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Original Article

Cardiac dysfunction in women with severe preeclampsia detected by tissue Doppler and speckle-tracking echocardiography

Gaoyun Pan[1], Deng Chen[1], Lixin Xu[1], Xinxin Dong[1], Liyi You[1], Zhangqian Zhu[1], Hongping Zhang[2], Yanjun Hu[2]

Departments of [1]Ultrasound, [2]Obstetrics, Wenzhou People's Hospital, Wenzhou Women and Children's Hospital, Wenzhou, China

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Abstract: Introduction: Preeclampsia is a multisystem disorder that can affect almost every organ. Cardiopulmonary morbidity is seen in a significant proportion of preeclamptic cases. Preeclampsia may be associated with the potential for significant myocardial damage. Aim: To test the hypothesis that severe preeclampsia (PE) provokes significant cardiac dysfunction using both tissue Doppler and speckle-tracking echocardiography. Materials and Methods: A total of 33 women with severe preeclampsia and 20 normotensive pregnant women were recruited. Tissue Doppler and speckle-tracking echocardiography were performed in all subjects. Results: Women with severe PE had higher IVSd, LVPWd, LVMI than healthy pregnant women. Septal and lateral annulus tissue Doppler velocity e' was significantly reduced in women with severe PE compared with healthy pregnant women. Average mitral inflow velocity early peak E to e' was significantly increased in women with severe PE compared with healthy pregnant women. Out of 33 patients, 17 (41.5%) patients had diastolic dysfunction, of which 4 (12.1%) patients had grade I and 13 (39.4%) had grade II. In control group, none of the subjects had diastolic dysfunction ($P<0.001$). In the severe PE group, 10 patients (30.3%) had left ventricular hypertrophy (LVH), while in the control group only 1 woman had LVH ($P=0.045$). Left ventricular ejection fraction was preserved in women with severe PE. 2D strain of apical four chamber view decreased in women with severe PE. Conclusion: Cardiac diastolic and systolic dysfunction can be present in women with severe preeclampsia. Left ventricular hypertrophy can occur in a proportion of women with severe preeclampsia. Tissue Doppler and speckle-tracking echocardiography is applicable and acceptable in detecting cardiac function changes in women with severe preeclampsia and can identify patients for early intervention to prevent heart failure.

Keywords: Cardiac dysfunction, severe preeclampsia, tissue Doppler, speckle-tracking, echocardiography

Introduction

Preeclampsia is a multisystem disease that can involve many organs. The pathological mechanism in this disorder is mainly ischemia and are known to affect the placenta, kidney, liver, brain, as well as heart [1-4]. Cardiorespiratory complication is seen in a significant proportion of preeclamptic women [5] and autopsy study have demonstrated that preeclamptic women have a higher prevalence of myocardial impairment than deaths in pregnancy from other causes [6]. Epidemiological study have also shown the close relationship between preeclampsia and premature morbidity and mortality from cardiovascular disease [7] which is thought to be related to shared cardiovascular risk factors. All these studies suggest that preeclampsia may be associated with the potential of significant myocardial damage. If cardiac dysfunction in preeclamptic women can be identified in early stage, it may be possible to prevent progression of this condition and save mothers from severe morbidity of acute heart failure. Echocardiography is widely used in detecting cardiac function, but conventional echocardiography play a little role in detecting myocardial dysfunction of early stage. Novel techniques such as tissue Doppler (TD) velocity and speckle-tracking echocardiography deformation indices are highly sensitive at detecting myocardial damage. The purpose of this study was to test the hypothesis that severe PE induces distinct cardiac dysfunction using both tissue Doppler and speckle-tracking echocardiography.

Table 1. Baseline Characters of controls and cases

	Control (n=20)	Severe PE (n=33)	P
Age (yrs)	28.7±5.1	30.5±6.0	0.286
Gestation (w)	34.7±3.4	34.7±5.0	0.969
BSA (m^2)	1.72±0.23	1.70±0.15	0.739
BMI	24.3±3.2	28.0±3.9	0.001
SBP (mmHg)	116±8.5	157.8±19.6	0
DBP (mmHg)	73.2±10.3	98.5±10.6	0

PE indicates preeclampsia; BSA,body surface area; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Materials and methods

Study subjects

This prospective study was carried out over a 2-year period from January 2014. A total of 33 women with singleton pregnancy and severe PE, without comorbidities, nonsmoking, and before starting any medication were asked to take part in the study. 20 normotensive, healthy, nonsmoking subjects matched for maternal age, gestation, and ethnicity were controls. Informed written consents were obtained from all subjects. Preeclampsia was defined as new onset, repeatedly high blood pressure (systolic blood pressure ≥140 mmHg and diastolic blood pressure ≥90 mmHg) occurring after 20 weeks' gestation with an additional organ system involvement. Women were classified as having severe disease if they had symptomatic disease, severe hypertension (systolic blood pressure ≥160 mmHg and diastolic blood pressure ≥110 mmHg), neurological complications or other significant organ derangement, according to the International Society for the Study of Hypertension in Pregnancy guidelines [8].

Echocardiography

The patients were examined in the left lateral decubitus position using a Vivid E9 commercial ultrasound scanner (version BT11; GE Vingmed Ultrasound AS, Horten, Norway) with phased-array transducers (M5S-D).

Conventional echocardiographic images were acquired, including parasternal long-axis and short-axis views and three standard apical views. For each view, three consecutive cardiac cycles were recorded during quiet respiration. Left atrium (LA) diameter, Left ventricular (LV) diameter and its wall thickness were measured using M-mode echocardiography. On the basis of apical four chamber and two-chamber views, LA and LV volumes and left ventricular ejection fraction (LVEF) were calculated according to Simpson's rule. The average of measurements of three cardiac cycles were calculated as the final measurement. Grayscale recordings were optimized for LV evaluation at a mean frame rate of 50 frames/sec. Color Doppler recordings were made to exclude valvular dysfunction. Doppler flow recordings were performed with a horizontal sweep velocity of 100 mm/sec. Global diastolic dysfunction was graded using a diagnostic algorithm based on the recommendations of European Association of Echocardiography and American Society of Echocardiography [9]. LA dilation is defined as LA volume index >34 ml/m^2.

For 2DE strain analysis, the software automatically tracked the contour on subsequent frames after three endocardial markers were placed in an end-diastolic frame. Adequate tracking could be verified in real time and corrected by adjusting the region of interest or by manually correcting the contour to ensure optimal tracking. Two-dimensional longitudinal strain was assessed in all three apical views. Average longitudinal strains were calculated for the 17 segments in relation to the strain magnitude at aortic valve closure. According to the strain definition, longitudinal systolic deformation was characterized as shortening, thus systolic indices generated a negative value.

Statistical analysis

Data were analyzed using SPSS 17 software (SPSS, Chicago, IL). Variables were compared using independent t-test. Proportions were compared using Chi-square or Fisher-exact test as appropriate. A value of $P<0.05$ was considered statistically significant and all tests were 2-sided.

Results

A total of 33 women with severe PE and 20 healthy pregnant women were recruited during the study period. These cases were closely matched (**Table 1**) for age and gestational age.

There were no significant differences in LA diameter, LA volume, LA volume index, left ventricular diastolic diameter(LVDd), left ventricu-

Table 2. Mean values of conventional, tissue Doppler and speckle-tracking echocardiography among the groups

	Control (n=20)	Severe PE (n=33)	P
LA (mm)	33.4±2.8	31.2±4.2	0.867
LAV (ml)	42.9±9.4	48.9±12.0	0.084
LAVI (ml/m^2)	25.1±6.1	28.5±6.1	0.087
LVDd (mm)	45.9±3.3	46.5±4.6	0.598
LVDs (mm)	29.9±3.1	30.1±4.0	0.891
EDV (ml)	92.8±22.0	88.8±29.4	0.646
ESV (ml)	41.8±12.7	42.5±13.2	0.874
IVS (mm)	8.2±0.9	9.5±1.0	0
LVPW (mm)	7.9±0.7	9.3±1.0	0
LVMI (g/m^2)	75.5±10.5	89.7±17.9	0.001
E (m/s)	0.82±0.25	0.91±0.19	0.162
A (m/s)	0.66±0.11	0.77±0.18	0.008
e'-sep (m/s)	0.10±0.03	0.07±0.02	0.001
e'-lat (m/s)	0.16±0.09	0.10±0.03	0.001
E/e'-sep	8.3±2.1	12.8±3.6	0
E/e'-lat	6.3±3.3	10.6±4.6	0.001
E/e'-avg	7.3±2.5	11.8±3.8	0
LVEF (%)	53.3±8.4	52.8±8.5	0.863
Strain-3ch (%)	-17.4±3.6	-15.4±3.2	0.062
Strain-4ch (%)	-20.0±3.6	-17.5±3.8	0.038
Strain-2ch (%)	-13.9±4.7	-14.2±4.8	0.861
Strain-avg (%)	-16.8±3.0	-15.8±3.2	0.271

LA indicates left atrium diameter; LAV, left atrial volume; LAVI, left atrial volume index; LVDd, left ventricular diastolic diameter; LVDs, left ventricular systolic diameter; EDV, left ventricular end-diastolic volume; ESV, left ventricular end-systolic volume; IVS, interventricular septum thickness; LVPW, left ventricular posterior wall thickness; LVMI, left ventricular mass index; E, mitral valve early peak velocity; A, mitral valve late peak velocity; e'-sep, septal annulus early tissue doppler velocity; e'-lat, lateral annulus early tissue doppler velocity; E/e'-sep, E to e'-sep; E/e'-lat, E to e'-lat; E/e'-avg, E to average e'; LVEF, left ventricular ejection fraction; Strain-3ch, global strain in apical 3 chamber view; Strain-4ch, global strain in apical 4 chamber view; Strain-2ch, global strain in apical 2 chamber view; Strain-avg, average global strain in three apical chamber views.

lar systolic diameter (LVDs), left ventricular end-diastolic volume (EDV), left ventricular end-systolic volume (ESV) between women with severe PE and healthy pregnant women. Women with severe PE had higher interventricular septum thickness (IVSd), left ventricular posterior wall thickness (LVPWd), and left ventricular mass index (LVMI) than healthy pregnant women. Mitral valve early peak velocity E was similar between women with severe PE and healthy pregnant women. Mitral valve late peak velocity A was greater in women with severe PE compared with healthy pregnant women (**Table 2**). Septal and lateral annulus tissue Doppler early velocity e' was significantly reduced in women with severe PE compared with healthy pregnant women (**Figure 1**). While Septal, lateral and average E/e' ratio was significantly increased in women with severe PE compared with healthy pregnant women. Out of 33 patients, 17 (41.5%) patients had diastolic dysfunction, of which 4 (12.1%) patients had grade I and 13 (39.4%) had grade II. In control group, none of the subjects had diastolic dysfunction (P< 0.001). In the severe PE group, 10 patients (30.3%) had left ventricular hypertrophy (LVH), while in control group only 1 woman had LVH (P=0.045). LA was dilated in 6 (18.2%) severe preeclamptic women and 3 (15%) in healthy pregnant women, there were no significant difference between the two groups (P=0.75), (**Table 3**).

For systolic function, LVEF was similar between women with severe PE and healthy pregnant women. As for speckle-tracking echocardiography, 2D strain was significantly different in apical four chamber view between women with severe PE and healthy pregnant women, but in apical three, two chamber views and average not.

Discussion

The main findings of this study are: 1) diastolic dysfunction was present in almost half of patients with severe preeclampsia. 2) Left ventricular systolic function was impaired in women with severe PE revealed by speckle-tracking echocardiography in apical four chamber view. 3) About 30% women with severe PE had left ventricular hypertrophy.

Risk factors for preeclampsia include nulliparity and risk factors for cardiovascular disease such as chronic hypertension, obesity, preexisting diabetes mellitus, hyperlipidemia, renal disease, and advanced maternal age [10]. Poor implantation of the placenta can precede the clinical onset of preeclampsia [11] and is related to an increase in uterine artery resistance that can be identified by Doppler ultrasound [12]. Furthermore, preeclampsia, like cardiovascular disease, is characterized by wide-ranging vascular endothelial dysfunction [13].

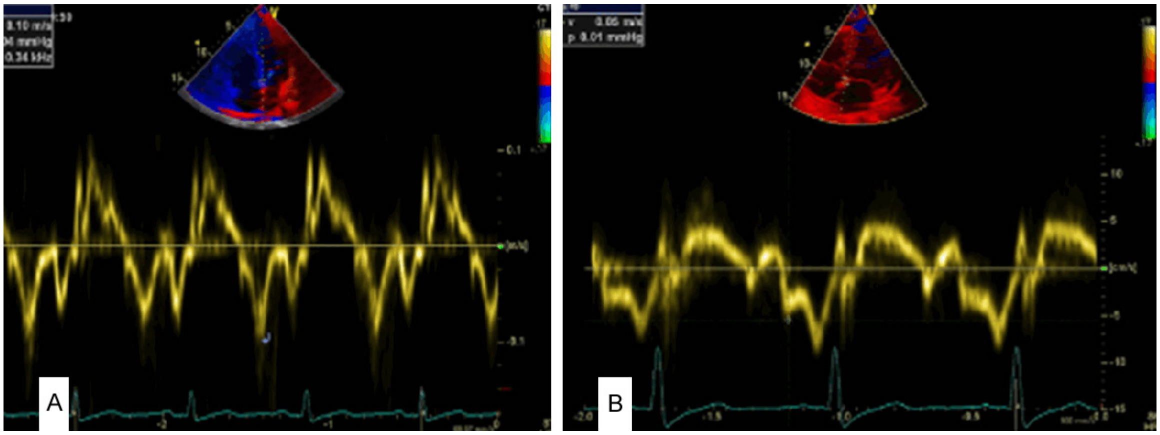

Figure 1. Septal mitral annulus tissue Doppler early velocity e' of women with severe PE compared with healthy pregnant women. Septal mitral annulus tissue Doppler early velocity e' of women with severe PE (B) decreased as compared with healthy pregnant women (A).

Table 3. Comparison of diastolic dysfunction and LVH in controls and cases

	Control (n=20)	Severe PE (n=33)	P
Diastolic dysfunction			
Normal	20 (100%)	16 (48.5%)	<0.001
Grade I	0	4 (12.1%)	<0.001
Grade II	0	13 (39.4%)	<0.001
LVH	1 (5%)	10 (30.3%)	0.045
LA dilation	3 (15%)	6 (18.2%)	0.75

LVH indicates left ventricular hypertrophy.

Diastolic dysfunction usually precedes the compromise of systolic function in hypertension and can lead to heart failure or pulmonary edema [14]. If this cardiovascular dysfunction can be revealed by an echocardiography in preeclamptic women, it may be possible to reduce the risk of heart failure by early intervention.

In the present study, the diastolic dysfunction was present in almost half of the patients with severe preeclampsia. Although almost two thirds of these patients had grade II diastolic dysfunction, none of the patients had diastolic dysfunction more than grade II in this study. Studies in patients with ischemic and hypertensive cardiac disorders have also demonstrated similar findings, termed "isolated diastolic dysfunction" [15]. The present study used mitral valve inflow pulsed Doppler and mitral annulus tissue Doppler velocity, which are well correlated with invasive indices of myocardial filling pressures and long-term cardiovascular risk. LV myocardial relaxation is an energy-dependent process that results in a rapid decrease in LV pressure after the end of contraction and during early diastole [9]. Hence, the process of myocardial relaxation is vulnerable in cardiovascular disorders and in PE. Muthyala [16] et al. showed that 39% women with severe preeclampsia demonstrated evident global diastolic dysfunction, while only 3% women with mild preeclampsia presented diastolic dysfunction, all of which were grade I diastolic dysfunction. Another study found that women with preeclampsia were more likely to arise diastolic dysfunction and had higher cardiac output in the second trimester as compared to normotensive women. Dennis [17] et al. found that women with severe preeclampsia presented diastolic dysfunction with a mean mitral valve E/septal e' ratio of 12.6. Melchiorre [18] found that in PE, diastolic dysfunction was significantly related to both increased afterload and increased LV mass. Moreover, diastolic function and longitudinal systolic indices were also independently related, therefore, simultaneous assessment of systolic and diastolic function is necessary.

Of systolic function, left ventricular ejection fraction was preserved in women with PE. Previous studies had similar findings [19, 20]. In speckle-tracking echocardiography, the global strain value in apical four chamber view in women with severe PE was decreased, which indicated that there was left ventricular systolic dysfunction in women with severe PE. Speckle-tracking echocardiography is a new technique which can track ultrasound speckle angle-independently. But there was no significant difference in global strain in women with PE in apical three and two chamber view compared with healthy pregnant women. This may be due to lower image quality of apical three chamber view and apical two chamber view, because lower image quality yields inaccurate speckle-tracking strain value.

A portion of women with severe PE showed evidence of LV hypertrophy and increased LV mass indices. These alterations are likely to be an adaptive response to lower the wall stress due to elevated afterload, thus maintaining the balance between myocardial oxygen demand and supply. This interpretation is affirmed by the finding that the LV end-systolic wall stress index between PE and controls remains unchanged. Independent associations between LV mass indices and hemodynamic indices were found in previous study [16]. These associations are consistent with a mechanically appropriate response to increased afterload, thus preserving myocardial contractility in PE. These assumptions are supported by the findings of other studies, which also showed that the ratio between LV mass and cardiac work indices is unchanged in PE [21]. LV concentric hypertrophy is known to be accompanied by subendocardial fibrosis both in hypertensive subjects and from autopsy data. The coexistence of LV hypertrophy and longitudinal systolic dysfunction in PE implies that there is subendocardial damage, for the longitudinal myocardial fibers are mainly distributed in the subendocardium. This assumption is validated by the autopsy finding of subendocardial ischemia in severe PE with adverse outcome [22].

Several limitations have to be taken into account for the present study. First, the case number of the study is small. Second, this study was a single-point study and not a serial study before and after interventions. It is therefore not possible to make any inference about the effect of treatment interventions on cardiac function in these women. Moreover, this study did not include women with mild preeclampsia due to insufficient case. Advanced study ranging widely should be performed to validate the conclusions.

In conclusion, the left ventricular dysfunction can be present in women with severe preeclampsia. Left ventricular hypertrophy can occur in a proportion of women with severe preeclampsia. Tissue Doppler and speckle-tracking echocardiography is applicable and acceptable in detecting both diastolic and systolic cardiac dysfunction in women with severe preeclampsia and can identify patients for early intervention to prevent progression of the condition and save mothers from severe morbidity of acute heart failure. Advanced study of tissue Doppler and speckle-tracking echocardiography of preeclampsia is proposed to investigate the improvement of cardiac function with treatment and residual difference postpartum.

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Disclosure of conflict of interest

None.

Address correspondence to: Dr. Gaoyun Pan, Department of Ultrasound, Wenzhou People's Hospital, Wenzhou Women and Children's Hospital, 57 Canghou Road, Wenzhou 325000, China. Tel: +86-57788059873; E-mail: 853701271@qq.com

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