






Efficacy of shear wave elastography in predicting preeclampsia in the first trimester

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SUMMARY

OBJECTIVE: This study aimed to investigate the predictive value of shear wave elastography (SWE) for preeclampsia (PE) in first-trimester pregnancies.

METHODS: Singleton pregnant women aged 18–45 years, who underwent routine first-trimester prenatal examinations (11–13 weeks+6 days) were enrolled. Pregnancies with anterior placenta and normal first-trimester screening test results were included in the study group. The SWE measurements of six areas of the placenta were performed, and the mean value was estimated. The perinatal outcomes and the demographic data were also collected. The receiver operating characteristic curve analysis was used for the accuracy of predicting PE.

RESULTS: This study consisted of 84 patients, of which 9 were diagnosed with PE during the follow-up. The mean SWE value of the PE patients was higher than that of patients with normal pregnancies ($p=0.002$). The analysis showed that the optimal cutoff value was 7.43 kPa to predict PE in the placentas of first-trimester pregnancies, with 88% sensitivity and 78% specificity.

CONCLUSIONS: The SWE values of the placenta in the first trimester were different between normal patients and those who are subsequently developing PE. SWE may be a suitable tool for predicting PE in pregnant women.

KEYWORDS: Shear wave elastography. Preeclampsia. High-risk pregnancy. First-trimester screening.

INTRODUCTION

Shear wave elastography (SWE) is a type of sonoelastography method that measures the stiffness and elasticity of soft tissues¹. This new technique has already been used in the differential diagnosis of diseases such as hepatic fibrosis, tumors, and inflammation in musculoskeletal tissues^{1,2}. Recently, it has become popular in screening the elasticity of the placenta in high-risk pregnancies such as those with preeclampsia (PE), intrauterine growth restriction, and placental dysfunction³⁻⁵. The application of SWE is considered safe during pregnancy, and performing this technique has already been documented in obstetrics^{5,6}.

PE, a known multisystem disease, generally affects 2–5% of pregnant women, and it is associated with a perinatal and neonatal mortality rate of 10%^{7,8}. Many studies have been conducted to predict and prevent PE⁹⁻¹¹. They investigated maternal factors including maternal pulse wave analysis, mean arterial blood pressure, uterine artery pulsatility index (UtA-PI), serum placental protein 13, serum pregnancy-associated plasma protein A (PAPP-A), and placental growth factor^{7-9,12}. While the cause of PE remains an enigma, clinical and pathological studies suggest that the placenta is central in the pathogenesis of this syndrome. Instead of combining the laboratory markers, the use of a noninvasive ultrasound method for screening

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the placenta seemed appealing. Therefore, we aimed to investigate the predictive value of SWE for PE in first-trimester single-euploid pregnancies.

METHODS

This prospective study included singleton pregnant women aged 18–45 years, who underwent routine first-trimester prenatal examination (11–13 weeks+6 days) between May 2019 and December 2019 at a tertiary hospital. Ethical documents, including the protocols as per the Declaration of Helsinki, were approved by the local Institutional Review Board (Approval number: 2019/50), and written informed consent was obtained from all patients.

Patients with normal first-trimester screening test results (single-euploid pregnancies) were enrolled in the study group. Exclusion criteria were multiple gestations, pregnancies with fetal anomalies, abnormal placental location, and uterine malformations. Patients with systemic autoimmune diseases (chronic hypertension, diabetes, hepatitis, etc.), history of PE, high blood pressure, and smoking habits were also excluded.

First-trimester prenatal examinations including nuchal translucency (NT) and UtA-PI of both maternal sides were performed as previously described^{13,14}. Routine laboratory markers, including PAPP-A and beta-human chorionic gonadotropin (β -hCG) for the first-trimester screening test, were also obtained. Measurements were expressed as multiples of the median (MoM) values according to the percentiles adjusted for fetal crown rump length. Additionally, SWE was performed during the ultrasonographic evaluation of the first trimester. All ultrasonographic measurements were conducted by a single perinatologist. Patients with anterior placenta were included in the study to avoid reducing the effectiveness of the method. Considering the disc-like structure of the placenta, it was divided into the following six regions for measurement: maternal right, maternal central, maternal left, fetal right, fetal central, and fetal left. The mean arithmetic value was calculated. The SWE measurements of the six areas of the placenta were performed for every patient to record the measurements from different parts of the placenta. Since the placental structure is small in the first trimester and the measurement areas were close to each other, an average value was calculated. The demographic data and the detailed medical and obstetrical history were examined and recorded during patient admission.

Perinatal outcomes, including the delivery week and birth weight, were also recorded. All patients were followed up at the perinatology clinic, and the delivery timings were organized

individually based on obstetrical indications. PE was diagnosed according to the following guidelines: two measurements of diastolic blood pressure ≥ 90 mmHg of at least 4 h apart in a previously normotensive woman and proteinuria ≥ 300 mg in 24 h; or two readings of at least “++” on the dipstick analysis of midstream urine or catheter specimen urine (if no 24-h urine collection is available) after 20 weeks of gestation¹⁵. The primary measurement outcome was to predict PE by using SWE in the normally detected first-trimester screening.

Shear wave elastography

SWE is a safe, noninvasive technique with the advantage of being performed in the same session as the routine antenatal scanning^{2,6}. There is no need to wait for the results like other screening markers; SWE measurement can alleviate patient anxiety. The stiffer the tissue, the higher is the shear wave velocity (SWV). Samsung HS70A ultrasound system with a Samsung CA1-7A convex transducer was used. SWE measures alterations in tissue deformation, reflective of its elastic properties when an internal or external force is applied. Once force is applied, tissue displacement can then be displayed directly as an image property, as SWE. During the examination, patients were made to lie in the supine position, breathing levels were kept steady to prevent noise and artifacts, and a minimum pressure was applied on the transducer to eliminate misleading tissue compression. A region of interest box of 10×10 mm was positioned on the placenta, and six measurements were obtained from the central and peripheral zones of the placenta while avoiding vascular structures (Figure 1). All measurements were obtained in kPa formats.

Statistical analysis

Statistical Package for the Social Sciences version 20 program (SPSS Inc., Chicago, Illinois, USA) was used for the statistical evaluation of the data obtained in this study. The continuous data were summarized as mean and standard deviation, while the categorical data were summarized as numbers and percentages. The receiver operating characteristic (ROC) curve was used to investigate the accuracy of predicting the presence of PE. According to this method, for the best test definition, the sensitivity was 100%, the area under the curve (AUC) was 1, and the diagnostic value of AUC was $p < 0.05$.

The sampling size was calculated based on the ability of the SWE measurements to predict PE in pregnancies by the ROC analysis. In this case, considering the structure of the ROC curve, the value of the AUC was assumed to be approximately 0.85 and the minimum sample size at 80% power at a 10% error level was determined in 76 patients.

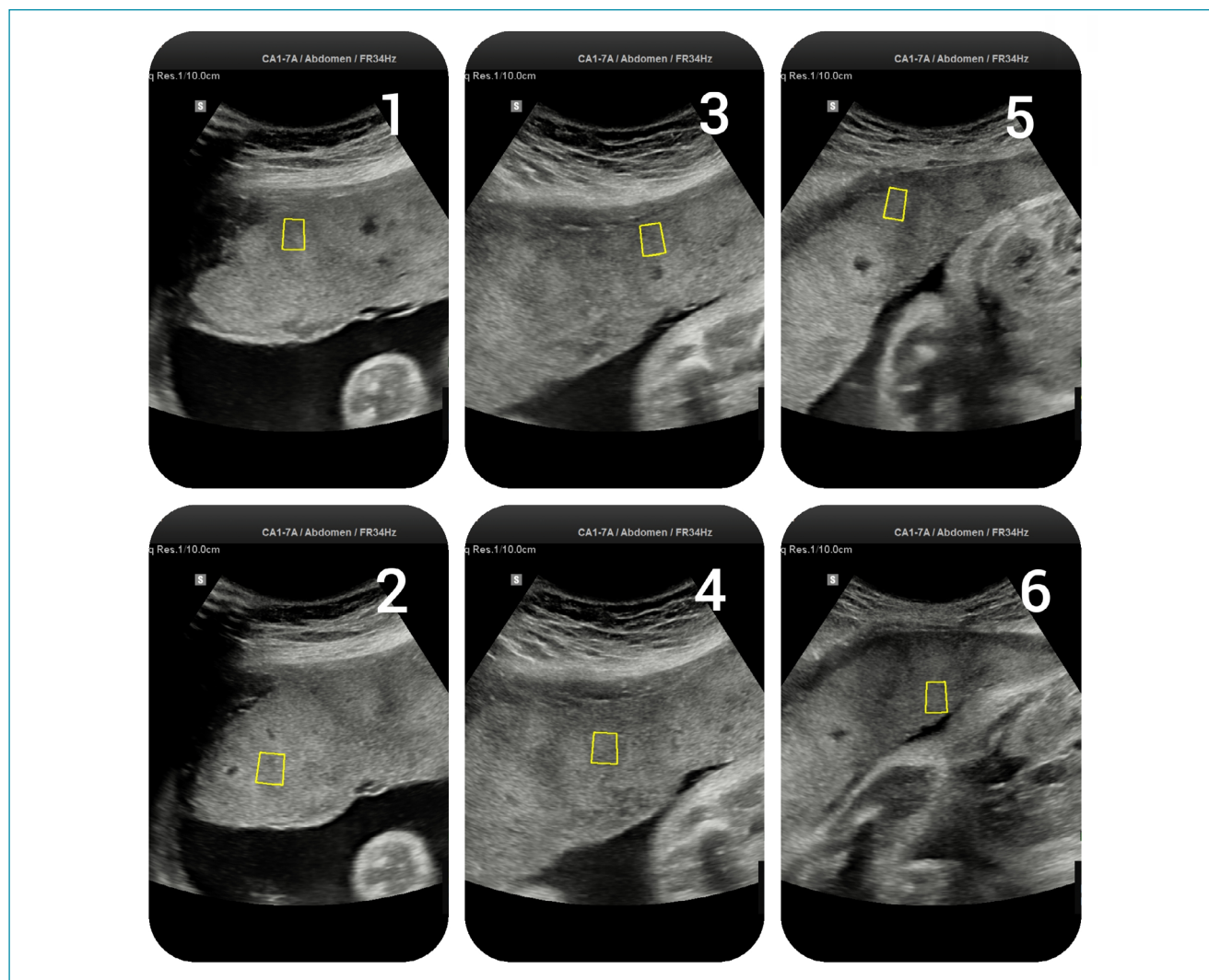


Figure 1. Placental measurements were obtained from central and peripheral zones of placenta while avoiding vascular structures. Numbers 1, 3, and 5 were maternal side and 2, 4, and 6 were fetal side; respectively.

RESULTS

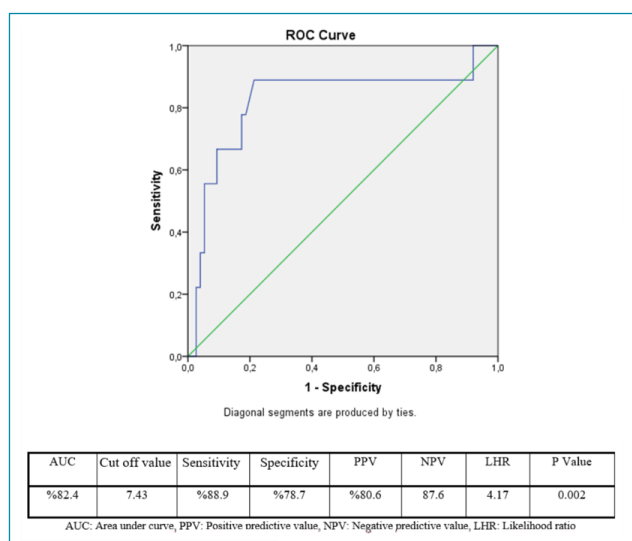
This study included 113 pregnancies, of which 11 patients were lost to follow-up and 1 to abortion. All pregnancies were followed up until delivery. Patients who subsequently developed gestational diabetes mellitus, gestational hypertension, and fetal growth restriction were excluded. Since it is not clear which patient will be diagnosed with PE according to the follow-ups in the first trimester, a long time was required in terms of the follow-up period and results. The final study population consisted of 84 patients, of which 9 were diagnosed with PE later during the follow-up. The characteristics of the patients, including pregnancy outcomes and the results of screening tests, are shown in Table 1. Pregnancies with PE had earlier deliveries and lower birth weights. The mean age of the women in this study was 29 ± 5.13 years,

and the mean gestation period was 11 weeks and 6 days. All mothers and babies were healthy, and only two babies were taken to the neonatal intensive care unit. There was no statistically significant difference between the patients with PE and those with normal pregnancies regarding age, gravidity, parity, body mass index, and the results of first-trimester screening tests, except for the mean SWE value. The mean SWE value in the PE patients was significantly higher than that of the patients with normal pregnancies ($p=0.002$). The ROC analysis for the mean values of SWE showed that the optimal cutoff value was 7.43 kPa to predict PE in the placentas of first-trimester pregnancies, with 88% sensitivity and 78% specificity (Figure 2). Regarding the detection rates including NT, PAPP-A, β -hCG, and UtA-PI for PE, there was no better prediction parameter than the mean value of SWE.

Table 1. Summary of characteristics of the patients, pregnancy outcomes, and the results of screening tests between groups (preeclampsia and normal pregnancies).

	Normal pregnancies (n=75)	Preeclampsia (n=9)	p-value
Age (year)	29.93±4.29	26.77±7.13	0.081
Gravidity (min–max)	2 (1–7)	2 (1–7)	0.828
Parity (min–max)	1 (0–3)	1 (0–3)	0.847
BMI	25.47±2.93	25.61±4.22	0.926
Birth (weeks)	38.66±1.09	36.22±2.63	0.024
Birth weight (g)	3390±372	2782±646	0.023
PAPP-A (MoM)	1.22±0.81	1.05±1.01	0.564
β-hCG (MoM)	1.16±0.91	1.20±0.99	0.905
NT (MoM)	0.94±0.23	0.97±0.26	0.736
UtA-PI			
Right	1.15±0.55	1.28±0.52	0.933
Left	1.08±0.50	1.28±0.61	0.279
SWE (mean)	6.03±2.23	9.04±2.57	0.04
SWE (min–max)	2.37–13.78	3.43–11.77	

BMI: body mass index; PAPP-A: pregnancy-associated plasma protein A; MoM: multiples of the median; β-hCG: human chorionic gonadotropin; NT: nuchal translucency; UtA-PI: uterine artery pulsatility index; SWE: shear wave elastography; p<0.05 indicates the statistical significance.

**Figure 2.** The receiver operating characteristic curve analysis for the positive and negative likelihood ratio of the value of 7.43 kPa.

DISCUSSION

In this study, we found that a mean SWE value above 7.43 kPa predicted PE with very high sensitivity and specificity in low-risk pregnancy patients with normal first-trimester screening test results.

Fujita et al.¹⁶ measured point SWV to evaluate the placental elasticity for predicting the onset of PE in the second trimester. They examined 16–32 weeks of singleton pregnancies with anterior placenta and compared values between 185 low-risk and 36 high-risk patients for PE¹⁶. A higher SWV was found in the high-risk group¹⁸. Therefore, it has been suggested that SWV can be used as a parameter to predict the onset of PE. Similarly, higher placental SWV values were observed in the second- and third trimester of pregnancies with mild-severe PE or gestational hypertension as compared with the controls^{3,17}. The UtA-PI value was found to be significantly higher in the PE group than in the controls of these studies^{3,17}.

Cimsit et al.⁵ investigated SWE in the placentas of normal pregnancies (n=101) and those complicated with PE (n=28) at 20–23 weeks of gestation. A higher overall mean value of SWE was found in pregnancies complicated with PE as compared with the controls (7.01 kPa vs. 2.53 kPa). There was no statistically significant difference in the SWE values between the center and edges of the placenta in both groups. UtA notching was detected in the PE group (60.7% bilateral and 39.2% unilateral). The SWE findings were in line with the results of our study, even in the second trimester. The efficacy of UtA-PI for the prediction of PE was found to be low and variable¹⁸. Although the first-trimester screening tests to detect aneuploidy have become an essential part of perinatology with recent evidence of serum or ultrasound markers, their results for the prediction of PE are not impressive¹⁹.

In our study, there was no difference between the UtA-PI values and the results of the other first-trimester screening tests. Since patients with normal first-trimester screening test results were included in this study, it could explain the nonsignificant difference between the two groups. The mean SWE value in patients with PE was significantly higher than in patients with normal pregnancies (p=0.04). The reason could be inflammation and resistance in the fetal–maternal unit (atherosis, infarction, and hyperplasia)²⁰. PE should not be considered as a single form with different underlying pathophysiological conditions.

In a recent study²¹, compared with healthy pregnancies, placentas of preeclamptic pregnancies were found stiffer and more heterogeneous. Placental stiffness was not affected by the gestational age or the severity of PE. In another point of view, the process of PE is known to be started in the first trimester, and pharmacological intervention with medications such as low-dose aspirin is recommended to reduce the prevalence of complications. But, there is still a lack of knowledge that plays

a major role in pathology, inflammation, or factors leading to inadequate invasion of the placenta. Both the insufficient invasion to the maternal unit and the tissue inflammation or changes were reported as stiffness in SWE in PE or fetal growth restriction. Therefore, it should be the answer to the high SWE values in our study results in the first trimester.

The major strength of our study was the SWE measurement in the first-trimester placenta and the follow-up for maternal and fetal outcomes. We believe that SWE can effectively predict PE in the first trimester.

Our study has some limitations. First, the posterior placenta was not evaluated due to the technical limitations of the SWE. Second, the distribution of PE cases was appeared to be higher than that of normal cases because the study was conducted in a tertiary hospital. Moreover, the study may be improved with larger patient numbers.

CONCLUSIONS

The SWE values differed between normal pregnancies and those that are subsequently developing PE in the first trimester. SWE may be a suitable tool, and we suggest its use clinically to predict PE.

AUTHORS' CONTRIBUTIONS

HAS: Conceptualization, Funding acquisition, Methodology, Resources, Software, Supervision, Writing – original draft. **GU:** Conceptualization, Project administration, Resources, Writing – original draft, Writing – review & editing. **HN:** Data curation, Investigation, Visualization, Writing – review & editing. **BC:** Data curation, Investigation, Validation. **SG:** Formal analysis, Project administration, Validation. **OP:** Formal analysis, Funding acquisition, Visualization.

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