ARTICLE

Blood pressure variability correlates with right ventricular strain in women with gestational hypertension and preeclampsia

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The aim of this study was to evaluate the short- and long-term blood pressure (BP) variability and right ventricular (RV) remodeling in women with gestational hypertension and preeclampsia, as well as their association. This cross-sectional study included 161 pregnant women (56 normotensive controls, 55 patients with gestational hypertension, and 50 patients with preeclampsia) after 20 weeks of gestation. All women underwent 24-h ambulatory BP monitoring and echocardiographic examination. Our findings showed that 24-h, daytime and nighttime systolic and diastolic BPs, as well as visit-to-visit systolic and diastolic BPs, were significantly higher in women with gestational hypertension and preeclampsia than in control group. Parameters of short- and long-term BP variability gradually increased from controls, throughout women with preeclampsia, to those with gestational hypertension. RV diameter, E/e′ and PAP were significantly higher in women with gestational hypertension and preeclampsia than in controls. Global and free wall RV longitudinal strains, as well as corresponding endo- and epicardial strains, gradually reduced from controls to women with preeclampsia. Parameters of short- and long-term BP variability were independently associated with global and free wall RV longitudinal strain. In conclusion, short- and long-term BP variability was higher in women with pregnancy-induced hypertensive disorders. RV diastolic function and mechanics were deteriorated in these women comparing with controls. A significant association between BP variability and RV longitudinal strain underlines the importance of determination of short- and long-term BP variability during pregnancy.

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INTRODUCTION

Hypertensive disorders in pregnancy represent one of the most common complications during gestation. This entity includes several hypertensive disorders (pregestational hypertension, gestational hypertension, preeclampsia, and preeclampsia superimposed on chronic hypertension) and all of them are associated with increased morbidity and mortality during pregnancy and particularly in its late stage [1]. Some studies even confirmed increased mortality risk, Alzheimer's disease, diabetes, ischemic heart disease, and stroke among women who experienced hypertensive disease of pregnancy [2]. The complexity of this type of hypertensive disorder is multisystem organ damage which involves heart, kidneys, liver, and vascular system.

Left ventricular (LV) remodeling in hypertensive disorders in pregnancy and particularly in gestational hypertension and preeclampsia has been extensively investigated in the last few decades [3–5]. However, right ventricular (RV) structural, functional, and mechanical changes are still mainly unrevealed. Scarce data are conflicting because some authors reported significant functional changes in terms of increased RV diameter, elevated pulmonary pressure and reduced RV longitudinal mechanics—strain [6–9], whereas other studies demonstrated no difference in RV structure and function between normotensive controls and pregnant women with hypertensive disorders [10, 11].

The effect of blood pressure (BP) variability in pregnancy is also uncertain. Data are scarce and mainly based on mid- and long-term BP variability that was based on office BP measurements, which were made during each clinical visit—visit-to-visit variability [12, 13]. Studies showed that visit-to-visit BP variability was associated with gestational hypertension and preeclampsia [12], as well as with risk of adverse birth outcomes in pregnant women without proteinuria or chronic hypertension [13]. Recent investigation reported that short-term BP variability obtained by 24-h ambulatory BP monitoring correlated with subclinical echocardiographic changes and microalbuminuria in normotensive women with history of preeclampsia or eclampsia [14]. The relationship between BP variability and RV remodeling has not been investigated so far.

The current study aimed to investigate RV structural, functional and mechanical changes, short- and long-term BP variability, as well as their relationship in women with gestational hypertension and preeclampsia.

METHODOLOGY

The present cross-sectional investigation involved 161 pregnant women (56 normotensive controls, 55 patients with gestational hypertension, and 50 patients with preeclampsia) after 20 weeks of gestation. Controls were selected from healthy pregnant women

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who were of similar age and gestational age as patients with gestational hypertension and preeclampsia. Gestational hypertension was defined as office systolic BP ≥ 140 mmHg and diastolic BP ≥ 90 mmHg occurring after 20 weeks of gestation with no proteinuria [15]. Preeclampsia was defined as BP ≥ 140 mmHg systolic or ≥90 mmHg diastolic BP on 2 different occasions, and a urine protein ≥300 mg in 24 h occurring after 20 weeks of gestation [15]. Patients with congenital heart disease, valvular heart disease, coronary artery disease, pulmonary disease, diabetes mellitus excluding gestational diabetes, and inadequate echocardiographic images (3 women) were excluded from the study.

Anthropometric measures (height, weight) and laboratory analyses (fasting glucose level, total cholesterol, creatinine, hemoglobin level and 24-h urine protein level), as well as current antihypertensive treatment, were investigated in all patients. Body mass index (BMI) and body surface area (BSA) were calculated for all patients. All women underwent a 24-h BP monitoring and echocardiographic examination. The echocardiographic examination was performed at the same day when 24-h ABPM was performed (just before putting BP monitor or just after removing it next day). The study was approved by the local Ethics Committee, and informed consent was obtained from all the participants.

Clinic BP and 24-h ambulatory BP measurements

Clinic arterial BP values were obtained by a calibrated sphygmomanometer in the morning hours by measuring the average value of the two consecutive measurements in the sitting position. BP was measured ≥2 times in separate occasions before hypertension disorder was diagnosed and ≥5 after hypertension was diagnosed. These values were used for calculation of visit-to-visit BP variability.

Schiller BR-102 plus system (Schiller AG, Baar, Switzerland) was used for noninvasive 24-h ambulatory BP monitoring. The device was programmed to obtain BP readings at 30-min intervals during the whole day. The recording was then analyzed to obtain a 24-h, daytime and nighttime average systolic and diastolic blood pressure according to the guidelines [16].

24-h BP variability has been evaluated by two different group of indices: (i) standard deviation (SD) of average 24-h BPs; and (ii) coefficient of variation (CV) of daytime, nighttime, and 24-h BPs that represents the average SD of BP divided by the corresponding mean BP and multiplied by 100 [CV = (SD/BP average values) × 100]. Nocturnal BP decline was calculated for all patients.

The visit-to-visit variability was determined by SD or CV of either systolic or diastolic BP from baseline through delivery.

Echocardiography

Echocardiographic examination was performed by a Vivid 95 ultrasound machine (GE Healthcare, Horten, Norway). The values of all 2D parameters were obtained as the average value of three consecutive cardiac cycles. LV diameters, interventricular septum, posterior wall thickness and relative wall thickness were evaluated in long-axis parasternal view [17]. LV ejection fraction (EF) was assessed by the modified Simpson's method of discs. LV mass was calculated by using the formula of the American Society of Echocardiography [17], and indexed for BSA.

Transmitral Doppler inflow and tissue Doppler velocities were obtained in the apical 4-chamber view. Pulsed Doppler measurements included the ratio between the transmitral early and late diastolic peak flow velocity (E/A). Tissue Doppler imaging was used to obtain LV myocardial velocities at the septal and lateral segment of the mitral annulus during early and late diastole (e′ and a′).

Right ventricle and atrium

The RV internal diameter was measured in the basal RV segment in apical 4-chamber view [18]. RV thickness was measured in the subcostal view. RA maximal volume was obtained in the 4-chamber view during ventricular end-systole and indexed for BSA. Fractional area change (FAC) was calculated as the percentage of change in RV area during systole: (end-diastolic area − end-systolic area)/end-diastolic area [18]. Tricuspid inflow (E) and tissue Doppler velocities (e'_t, s_t) were evaluated in the apical 4-chamber view [18], and E/e'_t ratio was calculated. RV systolic blood pressure (PAP) was assessed in the patients with minimal/mild tricuspid regurgitation and it was feasible to calculate in 144 (89%) of patients. Tricuspid annular plane systolic excursion (TAPSE) has been measured in all participants, according to the guidelines [18].

Two-dimensional right ventricular strain and strain rate

2D strain imaging was performed by using 3 consecutive cardiac cycles of 2DE images in the apical 4-chamber view. EchoPAC 202 (GE-Healthcare, Horten, Norway), as a commercially available software, was used for the 2D strain analysis.

The automatic tracking of the endocardial contour was performed in end-systole and it was carefully verified, the region of interest was manually corrected to ensure optimal tracking and inclusion of the entire RV thickness. After delineating the region of interest, software allowed the investigation of 3 myocardial layers: endocardial, mid-myocardial and epicardial. Mid-myocardial strain is calculated as the average of endo- and epicardial strain and it was equal to global longitude al strain. All strain parameters were determined for the RV lateral wall and global RV, separately.

Statistical analysis

Continuous variables were presented as mean ± SD and were compared by the analysis of equal variance (ANOVA), as they showed normal distribution. Tukey HSD post hoc analysis was used for the comparison between different groups. Differences in proportions were compared by the χ^2 test. Univariable and multivariable regression analyses were used for determining the association between different BP variability and echocardiographic parameters. Four models for multivariable regression analyses were used to determine the association between BP variability indices and RV global longitudinal and free wall strain.

Model 1 consists of age, BMI, use of antihypertensive medications, LVEF, LVMI, E/e′, 24-h SBP, and SD (24-h SBP)). Model 2 involves age, BMI, use of antihypertensive medications, LVEF, LVMI, E/e′, 24-h SBP, and CV (24-h SBP). Model 3 includes age, BMI, use of antihypertensive medications, LVEF, LVMI, E/e′, V-to-V SBP, and V-to-V SD (24-h SBP). Model 4 involves age, BMI, use of antihypertensive medications, LVEF, LVMI, E/e′, V-to-V SBP, V-to-V CV (24-h SBP), and V-to-V ARV (SBP). The p value <0.05 was considered statistically significant.

RESULTS

There was no difference in age between controls, women with gestational hypertension and preeclampsia (Table 1). BMI was higher in patients with preeclampsia than in controls (Table 1). Laboratory parameters (plasma glucose, serum creatinine levels, cholesterol, and hemoglobin level) were similar between three groups (Table 1). 24-h proteinuria gradually increased from control group, across women with gestational hypertension, to those with preeclampsia (Table 1). There was no difference in prevalence of gestational diabetes between three observed groups and the use of antihypertensive therapy between patients with gestational hypertension and preeclampsia (Table 1). Gestational week at the time of examination (24-h ABPM and echocardiographic evaluation) was similar between three groups (Table 1).

Ambulatory blood pressure monitoring and clinical BP measurements

24-h, daytime and nighttime systolic and diastolic BP were higher in women with gestational hypertension and preeclampsia than in controls (Table 2). BP variability parameters—SD and CV gradually

Table 1. Demographic characteristics and clinical parameters of study population.

	Controls ($n = 56$)	Gestational hypertension ($n = 55$)	Preeclampsia ($n = 50$)	p
Age (years)	30 ± 4	31 ± 5	31 ± 5	0.436
BMI (kg/m^2)	28.2 ± 5.4	29.0 ± 6.1	31.1 ± 5.9[a]	0.033
Parity	1 (1–3)	2 (1–3)	2 (1–3)	0.837
Gestational age (weeks)	31 ± 4	31 ± 3	32 ± 4	0.285
Plasma glucose (mmol/l)	4.9 ± 0.4	4.8 ± 0.5	5.0 ± 0.6	0.129
Total cholesterol (mmol/l)	4.6 ± 0.5	4.7 ± 0.6	4.7 ± 0.6	0.568
Serum creatinine (μmol/l)	78 ± 11	81 ± 9	80 ± 10	0.280
Hemoglobin (mg/dl)	11.8 ± 1.5	12.1 ± 1.7	11.6 ± 1.6	0.274
24-h urine protein level (mg/day)	86 ± 21	143 ± 35	969 ± 311[a,b]	<0.001
Gestational diabetes (%)	1 (1.5)	2 (3.6)	2 (4)	0.774
Antihypertensive therapy (%)	–	22 (40)	24 (48)	0.674
Gestational age at time of examination (weeks)	32 ± 3	31 ± 4	32 ± 4	0.266

BMI body mass index.
[a]$p < 0.05$ for controls vs. preeclampsia.
[b]$p < 0.01$ for preeclampsia vs. gestational hypertension.

Table 2. Ambulatory blood pressure measurements.

	Controls ($n = 56$)	Gestational hypertension ($n = 55$)	Preeclampsia ($n = 50$)	p
24-h ambulatory blood pressure monitoring				
24-h				
SBP (mmHg)	108 ± 6	123 ± 7[a]	121 ± 8[b]	<0.001
DBP (mmHg)	67 ± 4	76 ± 5[a]	74 ± 4[b]	<0.001
Daytime				
SBP (mmHg)	113 ± 7	128 ± 9	125 ± 8	<0.001*
DBP (mmHg)	70 ± 4	79 ± 5[a]	77 ± 6[b]	<0.001
Nighttime				
SBP (mmHg)	100 ± 5	111 ± 6[a]	110 ± 7[b]	<0.001
DBP (mmHg)	61 ± 4	70 ± 5[a]	68 ± 5[c]	<0.001
Nocturnal reduction rate (%)				
SBP (%)	11.7 ± 3.1	13.1 ± 3.8	12.2 ± 3.4	0.100
DBP (%)	12.7 ± 3.4	11.5 ± 2.9	11.6 ± 3.0	0.084
SD				
24 h SBP	8.7 ± 1.6	17.3 ± 4.1	14.7 ± 3.5	<0.001**
CV				
24 h SBP	8.0 ± 1.5	14.1 ± 2.5	12.1 ± 2.3	<0.001**
Clinic blood pressure measurement				
SBP (mmHg)	116 ± 6	133 ± 9[a]	130 ± 7[b]	<0.001
DBP (mmHg)	72 ± 4	83 ± 6	80 ± 6	<0.001*
SD	8.0 ± 1.9	15.3 ± 3.3	12.8 ± 3.1	<0.001**
CV	7.6 ± 1.3	13.1 ± 2.3	11.0 ± 2.0	<0.001**

DBP diastolic blood pressure, *CV* coefficient of variation, *SBP* systolic blood pressure, *SD* standard deviation.
*$p < 0.05$ for all comparisons, **$p < 0.01$ for all comparisons.
[a]$p < 0.01$ for controls vs. gestational hypertension.
[b]$p < 0.01$ for controls vs. preeclampsia.
[c]$p < 0.01$ for gestational hypertension vs. preeclampsia.

increased from controls, across women with preeclampsia, to those with gestational hypertension.

Visit-to-visit systolic and diastolic BPs were higher in patients with gestational hypertension and preeclampsia than in controls (Table 2). Visit-to-visit BP variability (SD and CV) gradually increased from controls, across preeclampsia, to gestational hypertension.

Echocardiographic parameters

LV diameters, septum and relative wall thickness, as well as LVMI, were higher in patients with gestational hypertension and preeclampsia than in controls (Table 3). LVEF was similar across three groups. Patients with gestational hypertension and preeclampsia had significantly lower E/A ratio than controls. Mitral E/e

Table 3. Echocardiographic parameters of left ventricular structure and function in the study population.

	Controls ($n = 56$)	Gestational hypertension ($n = 55$)	Preeclampsia ($n = 50$)	p
LV parameters				
LVEDD (mm)	46 ± 4	47 ± 4	48 ± 3[b]	0.024
LVESD (mm)	26 ± 3	30 ± 4[a]	31 ± 4[b]	<0.001
IVS (mm)	7.6 ± 1.0	8.2 ± 1.1[a]	8.4 ± 1.2[b]	<0.001
RWT	0.33 ± 0.02	0.35 ± 0.04[a]	0.35 ± 0.03[b]	<0.001
LVMI (g/m^2)	63 ± 7	77 ± 12[a]	74 ± 11[b]	<0.001
EF (%)	62 ± 3	61 ± 3	61 ± 4	0.198
E/A ratio	1.20 ± 0.15	1.11 ± 0.17[a]	1.06 ± 0.13[b]	<0.001
E/e′$_m$ ratio	5.5 ± 1.2	6.8 ± 1.4	8.2 ± 2.3	<0.001**
RV parameters				
RV basal diameter (mm)	23 ± 2	27 ± 3[a]	28 ± 3[b]	<0.001
RV thickness (mm)	3 ± 0.5	3.2 ± 0.8	3.1 ± 0.6	0.268
TAPSE (mm)	24 ± 2	24 ± 3	23 ± 3	0.096
FAC (%)	52 ± 3	50 ± 4[a]	49 ± 4[b]	<0.001
RAVI (ml/m^2)	17 ± 3	20 ± 4[a]	22 ± 4[b]	<0.001
E/e′$_t$ ratio	3.4 ± 0.7	4.5 ± 1.0	4.9 ± 1.3	<0.001*
s$_t$ (cm/s)	14 ± 3	13 ± 3	13 ± 2	0.089
PAP (mmHg)	23 ± 3	27 ± 4	30 ± 4	<0.001**
Right ventricular strain parameters				
Global longitudinal strain (%)				
Global RV	−24.5 ± 3.3	−22.1 ± 2.8	−20.6 ± 2.5	<0.001*
Free wall RV strain (%)	−26.3 ± 4.2	−24.4 ± 3.9	−22.5 ± 3.5	<0.001*
Layer-specific longitudinal strain for global RV (%)				
Endocardial	−26.1 ± 3.9	−24.3 ± 3.2	−22.1 ± 3.0	<0.001*
Epicardial	−22.8 ± 3.1	−19.9 ± 2.5[a]	−19.0 ± 2.1[b]	<0.001
Layer-specific longitudinal strain for free wall RV (%)				
Endocardial	−28.6 ± 4.3	−26.6 ± 4.1	−24.4 ± 3.9	<0.001*
Epicardial	−24.0 ± 3.4	−22.4 ± 3.1	−20.8 ± 2.7	<0.001*

A late diastolic mitral flow (pulse Doppler), *E* early diastolic mitral flow (pulse Doppler), *e′$_m$* average value of early diastolic flow velocities across the septal and lateral segments of mitral (e′) annulus obtained by tissue Doppler, *e′$_t$* value of early diastolic flow velocities across the lateral segment of tricuspid (e′) annulus obtained by tissue Doppler, *EF* ejection fraction, *FAC* fractional area change, *IVS* interventricular septum, *LVMI* left ventricular mass index, LVEDD-left ventricle end-diastolic dimension, LVESD-left ventricle end-systolic dimension, *PAP* pulmonary arterial pressure, *RAVI* right atrial volume index, *RV* right ventricle, RWT-relative wall thickness, *s′* value of systolic flow across the lateral segment of tricuspid annulus, *TAPSE* tricuspid annular plane systolic excursion.
*$p < 0.01$ for all comparisons.
**$p < 0.01$ for all comparisons.
[a]$p < 0.01$ for controls vs. gestational hypertension.
[b]$p < 0.01$ for controls vs. preeclampsia.

′ gradually and significantly increased from control group to women with preeclampsia (Table 3).

RV diameter was significantly higher in women with gestational hypertension and preeclampsia than in controls (Table 3). RV thickness, TAPSE and s′ were similar between observed groups. FAC was lower in women with gestational hypertension and preeclampsia than in controls. RAVI was higher in women with women with pregnancy-induced hypertension than in control group (Table 3). Tricuspid E/e′ ratio and PAP gradually increased from controls, throughout women with gestational hypertension, to those with preeclampsia.

Global and free wall RV longitudinal strains, as well as corresponding endo- and epicardial strains, gradually decreased from controls, across patients with gestational hypertension, to women with preeclampsia (Table 3).

Univariable and multivariable regression analysis

LVEF, LVMI, PAP, 24-h systolic BP and visit-to-visit systolic BP and corresponding indices of BP variability were related with RV global and free wall longitudinal strains (Table 4). LVMI, 24-h systolic BP and both parameters of BP variability were associated with global and free wall RV longitudinal strains independently of other echocardiographic and demographic parameters (Models 1 and 2). Visit-to-visit systolic BP, as well as parameters of BP variability, was significantly and independently associated with global and free wall RV longitudinal strains (Models 3 and 4).

DISCUSSION

Our investigation revealed several important findings summarized as follows: (i) short- and long-term BP variability gradually and significantly increased from controls, across women with pre-eclampsia, to those with gestational hypertension; (ii) RV structural, functional and mechanical remodeling was found in patients with gestational hypertension and preeclampsia; (iii) parameters of short- and long-term BP variability were independently of demographic, clinical and echocardiographic parameters associated with RV global and free wall longitudinal strains.

Table 4. Associations of 24-h and visit-to-visit blood pressure variability indices and RV longitudinal strain (univariate and multivariate regression analysis).

	RV global longitudinal strain (%)					RV free wall longitudinal strain (%)				
	β	β (M1)	β (M2)	β (M3)	β (M4)	β	β (M1)	β (M2)	β (M3)	β (M4)
Age (years)	−0.13	−0.08	−0.11	−0.10	−0.06	−0.16	−0.14	−0.10	−0.13	−0.09
BMI (kg/m^2)	−0.15	−0.11	−0.13	−0.12	−0.10	−0.12	−0.08	−0.11	−0.10	−0.12
LVEF (%)	0.24†	0.14	0.12	0.13	0.12	0.25†	0.12	0.17	0.22†	0.16
LVMI (g/m^2)	−0.30‡	−0.25†	−0.27†	−0.23†	−0.31‡	−0.30‡	−0.26†	−0.25†	−0.25‡	−0.24†
E/e′$_m$ ratio	−0.20†	−0.12	−0.15	−0.11	−0.12	−0.21†	−0.15	−0.13	−0.15	−0.12
PAP (mmHg)	−0.38‡	−0.28†	−0.23†	−0.32‡	−0.35‡	−0.34‡	−0.32‡	−0.27‡	−0.29‡	−0.28†
24-h SBP (mmHg)	−0.32‡	−0.31†	−0.26†	–	–	−0.26†	−0.15	−0.16	–	–
SD (24-h SBP)	−0.37‡	−0.32‡	–	–	–	−0.31‡	−0.26†	–	–	–
CV (24-h SBP)	−0.39‡	–	−0.31‡	–	–	−0.29‡	–	−0.26†	–	–
V-to-V SBP (mmHg)	−0.40‡	–	–	−0.34‡	−0.31‡	−0.38‡	–	–	−0.22†	−0.30‡
V-to-V SD (SBP)	−0.35‡	–	–	−0.27‡	–	−0.30‡	–	–	−0.29†	–
V-to-V CV (SBP)	−0.42‡	–	–	–	−0.34‡	−0.36‡	–	–	–	−0.28†

CV coefficient of variation, *E* early diastolic mitral flow (pulse Doppler), *e′* early diastolic flow velocity across the septal segment of mitral (e′) annulus (tissue Doppler), *EF* ejection fraction, *LV* left ventricle, *LVMI* left ventricular mass index, *M1* model 1 (age, BMI, use of antihypertensive medications, LVEF, LVMI, E/e′, 24-h SBP, and SD (24-h SBP)), *M2* model 2 (age, BMI, use of antihypertensive medications, LVEF, LVMI, E/e′, 24-h SBP, and CV (24-h SBP)), *M3* model 3 (age, BMI, use of antihypertensive medications, LVEF, LVMI, E/e′, V-to-V SBP, and V-to-V SD (24-h SBP)), *M4* model 4 (age, BMI, use of antihypertensive medications, LVEF, LVMI, E/e′, V-to-V SBP, V-to-V CV (24-h SBP), and V-to-V ARV (SBP)), *RV* right ventricle, *SBP* systolic blood pressure, *SD* standard deviation, *V-to-V* visit to visit.
$^{\dagger}p < 0.05$.
$^{\ddagger}p < 0.01$.

Our findings showed that indices of short- and long-term of BP variability gradually increased from controls, across women with preeclampsia, to those with gestational hypertension. Large study that included almost 1000 patients with gestational hypertension and preeclampsia investigated visit-to-visit BP variability in second and third trimester and reported similar results with significantly higher BP variability among women with gestational hypertension and preeclampsia than in normotensive controls [12]. In maximally adjusted models, authors showed that visit-to-visit BP variability was associated with gestational hypertension and preeclampsia [12]. The novelty of our study is inclusion of short-term BP variability and conclusion that short- and long-term BP variability assessments could be interchangeably used in clinical practice for all women with hypertensive disorders in pregnancy.

Existing data show a significant discrepancy between studies regarding RV remodeling. Caglar et al. reported a significant enlargement of RV and RA, and deterioration of RV systolic and diastolic function in women with preeclampsia comparing with controls [19]. Some researches reported enlarged RV, increased pulmonary arterial pressure and reduced RV longitudinal strain in patients with pregnancy-induced hypertension [6–9], whereas others did not find significant difference between these patients and normotensive controls [10, 11].

Our results revealed that RV global and free wall longitudinal strains gradually decreased from controls, across women with gestational hypertension, to those with preeclampsia. The same results were obtained for RV endocardial and epicardial strains for the global and free wall RV. In patients with acute preeclampsia RV global strain was significantly lower than in normotensive controls and this was particularly noticed for basal and apical RV segments [6, 9]. Yu et al. reported lower RV longitudinal strain in women with preeclampsia than in normotensive controls, [3], whereas other studies found no difference in RV global longitudinal strain [8, 11].

The novel finding of the present study is the evaluation of global and free wall RV longitudinal strain, as well as assessment of layer-specific strain in this population. This analysis enabled the detection of endo- and epicardial RV changes in patients with pregnancy-induced hypertension and revealed that all myocardial layers are equally affected in these patients. Moreover, 24-h and visit-to-visit systolic BP and BP variability were independently associated with RV global and free wall longitudinal strains.

RV longitudinal strain is still in normal range in our study population, but this is expected for hypertensive patients [20, 21]. However, the recent meta-analysis in COVID-19 patients revealed that each 1% decrease in RV longitudinal strain was associated with 25% higher risk of poor outcome (OR 1.25, 95% CI: 1.15–1.35, $p < 0.001$) [22], which could have a great implication in our study that found ~2% absolute reduction in RV longitudinal strain in women with gestational hypertension and almost 4% in patients with preeclampsia.

There are several potential mechanisms that could explain RV remodeling in our study population. RV enlargement and increased RV filling pressure (elevated E/e′) could be explained by the volume-overloaded state in hypertensive pregnant women [23]. Increased pulmonary resistance in gestational hypertension and preeclampsia, the consequence of reduced LV compliance and increased LV diastolic filling pressures, might also induce the reduction in RV longitudinal strain [24]. This hypothesis was partially supported by increased mean pulmonary artery pressure in gestational hypertension and preeclampsia in our study. Previous study also reported that RV dysfunction was associated with elevated pulmonary vascular resistance due to increased LV filling pressure, which was also confirmed in our study [24]. Cardiac magnetic resonance detected LV interstitial edema in 40% of preeclamptic women and it is reasonable to hypothesize that similar changes occur in the RV, which might be responsible for deterioration of RV strain in women with gestational hypertension and preeclampsia.

Our findings have several important clinical implications. Short-term BP variability, obtained from 24-h ABPM, is equally important as long-term BP variability derived from visit-to-visit BP measurements in prediction of RV remodeling in women with pregnancy-induced hypertension. This indicates that 24-h ABPM can be a reliable method for evaluation of BP and BP variability in pregnant women. This method is fast, inexpensive and widely available. Considering the relationship between parameters of BP variability and RV remodeling, our results indicate that impaired BP variability could predict the existence of subclinical impairment of RV mechanics, which might be partly responsible for cardiac

complications, including heart failure during and after pregnancy. The reduction in RV longitudinal global and layer-specific strain that we found in pregnancy-induced hypertension is not the part of physiological adaptation to pregnancy and it might be associated with adverse outcome of patients. Nevertheless, follow-up data are missing and this should serve as hypothesis for further investigations in this field.

LIMITATIONS

The present study has several limitations. Visit-to-visit BP variability in pregnancy could be challenging due to difficulty to define a baseline BP from which to make comparisons. However, at least 2 BP measurements from the first 20 weeks of gestation were available and therefore this problem was overcome. Preeclampsia was diagnosed in majority of patients before 32 gestational weeks and therefore we could not compare RV remodeling between women with early and late preeclampsia. Data about altered uterine artery Doppler are not available and it was not possible to determine the cause responsible for preeclampsia: placental, maternal or both. The appropriate visualization of the RV for assessment of longitudinal strain in pregnant women, particularly in the last trimester, could be difficult, but we succeeded to make adequate acquisitions in almost all participants. Due to COVID-19 pandemic the follow-up of our patients was not performed and outcome is unknown, which is additional limitation of the present study. The causal relationship between BP variability and RV structure and function could not be adequately evaluated due to a cross-sectional nature of this investigation.

CONCLUSION

Women with gestational hypertension and preeclampsia had significantly higher short- and long-term BP variability than normotensive controls. RV global and free wall longitudinal strains gradually and significantly reduced from control subjects, throughout patients with gestational hypertension, to preeclamptic women. Endo- and epicardial RV longitudinal strains were equally affected in women with pregnancy-induced hypertension. Parameters of short- and long-term BP variability were independently of clinical and echocardiographic parameters and BP associated with global and free wall RV longitudinal strains. Our findings highlighted the importance of short- and long-term BP variability, which can be used interchangeably, as a significant set of parameters that may indicate pregnant women who are at risk of adverse RV remodeling during and after pregnancy. Longitudinal studies with larger number of patients are necessary to investigate the potential predictive role of BP variability and subclinical RV changes in women with pregnancy-induced hypertension on long-term outcomes.

Summary table

What is known about topic

- Pregnancy-induced hypertensive disorders are associated with adverse outcome
- Left ventricular mechanics may be impaired in pregnancy-induced hypertensive disorders
- Visit-to-visit blood pressure variability is increased in women with gestational hypertension and preeclampsia

What this study adds

- Right ventricular mechanics is deteriorated in women with gestational hypertension and preeclampsia in comparison to normotensive pregnant women
- Short-term blood pressure variability measured during 24-h blood pressure monitoring is also increased in women with gestational hypertension and preeclampsia
- Long- and short-term blood pressure variability parameters were associated with right ventricular mechanics in women with gestational hypertension and preeclampsia

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COMPETING INTERESTS

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ADDITIONAL INFORMATION

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