Eco Doppler Investigation of Utero-placental Circulation in High-risk Pregnancies

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Introduction: Inadequate trophoblastic invasion of spiral arteries is associated with intrauterine growth retardation, pregnancy induced hypertension, preeclampsia, and abruptio placentae. The ability to accurately identify pregnant women who will develop these complications is limited. Predictive tests are further challenged by difficulty in the timing of the measurements, because the structural and biochemical characteristics of the placenta change with increasing gestational age. Improvements in ultrasound technology provide potentially useful novel tools for evaluating placental structure.
Aim of our study: To develop methods for early screening of high-risk pregnancies (studying the circulation in the utero-placental arteries — impedance to flow).
Material and methods: We have followed-up pregnant women in their first and second trimesters, who presented for pregnancy care in our unit. Results were calculated using Student-test and Chi-test (for the presence or absence of prothodiastholic notch).
Results: Impedance to flow and the frequency of the prothodiastholic notch decrease in the uterine arteries with the evolution of pregnancy. Changes in the resistance of uterine arteries during pregnancy show different patterns in certain obstetrical risk groups: obesity, smoking in pregnancy, uterus with previous interventions (scar from C-section) with the placenta on the anterior wall, pregnancies with „Vanishing Twin Syndrome". In these groups we noticed a greater resistance in the uterine arteries.
Conclusions: These pregnancies should have an intensified follow-up.

Keywords: utero-placental circulation, high-risk pregnancy, doppler

Introduction

Uterine blood irrigation is mainly achieved by the two uterine arteries, and to a lesser extent by the two ovarian arteries. These vessels show anastomosis in the uterine horn. Arcuate arteries originate from the uterine artery. From these arteries, radial arteries penetrate the outer third of the myometrium. From these vessels originate basal arteries and spiral arteries supplying the myometrium, decidua and the intervilous space. In a mature placenta there are about 100 spiral arteries ending in the intervilous space.

Ovular sac implantation and placental development has an important role in the further development of pregnancy. In this process, the trophoblasts have a key role, invading spiral arteries of the myometrium, thus causing a decrease in the vascular resistance of the uterine artery. During pregnancy, a transformation of these spiral arteries into utero-placental arteries is necessary to increase blood flow for fetal growth. The utero-placental arteries show dilated lumen, lack of muscle and elastic layers, endothelial disruption, thrombus, fibrin deposits. This physiological conversion of the spiral arteries into utero-placental arteries, described by Brosens (1967) and Pijnenborg (1983), occurs in two stages: the first wave of trophoblastic invasion occurs in the first trimester and produces the transformation of the decidual segment of spiral arteries, and the second wave is in the second trimester, causing changes in the myometrial segment of these arteries. The diameter of these vessels changes from 15–20 mm to 300–500 mm (with the decrease of vascular resistance).

Vascular resistance in the uterine arteries decreases in time. The initial decrease in resistance, up to 24–26 weeks of pregnancy, is due to trophoblastic invasion. The decrease in the third trimester is due to the persistence of a hormonal effect on vascular elasticity. Vascular resistance is lower in the homolateral uterine artery due to the area of lateral placentation. This highlights the fact that the change described above in the spiral arteries occurs only in the placental site.

Doppler indices measured in the uterine arteries:
RI = (S–D)/S (Pourcelot, 1974);
PI = 2(S–D)/(S+D) (Gosling, 1976);
S/D Ratio = S/D (Stuart & Drumm, 1980);
S = systolic peak (max. velocity);
D = end diastolic flow.

With the utero-placental vessel dilation, the prothodiastholic notch present in the first and second trimester of pregnancy, usually disappears in the third trimester in normal pregnancies. The inadequate trophoblastic invasion of spiral arteries is associated with intrauterine growth retardation, pregnancy induced hypertension, preeclampsia, and abruptio placentae.

The aim of our study was to develop methods for early screening of high-risk pregnancies (studying the circulation in the utero-placental arteries).

Material and methods

Type of study: case-control.

Material

- We have followed-up pregnant women in the first and second trimesters, who were admitted to our unit for

Table I. RI, PI and the frequency of the prothodiastholic notch in the uterine arteries with the evolution of pregnancies

Week	RI	PI	Notch ++ (%)	Notch +0 (%)	Notch 00 (%)
11	0.73 ± 0.06	1.42 ± 0.38	100	0	0
12	0.71 ± 0.07	1.60 ± 0.50	98.5	1.5	0
13	0.70 ± 0.08	1.63 ± 0.56	96.3	3.7	0
16	0.64 ± 0.08	0.97 ± 0.20	84.4	10.4	5.2
17	0.60 ± 0.09	0.87 ± 0.19	60.7	25	14.3
18	0.58 ± 0.08	0.83 ± 0.16	44.4	27.8	27.8
19	0.56 ± 0.08	0.79 ± 0.18	30.5	39	30.5
20	0.55 ± 0.07	0.78 ± 0.14	18.7	31.3	50
21	0.54 ± 0.07	0.75 ± 0.14	18.7	37.5	43.8
22	0.54 ± 0.05	0.74 ± 0.10	22.7	22.7	54.6
23	0.52 ± 0.06	0.72 ± 0.12	25	21.2	53.6
24	0.49 ± 0.07	0.66 ± 0.13	15	10	75
25	0.51 ± 0.07	0.7 ± 0.13	16	16	68
26	0.50 ± 0.08	0.69 ± 0.16	5.9	5.9	88.2
27	0.49 ± 0.05	0.65 ± 0.09	5.1	6.5	88.4
28	0.5 ± 0.06	0.67 ± 0.13	3.3	5.5	91.2

Notch ++: notch in both uterine arteries, Notch +0: notch in one uterine artery, Notch 00: notch absent in both uterine arteries

pregnancy care (n = 291: 285 monofetal, six twin pregnancies of which 3 with "Vanishing Twin Syndrome")

- Features of pregnant women we have followed-up:
  - Age: 28.5±3.72 years (variability coefficient: 13%);
  - Body mass index (BMI) in the first trimester: 22.57±3.34 kg/m^2 (variability coefficient: 14.8%);
  - 51.06% had a history of pregnancy, 48.94% were pregnant for the first time;
  - 42.55% had a history of giving birth;
  - 17.02% had a history of miscarriage;
  - None of the pregnant women suffer from hypertension.
- Inclusion criteria:
  - Agreement to the informed consent;
  - Desired, intrauterine pregnancies, with live fetus;
  - Age of the pregnancy: 11 weeks – 13 weeks + 6 days;
  - CRL (crown-rump length): 6.25±7.6 mm (variability coefficient: 12.77%).

Methods

- We studied with ultrasound the following parameters (abdominal probe, single observer):
  - Biometry;
  - Morphology;
  - Utero-placental circulation (uterine arteries, bilateral) with color Doppler and pulse wave Doppler. We calculated average uterine artery resistance index (RI) and pulsatility index (PI). We followed-up the presence or absence of prothodiastholic notch in both uterine arteries.
- Moments of ultrasound scans:
  - At the diagnosis of pregnancy (in the first trimester);
  - At the end of the first trimester (11 weeks – 13 weeks + 6 days);
  - At 16–19 weeks;
  - At 20–24 weeks;
  - After 24 weeks.
- Control group features:
  - monofetal pregnancies;
  - maternal BMI: 18.5–24.9 kg/m^2;
  - without intake of progestogens (for imminent abortion or prophylactic);
  - without smoking in pregnancy or before conception;
  - without previous interventions on the uterus (C-section, myomectomy).

The results were calculated using Student-test (for RI and PI) and Chi-test (for the presence or absence of prothodiastholic notch).

Table II. Changes in uterine artery resistance (RI) during pregnancy in certain obstetrical risk groups

RI	11w–13w+6d	16w–19w	20w–24w	25w–28w
BMI >30	0.69 ± 0.09	**0.72 ± 0.09**	**0.59 ± 0.08**	**0.61 ± 0.09**
BMI: 25–29.9	0.71 ± 0.07	0.58 ± 0.09	0.52 ± 0.07	0.51 ± 0.06
Control	0.70 ± 0.08	0.58 ± 0.08	0.54 ± 0.07	0.49 ± 0.06
BMI <18.5	0.73 ± 0.07	0.57 ± 0.14	0.52 ± 0.10	0.51 ± 0.06
OP	0.70 ± 0.07	0.59 ± 0.08	0.52 ± 0.06	0.49 ± 0.06
IP and MP	0.71 ± 0.06	0.57 ± 0.09	0.55 ± 0.09	0.51 ± 0.07
Prog for IA	0.70 ± 0.06	0.60 ± 0.09	0.51 ± 0.03	0.46 ± 0.04
Prog prophylact	0.70 ± 0.07	0.63 ± 0.09	0.53 ± 0.08	0.47 ± 0.06
S. during pregnancy	0.73 ± 0.09	0.58 ± 0.08	0.56 ± 0.10	**0.54 ± 0.10**
S. before pregnancy	0.71 ± 0.06	0.60 ± 10	0.53 ± 0.06	0.49 ± 0.07
US PI. anterior	0.72+/+0.04	0.56 ± 0.08	**0.58 ± 0.04**	**0.54 ± 0.06**
US PI. post/ fund	0.75 ± 0.04	0.60 ± 0.04	0.55 ± 0.06	0.49 ± 0.04
VTS (n=3)	**0.80**			
T (n=3)	**0.59**			

OP: nulliparous, IP: primiparous, MP: multiparous; IA: imminent abortion; Prog.: progestogens intake; S: smoking; US: uterus scar; VTS: Vanishing twin sy; T: Twin pregnancy with both fetus alive; PI: placenta

Table III. Changes in uterine artery impedance to flow (PI) during pregnancy in certain obstetrical risk groups

PI	11w–13w+6d	16w–19w	20w–24w	25w–28w
BMI >30	1.36 ± 0.44	**1.16 ± 0.22**	**0.85 ± 0.18**	**0.91 ± 20**
BMI: 25–29.9	1.61 ± 0.52	0.85 ± 0.19	0.71 ± 0.13	0.69 ± 0.12
Control	1.56 ± 0.50	0.83 ± 0.17	0.75 ± 0.14	0.67 ± 0.12
BMI <18.5	1.63 ± 0.53	0.83 ± 0.27	0.71 ± 0.18	0.70 ± 0.12
OP	1.62 ± 0.56	0.86 ± 0.18	0.72 ± 0.10	0.66 ± 0.12
IP and MP	1.55 ± 0.40	0.81 ± 0.20	0.77 ± 0.17	0.69 ± 0.14
Prog for IA	1.58 ± 0.36	0.88 ± 0.20	0.69 ± 0.05	0.60 ± 0.08
Prog prophylact	1.91 ± 0.89	0.98 ± 0.20	0.74 ± 0.15	0.61 ± 0.11
S. during pregnancy	1.70 ± 0.56	0.83 ± 0.17	0.78 ± 0.20	**0.76 ± 0.20**
S. before pregnancy	1.59 ± 0.43	0.88 ± 0.22	0.72 ± 0.12	0.66 ± 0.13
US PI. anterior	1.61+/+0.22	0.78 ± 0.20	**0.83 ± 0.08**	**0.74 ± 0.12**
US PI. post/ fund	1.50 ± 0.30	0.88 ± 0.08	0.77 ± 0.11	0.65 ± 0.04
VTS (n=3)	**1.36**			
T (n=3)	**0.86**			

OP: nulliparous, IP: primiparous, MP: multiparous; IA: imminent abortion; Prog.: progestogens intake; S: smoking; US: uterus scar; VTS: Vanishing twin sy; T: Twin pregnancy with both fetus alive; PI: placenta

Results

RI, PI and the frequency of the prothodiastholic notch decrease in the uterine arteries with the evolution of pregnancies are presented in Table I. Resistance in the uterine arteries shows an exponential decrease during pregnancy. The frequency of the prothodiastholic notch decreases after the end of the first trimester.

Changes in uterine artery resistance during pregnancy, show different pattern in certain obstetrical risk groups (Tables II and III):

- Obesity appears to adversely affect the decrease in uterine artery resistance. Compared with the control group, we found a greater resistance in this group during pregnancy:
  - RI 16w–19w: 0.72±0.09 vs. 0.58±0.08, p <0.05 (0.004);
  - RI 20w–24w: 0.59±0.08 vs. 0.54±0.07, p >0.05;
  - RI 25w–28w: 0.61±0.09 vs. 0.49±0.06, p <0.05 (0.003).
- We have not noticed any significant difference between nulliparous and primiparous/multiparous pregnancies in terms of uterine artery resistance.
- We have not noticed any significant difference between the control group and those who received progestogens for imminent abortion (first trimester metrorrhagia), or those who received progestogens for prophylactic considerations.
- Smoking during pregnancy seems to affect impedance to flow in the uterine arteries after 24 weeks (RI 25w–28w: 0.54±0.10 vs 0.49±0.06, p = 0.07). We can't say the same about the preconceptional smoking.
- Uterus with previous interventions (scar from C-section) with the placenta on the anterior wall seems to have a higher resistance in uterine arteries in the control group after 20 weeks, but this difference was not found statistically significant:
  - RI 20w–24w: 0.58±0.04 vs. 0.54±0.07, p >0.05;
  - RI 25w–28w: 0.54±0.06 vs. 0.49±0.06, p >0.05.
- Uterus with previous interventions (scar from C-section) with the placenta on the posterior or fundic wall shows no difference from the control group in terms of resistance in uterine arteries.
- In twin pregnancies we noticed a smaller resistance in uterine arteries from late first trimester of pregnancy where both fetuses were alive, and greater resistance where one of the fetuses wasn't alive ("Vanishing Twin Syndrome").

Discussions

The mean uterine artery resistance and prevalence of prothodiastholic notch shows a linear decrease with the evolution of pregnancy between weeks 11 and 14. [1]. Severe maternal smoking (>10 cigarettes/day) significantly influences (in negative direction) the circulatory indices at the end of the first trimester. The risk of intrauterine growth retardation is high in these pregnancies [2].

Some studies have found a higher vascular resistance in pregnancies with vaginal bleeding and subchorial hematoma [3]. There are studies, that measured the difference between PI maximum and minimum in both uterine arteries at 6–12 weeks of pregnancy. They found that discordant IP values associate with spontaneous abortion (RR = 2.9, CI:1.5–5.8, p <0.05), suggesting involvement of an ischemic factor in this pathology [4].

Other studies haven't noticed any significant difference in utero-placental circulation (RI, PI) between normal pregnancies and imminent abortions [5,6].

Most studies agree that Doppler investigation of uteroplacental circulation in the first trimester, in pregnancies with vaginal bleeding, does not change treatment strategy.

Preeclampsia and intrauterine growth restriction are major contributors to perinatal morbidity and mortality worldwide. The ability to accurately identify pregnant women who will develop these complications is limited. This greatly impairs the development and testing of preventive interventions. Predictive tests are further challenged by difficulties in the timing of the measurements. The structural and biochemical characteristics of the placenta change with increasing gestational age. The ideal screening test would accurately predict the development of adverse pregnancy outcomes early enough to provide a window for preventive interventions. Improvements in ultrasound technology provide potentially useful novel tools for evaluating placental structure, but the measurements need to be standardized in order to be useful [7].

Most studies agree with the following [8]:

- Increased impedance to flow in the uterine arteries in both high-risk and low-risk pregnancies is associated with increased risk for subsequent development of preeclampsia and intrauterine growth restriction.
- Women with normal impedance to flow in the uterine arteries constitute a group that have a low risk of developing obstetric complications related to uteroplacental insufficiency.
- Increased impedance to flow in the uterine arteries at 24 weeks of gestation is found in about 5% of pregnancies attending routine antenatal care. The prevalence of high impedance at 20 weeks is about 2–3 times higher than at 24 weeks.
- Increased impedance to flow in the uterine arteries in pregnancies attending routine antenatal care identifies about 50% of patients who subsequently develop pre-eclampsia. Abnormal Doppler is better in predicting severe rather than mild pre-eclampsia. The sensitivity for severe pre-eclampsia is about 75%.
- Increased impedance to flow in the uterine arteries in pregnancies attending routine antenatal care identifies about 30% of patients who subsequently develop intrauterine growth restriction. Abnormal Doppler is better in predicting severe (birth weight below the 3rd centile or growth restriction requiring delivery before 35 weeks) rather than mild growth restriction.

- In pregnancies with increased impedance to flow in the uterine arteries, prophylactic treatment with low-dose aspirin or vitamins C and E may reduce the risk for subsequent development of pre-eclampsia.

Conclusions

1. RI, PI and the frequency of the prothodiastholic notch decrease in the uterine arteries with the evolution of pregnancy.
2. Changes in uterine artery resistance during pregnancy, show different patterns in certain obstetrical risk groups: obesity, smoking during pregnancy, uterus with previous interventions (scar from C-section) with the placenta on the anterior wall, pregnancies with „Vanishing Twin Syndrome". In these groups we noticed a greater resistance in the uterine arteries.

References

1. Gómez O, Martínez JM, Figueras F, Del Río M, Borobio V, Puerto B, Coll O, Cararach V, Vanrell JA – Uterine artery Doppler at 11-14 weeks of gestation to screen for hypertensive disorders and associated complications in an unselected population. Ultrasound Obstet Gynecol. 2005 Oct;26(5): 490–4.
2. Rizzo G, Capponi A, Pietrolucci ME, Arduini D – Effects of maternal cigarette smoking on placental volume and vascularization measured by 3-dimensional power Doppler ultrasonography at 11+0 to 13+6 weeks of gestation., Am J Obstet Gynecol. 2009 Apr; 200(4):415.e1–5. Epub 2008 Dec 13.
3. Pellizzari P, Pozzan C, Marchiori S, Zen T, Gangemi M – Assessment of uterine artery blood flow in normal first-trimester pregnancies and in those complicated by uterine bleeding. Ultrasound Obstet Gynecol. 2002 Apr;19(4): 366–70.
4. Leible S, Cumsille F, Walton R, Muñoz H, Jankelevich J, Sepulveda W – Discordant uterine artery velocity waveforms as a predictor of subsequent miscarriage in early viable pregnancies. Am J Obstet Gynecol. 1998 Dec;179(6 Pt 1): 1587–93
5. Persona-Sliwińska A, Brazert J, Biczysko R – Transvaginal color Doppler study of the uteroplacental circulation in early pregnancy, Ginekol Pol. 1998 Sep;69(9): 682–92
6. van den Elzen HJ, Cohen-Overbeek TE, Grobbee DE, Wladimiroff JW – The predictive value of uterine artery flow velocity waveforms in miscarriage in older women. Br J Obstet Gynaecol. 1993 Aug;100(8): 762–4
7. Zhong Y, Tuuli M, Odibo AO – First-trimester assessment of placenta function and the prediction of preeclampsia and intrauterine growth restriction. Prenat Diagn. 2010 Feb 17
8. Nicolaides K, Rizzo G, Hecker K, Ximenes R – Doppler in obstetrics, ISUOG ducational series, www.centrus.com.br\DiplomaFMF\SeriesFMF\doppler\index-doppler.htm, 2002