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The effect of uterine and spiral artery Doppler velocimetry in predicting miscarriage in threatened miscarriage patients

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Abstract

Background/Aim: Doppler sonography was used to investigate the effect of abnormal placentation on early and late pregnancy complications with conflicting results on changes in uterine blood flow and spiral arteries in early pregnancy. This study aimed to compare the uterine and spiral artery Doppler findings between healthy pregnant women and patients with threatened miscarriage.
Methods: In this prospective case-control study, the uterine and spiral artery Doppler findings of 60 patients with threatened miscarriage between 12-20 weeks of gestation were compared with those of 60 healthy pregnant women at similar gestational weeks. Resistance index, spiral artery pulsatility index, systolic/diastolic ratio, and uterine artery Doppler values were evaluated.
Results: The patients in the threatened miscarriage group had a higher mean age than those in the control group ($P<0.001$). No significant difference was found between the groups in terms of uterine artery and spiral artery resistance index, systolic/diastolic ratio, and pulsatility index values ($P>0.05$ for each).
Conclusions: Our results showed that there was no significant difference between the indexes of spiral and uterine artery in Doppler ultrasonography. Further studies are needed to evaluate uterine vascular bed alterations to predict the threatened miscarriage prognosis in the first trimester.

Keywords: Resistance index, Pulsatility index, Spiral artery Doppler, Threatened miscarriage, Uterine artery Doppler

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Introduction

Based on the definition of the World Health Organization, miscarriage is defined as the expulsion of all or part of the embryo, fetus, or its attachments outside the uterine cavity within the first 20 weeks of pregnancy. Miscarriage is a common pregnancy complication that occurs in approximately 15% of clinically defined pregnancies [1]. After the pregnancy is detected on ultrasound, this rate decreases to 1.6-6.7% on average [2, 3]. Threatened miscarriage means the occurrence of vaginal bleeding when the cervix is closed, and the fetus is in the uterine cavity during pregnancy. Pelvic pain may or may not accompany the threatened miscarriage. It has been reported that the risk of miscarriage is 2.5 times higher in patients suffering from threatened miscarriage, which is of foremost importance for families' and women's psychological statuses [4].

Extravillous trophoblast should invade the myometrium, maternal decidua, and blood vessels for healthy placentation [5, 6]. With the use of Doppler sonography, the effect of abnormal placentation on early and late complications of pregnancy has been investigated. A non-invasive method that evaluates uteroplacental circulation is the high-frequency transvaginal Doppler sonography. Abnormal velocity waveforms in early pregnancy are related to pregnancy complications, including preeclampsia and intrauterine growth retardation (IUGR) [7, 8]. Few studies have examined the pulsatility index (PI) of the uterine artery, especially under 11 weeks [9]. There are conflicting results regarding changes in the uterine blood flow and spiral arteries in early pregnancy. In many studies, power analysis shows that the number of patients is insufficient. This study aims to compare the uterine and spiral artery Doppler findings between healthy pregnant women and patients with threatened miscarriage.

Materials and methods

Ethics Committee approval was obtained from the Ethics Committee of Beykoz University, Turkey (Permission granted/CAAE number: 30/09/2019 Decision no:1). This prospective case-control study was conducted in accordance with the Helsinki Declaration, in a tertiary hospital between October 2019 and June 2020.

Sociodemographic data such as BMI and age, parity, history of miscarriage, and gestational weeks of the patients were recorded. Sixty volunteers with threatened miscarriages between the 12^{th}-20^{th} gestational weeks admitted to the Obstetrics and Gynecology Department were included in the study. Transvaginal ultrasonography is our routine evaluation in patients presenting with bleeding in early gestational weeks. Transvaginal ultrasonography, which was routinely performed at the time of hospitalization, and uterine and spiral artery Doppler ultrasonography were performed in lithotomy position in 60 volunteering patients between the 12^{th}-20^{th} weeks of pregnancy, and the results were compared with 60 healthy pregnancies at similar gestational weeks. Exclusion criteria included patients with ectopic pregnancy, multiple pregnancy, miscarriages, hypertension, diabetes, immunologic, renal, hematologic, or heart diseases. Doppler ultrasound was performed with the same persons (N.T.O and T.G) in each hospital with the same type of ultrasound device (Siemens, Acuson S1000 Ultrasound System). The Doppler scanner is compatible with color, has spectral Doppler capacity and a convex-array transducer of 12-MHz. Fetal anomalies, crown-rump length (CRL) measurement, and pregnancy viability were assessed and recorded. The pulse repetition frequency was 2.5 kHz and the high-pass filter was set at a minimum. For Doppler sonographic examination, the maximum attainable mechanical and thermal indices were 1.0 and 1.2, respectively. The sampling gate size was adjusted to be 2 mm. The midsagittal uterine section was visualized and the cervical canal was observed. The probe was not moved laterally until the paracervical vascular plexus was visualized. After color Doppler initialization and detection of the uterine artery, cranially turning the probe caused it to ascend toward the uterine corpus. There were records of the measurements of the uterine artery with spectral Doppler before it branched into the arcuate artery. Once the angle of insonation was below 30^{o}, a spectral Doppler gate appeared over the vessel. To update the tracing, at least three consecutive flow velocity waveforms with adequate quality were verified through measurements of the bilateral uterine artery including pulsatility index (PI), systolic/diastolic (s/d) ratio, and resistance index (RI). There were spiral arteries in the medial third myometrium. The lowest feasible color-gain settings were examined with Doppler ultrasonography. The gain was gradually increased to view the flow pattern. Waveforms of the flow velocity were recorded after finding the flow. At least three satisfactory waveforms were used to calculate the spectral Doppler values. Spiral and bilateral uterine arteries' RI, PI, and s/d values were saved.

Both Lin's Intraclass Correlation Coefficient (ICC) (two way-mixed, absolute agreement, average measurements) and Concordance Correlation Coefficient (CCC) were used to evaluate intra- and inter-observer generalizability and reliability at 95% Confidence Interval (CI). The first and the second measurements of Operator A were crosschecked to investigate the intra-observer reproducibility, which was evaluated using the mean values of the first and second measurements of each operator. The blinded method was used for the examination three times as follows: Observer A performed the first scan, Observer B performed the second scan to check interobserver reproducibility, and Observer A performed the scan once more to check intra-observer reproducibility. To determine the concordance correlation coefficient (CCC) with adequate precision (95% CI width = 0.20) at ≥0.70 (10), a sample size of 120 individuals was needed. CCC values of <0.70 indicated very poor reproducibility [10].

In a reference study evaluating threatened miscarriage patients, the uterine artery s/d ratio was 5.3 (4.6-6.7) in the threatened miscarriage group and 4.3 (3.5-6.1) in the control group. With the mean of two groups compared with the student t-test, calculation of the sample size with G*Power 3.1 (http://www.gpower.hhu.de/) showed that a minimum of 57 patients per group was needed for 80% power and 0.05 type 1 error. A third-party expert's opinion was used to prevent any potential bias.

Statistical analysis

Statistical analyses were performed with SPSS 23.0 software. Categorical values were presented as numbers and percentages, and continuous data were given as mean, deviation, and minimum-maximum values. To compare the continuous

measurements between groups, independent student t-test analysis was applied to binary variables by controlling distributions. A *P*-value of <0.05 indicated statistical significance in all tests.

Results

One hundred and twenty patients were included in the study voluntarily. The mean age of the patients in the threatened miscarriage group was significantly higher than that in the control group ($P<0.001$) (Table 1). The remaining sociodemographic and obstetric data, namely, parity, history of miscarriage, BMI, and gestational week were similar between the two groups ($P>0.05$) (Table 1). There was no significant difference between the groups in terms of uterine and spiral artery PI, RI, s/d values ($P>0.05$) (Table 2). We found that there was moderate intra-observer reproducibility of the CCCs between 0.92-0.95 and moderate inter-observer reproducibility of the CCCs between 0.91-0.95 in transvaginal ultrasonography performed by experienced operators.

Table 1: Baseline characteristics of studied participants

	Threatened Abortion (n=60) mean(SD)	Healthy Pregnant (n=60) mean(SD)	*P*-value
Age	29.97(6.69)	24.43(5.03)	0.001
Parity	1.98(0.98)	1.57(0.67)	0.080
History of early pregnancy loss (≤12 weeks)	0.18(0.43)	0.24(0.43)	0.619
Body mass index (kg/m²)	26.45(4.41)	24.71(4.10)	0.118
Gestational age (weeks)	14.31(2.19)	14.57(2.27)	0.652

SD: standard deviation

Table 2. Spectral Doppler measurements between groups

	Threatened Abortion (n=60) mean(SD)	Healthy Pregnant (n=60) mean(SD)	*P*-value
Uterine artery PI	1.59(0.31)	1.58(0.36)	0.934
Uterine artery RI	0.70(0.05)	0.71(0.07)	0.536
Uterine artery S/D	4.9(1.44)	4.6(1.28)	0.230
Spiral artery PI	0.51(0.10)	0.51(0.10)	0.792
Spiral artery RI	0.35(0.05)	0.37(0.06)	0.163
Spiral artery S/D	4.16(0.92)	4.05(1.21)	0.576

SD: standard deviation, PI: pulsatility index, RI: resistance index, S/D: systolic/diastolic

Discussion

Uteroplacental circulation is not fully elucidated. There is an association between vascular remodeling disruption on the maternal-fetal surface and complications of pregnancy [11]. It has been reported that intensive vascular remodeling during early pregnancy is important in healthy progression. Determining the uteroplacental vascular changes from implantation until the end of the pregnancy may be diagnostic in the clinical management of early pregnancy loss and pregnancy complications [12]. The resistance index of the spiral artery decreases after the 5th gestational week. This is shown to reduce local arterial resistance in vascular remodeling caused by trophoblast invasion [13]. A study conducted by Pellizzari et al. [14] showed no significant difference in resistance indexes between the 6th-12th gestational weeks, which is in line with our study results. In a study by Özkan et al. [15], no significant difference was found in resistance index, spiral artery pulsatility index, and systolic/diastolic ratio values, but systolic/diastolic ratio was higher in uterine artery values in the miscarriage group. In the study by Roberts et al. [16], it was shown that maternal blood flow to placental intervillous space starts from the 6th week. The uterine artery systolic/diastolic ratio was promising in predicting adverse outcomes. However, although abnormal placentation starts from the beginning of pregnancy, it can become more evident at the end of the first and second trimesters [15]. There may be very small vascular changes in the uteroplacental circulation in the first trimester, and the uterine artery velocity waveform is changed through its localization. In a few studies evaluating the small vessels of the vascular uterine bed, including the spiral artery and subchorionic vessels, a significant association was reported between abnormal Doppler findings and pregnancy results, while no significant association was found in the other studies [17, 18]. In the study conducted by Ozkaya et al. [19], the increase in the uterine and spiral artery resistance indexes increased the risk of miscarriage, placental abruption, preterm labor, and IUGR in a limited number of cases, which is not in line with our study results. Guedo-Martin et al. [9] reported an age-related reduction of RI and PI values of the uterine artery from 6 weeks to 10 weeks. The study conducted by Özkan et al. [15] reported that uterine and spiral arteries showed different changes in early pregnancy, and spontaneous abortion risk might increase in pregnancies with high spiral artery RI at the 5th and 6th weeks. When spiral artery RI is normal, decreased uterine artery RI in the placental area may occur with a locally developing shunt [20]. Sheehata et al. [21] found no significant difference between the Doppler indices of the uterine artery. The patients' ages were significantly higher in the spontaneous abortion group than in the ongoing pregnancy group, which is consistent with previous studies reporting that inappropriate and inadequate progesterone secretion increases miscarriage rate due to ovarian aging [21, 22]. In our study, age was significantly higher in the threatened miscarriage group and no significant differences were found in the indexes of spiral and uterine arteries by Doppler ultrasonography.

Limitations

Two observers examining the variables can be considered as a study limitation. However, the use of the same quality ultrasound machine has been the factor that improves the reproducibility of the study.

The major strength of this research is the fact that it was conducted with transvaginal measurements, in line with the Guidelines of the International Society of Ultrasound in Obstetrics and Gynecology [23]. The ultrasound scans were entirely detached, observers were blinded to their results, and the results were analyzed and interpreted attentively.

Conclusion

In the first trimester, fetal structural changes are detected most, and hemodynamic evaluation is not given enough importance. There are important limitations of investigating the spiral and uterine artery indexes in the early weeks of pregnancy. There should be more studies to explain the relationship between histological findings of vascular remodeling and spiral artery resistance in Doppler ultrasonography and evaluation of the uterine vascular bed alterations for prediction of the prognosis of threatened miscarriage in the first trimester.

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