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Original Research

Does the placental strain ratio correlate with the umbilical artery Doppler values?

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Summary

Objective: The aim of this study is to reveal whether there is any relationship between strain elastography (SE) values and Doppler ultrasonography (US) findings, and to investigate the availability of SE in early diagnosis of preeclampsia (PE). *Material and Methods:* The authors examined 21-24 week old patients who applied to this clinic for anomaly screening. Only 55 pregnant women with anterior or anterolateral placental placement were included in the study. Doppler US data and placental strain elastography values were compared statistically. *Results:* There was an inverse correlation between umbilical artery resistance index (RI) values and placental strain ratios. *Discussion:* Histopathological examination shows that, as a result of the increasing extracellular matrix proteins due to increased inflammation, elasticity in the placental tissue decreases, and this may lead to an increase in placental stiffness. Also it is known that, abnormal Doppler US findings are considered to be a weak positive predictor of placental insufficiency. Therefore the present authors compared Doppler US with placental elastography and found an inverse correlation between umbilical artery RI value and placental strain ratio. *Conclusion:* Placental elasticity can be used for placental abnormalities in addition to other methods, but further studies are needed to use placental elasticity as a positive predictive marker for placental insufficiency.

Key words: Placental elastography; Doppler US; Placental insufficiency; Preeclampsia.

Introduction

Sonoelastography is an assistant method of conventional ultrasound that measures the elasticity of tissue. Strain elastography (SE) or real time sonoelastography gives the relative tissue hardness by calculating the rate of strain between target and reference tissue texture [1, 2]. SE is widely used in differentiating normal tissue from neoplasia, inflammation and fibrosis in breast, thyroid, prostate, and liver imaging [3, 4]. However, there is a limited number of article that use SE in the placenta.

Preeclampsia (PE) is a serious clinical condition that can lead to placental dysfunction, fetal growth retardation, and fetal and maternal loss. PE can be diagnosed clinically with the presence of hypertension and proteinuria. Ultrasonography (US), Doppler ultrasonography (DUS), non-stress test (NST), and biophysics profile constitute the tests help to identify it. Umbilical and uterine artery DUS findings may be an early messenger of PE and intrauterine growth retardation (IUGR) [4, 5]. However, any test that was developed up to now does not have sufficient sensitivity for the diagnosis of PE.

The aim of this study is to reveal whether there is any relationship between SE values and Doppler US findings, and to investigate the availability of SE in early diagnosis of PE.

Materials and Methods

This study was approved by the Ethics Committee of the University. Every patient included in the study was informed about the study and a voluntary consent form was obtained.

Fifty-five cases of 21-24 weekly pregnant women joined the study. Only the pregnant women with anterior placements of placentas were included in this study. Gestational weeks (GW) were determined according to the last menstrual period. The cases of the largest vertical amniotic pocket calculated under 2 cm were evaluated as oligohydramnios and were not included in the study. There was no clinical findings of fetal distress in any cases. Cases were evaluated according to maternal age, gestational week, subcutaneous fat thickness, placental thickness, morphology, gravid, parity, and abortion data.

All ultrasound examinations were performed with 6-MHz MF convex transducer. US elastography was performed by two radiologist with at least five years' experience. In all cases, B-mode US and US elastography were performed in the supine position.

US elastography were performed in the supine position, with 6.1-MHz convex probe as sequential light-level compression and decompression perpendicular to the skin. Simultaneous sinusoidal waves are followed and data was imported. Palpation speed, amplitude, and persistence was important for the optimization. For this purpose, before starting the study, ten healthy pregnant women were examined for standardization of the elastography technique. The two radiologist who applied SE were blinded to the US and Doppler imaging findings and patient histories. Placenta strain rate (target tissue strain/ reference tissue strain) were performed as semi-quantitatively. The authors selected the sub-

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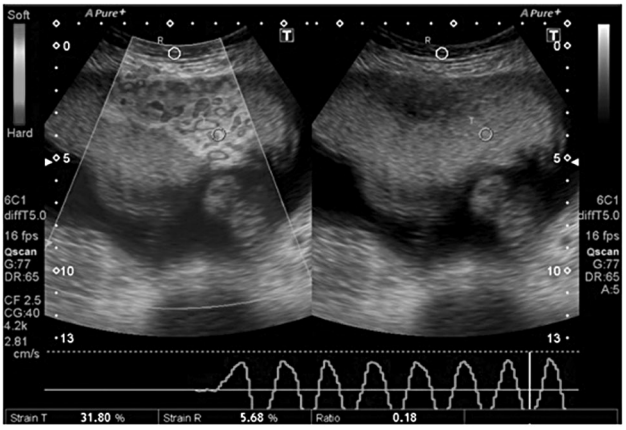

Figure 1. — Measurement of placental strain ratio using subcutaneous fat as reference.

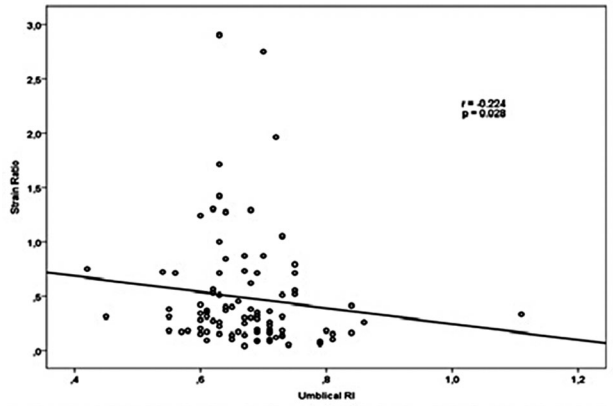

Figure 2. — An inverse correlation is seen between placental strain ratios and umbilical artery RI values.

cutaneous adipose tissue as a reference point and the central portion of the placenta as the target point (Figures 1 and 2). In order to achieve the same press effect, reference, and the target points were designated on the same plane. Smaller than 5 mm^2 region of interest (ROI) were selected for the elastography examinations.

Because SE is a dependent examination to the applied pressure, for optimal evaluation, the selection of the region to be examined is important. For this reason the authors included anterior and anterolateral located placentas to this study, and they made the measurements from the anterior part of the anterolateral located placentas.

Second point is due to the structure of the convex probe, equal pressure at each point in the study area cannot ensured. Therefore the authors believe that in the measurements of the reference point and the target point, ROI's should be selected from the same plane where the pressure is applied. For this purpose, by accepting the center of the probe as reference line, they chose the reference and the target points from the middle line of the images as distinctly from the other studies.

Uterine and umbilical artery Doppler values were calculated by two radiologists with at least five years' of experience. Pulse wave Doppler examinations were performed at mild left lateral position of the patients in the absence of maternal and fetal movements. Doppler US was applied with the sampling gate set at 2 mm and the angle of implementation less than 60°.

Umbilical artery measurements were obtained from at least three separate points of free-floating portion of the umbilical artery and their averages were taken. Resistivity and pulsatility indices (PI and RI) were measured automatically from five similar heart rates in the continuum. The uterine artery PI and RI values were measured from the entry point to the placenta using the same method. Umbilical and uterine artery RI and PI values were divided into two groups including normal and abnormal, by reference to Bahlmann *et al.* [6, 7] studies.

SPSS 22.0 program was used for analysing data. For suitability of normal distribution of data Shapiro-Wilk test and for homogeneity of variance the Levene's test was used. For comparison of two independent groups, Mann-Whitney U test was evaluated by Monte Carlo simulation technique. To examine the correlations between the variables, Spearman's Rho test was used. Data were examined with a 95% confidence level and p value less than 0.05 was considered statistically significant.

Results

Patients' age ranged between 17 to 43 (mean 27.9 ± 5.9) years and GW 21 to 24 (mean 22.6 ± 0.8) weeks.

Placental thickness on the vertical axis ranged between 13.9 to 43.2 (mean 25.2 ± 6.3) mm. The thickness of the subcutaneous fat tissue ranged between 7.7 to 34 (mean 16.9 ± 4.6) mm. Eighteen cases had abnormal umbilical artery RI and PI values, and 23 cases had abnormal uterine artery RI and PI values. There was no correlation between strain ratio values with maternal age, gravity, gestational week, placental thickness, and subcutaneous fat thickness (Table 1). An inverse correlation was found between umbilical artery RI values and placental strain ratios (p= 0.02; r= -0.22) (Figure 2).

Discussion

Previous studies showed that there was a correlation between placental elasticity and PE. It is unclear whether this difference is associated with placental insufficiency or placental insufficiency with IUGR.

The pathogenesis of PE is a complex issue. Histopathological examination shows a state that increased placental infarcts, sclerotic changes in the arteries, intervillous thrombosis and inflammation, and reduced placental weight is [8, 9]. As a result of the increase of extracellular matrix proteins due to increased inflammation, elasticity in the placental tissue decrease [10]. This may lead to an increase in placental stiffness. For this reason, it can be considered that the elasticity of the placenta can be measured with US elastography to contribute to the diagnosis of PE. However, contrary to other tissues, studies on placental elasticity have not been performed for a long time due to the possibility that the increase in heat during use of US elastography may damage the fetus. Herman *et al.* [11] showed that during the study they performed, the increase in tissue heat during ultrasound elastography was within safe limits as deter-

Table 1. — *Correlation data.*

Placental strain ratio	Umb. RI	Umb. PI	Uter. RI	Uter. PI	Mat. age	Grav.	Gest. week	Plac. thick.	Subc. fat thick.
Spearman's Rho									
Correlation coefficient	-0.224	-0.199	0.003	0.007	0.063	0.118	0.153	0.159	-0.005
Sig. (2-tailed)	0.028	0.051	0.980	0.945	0.544	0.251	0.138	0.122	0.958

mined by the FDA. Sugitani *et al.* [12] demonstrated that elastography does not thermally change histologically in the ex-vivo study performed on placenta and that US elastography is a safe assay. On these developments, in-vivo studies have been started with US elastography in the placenta.

In the literature review, the present authors found few articles related to placenta elasticity [8, 13-18]. The majority of them were performed using the shearwave elastography method, two of which were animal experiments [13-17]. The authors observed two articles that studied placenta elasticity with strain elastography. One of these is an ex-vivo study [8] by Durhan *et al.*, the other is an in-vivo study by Cimsit *et al.* [18].

In the ex-vivo study, Sigutani *et al.* reported that the placenta was classified in three groups as IUGR, PE-diagnosed, and normal pregnancy. A statistically significant increase in placental stiffness was found in the group with IUGR compared to the normal group, but there was no statistically significant difference between PE patients and normal group. In both Cimsit *et al.*, and Kılıc *et al.* studies, patients with PE were collected in a single group regardless of the presence of IUGR, and they found a statistically significant increase in placental stiffness in this group according to the normal group of patients. This may suggest that PE is not sufficient to cause an increase in placental stiffness and should be accompanied by IUGR.

In the present study, the patients could not be followed until birth, because their follow-up was performed in other centers and the patients came to this clinic just to scan for birth anomaly. Therefore, it is not possible to determine whether the fetuses were retarded at birth. The given birth of the majority of the pregnant women outside of this University can be attributed to the fact that they did not have major problems during the pregnancy. It may be thought that this may have led to IUGR being less visible in the present cases. The fact that there is no significant difference between the Doppler data and the placental elasticity in this study can be explained by this situation.

The first study showing placental elasticity as a strain was performed by Cimsit *et al.* [10]. In this study, SE data were found to be different in the case of second trimester early-onset PE, from the normal group. In 2016 Durhan *et al.* [8], evaluated placentas ex-vivo by histopathological and US elastography methods in cases with IUGR. They found that all placental levels had higher stiffnesses than the control group in IUGR cases. In the present study, the authors found an increase in stiffness of the placenta by SE although it did not reach statistical significance.

As is known, Doppler US abnormal findings are considered to be a weak positive predictors of placental insufficiency (8-33%) [19-21]. Cimsit *et al.* found a correlation with SE data by accepting notching in the uterine artery as a positive predictive factor for PE. Kilic *et al.* found a weak correlation between the RI and PI values of the uterine artery and the SE data in their study. The present authors did not find a study comparing Doppler values of umbilical arteries with SE in this literature search. They investigated the umbilical artery RI and PI values in addition to uterine arteries in this study, and investigated whether there was a positive predictive contribution to PE placental insufficiency. As a result, they found an inverse correlation between strain ratio values and umbilical artery RI values.

Studying only those pregnancies for anomaly scan and the absence of third-trimester pregnancies may be the limitations of the study. The most important limitation is that the patients with PE are not in the study group because of the necessity of performing the follow-ups of the patients out of this hospital.

Conclusion

In the present study, the authors found a correlation between placenta elasticity and Doppler findings. For the first time in this study, the relation between the values of umbilical artery Doppler results and SE values was determined.

Placental elasticity can be used for placental abnormalities in addition to other methods, but further studies are needed to use placental elasticity as a positive predictive marker for placental insufficiency.

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