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Blood flow volume of uterine arteries in human pregnancies determined using 3D and bi-dimensional imaging, angio-Doppler, and fluid-dynamic modeling

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ABSTRACT

The primary aim of this pilot study was to study uterine artery (UtA) blood flow volume in uneventful human pregnancies delivered at term, at mid and late gestation by means of 3D and bi-dimensional ultrasound imaging with angio-Doppler combined with fluid-dynamic modeling. Secondary aims were to correlate flow volume to placental site and to UtA Pulsatility Index (PI).

Women with singleton, low-risk pregnancies were examined at mid and late gestation. The structure and course of the uterine artery (UtA) was studied in each patient by means of 3D-angio-Doppler and included vessel diameter D, blood flow velocity and PI (measured along the UtA). Fetal weight estimation and placental insertion site were assessed by ultrasound. A robust fluid-dynamic modeling was applied to calculate absolute flow and flow per unit fetal weight.

Mean UtA diameter and blood flow velocity increased significantly ($p < 0.0001$) from mid-gestation to late gestation from 2.6 mm and 67.5 cm/s, to 3.0 mm and 85.3 cm/s, respectively, yielding an increasing absolute flow troughout gestation. h coefficient, derived by fluid-dynamic modeling to calculate mean velocity, increased significantly from 0.52 at mid-gestation to 0.57 at late gestation. UtA blood flow volume ml/min/kg-fetal weight was significantly higher at mid-gestation than at late gestation (535 ml/min/kg vs 193 ml/min/kg; $p < 0.0001$). In cases with strictly lateral placentas the ipsilateral UtA accommodates at mid and late gestation 63% and 67% of the total UtA flow. In central placentas UtA flow was evenly distributed between the two vessels. An inverse correlation was observed between PI and blood flow volume ml/min/kg (Pearson's coefficient $r = -0.54$).

Our work confirms the technological and methodological limitations in the measurement of uterine artery blood flow. However, Doppler measurements supported by three-dimensional angio imaging of the uterine vessel, high resolution imaging and diameter measurement, and a robust mathematical model of local circulation adds a genuine new area of investigation into human uterine circulation during pregnancy.

1. Introduction

Utero–placental blood flow provides nutrients and oxygen for feto–placental growth. Trophoblast migration into the spiral arteries wall leads to larger lumen diameter, which combine to reduce impedance to flow into the developing intervillous space. Changes at the cellular level and the impact of progressive shear stress due to increased flow dramatically modify the blood volume accommodated by the uterine arteries with each cardiac cycle. Evidence of a correlation between placental lesions and increased impedance to utero–placental flow has been observed consistently in complicated human pregnancies by Doppler velocimetry [1–4]. Despite a robust pathological background and the extensive clinical usage of uterine Doppler velocimetry in high risk pregnancies, only a few studies have attempted the quantification of actual blood flow volume. Table 1 briefly describes the different techniques to calculate uterine blood flow volume and the wide range of results obtained, which were initially described in the 1950s. With updated technology reproducibility of ultrasound and Doppler measurements for blood flow volume does not seem to pose a major limitation [11]. The major challenge not thoroughly addressed in previously published works concerns the evaluation

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Table 1
Different techniques adopted to calculate uterine blood flow volume and results reported from 1955 to 2007.

Author	Uterine Arteries sampling site	Technique	Vessel diameter	Mean spatial blood velocity	Weeks of gestation	Flow volume (ml/min) mean ± SD
Metcalfe J, 1955 [5]	Bilateral Common trunk	N_2O infusion			37–40	492 ± 195
Thaler I, 1989 [6]	Unilateral, ascending branch	Transvaginal Color-Pulsed wave Doppler	Ultrasound imaging		37–40	342
Palmer SK, 1992 [7]	Unilateral, Common trunk	Transabdominal Color, pulsed Doppler	Ultrasound imaging		36	312 ± 22
Konje JC, 2001 [8]	Bilateral, Common trunk	Transabdominal Power, pulsed Doppler	Angio-Doppler imaging	Automatic Doppler derived T.A.M.	21, 38	513 ± 127, 970 ± 193
Jeffreys RM, 2006 [9]	Unilateral ascending branch	Transabdominal Power, pulsed Doppler	Ultrasound imaging		28–36	267 ± 73[a]
Wilson MJ, 2007 [10]	Bilateral[b] Not determined	Transabdominal Power, pulsed Doppler	Color Doppler derived	Automatic Doppler derived T.A.M.	20, 36	400 480

[a] Measured in a single vessel. The aim of the study was to assess blood flow estimation under varying conditions – exercise, different recumbent positions etc.
[b] European pregnant women at 4000 m altitude.

of the mean spatial blood velocity [12]. An efficient and robust solution is to deduce the mean spatial velocity by scaling the maximum velocity measured in the investigated area with a Spatial Velocity Distribution Coefficient [13,14]. The value of this methodology is enhanced by three-dimensional imaging and high resolution of sonographic imaging of uterine vessels. Its application could eventually help explain the poor specificity of impedance indices of the uterine arteries. The primary aim of this study was to apply a fluid-dynamic modeling to assess the mean spatial velocity in the uterine artery (UtA) necessary to calculate the blood flow volume in a cohort of uncomplicated pregnancies at mid-gestation and in the third trimester. The secondary aim was to correlate flow volume to strictly defined placental site and to determine the correlation between UtA blood flow volume and UtA pulsatility index (PI).

2. Materials and methods

2.1. Study population

Women with singleton, low-risk, and uncomplicated pregnancies scheduled for routine ultrasound screening examinations were asked to participate in this prospective study. According to the Italian National Health Service, a routine ultrasound examination is offered at approximately 20 (mid-gestation) and at third trimester around 32 weeks of gestation. The following demographic, sonographic and Doppler findings were considered as inclusion criteria: Caucasian ethnicity, low-risk singleton pregnancies, sonographic assessment of gestational age in the first trimester, normal mean UtA PI at the time of first examination and throughout gestation, maternal blood pressure within the normal ranges until delivery. Exclusion criteria were: chromosomal abnormality, structural malformations, and maternal chronic diseases; obstetrical history with gestational hypertension preeclampsia, HELLP syndrome, IUGR, abruptio placentae, gestational diabetes, unexplained fetal loss/intrauterine fetal death, tobacco/alcohol use. In addition to this, cases with an unclear vessel anatomy or a markedly twisted vessel were excluded. An informed consent for participation in the study was obtained from each eligible patient. Gestational age at delivery, birth weight, neonatal outcome were recorded. Seventy-one singleton normal pregnancies were recruited for the study.

2.2. Ultrasonic procedures

All examinations were performed (S.R., S.B., A.P.) between 9.00 and 1:00 with a maximum examination length set at 45 min. A learning curve was observed for the duration of the examination along the time period of this study, especially as regards the assessment of the vessels anatomy. Uterine artery blood flow volume measurements on each side were performed with the woman in a semi-recumbent position.

2.2.1. Anatomical and biometrical examination

The anatomy of the UtA and its corporal and cervical branches was studied in each patient by means of 3D-angio-Doppler in order to identify the UtA before any visible vascular division (Fig. 1a) (Voluson Expert General Electric Healthcare). Vessel diameter D, blood flow velocity and PI were measured along the UtA, approximately 15 mm upstream to vessel bifurcation on the common trunk of the uterine artery. Measurements were taken for both right and left UtA. Diameters were measured on a perpendicular B-mode view of the longitudinal vessel section, at the maximum magnification. The lumen of the vessel was visualized by the color power angiography and the diameter was measured on a gray-scale image after reducing the color box, by placing the calipers at the inner edges of the vessel itself at the specular reflection (Fig. 1b). The average of three repeated measurements of vessel diameter was served as the final diameter. A lateral placenta was defined when the mid–sagital plane of the uterus was not reached by the medial edge of the placenta.

2.2.2. Doppler interrogation of uterine vessels

UtA blood flow velocity and PI were measured with a Doppler beam angle <30 (Fig. 1c). Angular correction of velocity was performed. The time-average maximum velocity along the cardiac cycle (V_{max}) and the mean PI over 3–5 cardiac cycles were utilized. The heart rate was also recorded, as required for the evaluation of Womersley number (see Appendix). The blood flow rate (ml/min) through each UtA was calculated according to the formula $Q = h\overline{V}_{max}\pi D^2/4$. (see below for definitions). UtA volume flow was calculated separately for each the right and left uterine artery and total UtA volume flow was calculated as the sum of the flow from both vessels.

Fetal Biometry. Routine fetal biometry (biparietal diameter, head and abdominal circumference, and femur length) and placental site were recorded after completion of uterine artery measurements bilaterally. Fetal weight was estimated according to Hadlock's formula [15].

2.2.3. Mathematical model of the uterine arterial velocity profiles

The UtA in the tract between its origin from the internal iliac artery and the cervical–corporal bifurcation usually shows a roughly straight path with constant diameter and no branching, and its flow in normal pregnancies is a pulsatile, forward, laminar flow [16]. Along such a vessel, within the so-called 'entrance region', the spatial velocity profile undergoes development from an initial shape at the inlet to a fully developed profile some distance downstream [17]. The spatial velocity profile of arterial blood flow along the UtA and corresponding Spatial Velocity Distribution Coefficient (h) were calculated on the basis of Reynolds and Womersley numbers, two dimensionless quantities describing the vessel hemodynamics. These were specifically evaluated for each right and left uterine arterial vessel on the basis of the measured diameters (D), blood time-averaged maximum velocities and heart rate, while mean values obtained in pregnant women [18] were used for maternal blood properties (3.3 cP and 1.06 g/cm^3 for the viscosity and density, respectively). Moreover, the distance (L) from the internal iliac artery to the Doppler sampling site is expected to be between 3 and 5 cm, though the exact value for a specific UtA is not known since visualization of the UtA origin is not always achievable. A preliminary analysis showed that this L uncertainness has a negligible impact on the uterine h coefficient calculations, suggesting the use of a fixed value of 4 cm.

Finally, from the knowledge of L, D, Reynolds and Womersley numbers the h coefficient was evaluated for each specific case (see Appendix). This coefficient was used to scale down the measured time-averaged maximum velocity to a calculated time-averaged mean velocity. A similar approach was previously applied to evaluate spatial velocity profiles in mouse embryonic aorta [19].