Ultrasound Obstet Gynecol 2002; **19**: 366–370

Assessment of uterine artery blood flow in normal first-trimester pregnancies and in those complicated by uterine bleeding

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KEYWORDS: Early pregnancy, Pulsed and color Doppler, Threatened miscarriage, Transvaginal color Doppler, Uterine blood flow

ABSTRACT

Objective *To compare uterine artery blood flow in normal first-trimester pregnancies with those complicated by uterine bleeding.*

Methods *Uterine artery blood flow was investigated by transvaginal color Doppler in 46 pregnant women affected by uterine bleeding and in a control group of 35 women with normal intrauterine pregnancy. Gestational age ranged from the 6th to the 12th week. Three blood flow values were calculated, the pulsatility index, the resistance index and the peak systolic velocity. Results were compared between the two groups.*

Results *Of the 46 patients affected by uterine bleeding, 18 had an incomplete miscarriage, eight had a blighted ovum, five had a missed miscarriage and 15 continued their pregnancy until term and delivered liveborn infants. No significant differences were found in any of the three vascular indices between the normal and the pathological groups of patients. Uterine artery pulsatility and resistance indices decreased with gestational age in both normal and abnormal pregnancies but this change was not statistically significant. The peak systolic velocity significantly increased with gestational age in the control group but not in the pathological group. In patients with a retroplacental hematoma, uterine vascular resistance appeared higher than in those without a hematoma, while the peak systolic velocity showed no difference between the two groups.*

Conclusion *Doppler analysis of the uterine artery blood flow is unlikely to have a clinical role in the management of early pregnancies complicated by uterine bleeding.*

INTRODUCTION

The introduction of pulsed and color Doppler sonography into obstetrics has allowed the direct non-invasive investigation of the fetomaternal circulation. In particular, Doppler analysis of the uterine vessels has enabled the assessment of the major vascular events which occur during pregnancy. These events are represented by the decrease in vascular resistance and the increase in blood flow velocity which, associated with an increase in maternal cardiac output, are necessary for fetal development and growth[1–3].

Apart from providing useful information on the physiology of the uteroplacental circulation, pulsed and color Doppler has become a useful tool for monitoring fetal wellbeing in the second and third trimesters of pregnancy. It is now well established that complications of pregnancy such as pre-eclampsia, hypertension and intrauterine growth restriction are associated with important vascular alterations of the uterine and placental blood flows which can be easily detected by Doppler analysis[4–6].

The uteroplacental circulation is the result of the invasion of the trophoblastic tissue of the uterine spiral arteries, which occurs in two different phases. The first vascular invasion occurs from the 5th week of pregnancy and is followed by a second invasion in the 14th week[7–9]. These changes lead to a progressive decrease in the resistance to flow in uterine vessels and to an increase in blood flow directed to the pregnant uterus[2,7,10,11]. Some investigators have proposed studying the uteroplacental circulation in early pregnancy to determine if alterations of the early vascular events could influence pregnancy course and outcome[3,12–16].

This study set out to investigate uterine artery blood flow by transvaginal pulsed and color Doppler to determine if first-trimester pregnancies complicated by uterine bleeding have different blood flow patterns in comparison with normal pregnancies. In such cases, Doppler analysis of the uterine arteries would be of clinical value in the management of early pregnancies complicated by uterine bleeding.

METHODS

This was a 1-year prospective cross-sectional study including 46 patients with an early pregnancy complicated by uterine

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Accepted 20-12-01

bleeding and 35 patients with a normal first-trimester pregnancy who served as the control group. The gestational age ranged from the 6th to the 12th week. The study was carried out at the Department of Obstetrics and Gynecology at the University of Padova, Italy. All patients were informed of the purpose of the study and gave their consent.

Each patient underwent a single sonographic examination with a Siemens Sonoline Elegra ultrasound machine (Siemens, Munich, Germany) equipped with a 6.5-MHz transvaginal probe. All examinations were performed by the same physician. The high pass filter was set at 100 Hz and the spatial peak temporal average was 80 mW/cm^2 (according to the limits recommended by the American Food and Drug Administration for use in fetal medicine). A two-dimensional, B-mode scan was first performed to evaluate the state of the pregnancy and to determine the true gestational age by measuring the crown–rump length. Both uterine arteries were visualized at the level of the corporocervical junction by transvaginal color Doppler. A pulsed Doppler range gate was then placed across the artery, aiming for an angle of insonation close to 0° between the Doppler beam and the vessel. Flow velocity waveforms were obtained from both uterine arteries in all patients. After detection of blood flow and visualization of the uterine artery waveform, three flow indices were automatically calculated: the pulsatility index (PI), the resistance index (RI) and the peak systolic velocity (PSV). At least three consecutive, correctly imaged blood flow velocity waveforms were analyzed and the mean value was calculated for each of the three flow indices.

As suggested by Jurkovic *et al.*[2], who assumed that the uterine artery with the higher PSV contributed more to the placental blood supply, we selected this vessel for further analysis.

Reproducibility of the uterine artery Doppler measurements was calculated before starting the study using one-way analysis of variance (ANOVA) of replicate data. The uterine artery indices (PI, RI and PSV) were calculated during each of 14 Doppler evaluations performed sequentially on a young woman who volunteered. The mean values were 3.4 ± 1.1 standard deviations (SD) for PI, 0.90 ± 0.002 SD for RI and 37.8 ± 0.10 SD for PSV. The coefficients of variation were 0.32% for PI, 0.22% for RI and 0.26% for PSV.

Differences in uterine vascular RIs and PSV were calculated between the two groups (pregnancies affected by bleeding ($n = 46$) and normal gestations ($n = 35$)) for each gestational week. For both groups the relationship between gestational age and each of the three indices was studied. All pregnancies which continued were followed to term. Finally we analyzed the uterine artery blood flow in patients presenting with a retroplacental hematoma and in patients with no hematoma.

The mean and SD of values recorded for the three indices for each gestational week were calculated. The significance of the difference between the groups was determined by ANOVA. Pearson's correlation coefficient (r) was used for the correlation of each vascular index with gestational age; $P < 0.05$ was considered statistically significant in all tests. Statistical analysis was performed using the SPSS software (Chicago, IL, USA).

RESULTS

Eighty-one patients were included in the study: 44 were nulliparous and 37 were multiparous. The mean age of subjects was 30.9 (range, 17–45) years. Of the 46 patients affected by uterine bleeding 18 had an incomplete miscarriage, eight had a blighted ovum, five had a missed miscarriage and 15 continued their pregnancy to term and delivered liveborn infants. Among these patients only one pregnancy was affected by mild hypertension during gestation and this case developed no fetomaternal complications. A retroplacental hematoma was found in 10 patients of the 46 affected by uterine bleeding.

Of the 35 patients in the control group, 25 decided to interrupt pregnancy for psychosocial reasons at the 13–14th week of gestation and 10 continued their pregnancy to term without complications. Table 1 shows the distribution of patients according to gestational age.

The results of the uterine artery blood flow analysis are reported in Table 2. No significant differences were found in

Table 1 Distribution of patients according to gestational age

Gestational age (weeks)	*Abnormal group (n) (n = 46)*	*Control group (n) (n = 35)*
6	9	4
7	7	4
8	9	7
9	4	9
10	9	4
11	5	4
12	3	3

Table 2 Mean values of each vascular index of the uterine artery for each gestational age in the abnormal group ($n = 46$) and the control group ($n = 35$) of patients

Weeks of gestation	*Abnormal group (mean (SD))*			*Control group (mean (SD))*		
	PI	*RI*	*PSV (cm/s)*	*PI*	*RI*	*PSV (cm/s)*
6	2.46 (0.91)	0.84 (0.12)	37.77 (14.16)	2.16 (0.64)	0.79 (0.16)	31.75 (9.84)
7	3.06 (1.03)	0.90 (0.08)	52.42 (16.48)	2.60 (1.19)	0.87 (0.11)	52.00 (26.84)
8	2.93 (0.93)	0.89 (0.10)	50.33 (14.27)	2.32 (0.66)	0.79 (0.21)	44.28 (15.75)
9	2.88 (0.67)	0.86 (0.18)	45.75 (18.55)	2.44 (0.61)	0.86 (0.07)	49.00 (8.70)
10	2.29 (0.55)	0.83 (0.08)	40.00 (14.26)	1.88 (0.49)	0.83 (0.10)	60.00 (26.82)
11	2.21 (1.03)	0.81 (0.08)	39.80 (10.94)	2.11 (0.39)	0.81 (0.08)	42.50 (17.67)
12	2.28 (1.01)	0.82 (0.11)	47.33 (21.73)	1.95 (0.63)	0.77 (0.12)	64.33 (28.53)

PI, pulsatility index; RI, resistance index; PSV, peak systolic velocity.

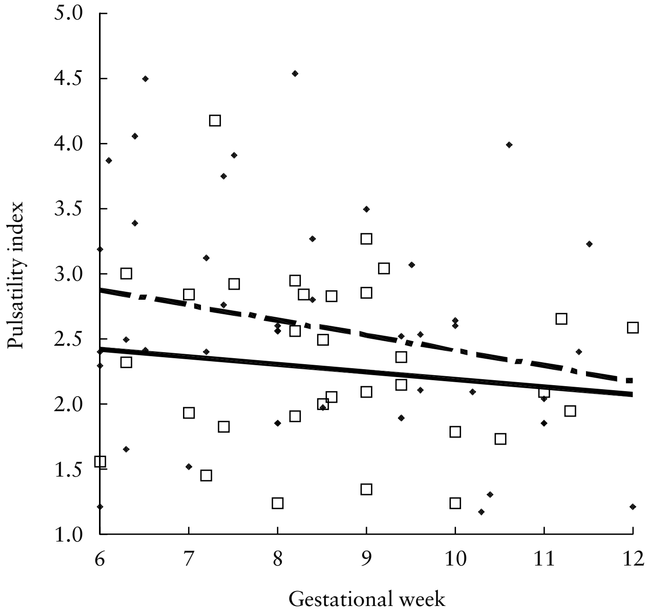

Figure 1 Scatterplot with linear regression lines showing changes of the pulsatility index with gestational age in normal (□, solid line) and pathological (◆, broken line) groups (pathological group: $P = 0.05$, $r^2 = 0.248$, slope = 0.117; control group: $P = 0.18$, $r^2 = 0.157$, slope = 0.05914).

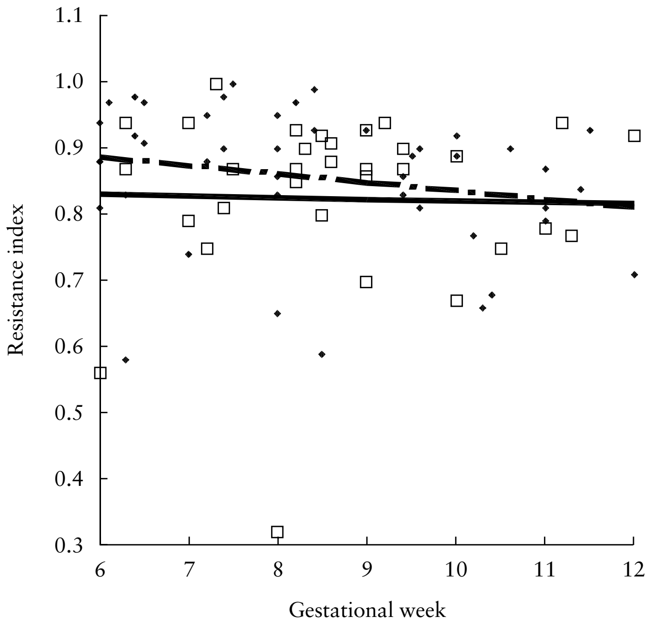

Figure 2 Scatterplot with linear regression lines showing changes of the resistance index with gestational age in normal (□, solid line) and pathological (◆, broken line) groups (pathological group: $P = 0.70$, $r^2 = 0.225$, slope = 0.01278; control group: $P = 0.42$, $r^2 = 0.033$, slope = 0.002471).

the three vascular index values between the normal group and that with uterine bleeding ($P = 0.054$ for PI; $P = 0.20$ for RI; $P = 0.31$ for PSV) (ANOVA).

Analysis of correlation (r) between each vascular index and gestational age showed that the PI and the RI decreased in both normal and abnormal pregnancies with advancing gestation but this change was not statistically significant. The PSV significantly increased with gestational age in the

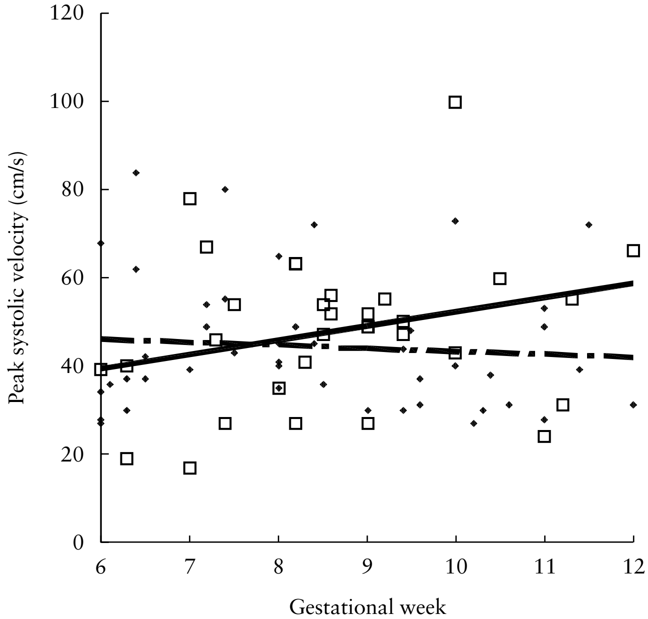

Figure 3 Scatterplot with linear regression lines showing changes of the peak systolic velocity with gestational age in normal (□, solid line) and pathological (◆, broken line) groups (pathological group: $P = 0.28$, $r^2 = 0.084$, slope = 0.685; control group: $P = 0.036$, $r^2 = 0.308$, slope = 3.275).

control group ($P = 0.036$), but not in the pathological group ($P = 0.28$). Figures 1–3 show the regression lines of the changes in the PI, RI and PSV with gestational age in the uterine artery for the two groups of patients.

Finally we considered patients presenting with retroplacental hematoma. The PI and the RI were higher than in those without hematoma ($P = 0.01$ for the PI; $P = 0.07$ for the RI), while the PSV showed no difference between the two groups ($P = 0.14$). Seven patients in this group miscarried.

DISCUSSION

Thanks to the new generation of pulsed and color Doppler equipment which makes it possible to map uteroplacental circulation from the first weeks of gestation[16], Doppler technology has been used to investigate early pregnancies complicated by uterine bleeding[3,12,13,17,18]. Indeed, the possibility to identify uteroplacental vascular alterations from the first trimester of pregnancy could provide a new diagnostic tool for the clinical management of early pregnancies complicated by uterine bleeding.

In this study, blood flow analysis was performed on the uterine artery because this vessel is easily recognized and detected[19] and this improves reproducibility of the results obtained by different physicians. Small vessels such as the peritrophoblastic vessels are more difficult to detect, and require sophisticated equipment, thus the results obtained may be more imprecise and may vary greatly[3,18–20].

It has been demonstrated that the vascular resistance and the PSV recorded from one of the uterine arteries are different from those obtained from the contralateral vessel[10,19,21]. One of the two uterine arteries prevails over the other one in almost all pregnancies, especially during the first weeks of gestation. In particular, the artery which is homolateral to the site of embryo implantation shows lower vascular resistance and higher blood flow[13]. Therefore abnormal blood flow patterns may be evident during the first trimester only in the dominant uterine artery. Thus in our study the uterine artery blood flow analysis was performed on the uterine vessel with the higher PSV, which is considered to be the dominant one[2].

In agreement with other studies[12,18,22] we did not find any significant differences in blood flow indices of the uterine artery between first-trimester pregnancies complicated by bleeding and those of the control group. This suggests that uterine artery blood flow analysis does not identify hemodynamic alterations which occur in abnormal early pregnancy. Most likely the vascular changes which compromise the uteroplacental circulation in the first trimester are too small and too localized to influence uterine artery velocity waveforms. The uterine artery represents the sum of the vascular resistance of the whole uterine vascular bed; thus small differences between normal and abnormal pregnancies cannot be detected. Some authors have proposed investigating the small vessels of the vascular uterine bed such as the spiral arteries and the subchorionic vessels[4,9,18]. Although some studies demonstrated an association between abnormal color Doppler findings in the decidual spiral arteries and prevalence of complicated pregnancies, other studies have not found such significant differences[12,13,15].

Recently Leible *et al.*[23] demonstrated that patients with a pregnancy ending in miscarriage show a different uterine artery blood flow pattern in comparison with patients whose pregnancy continues. The authors reported discordant uterine artery blood flow velocity waveforms with an abnormally high PI in one of the two uterine arteries in patients at risk of subsequent miscarriage. In particular the discordant uterine artery PIs were strongly associated with subsequent pregnancy loss. However, most cases of miscarriage reported in this work were missed miscarriages in which it has been demonstrated that the main cause of miscarriage is poor vascularization[14]. It is probable that in missed miscarriage, as suggested by the authors, the exclusion of one uterine artery may produce an ischemic injury which leads to pregnancy failure.

Most studies described in the literature have shown that vascular resistance of the uteroplacental bed declines with advancing gestation[7,12,24]. In our study, vascular RIs decreased with gestational age but these differences did not reach statistical significance in either group of patients. This may be due to the fact that we considered a narrow range of gestational weeks, from the 6th to the 12th, while most authors have studied a wider range, from the 4th to the 16–18th, and it has been demonstrated that the major hemodyamic changes occur around the 14th week of gestation[2,3,7,12]. On the other hand, in our study the PSV significantly increased with gestational age in the control group, but not in the pathological group. This result suggests two things: (1) during early pregnancy most of the uterine blood supply is probably due more to an increase of blood flow velocity than to a decrease of vascular resistance; (2) pregnancy ending in miscarriage has a lower blood flow supply than has normal ongoing pregnancy. However, differences in the PSV between normal and abnormal groups were not detectable by analysis of the absolute value of the PSV. Instead they became evident by analysis of their different trends with gestational age. It is likely that vascular alterations due to an abnormal placentation are present from the beginning of pregnancy, but they are detectable through Doppler analysis only from the beginning of the second trimester. Based on this we could speculate that pregnancies associated with greatly compromised uteroplacental circulation will miscarry, while pregnancies mildly compromised will continue but will risk developing complications such as intrauterine growth restriction and pre-eclampsia. This needs to be confirmed by prospective longitudinal studies, and should this hypothesis be confirmed, therapeutic support such as aspirin should be given to high-risk patients from the first weeks of gestation.

Finally, we considered patients presenting with a retroplacental hematoma. In these patients, impedance was greater than in those without hematoma. These data are in accordance with those of Kurjak *et al.*[12] who carried out research on the spiral arteries. In this work the phenomenon was attributed to the compression by the hematoma of neighboring vessels.

In conclusion, this study confirms the important role of color Doppler in understanding the different aspects of the pathophysiology of the uteroplacental circulation. However, today it is likely to have no clinical role in the management of early pregnancies complicated by uterine bleeding.

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