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RESEARCH ARTICLE

Comparison of Placental Strain Elastography Values Between Healthy Pregnant Women and Pregnant Women with Intrauterine Growth Restriction or Preeclampsia

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ABSTRACT

Objective: We aimed to determine strain elastography values in the placentas of healthy pregnant women and pregnant women with intrauterine growth restriction (IUGR) and preeclampsia (PE). To obtain more objective data, we also examined whether strain ratio values change with placental maturation at different gestational weeks.

Materials and Methods: In our prospective randomized study, 64 pregnant women were divided into groups according to the degree of placental maturation (placenta grades 1, 2, and 3) and the trimester they were in to determine strain elastography values. Strain rates of the target tissue (placenta) and subcutaneous adipose tissue were calculated.

Results: According to our study, there was no statistically significant difference between the degree of placental maturation and strain ratio values. Additionally, no significant difference was detected in the strain ratio values of healthy pregnant women in the second and third trimesters. However, in cases with preeclampsia and intrauterine growth restriction, strain ratio values were found to be statistically significantly higher, especially in pregnant women in the second and third trimesters. We found a moderate correlation between strain ratio values and uterine artery S/D. Additionally, we observed a moderate positive correlation between strain ratio and BMI.

Conclusion: Our findings indicate that placental elastography strain ratio values may increase in pregnant women with preeclampsia and IUGR. These results support previous studies. Furthermore, our study shows that placental elastography strain rate values are not affected by gestational age or placental maturation (second and third trimesters) in healthy pregnant women. Our study was conducted in a reference hospital with a limited number of patients and restricted ultrasound imaging facilities. Future research with a larger sample size and advanced imaging techniques is recommended to support these findings.

Keywords: Elastography, FGR, growth, healthy, placenta, preeclampsia, pregnancy, restriction, strain

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INTRODUCTION

Elastography is a method of determining tissue stiffness using radio frequency (RF) ultrasound signals and a transducer. The transducer uses a controlled pre-compression signal and a post-compression signal to calculate the strain rate versus depth and distance. This strain value varies according to the degree of stiffness of the tissue.[1] B-mode gray scale or color scale evaluation of tissue hardness is based on comparing the amount of flattening that the tissue is subjected to with the amount of flattening in an area adjacent to this tis-

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sue. This method is widely used to detect lesions in different organs such as breast, prostate, thyroid and lymph nodes.[2] Studies are ongoing to standardize normal and abnormal values of tissue stiffness in many different organs (breast, thyroid, prostate, kidney and spleen, lymph gland, placenta). Studies on the determination and standardization of placental tissue stiffness are limited and almost non-existent. Similarly, studies on how these values change in pregnancies complicated by preeclampsia and in uterine growth retardation are limited.[3] As known, the placenta is important in the development of fetal and maternal diseases during pregnancy. Abnormal placental development leads to diseases with feto-maternal morbidity and mortality such as intrauterine growth restriction and preeclampsia.[4–6] Uterine artery doppler is frequently used to predict preeclampsia and intrauterine growth retardation.[5,6] There are studies showing that placental elastography may be useful in predicting and detecting such placental dysfunctions.[7] Recently, the number of studies in this field has been increasing.[8]

Placental elastography is a relatively new field of study. This method has the potential to provide useful information about the structure and function of the placenta.[7] The level of stiffness of tissues can help us to learn about the pathological state of organs. For example, elastography is widely used in the diagnosis of mechanical findings such as hepatic fibrosis caused by liver cirrhosis or abnormal tissue stiffness indicating pathological findings in breast tumors.[9] Similarly, research suggests that placental elasticity and stiffness are altered in diseases such as preeclampcia and intrauterine growth restriction compared to normal pregnancies.[10] However, these previous studies did not focus on whether the gestational week affects placental elastography values. Studies on elastographic examinations performed in healthy pregnant women are limited. At different gestational weeks, the levels of placental firmness and whether there is a difference between them may be important. Placental strain ratio values are likely to increase in progressive gestational weeks without placental pathology. Although this is expected in relation to the increasing degree of placental maturation as the gestational week progresses, we could not find a study on this subject. For example, would the strain ratio values of a healthy placenta at 32 weeks differ from the placental strain ratio values at 24 weeks or 16 weeks? This is an unanswered question according to the literature at this stage. However, since the normal values of placental stiffness are not standardized, inconsistencies arise in defining abnormal results.[11,12] In addition, it is unclear whether placental elastography values are affected by parameters such as maternal age, gestational week, maternal body mass index, uterine artery doppler ultrasography pulsatility index (PI) values.[13] In our study, we aimed to determine strain elastography values in both normal pregnancies and complicated pregnancies such as preeaclampsia and intrauterine growth retardation.

MATERIALS and METHODS

This study was conducted prospectively. Our study received ethics committee approval from the Bulent Ecevit University Clinical Research Ethics Committee of the University Faculty of Medicine and the Declaration of Helsinki was complied with (decision dated 27.01.2016 and numbered 02). In addition, informed consent was obtained from each patient participating in the study. A total of 64 randomized patients with different gestational weeks were included in the study. The number of patients was determined by taking into account the number of patients in previous studies.[14] Pregnant women were divided into groups according to their trimester and placental maturation grade (grade 1, 2, 3). Placental stiffness was measured and recorded in 'kPa' by strain elastography in all pregnant women. These values were compared with those of pregnant women with placental dysfunction such as preeclampsia and IUGR. Intrauterine growth retardation and preeclampsia were analyzed. Elastography values, systolic and diastolic blood pressure values, gestational weeks, uterine artery doppler findings were recorded.[15] In addition, age, body mass index, singleton or multiple pregnancy, and presence of comorbidities were questioned. Estimated fetal weight and abdominal circumferences were measured and intrauterine growth retardation was determined.[16] Placental garade, uterine artery doppler systole/diastole (S/D) and pulsatility index (PI) findings were determined and recorded. Placental maturity grades were classified into grades according to the criteria described by Grannum et al.[17] Of the pregnant women, 22 had grade I, 23 grade II and 19 grade III placentas. To ensure standardization in placental elastography, we excluded multiple pregnancies, pregnant women with posteriorly located placentas, placental invasion anomalies, and morbid obesity.

Imaging and Strain Elastography

Strain elastography is a quantitative assessment using a mechanical force with reference to the area to be measured and a point in its neighborhood.[2] In image formation, controlled pressure is created on the tissue examined with a probe from the skin surface and the responses are evaluated. The units of measurement used in elastography are kilopascal (kPa) and shear wave velocity (m/sec). Measurement is basically done in the form of velocity measurement (m/sec).[7,12,18] Placental elastographic studies have been used to investigate

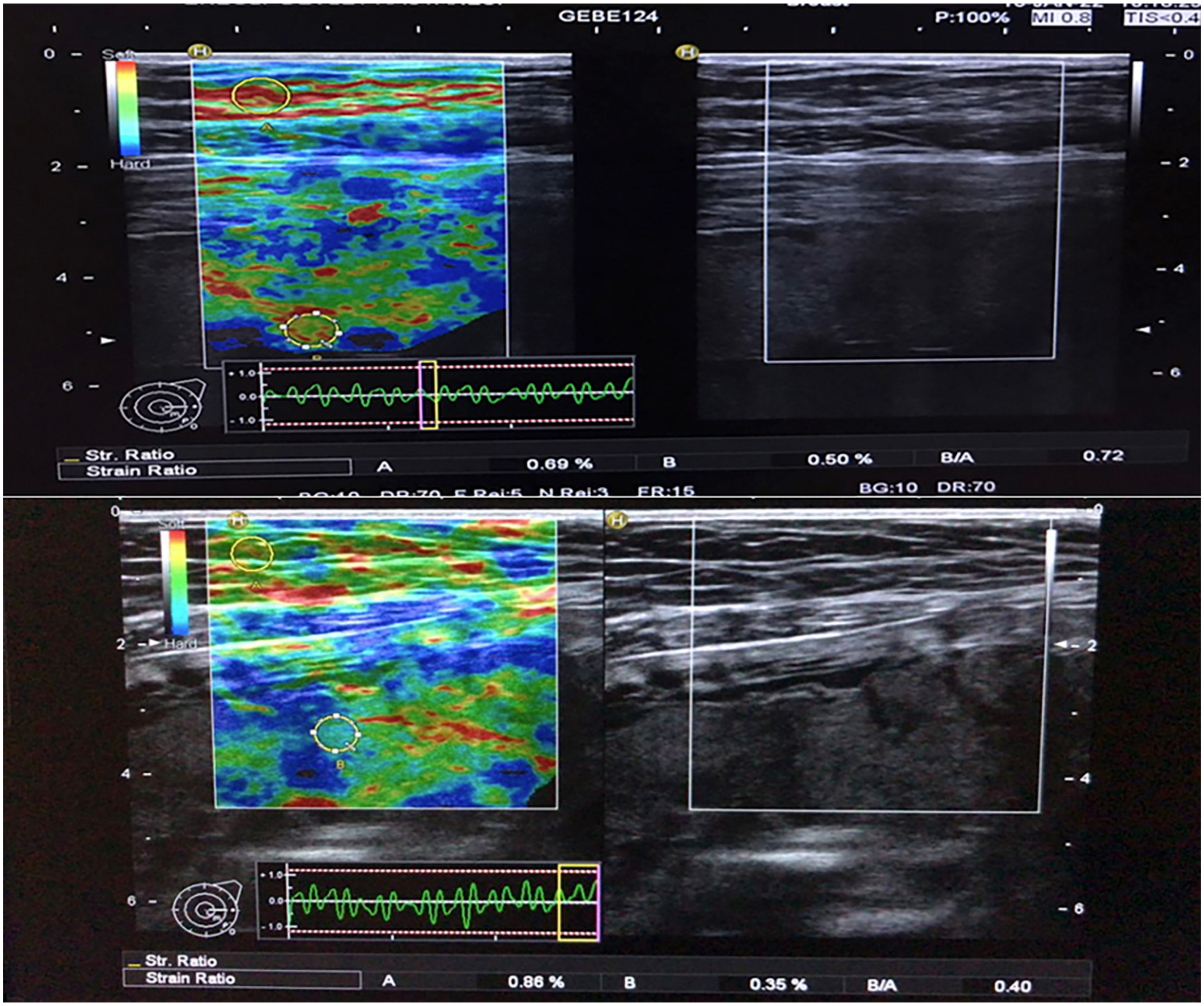

Figure 1. Placenta elastogrphy. The left side of the window is color-coded and the right side is gray scale imaging. One circle represents the subcutaneous adipose tissue and the other the placental region of interest. A normal sinusoidal wave may appear at the bottom of the screen. Indicates that the probe pressure is optimal. Numbers indicate strain values and percentages indicate the rate

obstetric pathologies associated with uteroplacental insufficiency.[13] Elastographic measurements were performed by an expert radiologist with approximately 5 years of experience in handsatography using high-resolution B-mode gray gray ultrasound. A Hi Vision Preirus ultrasonography system (Hitachi Aloka Medical, Ltd.) with a 5–13 MHz linear array transducer was used as the ultrasonography device. In measurements using the free hand technique, following activation of the mechanical elastography system (Elasto-Q), lateral movements were avoided during pressure application with the probe positioned perpendicular to the skin. Elastographic measurements were finalized after the compression and relaxation stages.[19] Measurements were blindly supervised by a second radiologist. Prior to elastography, fetal assessment and biometry measurements using gray scale, two-dimensional (2D) ultrasound were performed by an obstetrician and gynecologist according to the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) guidelines.[20] The ultrasound frequency mostly used for elastography is similar to B mode and no adverse effects on pregnancy are

Table 1. Some sociodemographic and pregnancy-related characteristics

Specifications	Median	1–3 quarter	Min-max
Age	27.00	24.00–31.75	18–40
Gestational week	30.00	24.25–33.00	14–38
Placenta grade	2	1.00–3.00	1–3
Trimester	3.00	2.00–3.00	2.00–3.00
Strain ratio	0.82	0.74–1.24	0.50–9.23
Uterine artery SD	2.15	1.90–2.60	1.50–3.80
BMI	24.00	22.00–2.00	18.00–33.00
Systolic TA	100.00	100.00–110.00	90.00–160.00
Diastolic TA	60.00	60.00–80.00	50.00–100.00
IUGR n (%)			
+	9 (14.1)		
–	55 (85.9)		
Preeclampsia n (%)			
+	11 (17.2)		
–	53 (82.8)		
Total n (%)	64 (100)		

Some sociodemographic and pregnancy-related features. SD: Sistol diastole; TA: Blood pressure arterial; BMI: Body mass index; IUGR: Intrauterine growth restriction

expected.[21] Only singleton pregnancies and patients with an anterior placenta were included in the study. After fetal biometric measurements were taken according to ISUOG guidelines, uterine artery doppler measurements were performed and recorded. Uterine artery doppler measurements were recorded by calculating pulsatility index and resistance index. First, the "Strain Ratio" ratios of the placenta, which is the target tissue, and the subcutaneous adipose tissue to be taken as reference were calculated.[20] Then the average strain ratio was calculated by finding the ratio between the target tissue and the reference tissue (Fig. 1). For the procedures, a randomized area, approximately away from vascular structures and lacunar areas, was used. Strain elastographic measurements were performed close to the uterus, close to the fetus and at mid-placental distance, respectively, and the average of the three regions was calculated as the elastographic strain ratio.[22,23] Mechanical indices did not exceed 1.5 and thermal indices did not exceed 1.7.[24]

Statistical Analysis

The statistical analysis was performed using IBM SPSS Statistics version 21.0 software (IBM Corporation, Armonk, NY, USA). The normality of the distribution of continuous variables was determined visually and analytically (Kolmogorov-Smirnov). Descriptive analyses were evaluated using medians and 1st-3rd quartile, minimum-maximum values for non-normally distributed variables. Categorical variables were expressed as numbers and percentages. Mann-Whitney U test and Spearman correlation test were used to analyze the data. The significance level for all statistical tests was set as $p<0.05$. Post hoc analysis was proformed with Dunn test.

RESULTS

Twenty-two of the pregnant women had grade I, 23 had grade II and 19 had grade III placentas. Intrauterine growth retardation was detected in 9 patients and preeclmapsia in 11 patients. Of the pregnant women in the study, 26 were in the early 2nd trimester and 38 were in the 3rd trimester (Table 1). Strain ratio was statistically significantly higher in cases with IUGR. While there was no statistically significant difference in pregnant women with grade 1 placenta, strain ratio was statistically significantly higher in cases with grade 2 and 3 IUGR. In pregnant women with preeclampsia and in those with preeclampsia in all three placental grades, strain ratio was statistically significantly higher than in those without preeclampsia (Table 2). In 2nd and 3rd trimester pregnant women, no statistically significant difference was found in Strain ratio values ($p>0.05$) (Table 3). IUGR (intrauterine growth restriction) In 2nd and 3rd trimester pregnant women with IUGR and preeclampsia, strain Ratio value was

Table 2. Comparison of strain ratio values in pregnant women according to some characteristics

	Strain ratio		
	Median	Min-max	p*
IUGR			<0.001
+	3.20	1.04–7.57	
–	0.80	0.50–9.23	
Grade 1 IUGR			0.052
+	2.40	1.04–7.57	
–	0.76	0.50–1.20	
Grade 2 IUGR			0.007
+	5.59	1.80–9.23	
–	0.80	0.50–3.20	
Grade 3 IUGR			0.037
+	3.80	2.46–6.26	
–	0.88	0.50–1.42	
Preeclampsia			<0.001
+	4.60	1.04–9.23	
–	0.79	0.50–3.20	
Grade 1 preeclampsia			0.011
+	2.40	1.04–7.57	
–	0.76	0.50–1.20	
Grade 2 preeclampsia			
+	5.59	1.80–9.23	0.001
–	0.80	0.50–3.20	
Grade 3 preeclampsia			0.008
+	3.80	2.46–6.26	
–	0.88	0.50–1.42	

*: Mann Whitney U test. Comparison of strain ratio values in pregnant women according to some characteristics. Elastography strain ratio in pregnant women with preeclampsia and IUGR. The relationship with placental maturation was analysed. IUGR: Intrauterine growth restriction

found to be statistically significantly higher (Table 4). There was a moderate positive correlation between strain rate and uterine artery SD and BMI (respectively, r=0.500, p<0.001; r=0.535, p<0.001 (Table 5).

DISCUSSION

Strain elastography is an ultrasonographic method used to detect tissue stiffness.[12,25,26] Strain elastography has a higher risk of variability depending on the practitioner, but a study suggests that it makes a diagnostic contribution as much as SWE elastography.[27] Physiopathologic processes during placental development predispose to diseases such as preeclampsia, intrauterine growth retardation and affect placental elasticity.[13,14] Therefore, placental elastographic studies may provide insight into the management of these diseases in the future. Our review of the literature has shown that there are some changes in the degree of placental stiffness especially in diseases such as preeclampsia and intrauterine growth retardation.[13] However, the degree of placental stiffness has not been standardized by strain elastography in a healthy placenta in normal pregnant women. In addition, there are no studies on whether placental stiffness varies in different trimesters or at different placental maturation. Our main aim in this study is to determine whether strain elastography values vary in grade 1–2–3 placentas and in pregnant women at different trimesters. In addition, we examined the effects of various demographic characteristics on placental strain ratio values. We also tried to determine whether there is a correlation between strain ratio values and pathologies associated with placental dysfunction such as preeclampsia and intrauterine growth retardation.

Table 3. Comparison of strain ratio values according to trimesters in pregnant women without IUGR and preeclampsia

	Strain ratio		
	Median	Min-max	p*
Trimester			0.524
2nd	0.76	0.50–1.20	
3rd	0.80	0.50–1.63	

*: Mann Whitney U Test. Comparison of strain ratio values according to trimesters of pregnant women without a diagnosis of IUGR (intrauterine growth restriction) and preeclampsia. IUGR: Intrauterine growth restriction

Sociodemographic characteristics of the pregnant women are shown in Table 1. According to our study, there was no statistically significant change in placental grade and strain ratio values in healthy pregnant women (Table 2). In our study, no significant difference was found in strain ratio values in healthy 2nd and 3rd trimester pregnant women (Table 3). Fifty-three pregnant women without placental pathology, preeclampsia and intrauterine growth retardation were analyzed and mean starin ratio values were measured in the range of 0.76–3.40 kPa. These values did not show a statistically significant difference in different trimesters. Grade 1 healthy placentas had 0.76 kps, grade 2 placentas had 0.80 kPa, grade 3 placentas had 0.88 kPa and these differences were not statistically significant. This suggests that possible increases in the degree of placental stiffness cannot be attributed to placental maturation or advanced gestational

Table 4. Comparison of strain ratio levels according to the development of IUGR and preeclampsia in different trimester pregnant women

	2nd trimester		3rd trimester	
Strain ratio	Median	Min-max	Median	Min-max
IUGR				
+	3.20	1.80–6.26	4.60	2.46–7.57
–	0.76	0.50–2.40	0.80	0.50–9.23
p*	0.008		0.002	
Preeclampsia				
+	2.40	1.80–6.6	5.59	2.46–9.23
–	0.76	0.50–3.20	0.80	0.50–2.60
p*	0.010		<0.001	

*: Mann Whitney U Test, IUGR (intrauterine growth restriction). Comparison of strain ratio levels according to IUGR and preeclampsia development status in different trimester pregnant women. IUGR: Intrauterine growth restriction

Table 5. Analysis of correlation* between strain ratio, uterine artery SD, BMI, age, and gestational age

	Uterine artery SD	Strain ratio	BMI	Age	Gestational week
Uterine artery SD					
r	1.000	0.500	0.234	0.043	-0.068
p	.		0.062	0.737	0.596
Strain ratio					
r	**0.500**	1.000	0.535	0.124	0.221
p	**<0.001**	.	0.000	0.328	0.080
BMI					
r	0.234	**0.535**	1.000	0.154	0.347
p	0.062	**<0.001**	.	0.225	0.005
Age					
r	0.043	0.124	0.154	1.000	0.127
p	0.737	0.328	0.225	.	0.317
Gestational week					
r	-0.68	0.221	**0.347**	0.127	1.000
p	0.596	0.080	**0.005**	0.317	.

: Examined with Spearman correlation. Analysis of the correlation relationship between strain ratio, uterine artery SD, BMI, age, and gestational week values. SD: Sistol diastole; BMI: Body mass index.

weeks, and it is definitely worth investigating for placental pathology. In healthy pregnant women, 2nd trimester strain ratio values were between 0.50–1.20 kPa and 3rd trimester starin ratio values were between 0.50–1.63 kPa. There is no study on these values in our literature review. However, gestational age and elastography Strain ratio values were examined in two different studies and no statistically significant difference was found in both studies as in our study. Wu et al.[11] the second and third trimester placental shear wave velocity results were found to be 0.63–1.81 kPa, similar to our study. In another study conducted by Li et al.[28] it was found to be 7.84 kPa and large differences were found between the measurements. In this study, unlike ours, share wave elastography (SWE) technique was used. Çimşit et al.,[2] placenta Strain ratio values were found between 0.82–0.97 in the 2nd and 3rd trimesters. These results are consistent with our results. In fact, a more mature placenta is expected to be stiffer due to calcification and fibrosis. However, according to the results of our study, if there is no triggering placental dysfunction in the placenta, there is no significant change in Strain ratio values according to gestational week. This is consistent with the knowledge that abnormal placental calcification is independent of gestational age.[28,29] It is not clear whether there is a relationship between placental elastographic values and parameters such as age, gestational week, placental grade, BMI, systolic blood pressure, diastolic blood pressure. Whether these variable parameters affect placental elsatographic values was included in our study. Accordingly, we found a moderate positive correlation between Strain ratio and BMI. This result was similar to previous similar studies. This result was similar to previous similar studies [2,13,14] (Table 5).

In a few studies on the degree of placental stiffness, it has been found that strain ratio values change with the deterioration of placental elasticity especially in diseases such as preeclampsia and intrauterine growth retardation.[13,14] In our study, like Kılıç et al.[14] we found significantly higher strain ratio values in patients with preeclampsia and intrauterine growth retardation, especially in grade 2–3 placentas and in pregnant women in the last two trimesters (Table 2, 4). This height was 3–10 times higher than the strain ratio values in healthy pregnant women with increasing placental maturation and advancing gestational weeks. In a different study, Cimşit et al.[2] Strain ratio values were 2 or 3 times higher (mean 2.16kPa) in pregnant women complicated with preeclampsia compared to healthy pregnant women. We found that placental stiffness was higher in pregnant women with intrauterine growth retardation compared to control groups (3.20Pa). This result is consistent with previous studies.[7,8,30] In our study, we did not find a significant difference in Grade 1 placentas, which suggests that elastography may be more useful in the middle and late period.

Also in our study, we investigated whether uterine artery doppler evaluation and placental strain elastography values differ. According to the results of our study, a moderate correlation was found between Strain ratio and uterine artery S/D (Table 5). Our results are in accordance with Kılıç et al.[14] and Karaman et al.[31] Our results show correlation with different studies conducted by Kılıç et al.,[14] placental strain ratio values increased as uterine artery resistance increased. In the future, the addition of placental strain elastography values to doppler parameters with larger-scale studies may have a place in the prediction of these diseases.

Since our study was designed to determine whether placental grade and placental elastography Strain ratio values change, the number of patients to be compared with preeclampsia and IUGR patients was partially limited. In addition, it was not easy to find pregnant women complicated with preeclampsia and IUGR because the hospital where the study was conducted was not a tertiary health care institution. The fact that there is no other study in which placental grade and Strain ratio values were examined makes our study different.

CONCLUSION

As a result, 64 pregnant women who were divided into grades according to the criteria specified by Grannum et al.,[17] were examined and placental elastography values were analyzed. Although Strain ratio values showed a minimal increase as placental grade increased in pregnant women not complicated with preeclampsia and IUGR, this difference was not statistically significant (grade1–0.76kPa, grade2–0.80kPa, grade3–0.88kPa) (Table 2). On the contrary, Strain ratio values were statistically significantly higher in pregnant women complicated with preeclampsia and IUGR. These results suggest that in the absence of pathologies affecting placental stiffness and elasticity, placental elastography Strain ratio values do not increase with placental grade or gestational age. This suggests that placental elastography can be used in conjunction with other ultrasonographic methods, especially in cases associated with placental pathologies such as preeclampsia or IUGR.

Disclosures

Ethics Committee Approval: The study was approved by the Bulent Ecevit University Clinical Research Ethics Committee (No: 02, Date: 27/01/2016).

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