

Lower Limb Vein Enlargement and Spontaneous Blood Flow Echogenicity Are Normal Sonographic Findings during Pregnancy

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ABSTRACT: *Purpose.* We studied pregnancy-induced changes in lower limb venous function.

Methods. We used plethysmography and sonography to assess the changes in venous wall distensibility, saphenous vein diameters, and spontaneous blood flow echogenicity in the common femoral veins in 190 consecutive women during and after uncomplicated pregnancies (total of 409 examinations).

Results. The percentage of women with clinical symptoms and signs of venous insufficiency increased significantly during pregnancy. The mean diameters of the great and small saphenous veins also increased significantly, while occlusive venous plethysmography showed a decrease in parameters indicating vein distensibility. Spontaneous blood flow echogenicity in the common femoral veins was clearly visible or marked in 6% of cases during the first trimester of pregnancy, 63% during the second trimester, and 96% during the third trimester, versus 6% after delivery ($p < 0.0001$). The mean hematocrit decreased and the mean fibrinogen concentration increased during pregnancy.

Conclusions. The increase in lower limb venous pressure seen during pregnancy leads to venous overdistention and worsens blood stasis. Decreased ve-

nous flow velocity and rheological alterations result in increased red cell aggregation, giving rise to spontaneous blood flow echogenicity. Spontaneous blood flow echogenicity is therefore a normal finding during pregnancy and should not be mistaken for venous thrombosis. © 2000 John Wiley & Sons, Inc. *J Clin Ultrasound* 28:407–413, 2000.

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Pregnancy may cause important changes in venous function that may result in vascular symptoms and complications.^{1,2} The underlying mechanisms are complex, and their relative importance remains debated. Possible factors are mechanical (eg, venous obstruction by the gravid uterus and the fetal head in the pelvis or plasma volume increase),^{3,4} hormonal,^{5,6} rheological,^{7,8} or functional (eg, changes in smooth muscle tone).^{6,9} An increase in venous wall compliance is a widely accepted consequence of pregnancy, but in vitro experiments have demonstrated that pregnancy causes alterations in the walls of capacitance veins that result in an apparent increase in blood volume at the expense of wall compliance.¹⁰ These changes involve an increase in venous tone and a decrease in venous distensibility in the

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lower limbs.⁶ Furthermore, red cell aggregation has been found to increase during normal pregnancy despite hemodilution; in addition, there is a decrease in whole blood viscosity largely determined by the decrease in hematocrit overcoming the increase in plasma viscosity.^{8,11}

Noninvasive means of detecting and measuring the changes in venous function during normal pregnancy would provide valuable information. We used plethysmography and sonography for the noninvasive evaluation of lower limb venous function in women with uncomplicated pregnancies to assess changes in venous diameter, wall compliance, and spontaneous blood echogenicity.

PATIENTS AND METHODS

Patients

Pregnant women referred to our institution were routinely offered physical examinations, laboratory tests, plethysmography, and sonography to monitor their lower limb venous function. The examinations took place during the first, second, and third trimesters of the pregnancy and during the first 5 months after delivery. We retrospectively reviewed the records of 190 consecutive pregnant women, identified from a search of all files, who met the study criteria. All women with uncomplicated pregnancies with or without lower limb venous insufficiency were included in the study if they had 1 or more examinations of lower limb venous function. Women were excluded if they had a complicated pregnancy (from any cause, including arterial hypertension or venous thrombosis); had a chronic disease such as diabetes, hypertension, or cardiac failure, regardless of whether drug therapy was required; or were receiving anticoagulant therapy or any other long-term systemic therapy. The 190 women underwent a total of 409 examinations (95 during the first trimester of pregnancy, 145 during the second trimester, 124 during the third trimester, and 45 during the postpartum period).

Examination Techniques

For each patient, the physical examination, plethysmography, and sonography were performed by the same physician. The patient was carefully interrogated about any past or present symptoms of chronic venous insufficiency (eg, lower limb pain, edema, paresthesia, and cramp, especially those aggravated by standing). The physical examination searched for signs of lower limb venous dis-

orders (eg, sural, gluteal, and vulvar varicose veins; hemorrhoids; varicosities; and edema).

We used a strain-gauge plethysmograph (Periflow, Janssen Scientific Instruments, Beerse, Belgium) for lower limb occlusive venous plethysmography. The patient was in a supine position, with her legs elevated 20 cm above the level of the left atrium by a foam block and her knees slightly flexed. Strain gauges (mercury in Silastic) were wrapped around the calf at its widest diameter. A pneumatic cuff was applied to the thigh above the knee and inflated to a pressure of 50 mm Hg, causing the calf blood volume to expand. When the equilibrium level was reached (ie, after approximately 2 minutes), the cuff was suddenly deflated. The percentage increase in volume of the calf ($\delta V\%$) in ml/100 ml was measured at the equilibrium level before cuff deflation. The maximum venous outflow (MVO) in ml/100 ml/minute was measured by drawing a tangent to the initial part of the downslope following cuff deflation. The emptying half-life ($T_{1/2}$) in seconds was measured as the delay between cuff deflation and the point where the downslope reached 50% of its total vertical amplitude. Plethysmography tracings were read and calculations made by an independent observer.

We used a continuous-wave Doppler system (Spectradop2 system, DMS, Montpellier, France) with 4- and 8-MHz transducers and real-time spectral analysis for the functional examination of the great and small saphenous veins in the left and right lower limbs. The patient was examined in a standing position. Upstream muscle compression, Valsalva's maneuver, and coughing were used to evaluate valve competence. We considered a venous reflux lasting for more than 1 second to be abnormal.

We used duplex systems (DRF400V system, Diasonics, Milpitas, CA, with a 7.5-MHz mechanical sector-array transducer; or 750SD system, CGR-Ultrasonics, Meaux, France, with a 7.5-MHz linear-array transducer) for gray-scale sonographic examination of the lower limb veins. The patient was examined in a supine position. The diameters (in mm) of the great and small saphenous veins were measured at the level of their junction with the deep venous system (the common femoral and popliteal veins, respectively). Spontaneous blood flow echogenicity was then graded in the common femoral vein as follows: grade 0, anechoic (absent); grade 1, barely visible echoes; grade 2, clearly visible echoes whose intensity remained lower than that of surrounding tissues; or grade 3, blood flow echogenicity equal

to or greater than the echogenicity of surrounding tissues (marked) (Figure 1).

Laboratory tests included measurements of hematocrit (%), blood fibrinogen (g/l), and relative blood viscosity (Hess's viscosimeter; normal blood viscosity versus water = 4.5).

Statistical Analyses

Continuous data during a given trimester were compared to those in other periods (trimesters of pregnancy or postpartum) using the Student's *t* test for paired data. Changes in paired categorical data from the first or second to the second or third trimester of pregnancy or from the second or third trimester to the postpartum period were compared using McNemar's test (binomial distribution method). Differences were considered signifi-

cant when *p* was less than 0.05. Statistical calculations were made using GraphPad Prism V3.0 and Statmate V1.0 (GraphPad Software, San Diego, CA).

RESULTS

From the first to the second and from the second to the third trimester of pregnancy, there were significant increases in symptoms ($p < 0.001$ for both comparisons) and signs ($p < 0.001$ for both comparisons) of venous insufficiency but no significant change in the valve incompetence of the great or small saphenous veins (Table 1). From the second and third trimesters to the postpartum period, there were significant decreases in symptoms of venous insufficiency ($p < 0.0001$) but no significant change in signs of venous insufficiency

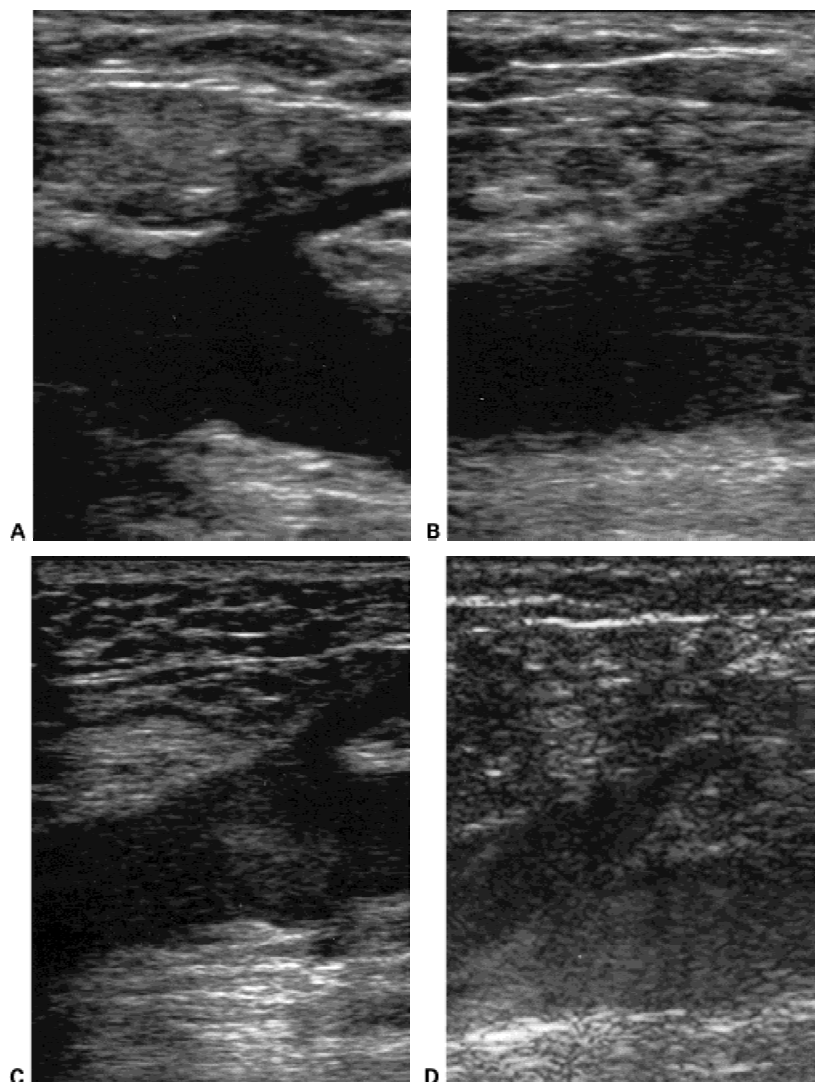


FIGURE 1. Examples of spontaneous blood flow echogenicity in the common femoral veins of pregnant women. (A) Grade 0; (B) grade 1; (C) grade 2; and (D) grade 3.

TABLE 1
Physical and Doppler Examination Results

Finding	No. Patients with Finding/No. Examined (%)			
	1st Trimester	2nd Trimester	3rd Trimester	Postpartum
Symptoms of venous insufficiency	55/95 (58)	115/144 (80)	96/117 (82)	17/41 (41)
Signs of venous insufficiency	43/93 (46)	95/140 (68)	89/116 (77)	27/41 (66)
Great saphenous vein valve incompetence	9/83 (11)	40/128 (31)	27/107 (25)	15/41 (37)
Small saphenous vein valve incompetence	18/86 (21)	36/129 (28)	37/109 (34)	20/41 (49)

or in great or small saphenous vein valve incompetence.

The mean diameter of the small saphenous veins significantly increased from the first to the second trimester ($p < 0.005$) but showed no significant change afterward. The mean diameter of the great saphenous veins was significantly greater in the second than in the first trimester ($p = 0.0042$) and in the third than in the second trimester ($p = 0.001$) and then decreased after delivery ($p < 0.001$) (Table 2).

On plethysmography, the mean $\delta V\%$ was significantly lower during the second trimester than during the first trimester and during the third trimester than during the second trimester ($p < 0.001$ for both comparison). The $\delta V\%$ significantly increased after delivery ($p < 0.0001$) (Table 2). There was no significant change in mean MVO between the first and second trimesters, between the second and third trimesters, or between the third trimester and the postpartum period. The mean postpartum $T_{1/2}$ was significantly greater than that during the first ($p = 0.0015$), the second ($p < 0.01$), and the third ($p < 0.0005$) trimesters of pregnancy (Table 2).

There were 166 measurements of blood viscosity, 193 measurements of hematocrit, and 107 measurements of fibrinogen concentration available for analysis. There was no significant change in relative blood viscosity between any of the trimesters or the postpartum period. The mean hematocrit was significantly lower during the second than during the first trimester ($p = 0.002$) and significantly higher after delivery than dur-

ing any trimester of pregnancy ($p < 0.05$). The mean blood fibrinogen concentration was significantly greater during the second than during the first trimester ($p = 0.018$) but showed no significant change during the third trimester or postpartum period (Table 2).

Spontaneous blood flow echogenicity was clearly visible or marked (grade 2 or 3) in 6% of cases during the first trimester of pregnancy, 63% during the second trimester, and 96% during the third trimester, versus 6% after delivery ($p < 0.0001$). Conversely, spontaneous blood flow echogenicity was absent or barely visible (grade 0 or 1) in 94% of cases during the first trimester of pregnancy, 37% during the second trimester, and 4% during the third trimester, versus 94% after delivery ($p < 0.0001$) (Table 3).

DISCUSSION

Our study confirms the significant increase in clinical symptoms and signs of venous insufficiency during uncomplicated pregnancy.^{1,2} We also found an increase in the diameters of the saphenous veins. The most notable plethysmographic result was a decrease in the $\delta V\%$ during pregnancy. Spontaneous blood flow echogenicity was seen in most patients during the second and third trimesters of pregnancy, and the hematocrit decreased and the fibrinogen concentration increased during pregnancy.

The relatively high rate of venous disorders that we found in pregnant women was not unexpected. Wenderlein¹ found that 43% of pregnant

TABLE 2
Sonographic and Plethysmographic Results

Finding	Mean $\pm$ Standard Deviation			
	1st Trimester	2nd Trimester	3rd Trimester	Postpartum
Great saphenous vein, mm	6.5 $\pm$ 1.0	6.9 $\pm$ 0.9	7.4 $\pm$ 1.1	6.4 $\pm$ 0.7
Small saphenous vein, mm	3.4 $\pm$ 0.7	3.6 $\pm$ 0.7	3.7 $\pm$ 0.7	3.7 $\pm$ 1.0
$\delta V\%$, ml/100 ml	2.9 $\pm$ 0.8	2.5 $\pm$ 0.6	2.1 $\pm$ 0.5	3.2 $\pm$ 0.6
MVO, ml/100 ml/minute	84 $\pm$ 22	79 $\pm$ 18	77 $\pm$ 17	79 $\pm$ 20
$T_{1/2}$, seconds	1.7 $\pm$ 1.1	1.6 $\pm$ 1.1	1.3 $\pm$ 0.9	1.9 $\pm$ 0.5
Hematocrit, %	37.0 $\pm$ 4.2	35.1 $\pm$ 3.9	33.6 $\pm$ 4.1	40.0 $\pm$ 3.4
Fibrinogen, g/l	3.2 $\pm$ 0.7	3.7 $\pm$ 0.7	4.2 $\pm$ 0.9	3.4 $\pm$ 1.1

LOWER LIMB VEINS DURING PREGNANCY

TABLE 3
Spontaneous Blood Flow Echogenicity in Common Femoral Veins during Pregnancy

Echogenicity	No. Patients with Finding/No. Examined (%)			
	1st Trimester	2nd Trimester	3rd Trimester	Postpartum
Grade 0	45/82 (55)	13/139 (9)	2/114 (2)	11/35 (31)
Grade 1	32/82 (39)	39/139 (28)	3/114 (3)	22/35 (63)
Grade 2	5/82 (6)	68/139 (49)	35/114 (31)	1/35 (3)
Grade 3	0 (0)	19/139 (14)	74/114 (65)	1/35 (3)

women had complaints of venous insufficiency, and Wienert¹² reported that 50% of pregnant women had edema of the legs. In our study, the Doppler ultrasound examination demonstrated an increasing rate of saphenous vein valve incompetence that persisted after delivery, suggesting that changes in venous function that occur during pregnancy can produce permanent anatomic lesions.

The reduction of the $\delta V\%$ of the calf that we observed is a somewhat paradoxical result in view of the increase in venous wall compliance during pregnancy reported by others.^{3,13} In fact, we measured not venous compliance itself but the calf blood volume increase produced by a 50 mm Hg counterpressure. This parameter is related to venous pressure (representing the difference between the actual venous pressure and the applied counterpressure), venous volume, and "venous wall compliance." Moreover, venous distention by increased blood pressure should reduce venous wall compliance because distention involves mostly the relatively nondistensible collagen components of the venous wall.¹⁴ Therefore, the decrease in $\delta V\%$ or related parameters that we and others¹⁵⁻¹⁷ found in pregnant women may be explained by increased lower limb venous pressure; however, our methods did not allow direct assessment of venous wall compliance or venous blood pressure. Hormone-induced smooth muscle cell relaxation in the venous wall should result in increased venous distensibility, as reported by some authors,^{9,13} especially in the forearms, while this effect may be reversed or masked by increased venous pressure in the lower limbs. Recently, Edouard et al⁶ demonstrated an increase in lower limb venous tone during normal pregnancy but little change in the upper limbs.

Increased pressure and increased venous compliance are possible causes of the increase in saphenous vein diameter that we observed in pregnant women. A significant increase in lower limb venous pressure during pregnancy is a well-established finding.¹⁸ An increase in lower limb vein diameter during pregnancy has been re-

ported by several authors,¹⁹⁻²¹ who pointed to the role of the pregnant uterus, which can slow down the blood flow from the venous system of the legs. In a longitudinal study of 21 singleton pregnancies, Baumann et al²² found that the time-averaged velocity of blood flow in the femoral vein remained lower during pregnancy than after delivery. Increased venous pressure resulting from vena caval compression by the gravid uterus seems likely to be the main cause of the saphenous vein enlargement and of the decrease in $\delta V\%$ that we noted.

Blood flow echogenicity has been extensively described in various conditions dominated by blood stasis and is generally believed to be related to red cell aggregation with formation of rouleaux; shear rate determines the degree of red cell aggregation when other conditions affecting red cell aggregation (eg, hematocrit, erythrocyte membrane conditions, and plasma macromolecules) are held constant.^{23,24} When blood stasis is induced, erythrocyte rouleaux are formed and become progressively larger, approaching the ultrasonic wavelength (about 0.2 mm at 7.5 MHz) and thus producing reflection and making swirling echoes appear in the vessel lumen.^{25,26} Alternatively, some authors argue that the association between spontaneous blood flow echogenicity and a propensity for thromboembolism implies that platelet aggregates are the most likely origin of in vivo ultrasound contrast in flowing blood.²⁷ In vitro, the addition of adenosine diphosphate to platelet-rich plasma results in the formation of multiple, discrete echoes that increase in size and intensity in a time- and dose-dependent manner, although the overall echogenicity of whole blood declines with the development of platelet aggregates.²⁸ Practically, platelet aggregates induced by adenosine diphosphate appear in dense clumps and in a flow-independent pattern, whereas erythrocytes suspended in saline solution have an intermediate echogenicity, as demonstrated in vitro in porcine blood.²⁹ Therefore, the swirling echogenicity of flowing blood, very commonly seen during sonographic examinations in humans, is

certainly related to red cell aggregation, while occasional echogenic clumps may be related to platelet aggregation. Ultrasonic backscatter from flowing whole blood depends on fibrinogen concentration when red blood cell aggregation exists.³⁰ As a matter of fact, several studies have demonstrated that red cell aggregation is considerably increased during normal pregnancy despite the hemodilution that occurs and that this increase may be attributed mainly to the increased fibrinogen concentration,^{11,31} also noted in our study. Changes in blood viscosity during pregnancy seem to be more complex; the influence of plasma viscosity on the resulting whole blood viscosity increases at higher shear rates, while the hematocrit appears to be the most important determinant of whole blood viscosity at lower shear rates.³² Eguchi et al⁸ suggested that decreased erythrocyte deformability and increased fibrinogen concentration are compensated for by decreased hematocrit and result in unchanged blood viscosity during uncomplicated pregnancy.

Our study had some limitations in design and conditions. First, for evident practical reasons, there was no examination before pregnancy; in addition, there was no control group of nonpregnant women. The postpartum status cannot be expected to reflect perfectly the basal, nonpregnant status since the delay before catamenial restoration is highly variable and since the delay between delivery and the postpartum examination varied by up to 5 months in our study. Our study was part of the routine follow-up of pregnant women, and any alteration of their usual management was avoided. Another potential limitation of the study was the way blood flow echogenicity was graded. An in vitro quantitative method for the analysis of the factors affecting blood echogenicity has been described by Kallio and Alanen³³ using digitization of the signal from an A-mode ultrasound scanner, integration, subtraction, and computer analysis of the signal. This is not possible in vivo because many parameters, including attenuation by interposed tissues, can interfere with overall echogenicity. Interobserver variability of subjective grading of spontaneous blood flow echogenicity has differed in previous studies.^{34,35} Fatkin et al used a five-level scale³⁶ and found a strong positive correlation of subjective grading with videodensitometry data³⁷; other authors have also used videodensitometry for the evaluation of spontaneous blood flow echogenicity.³⁸ Image processing techniques are being developed in our laboratory for automatic quantification of blood flow echogenicity. In this study, the four-level scale we used was simple enough to

allow semiquantitative grading. A final potential limitation of our study was that the physician performing the examination was aware of the pregnancy status of the patient; however, she was not aware of the plethysmographic and laboratory findings.

In conclusion, our study demonstrates that major changes in lower limb venous function occur during pregnancy and that most of them reverse after delivery. Enlarged saphenous veins and reduced calf capacitance suggest that increased venous pressure leads to overdistention and reduced compliance. Vena caval compression by the gravid uterus and increased intra-abdominal venous pressure are probably the main cause of the increase in lower limb venous pressure. Decreased flow velocities, with low shear rates on one hand and rheological alterations with increased fibrinogen concentration on the other hand, result in increased red cell aggregation; red cell aggregation gives rise to spontaneous blood flow echogenicity in the lower limb veins, which appears to be a normal finding during pregnancy and should not be mistaken for venous thrombosis.

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