

The value of hemodynamic parameters of uterine spiral arteries in predicting Gestational Diabetes Mellitus in first trimester

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Research Article

Keywords: Gestational diabetes mellitus, Uterine spiral arteries, Ultrasonography, Doppler, Hemodynamic

Posted Date: May 31st, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1632025/v1>

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Abstract

Purpose Early diagnosis of GDM and targeted blood glucose control treatment are crucial to improve maternal and infant health and to reduce the incidence of adverse pregnancy events. There is a lack of simple, effective and accurate screening methods that can be performed before 14 weeks of gestation. This study aimed to investigate the value of hemodynamic parameters of spiral artery in predicting GDM at 11 ~ 13 + 6 weeks of gestation.

Methods To investigate the value of hemodynamic parameters of uterine spiral artery in predicting GDM in first trimester. We conducted a prospective case–control study, involving 1054 singleton pregnancies in our obstetric clinic of Shanghai First Maternal and Infant Hospital from January 2020 to June 2021. According to the follow-up results, they were divided into normal group (938 cases) and GDM group (116 cases). All pregnant women examined by Doppler ultrasonography in first-trimester to measure uterine spiral arterial hemodynamic parameters, including pulsation index (PI), resistance index (RI), peak systolic flow velocity (PSV) and mean diastolic velocity (MDV). The hemodynamic parameters of the GDM group and normal group were compared, and ROC curve was drawn to evaluate the efficacy of uterine spiral artery PI in predicting GDM.

Results The PI value of uterine spiral artery in GDM group was higher than that in normal group (0.88 ± 0.16 vs. 0.63 ± 0.17), and the difference was statistically significant ($t = 14.932$, $P < 0.05$). The PSV and RI in GDM group were slightly lower than those in normal group, but the differences were not statistically significant ($P > 0.05$). The area under ROC curve of spiral artery PI for predicting GDM was 0.861 (95%CI: 0.827–0.895, $P < 0.05$), and PI 0.675 was the optimal threshold. The sensitivity and specificity of spiral artery PI for predicting GDM were 90.5% and 73.3%, respectively.

Conclusions: The changes of uterine spiral artery hemodynamic parameters at first-trimester of pregnancy may be related to the occurrence of GDM, and the PI value of uterine spiral artery has certain value in predicting GDM.

1. Introduction

The public health impact of Gestational diabetes mellitus (GDM) is becoming more and more apparent in China, Especially after the implementation of the “two-child policy” in October 2015. GDM might lead to the development of adverse effects on both the fetus and the mother, and also increases the risk of long-term diabetes after delivery^{1,2}. GDM can not only induce gestational hypertension and other complications of pregnancy. Moreover, it seriously affects the metabolism and secretion of maternal hormones. The prediction of gestational diabetes in early pregnancy has far-reaching significance. There is a lack of simple, effective and accurate screening methods that can be performed before 14 weeks of gestation. As a convenient, accurate and non-invasive medical technique, color Doppler ultrasound can reflect arterial blood supply directly^{3,4}. This study observed the changes of uterine spiral artery blood flow parameters in GDM patients during early pregnancy and their influence on pregnancy outcome, in order to

provide reference for clinical practice. The purpose of this study was to explore the predictive value of hemodynamic changes in GDM by comparing the ultrasonic Doppler parameters of uterine spiral artery between GDM pregnant women and normal pregnant women in first-trimester.

2. Methods

2.1 Objects

A prospective case-control study was conducted, recruited 1054 singleton pregnant women between December 2020 to January and February 2021 in Shanghai First Maternity and Infant Hospital, Tongji University, Shanghai, China. All subjects clearly understood the content and purpose of the study, voluntarily participated in the study and signed the informed consent. There were no significant differences in age, parity, weight, body mass index(BMI)and Crown rump length (CRL)between the two groups ($P > 0.05$ for all). Patients with GDM met the diagnostic criteria for GDM issued by the American Diabetes Association (ADA). Inclusion criteria were :(1) single pregnancy; (2) All patients received ultrasound Doppler examination in 11 ~ 13 + 6 weeks of gestation. (3) Pregnancy outcomes were obtained through follow-up. Exclusion criteria were: (1) previous adverse pregnancy history; (2) other medical and surgical complications except GDM; (3) Fetal abnormalities were found during pregnancy. According to the diagnostic criteria of GDM ⁵, 1054 pregnant women were divided into normal group (938 cases) and GDM group (116 cases) according to follow-up results. This study was reviewed and approved by the ethics Committee of Shanghai First Maternal and Infant Hospital.

2.2. Instrument

Philips iU22 color Doppler ultrasound diagnostic instrument, probe type C5-1, frequency 3.5MHz. All pregnant women were examined by ultrasound Doppler at 11 to 13 + 6 weeks of gestation. The pregnant women were in supine position and breathing peacefully. First, the conventional parameters such as Crown Rump Length (CRL) and fetal heart rate were measured. Then, the spiral artery blood flow spectrum of placenta attached to uterine muscle wall was observed and measured. The Angle between the acoustic beam and the direction of the artery should not exceed 20 degrees, and the sampling volume is adjusted by about 2 mm to obtain spectral patterns of at least 3 cardiac cycles and obtain hemodynamic parameters, including systolic/diastolic ratio (S/D), pulsation index (PI), resistance index (RI), peak systolic flow velocity (PSV), mean diastolic velocity (MDV).

2.3. Statistical analysis

SPSS 21.0 statistical software was used for statistical analysis of the data. The pregnant women's age, CRL, PI, S/D and PSV were all measurement data, in line with normal distribution, represented by $\bar{x} \pm s$. Independent sample T test was used for comparison between the GDM group and the normal group. ROC curve was used to analyze the area under the curve, cut-off, and specificity of PI in predicting GDM. $P < 0.05$ was considered as statistically significant difference.

3. Results

3.1 Comparison of general data between the GDM group and the normal group, among 1054 pregnant women, there were no significant differences in age, CRL and BMI between the GDM group and the normal group in first-trimester (all $P > 0.05$, Table 1).

Table 1
Comparison of general data between GDM group and normal group ($\bar{x} \pm s$)

groups	n	Parities	Age(years)	Weight	BMI	CRL
GDM group	116	0.38 ± 0.48	30.59 ± 3.8	61.24 ± 3.67	23.54 ± 1.9	62.84 ± 5.9
Normal group	938	0.34 ± 0.49	30.69 ± 4.0	60.59 ± 4.9	23.19 ± 2.1	60.13 ± 6.5
t	-	0.87	0.26	0.92	1.85	4.24
P	-	0.36	0.61	0.34	0.98	0.67
GDM: Gestational diabetes mellitus, BMI: Body Mass Index, CRL: Crown rump length						

3.2 The uterine spiral artery PI value in GDM group was higher than that in normal group (0.88 ± 0.16 vs. 0.63 ± 0.17), and the difference was statistically significant ($t = 14.932$, $P < 0.05$). The RI and PSV of the GDM group were slightly lower than those of the normal group, but the differences were not statistically significant ($P > 0.05$, Table 2, Fig. 1).

Table 2
Comparison of hemodynamic parameters of uterine spiral arteries between GDM group and normal group at first-trimester

groups	n	S/D	PI	RI	PSV	MDV
GDM group	116	2.44 ± 0.30	0.88 ± 0.16	0.45 ± 0.10	58.92 ± 4.12 cm/s	26.02 ± 2.33 cm/s
Normal group	938	2.38 ± 0.34	0.63 ± 0.17	0.47 ± 0.05	59.66 ± 2.01 cm/s	26.27 ± 2.17 cm/s
t	-	1.906	14.932	1.041	0.893	1.18
P	-	0.059	0.000*	0.298	0.374	0.238
GDM: gestational diabetes mellitus, S/D: systolic/diastolic ratio, PI: pulsing index, RI: resistance index, PSV: peak systolic flow velocity, MDV: mean diastolic velocity						

3.3 Based on the diagnostic criteria for GDM⁶, the area under ROC curve for predicting GDM by spiral artery PI was 0.861 (95%CI: 0.827–0.895, $P < 0.05$), and PI 0.675 was the optimal threshold. The

sensitivity and specificity of spiral artery PI for predicting GDM were 90.5% and 73.3%, respectively. (Fig. 2)

4. Discussion

Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance resulting in hyperglycemia with first occurrence or detection during pregnancy. GDM is seriously harmful to both the woman and the fetus. GDM women are prone to complications of gestational hypertensive disease, polyhydramnios, and premature rupture of fetal membranes, infection and premature birth⁷. In addition, the fetus is prone to spontaneous abortion, malformation and hypoxia even intrauterine death. More than 80% of pregnant women with diabetes have GDM. The prevalence of GDM in China is 4%-15%. The prevalence rate in North, central and East China is higher than that in other regions, and has a significant upward trend in recent years^{8,9}. In this study, the ratio of GDM to non-GDM pregnant women was 1:8.1. GDM has great harm to both mothers and children. The etiology and pathogenesis are not yet clear, which may be related to environmental factors, genetic factors, insulin resistance, adipocytokine and inflammatory factors¹⁰.

Studies have confirmed that vascular remodeling disorders at the maternal-fetal interface are widely associated with pregnancy complications. Vascular remodeling highly intensive in early pregnancy is an important determinant of pregnancy outcome¹¹⁻¹³. The uterine spiral artery passes through the placenta and provides the fetus with the nutrients needed for growth and development. In the first 3 months of pregnancy, the uterine spiral artery undergoes a recast process to establish enough blood perfusion placentas for optimal nutrition and metabolite exchange to meet the needs of the fetus^{14,15}. In the recast process, the smooth muscle and elastic fibers of the uterine spiral artery medium disappear and are replaced by fibrinoid substances, and the lumen expands gradually from the distal end to the proximal end, resulting in decreased vascular bed resistance and increased blood flow¹⁶, thus facilitating the occurrence and development of the placenta. Animal experiments have found that trophoblast infiltration and spiral artery remodeling disorders in diabetic rats may lead to placenta damage and insufficient nutrient supply, and ultimately lead to fetal weight loss¹⁷. Hemodynamic changes of spiral arteries can be used to evaluate the process and degree of spiral artery recasting, which is closely related to placenta development. Currently, the most frequently studied hemodynamic parameter is PI, which is indirectly obtained by the formula and is not affected by the sample angle. PI is the ratio of peak systolic blood flow velocity to average blood flow velocity, which can comprehensively reflect the maximum and average blood flow velocity and vascular bed resistance. This study found that the uterine spiral artery PI in GDM group was higher than that in normal group in first-trimester. Therefore, it is speculated that the increase of PI may be related to the occurrence of GDM. The mechanism may be as follows: on the one hand, the GDM group may not meet the diagnostic criteria of elevated blood glucose during first-trimester, but has abnormal glucose tolerance, which is not conducive to the recast process of the uterine spiral artery; On the other hand, the increase of PI in the uterine spiral artery means increased blood supply resistance, which in turn affects the development of placenta. The placenta has an endocrine function, which can secrete estrogen, progesterone, placental lactin, cortisol, insulinase and other substances with

insulin resistance¹⁸. Placenta with abnormal development will directly affect hormone secretion, and the changes of hormones will lead to further changes in immune-endocrine regulation of the maternal-fetal interface, resulting in GDM. The specific mechanism remains to be confirmed by further studies.

The early screening of GDM is of great clinical significance, but at present, it is mainly carried out by oral glucose tolerance test (OGTT) at 24–28 weeks of gestation¹⁹. The results of this study showed that there was no significant difference between GDM and normal pregnant women in conventional obstetric color Doppler ultrasonography, that is, GDM could not be predicted by two-dimensional images or color Doppler. When measuring the hemodynamic parameters of uterine spiral arteries, it was found that the PI value of the GDM group was higher than that of the normal group, and the difference was statistically significant. Moreover, it was found by ROC curve that the sensitivity and specificity of GDM prediction were 90.5% and 73.3% when PI increased by more than 0.675 as the threshold value. The area under ROC curve was 0.861, indicating that PI had a certain predictive value for GDM, that is, it was feasible to predict the occurrence of GDM by measuring PI value of uterine spiral artery at 11 ~ 13 + 6 weeks of gestation. In conclusion, the changes of uterine spiral artery hemodynamics at 11 ~ 13 + 6 weeks of pregnancy may be related to the occurrence of GDM, and the PI value of uterine spiral artery has certain value in predicting GDM.

Declarations

Ethics approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The research protocol was approved by the ethics committee of Shanghai First Maternity and infant Hospital.

Consent to participate

Informed consent was obtained from all individual participants included in the study.

Consent to publish

The authors affirm that human research participants provided informed consent for publication of the images in Figure 1a, 1b.

Author Contributions

L W: Data Collection, Manuscript writing. M R: Data collection and analysis. P C: Project development. HM K and XY M: Manuscript editing. All authors read and approved the final manuscript.

Conflict of interest

The authors declared that they have no conflicts of interest to this work.

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Figures

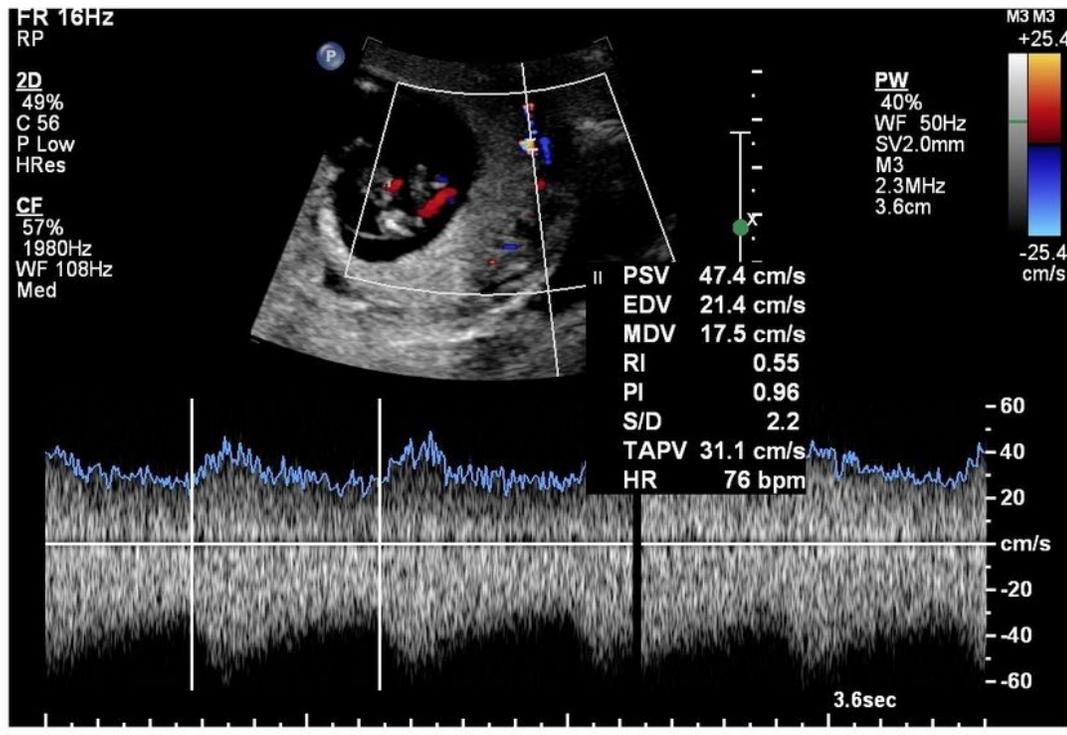
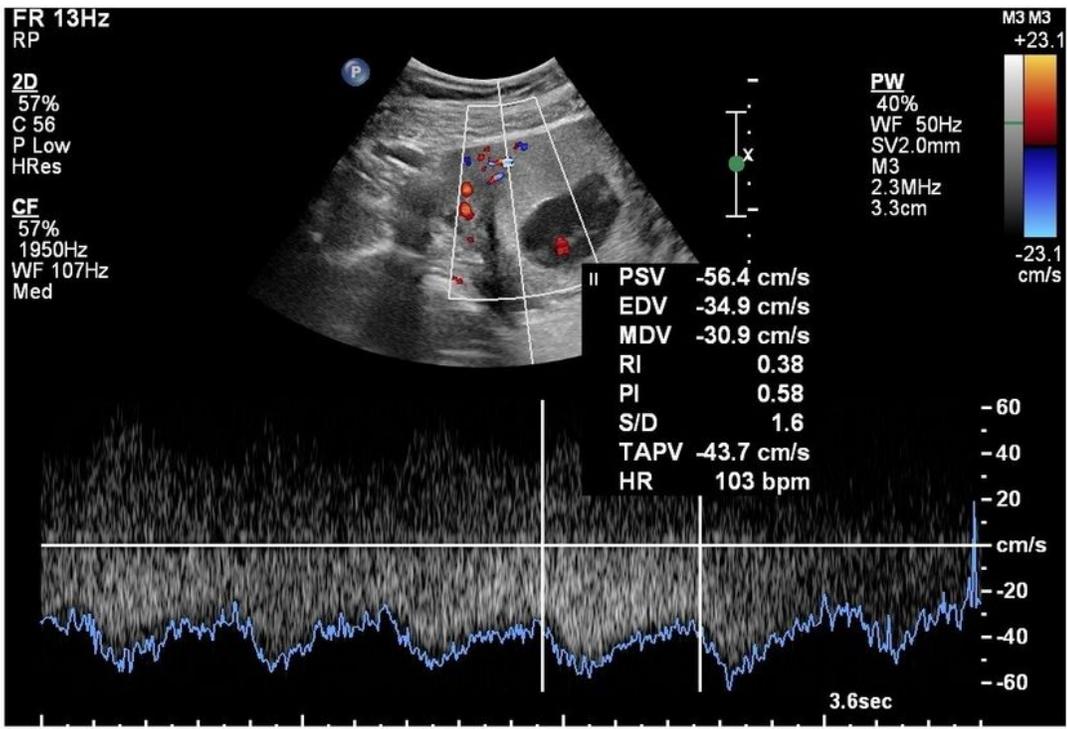
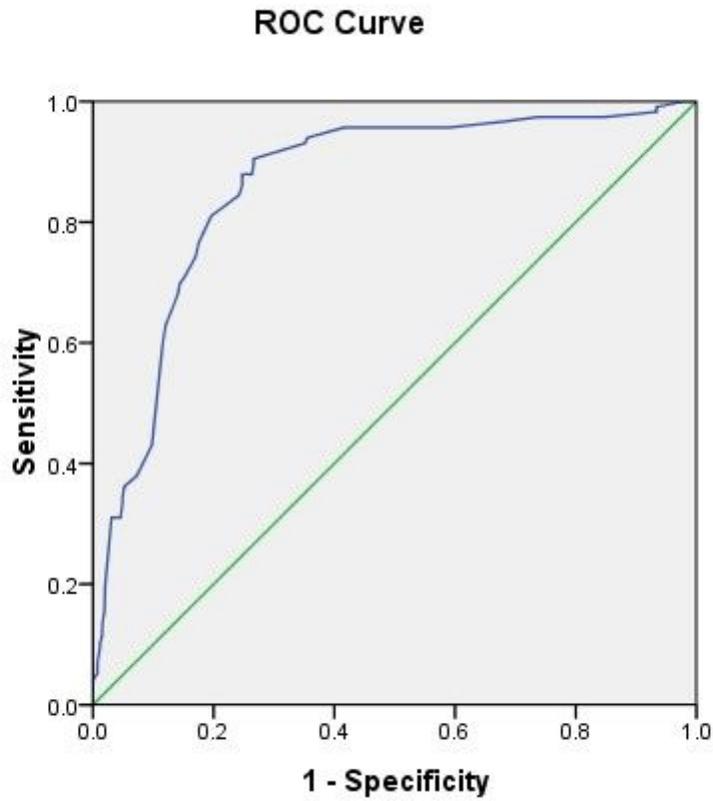


Figure 1

(a, b) Doppler images of uterine spiral artery in normal and gestational diabetic women

1a shows Doppler flow of normal uterine spiral artery in pregnant women. 1b shows Doppler flow of uterine spiral artery in gestational diabetic women



Diagonal segments are produced by ties.

Figure 2

ROC curve of uterine spiral artery pulsatility index in predicting gestational diabetes mellitus

The area under the curve was 0.861, and the cut-off of PI was 0.675. The sensitivity and specificity of GDM prediction was 90.5 % and 73.3 %, respectively.