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Placental elasticity evaluation using virtual touch tissue quantification during pregnancy

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ABSTRACT

Introduction: Virtual touch tissue quantification (VTTQ) has been developed to evaluate tissue elasticity. Our previous study using delivered placentas showed increased elasticity in fetal growth restriction (FGR). Therefore, we investigated changes in placental elasticity during pregnancy, including complicated pregnancies.

Methods: Based on complications, 199 women were divided into 5 groups (normal, FGR, pregnancy induced hypertension (PIH), diabetes mellitus and collagen disease), and shear wave velocity (SWV) of the placenta, measured using VTTQ, was compared. A cross-sectional study was performed with the 143 normal cases to construct the reference range. The association between placental SWV and the expression ratio of collagen fibers in the placenta stained with Masson's trichrome was determined.

Results: The SWV was safely measured for all participants. The correlation between SWV and gestational weeks was not significant. The mean ± SD SWVs in the normal, FGR, and PIH groups were 0.98 ± 0.21, 1.28 ± 0.39, and 1.60 ± 0.45 m/sec, respectively. The FGR and PIH groups had significantly higher SWVs than that of the normal group. SWV and the expression ratio of collagen fibers were significantly correlated.

Discussion: Based on the present findings, changes in SWV during pregnancy were associated with placental fibrosis, and increased SWV in PIH and/or FGR cases might be influenced by infarction, ischemic changes, and inflammation, as well as fibrosis. In conclusion, the measurement of placental SWV is potentially useful to evaluate the condition of the placenta during pregnancy.

1. Introduction

Virtual touch tissue quantification (VTTQ) based on acoustic radiation force impulse (ARFI) imaging is a new non-invasive method to quantitatively evaluate tissue elasticity. With VTTQ, a short acoustic push pulse is generated that causes a minute displacement of the targeted tissue, which propagates a lateral shear wave velocity (SWV; m/sec) that can be measured. Because SWV is correlated with Young's modulus, which is an index of elasticity [1], VTTQ can be used to evaluate tissue elasticity, where faster SWV speeds and smaller displacements are associated with stiffer tissues and vice versa. VTTQ has recently been used in various parenchymal organs and to diagnose liver fibrosis, breast nodules, and thyroid tumors [2–6].

Placental pathological findings, such as infarction and ischemic changes, are poor prognostic indicators of fetal growth restriction (FGR) or fetal acidosis. However, histological changes of the placenta are usually revealed only after delivery, and the evaluation of these changes during pregnancy is impossible.

In our previous study with *ex vivo* placentas, ARFI caused no apparent histological damage to the placental tissue [7], leading us to believe that VTTQ could be safely performed with pregnant women. In addition, our study showed clinically that the SWV in the group with FGR was significantly higher than that of the group without growth restriction [7]. However, VTTQ during pregnancy for the observation of placental tissue has not been reported. Therefore, we investigated placental elasticity using VTTQ during pregnancy. In addition, to provide clinical data, we investigated

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Abbreviations

ARFI	acoustic radiation force impulse
DM	diabetes mellitus
FGR	fetal growth restriction
MCA	middle cerebral artery
NP	normal pregnancy
PIH	pregnancy induced hypertension
ROI	region of interest
RI	resistant indices
SWV	shear wave velocity
SD	standard deviation
UmA	umbilical artery
VTTQ	virtual touch tissue quantification

changes in SWV with increasing gestational age and between normal and complicated pregnancies.

2. Materials and methods

2.1. Participants

Pregnant Japanese women between 17 and 40 weeks of gestation who had a prenatal check-up at Kyushu University Hospital between December 2011 and October 2014 (n = 199) were eligible. Women with a singleton pregnancy and whose placenta was located on the anterior uterine wall were included. Women with a multiple gestation, fetus with malformations, or aneuploidy were excluded. Informed consent was provided by the participants, and the study protocol was approved by the Bioethics Committee of Kyushu University.

The participants were divided into 5 groups: normal pregnancy (NP) group: without any maternal or fetal complications except for preterm birth (n = 143); FGR group: with an estimated fetal weight less than the mean − 1.5 standard deviation (SD) of the Japanese standard for the gestational week on ultrasonography [8] (n = 21); pregnancy induced hypertension (PIH) group: based on the Japanese definition [9] of PIH (systolic and/or diastolic blood pressure >140 and 90 mmHg, respectively), including preeclampsia or superimposed PIH (n = 15); diabetes mellitus (DM) group: diagnosis of abnormal glucose tolerance [10], including gestational diabetes mellitus, overt DM in pregnancy and DM complicated before pregnancy (n = 13); and collagen disease (CD) group: complicated with collagen disease, such as systematic lupus erythematosus and Sjogren syndrome (n = 7). For the participants in the complicated groups, all of the SWV values were measured after the diagnosis. Five cases diagnosed with PIH had other complications (FGR, n = 2; collagen disease, n = 1; FGR and collagen disease, n = 1; and gestational diabetes mellitus, n = 1) and were included in the PIH group. None of the participants were treated with an antihypertensive.

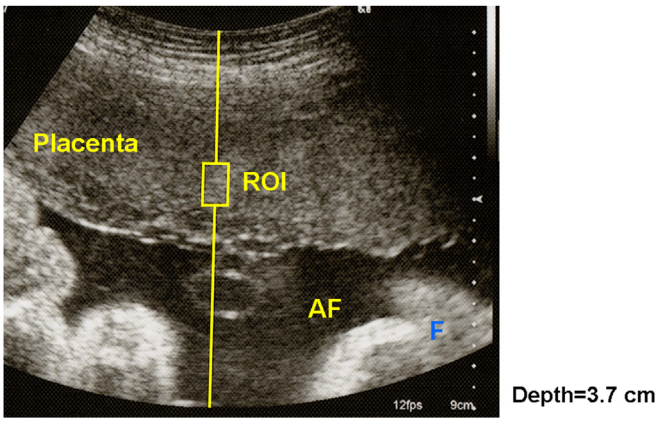

Fig. 1. Measurement of shear wave velocity in a placenta using virtual touch tissue quantification. The region of interest (ROI) was placed at a depth of 3.7 cm from the subcutaneous layer in the placenta at 34 weeks of gestation. AF: amniotic fluid, F: fetus.

The clinical characteristics, reported as median (range) of each group are shown in Table 1.

2.2. Measurement of the shear wave velocity

For all participants, after a routine prenatal check-up using B-mode and Doppler ultrasonography, SWV was measured using a VTTQ unit with a 4C1 convex probe (2.0–4.5 MHz) (ACUSON S2000; Mochida Siemens Medical, Tokyo, Japan) (Fig. 1), with a thermal index of bone and mechanical index of <0.43 and 1.3–1.7, respectively.

The participant was asked to take a shallow breath, and the observer confirmed that the fetal movement was not severe and the placental tissue was as horizontal as possible. A region of interest (ROI) was fixed at a depth of 1–8 cm from the subcutaneous tissue in the placenta on the anterior uterine wall, and the site of cord insertion and placental margin were excluded from the measurement site. The mean value of 5 measurements at each site was used for analysis.

2.3. Analysis of the shear wave velocity

2.3.1. Factors affecting the shear wave velocity measurements

The influence of maternal breathing, fetal movement, and the depth of the ROI on the SWV measurement was investigated in 10 cases randomly selected from the NP group. For maternal breathing, we compared the SWV at the same measurement site between

Table 1
Clinical characteristics of each group.

	NP (n = 143)	FGR (n = 21)	PIH (n = 15)	DM (n = 13)	CD (n = 7)
Maternal age	31 (19–45)	31.5 (26–45)	35 (21–41)	34.5 (29–41)	30 (25–39)
BMI	23.5 (16.1–34.2)	23.5 (16.1–34.2)	22.3 (20.5–37.7)	26.3 (19.4–41.9)	21.9 (17.8–24.0)
GW at measurement	31.0 (17.0–40.6)	36.3 (21.9–39.6)	34.3 (17.4–39.3)	31.7 (24.1–37.4)	25.0 (18.0–37.3)
GW at birth	38.9 (32.3–41.0)	37.4 (27.7–40.1)	34.0 (24.0–40.0)	38.5 (33.6–41.6)	39.6 (38.4–40.1)
BW	2940 (1780–3750)	1990 (565–2660)	1753 (324–3890)	2950 (2145–3360)	2885 (2350–3115)
Apgar score at 5 min	9 (5–10)	9 (6–10)	9 (6–9)	9 (9–10)	9 (9–10)
UmA pH	7.31 (7.11–7.46)	7.27 (7.22–7.38)	7.30 (7.14–7.32)	7.30 (7.21–7.36)	7.35 (7.33–7.38)

Data are shown as median and range.
NP: normal pregnancy, FGR: fetal growth restriction, PIH: pregnancy induced hypertension, DM: diabetes mellitus, CD: collagen disease, BMI: body mass index, GW: gestational week, BW: birth weight, UmA: umbilical artery.

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