive pelvic trauma at the age of 3 years, had undergone ligation of the left external iliac vein (Table II). APG demon-

Table II. Hemodynamic changes in left leg of patient 1

	APG					*Duplex*			
Trimester	*OF*	*VV*	*VFI*	*EF*	*RVF*	*CFVd*	*SFJd*	*POPVd*	*SPJd*
First	35.4	104	53	24.0	68.3	.44	.70	.68	.38
Late 3rd	36.5	88.5	.52	24.9	45.2	.66	1.16	.95	.48
Postpartum	27.4	107	.57	24.8	4.7	.63	.52	1.05	.68

CFV and GSV (SFJ) reflux by duplex was seen at each of seven visits.
Abbreviations as in Table I.

Table III. Hemodynamic changes in left leg of patient 2

	APG					*Duplex*			
Trimester	*OF*	*VV*	*VFI*	*EF*	*RVF*	*CFVd*	*SFJd*	*POPVd*	*SPJd*
First	28.1	73.2	2.0	61.5	24.6	.94	.57	.28	.21
Late 3rd	29.2	74.0	1.5	37.2	53.4	.75	.58	.89	.51
Postpartum	30.3	82.5	2.45	69.7	48.5	.94	.52	.66	.53

Continuous flow at CFV, and CFV and POPV reflux by duplex was seen at each of seven visits.
Abbreviations as in Table I.

strated moderate outflow obstruction (OF 35.6%) before conception, which did not deteriorate (OF 36.5% late third TM). Her VFI remained unchanged, although CFVd and SFJd increased at late third TM and decreased after delivery, similar to women in the NVD group. She was treated with 30 to 40 mm Hg below-knee compression stockings, and her mild preconception left leg symptoms remained stable. She delivered uneventfully at term by Caesarian section.

Patient 2 (G6P4Ab1) had had a postpartum left iliofemoral deep venous thrombosis 12 months before study enrollment. Moderate left leg pain and swelling persisted despite a 6-month course of anticoagulation. She was treated with below-knee compression and subcutaneous heparin throughout her new pregnancy. A vaginal delivery was uneventful. Although serial duplex scans demonstrated proximal venous obstruction and CFV and POPV reflux, OF did not deteriorate, and VFI remained low and unchanged (Table III). Changes in POPVd and saphenopopliteal junction diameter (SPJd) were inconsistent for both patients.

DISCUSSION

These data describe the anatomic and physiologic changes in lower extremity venous hemodynamics associated with pregnancy in eight women. Six women in the NVD group showed no clinically significant deterioration in vein function, although statistically significant increases in VFI, CFVd, and SJFd did occur by late third TM. VFI, CFVd, SFJd, and POPVd decreased when late third TM studies were compared with postpartum studies. Neither of two women in the DVO group showed worsening obstruction or onset of reflux in late third TM. Prophylactic anticoagulation during pregnancy may have prevented a recurrent deep venous thrombosis in patient 2 with severe preexisting obstruction. Both women in the DVO group delivered uneventfully.

It is possible that OF by APG is a poor measure of obstruction in pregnant women. The gravid uterus at least partially obstructs the inferior vena cava in late pregnancy with a woman in the supine position. Her leg veins may incompletely empty because of caval compression despite the supine and leg elevated position. Therefore, because the air-filled APG cuff measures relative volume changes only, the recorded venous volume may represent the difference between full and fuller; that is, it may underestimate the true calf venous volume. Underestimating calf venous volume would cause OF (%) to rise, failing to reflect increasingly severe obstruction. This concern about plethysmography is raised by Skudder et al.[7] Optimal estimates of OF might be better obtained with a pregnant woman in the left or right lateral decubitus position. Our data did not show decreases in the venous volume part of OF or rising OFs, which might support this concept. It is also possible that we failed to study women at maximum uterine enlargement, although the last third TM studies were performed at almost 39 weeks, an average of 15 days before delivery.

All women except one in our series tolerated the prolonged supine position required for duplex and APG studies well. Bilateral duplex studies averaged 40 minutes. The woman who did not tolerate this

position gained 84 pounds and had extreme pedal edema during pregnancy. She reported severe shortness of breath in both the supine and lateral recumbent positions. No woman developed clinical symptoms consistent with the "supine hypotensive syndrome," although we did not measure pulse or blood pressure routinely during duplex and APG studies. Because only approximately 11.2% of women will have this syndrome,[8] perhaps no woman in this small series had the anatomic configuration and degree of uterine flaccidity necessary to produce significant caval compression when lying supine. However, there is little doubt that uterine compression of the inferior vena cava, iliac veins, and possibly aorta can occur and have important effects on maternal cardiovascular function.[9-15]

Firm conclusions about the relative contribution of obstruction to the development of varicose veins in pregnant women are difficult. Significant obstruction as measured by APG did not occur in our series, although increased CFVd and SFJd may suggest its presence to some degree. Increases in CFVd and SFJd might also occur as a result of increased vein wall distensibility or increased venous flow associated with late pregnancy. Significant reflux, which could result from obstruction, also did not occur. The statistical increase in VFI may be the result of increased arterial inflow as a result of increased maternal cardiac output. Certainly, increased hydrostatic pressure is not the sole mechanism by which pregnant women get spider and varicose veins. Sadick[5] noted that "30% of patients noting varicose or telangiectatic veins related to pregnancy noted onset during the first trimester of pregnancy, while 24% noted the onset during the second or third trimesters." Forty-nine percent actually noted onset after delivery. Sadick concluded that hormonal factors such as estrogen and progesterone or other angioproliferative factors must account for the early development of venous disease in this large subset of patients. In addition, Mullane[16] states that 70% to 80% of women develop varicose veins during the first trimester, 20% to 25% during the second trimester, and 1% to 5% during the third trimester. Goldman[17] nicely summarizes the existing data with respect to hormonal influence on the venous system.

Similar to OF, residual volume fraction values remained unchanged as women progressed from first to late third TM of pregnancy. The lack of decrease in OF or ejection fraction and minimal increase in VFI support this finding. Therefore estimated ambulatory venous pressures did not rise as might be expected during pregnancy and given our finding of CFV and SFJ enlargement.

No woman in our series had development of varicose veins. This fact may be due to their young average age at 26.6 years. Dindelli et al.[10] found that the relative risk (RR) of developing venous disease in pregnancy increased with age; it is least for women ≤24 years of age and is 4.0 for those ≥35 years of age. Parity also had an influence on development of venous disease. Compared with primiparae, the estimated RR was 2.0 for women reported to have given birth to one child or more. Three of six women in the NVD group in our study were primiparae and were therefore at less risk. And finally, only three women in the NVD group in our study reported a family history of varicose veins, a factor for which these authors found an RR of 5.8. Half of our group may therefore lack the genetic predisposition important for development of venous disease.

Finally, both patients in the DVO group tolerated pregnancy well. Patient 1 had minimal symptoms throughout the pregnancy. She was treated with compression alone. Her preconception clinical picture suggested good collateralization around the left external iliac vein injury, which had occurred 25 years previously. This patient had been advised to consider surrogate motherhood. Patient 2, with a history of postpartum deep venous thrombosis 1 year before this pregnancy, was less well compensated by both clinical and APG criteria. Her preconception left leg edema was moderate and well controlled by compression therapy. Subcutaneous heparin injections were instituted in the first TM, increased in the second and third TM, and continued 4 weeks after delivery. No additional morbidity was related to these injections.

In summary, we have shown small but statistically significant lower extremity venous hemodynamic changes in a carefully studied group of eight pregnant women, two with known DVO. Women in the NVD group were young, 50% were primiparae, and only 50% had a positive family history, which may explain why no woman developed varicose veins. Women in the DVO group fared well from both a hemodynamic and clinical standpoint but must be approached with caution. The mechanisms by which pregnancy leads to varicose vein formation are probably multiple, and whether pregnancy has a primary effect or simply acts as an accelerator of the process in susceptible women is still unknown.

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