3D power Doppler ultrasound assessment of placental perfusion during uterine contraction in labor

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A R T I C L E I N F O

A B S T R A C T

Introduction: To assess placental perfusion during spontaneous or induced uterine contraction in labor at term using placental vascular sonobiopsy (PVS) by 3D power Doppler ultrasound with the VOCAL imaging analysis program.
Method: PVS was performed in 50 normal pregnancies (32 in spontaneous labor group [SLG], and 18 in induced labor group with oxytocin or prostaglandin $F_{2\alpha}$ [ILG]) at 37—41 weeks of gestation to assess placental perfusion during uterine contraction in labor. Only pregnancies with an entirely visualized anterior placenta were included in the study. Data acquisition was performed before, during (at the peak of contraction), and after uterine contraction. 3D power Doppler indices such as the vascularization index (VI), flow index (FI), and vascularization flow index (VFI) were calculated in each placenta.
Results: There were no abnormal fetal heart rate tracings during contraction in either group. VI and VFI values were significantly reduced during uterine contraction in both groups (SLG, −33.4% [−97.0−15.2%], and ILG, −49.6% [−78.2−−4.0%]), respectively ($P < 0.001$). The FI value in the ILG group was significantly lower during uterine contraction ($P = 0.035$), whereas it did not change during uterine contraction in the SLG group. After uterine contraction, all vascular indices returned almost to the same level as that before uterine contraction. However, the FI value in ILG (−8.6%, [−19.7−16.0%]) was significantly lower than that in SLG (2.4%, [−13.4−38.1%]) after uterine contraction ($P < 0.05$). All 3D power Doppler indices (VI, FI, and VFI) during uterine contraction (at the peak of contraction) showed a correlation greater than 0.7, with good intra- and inter-observer agreements.
Discussion: Our findings suggest that uterine contraction in both spontaneous and induced labors causes a significant reduction in placental perfusion. Reduced placental blood flow in induced uterine contraction has a tendency to be marked compared with that in spontaneous uterine contraction. To the best of our knowledge, this is the first study on the non-invasive assessment of placental perfusion during uterine contraction in labor using 3D power Doppler ultrasound. However, the data and their interpretation in the present study should be taken with some degree of caution because of the small number of subjects studied. Further studies involving a larger sample size are needed to assess placental perfusion and vascularity using PVS during normal and abnormal uterine contractions in normal and high-risk pregnancies.

1. Introduction

In spontaneous uterine contraction, maternal placental blood flow before labor was reported to be 4.5% of the cardiac output, decreasing to 2.9% (35.5% decrease) during uterine contraction, and increasing to 7.2% (60% increase) after contraction in pregnant rhesus monkeys [1]. Reduction of placental blood flow during spontaneous uterine contraction was also $30 \pm 8\%$ in dogs and $35 \pm 12\%$ in rabbits [2]. On the contrary, in induced uterine contraction with oxytocin and prostaglandin E_2, uterine contraction led to a marked reduction (average: 73%) of the placental blood flow in pregnant rhesus monkeys, and the placental blood flow partially recovered after the uterine contraction [3]. These reductions of placental blood flow on induced uterine contraction with oxytocin were $43 \pm 16\%$ in dogs, and $46 \pm 13\%$ in rabbits [2].

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However, to the best of our knowledge, there are no available data on the change in placental blood flow during uterine contraction in the human placenta.

Placental vascular sonobiopsy (PVS) using three-dimensional (3D) power Doppler ultrasound with VOCAL imaging histogram analysis is a novel technique to quantitatively and qualitatively assess the vascularization and blood flow in the placenta [4–6]. Moreover, PVS is a valid alternative for evaluation of the placental vascularity and blood flow when visualization of the entire placenta is not feasible [7]. In the present study, we assessed placental perfusion during spontaneous or induced uterine contraction in labor at term using PVS.

2. Patients and methods

2.1. Patients

In the period from July 2012 to May 2015, 73 women with normal singleton pregnancies in labor at 37–41 weeks of gestation were studied cross-sectionally. The women were recruited randomly. The fetal age was calculated from the first day of the last menstrual period, with confirmation by first-trimester ultrasound. Women with gestational diabetes, chronic hypertension, maternal systemic disease, or taking antihypertensive medications were not enrolled. Of the 73 women, 23 (31.5%) were excluded because of insufficient data acquisition due to severe artifacts caused by uterine contraction or maternal movements. Therefore, 50 women (32 in a spontaneous labor group [SLG], and 18 in an induced labor group with oxytocin or prostaglandin $F_{2\alpha}$ [ILG]) underwent further investigation. Indications of induced labor were a weak labor in 11 women, and post-term pregnancy in 7 women. Clinical characteristics of the subjects in each group are shown in Table 1. The umbilical artery pulsatility index in all subjects was normal at 26 to 29 weeks of gestation. The growth of all fetuses was normal, and there were no abnormalities during pregnancy. This study was approved by the Kagawa University Graduate School of Medicine Ethics Committee, and standardized written informed consent was obtained from all women.

2.2. Ultrasound examination

A single experienced observer (M.S.) performed all 3D power Doppler ultrasound scans using a Voluson E8 A6 2.4 (GE Healthcare Japan, Tokyo, Japan) with a transabdominal 1–4 MHz transducer (RAB2-5-D) at the first stage of labor. At each examination, each placenta was confirmed to be located in an anterior position. 3D power Doppler ultrasound was employed for a representative placental vascular tree volume based on the following procedure, described in detail in our previous investigations [4–6]. The maximal sensitivity was ensured by setting the pulse repetition frequency (PRF) to 0.6 kHz and the wall motion filter to 'low'. The following constant default instrument settings (corresponding to the manufacturer's Doppler power setting) were used throughout the examinations: frequency, mid; dynamic, balance, 225; smooth, 4/5; ensemble, 11; line density, 8; power Doppler map, 4; artifact suppression, on; power Doppler line filter, 3; quality, normal. The power Doppler window was placed over the placenta, including its total thickness, from the basal to chorionic plates. The 3D volume box was positioned over the placenta at a fixed 65° angle. Volume acquisition was carried out within 16 s before (at the start of contraction), during (at the peak of contraction), and after uterine contraction (at the end of contraction) (Fig. 1).

As presented in detail in our previous studies [4–6], the examination of placental perfusion was performed using PVS. In the measurement of PVS, the power Doppler window is placed over the placenta, including its total thickness, from the basal to chorionic plates (excluding both of them). The spherical 3D volume is obtained between the basal and chorionic plates (Fig. 1). The VOCAL program automatically calculates color values (vascularization index [VI], flow index [FI], and vascularization flow index [VFI]) from the acquired sphere. A sequence of six placental sections separated by successive rotations of 30° is obtained, and 1 to 3 spherical sampling sites are chosen in each plane. Each spherical volume was taken at approximately equidistant intervals along the length of the placental image. Each index was an average value from those of 6–13 spheres in each placenta. A single experienced observer (M.S.) conducted all 3D Doppler ultrasound histogram analyses with the VOCAL program.

2.3. Statistical analysis

All statistical analyses were performed with SPSS statistical software, version 23 for Windows (SPSS Inc., Chicago, IL, USA). Differences in the maternal age, birth age, cervical dilatation, interval of uterine contraction, birth weight, and umbilical artery blood pH between SLG and ILG groups were assessed by the unpaired t-test. Differences in Apgar scores between the groups were investigated with the Mann-Whitney U test. The percent change of each index during uterine contraction was assessed by the Wilcoxon Signed-rank test. Differences in variables at each stage between SLG and ILG groups were investigated with the Mann-Whitney U test. Intra- and inter-class correlation coefficients were used as an expression of reliability [8]. Intra- and inter-class correlation coefficients were defined as the correlation between any two measurements from the same data during uterine contraction (at the peak of contraction). Their values ranged from zero to one; the latter indicates maximum reliability. Intra- and inter-observer variability were calculated according to Bland and Altman's procedure [9] in 20 samples (11 in SLG and 9 in ILG). Intra-observer variation was examined by M.S., and inter-observer variation was assessed by M.S. and J.N. This analysis consisted of a graph, in which the difference between the measurements (y-axis)

Table 1
Clinical characteristics of subjects.

Subject	n	Maternal age (yo)	Parity	Birth age (weeks)	Cervical dilatation (cm)	Uterine contraction interval (min)	Birth weight (g)	Apgar score		UApH
								1 min	5 min	
		Mean (SD)	Median (range)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Median (range)	Median (range)	Mean (SD)
Spontaneous labor	32	29.9 (5.4)	0 (0–2)	39.5 (0.9)	6.1 (3.1)	3.8 (0.9)	3028.9 (230.3)	8 (7–10)	9 (7–10)	7.31 (0.08)
Induced labor	18	29.6 (3.9)	0 (0–2)	40.5 (0.9)	5.9 (3.3)	3.3 (0.6)	3212.7 (295.8)	8 (5–9)	9 (7–10)	7.28 (0.08)
Significance		NS	NS	NS	NS	NS	NS	NS	NS	NS

yo, years olds; min, minute; SD, standard deviation; NS, not significant; UApH, umbilical artery blood pH.