



EVALUATION OF ASCENDING AORTA ELASTICITY PROPERTIES AND LEFT ATRIAL VOLUME INDEXES IN PREECLAMPSIA PATIENTS

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ABSTRACT

Preeclampsia (PE) is associated with long term cardiovascular function impairments in women. The aim of the study was to evaluate the left atrial volume (LAV) indexes and ascending aortic stiffness parameters in PE patients, and we aimed to evaluate any association between these two parameters. A total of 50 PE patients and 39 healthy pregnant controls (HP) were enrolled in this single-center, prospective, cross-sectional study. Aorta (Ao) diameters, Ao compliance, Ao M-Mode strain, Ao distensibility, Ao stiffness index, and Peterson's elastic modulus (Pa) parameters were measured and calculated besides LAV indexes. AoD, AoS, and Ao strain were significantly higher in PE group ($p < 0.05$ for all), while the Ao stiffness index was lower ($p = 0.009$). LVMI, mitral E, mitral A, mitral E/Em, deceleration time, and myocardial performance index were significantly higher in the PE group ($p < 0.05$ for all). LA maximum LAV index (LAVImax), minimum LAV index (LAVImin), and presystolic LAV index (LAVIp) were higher in the PE group compared with the HP group ($p < 0.001$ for all). Ao Strain value was positively correlated with LAVImax ($r: 0.254, p: 0.016$), LAVImin ($r: 0.385, p: 0.001$), and LAVIp ($r: 0.265, p: 0.011$). Aortic strain, aortic stiffness index, and LAV indexes were impaired in hospitalized PE patients. There was an association between the Ao strain, Ao stiffness index, and LAV indexes.

KEYWORDS : ascending aorta, preeclampsia, strain, distensibility, stiffness index, elastic modulus

INTRODUCTION

Preeclampsia (PE) is a multisystem disorder of pregnancy that affects 2-8% of pregnancies [1]. The diagnostic criteria for PE are the presence of new onset and persistent hypertension, together with significant proteinuria or fetal growth restriction after 20 weeks of gestation. It is an important cause of preterm birth, with associated long term consequences for infants and children. It is also associated with long term cardiovascular function impairments in women. Women with PE are at significant risk of chronic hypertension, stroke, and cardiac failure [2].

It was shown in previous studies pregnant patients with PE had a high cardiac output [3]. These changes occurred before the onset of hypertension and persisted in the postnatal period even once hypertension was controlled. It has been shown in later studies that cardiac output decreases and peripheral resistance increases when the clinical syndrome develops in women whose cardiac output was significantly increased during pregnancy due to PE [4].

Many parameters, such as pulse wave velocity and carotid intima media thickness, are used in the measurement of arterial stiffness and in the evaluation of cardiovascular diseases [5-8]. The elastic properties of the ascending aorta, which evaluate the stiffness of the ascending aorta, have also recently been studied in PE patients [9-13]. In previous studies such as these, patients with previous PE or a history of PE were included [9-12]. There are no data in the literature about morphological and functional alterations of the ascending aorta evaluated via aortic elastic parameters in hospitalized active PE patients. In our study, we intended to detect whether left atrial volume indexes and ascending aortic stiffness parameters were impaired in new onset PE patients without any cardiovascular risk factors. Additionally, we aimed to evaluate any association between left atrial volume indexes and ascending aortic stiffness parameters.

MATERIALS AND METHODS

Study Population

A total of 50 consecutive PE patients who were followed up in the obstetrics and gynecology clinic and intensive care unit and 39 healthy pregnant controls who were routinely recruited from the antenatal clinic were enrolled in this single-center, prospective, cross-sectional study between December 2021 and December 2022. All pregnant women were healthy and without a family history of premature heart disease. They had no any complicated pregnancies before.

Patients who met the diagnostic criteria of preeclampsia defined by the report of the National Collaborating Centre for Women's and

Children's Health, hypertension in pregnancy, and the National Institute for Health and Clinical Excellence were enrolled in the study. A patient is accepted as having PE if she has a blood pressure higher than 140/90 mmHg on two consecutive measurements 4 hours apart, in combination with significant proteinuria (> 300 mg total protein in 24-hour collected urine) developing after 20 weeks of gestation in previously normotensive patients. Baseline demographic data were obtained by an obstetrician during a clinical interview and laboratory samples were extracted prior to the examination. All pregnant women had no other risk factors for arterial stiffening including smoking, sleep apnea, in vitro fertilization conception, diabetes mellitus, hyperlipidemia and/or other cardiovascular diseases. Women with gestational hypertension and chronic hypertension were excluded. The study was designed and conducted with the approval of the local ethics review commission and in accordance with the Declaration of Helsinki. Informed consent forms were obtained from all patients (Harran University Ethical Committee, date: 13.12.2021, number: 21.22.02).

Transthoracic Echocardiography

Echocardiography was performed at rest with the patient in the left lateral decubitus position, with a VIVID S60 (General Electric, Horton, Norway) with a 3 MHz transducer, by an experienced cardiologist who was blinded to the clinical data. A one-lead electrocardiogram was recorded continuously during the echocardiographic examination. The thicknesses of the posterior wall (PwD) and interventricular septum (IVS), LV end-diastolic diameter (LVEDD), and LV systolic diameter (LVESD) were obtained using M-mode. The LV ejection fraction (LVEF) was calculated using Simpson's biplane method. The LV mass and LV mass index (LVMI) were calculated. The velocities and systolic times of the mitral lateral, mitral septal, and tricuspid lateral annular basal segments were acquired using pulsed Doppler and tissue Doppler echocardiography from the apical four-chamber view. LA volume (LAV) (mL/m²) was measured using the biplane area-length method [$LAV = (0.85 \times A1 \times A2) / L$ formula] in the apical four- and two-chamber view. The LA maximum (LAVmax), minimum (LAVmin), and presystolic (LAVp) volumes were recorded and normalized for body surface area to calculate LAV indexes (Fig 1B).

The elastic properties of the ascending aorta were calculated by measuring the systolic and diastolic diameters of the aorta 3 cm above the aortic valve in M-mode. Aortic systolic (AoS) was measured as the highest diameter of the ascending aorta in systole, while AoD was measured at the time corresponding to the peak of the QRS complex (Fig 1A). Measurements were made by drawing a perpendicular line

along the inner edges of anterior and posterior walls of the ascending aorta. The gain level was adjusted so that the junction surface of the endothelium and blood was best seen, and the average of the three recorded values was taken. Aortic elastic parameters;

-Aortic compliance (cm/mmHg) = $(AoS - AoD) / (SBP - DBP)$,

-Aortic M-Mode strain (%) = $100 \times [(AoS - AoD) / AoD]$,

-Aortic distensibility $(10^{-7} Pa^{-1}) = 2 \times (AoS - AoD) / AoD \times (\text{pulse pressure})$,

-Aortic stiffness index = $LN(SBP/DBP) / (Ao \text{ Strain})$,

-Peterson's elastic modulus (Pa) = $AoD \times (\text{pulse pressure}) / (AoS - AoD)$ [14,15].

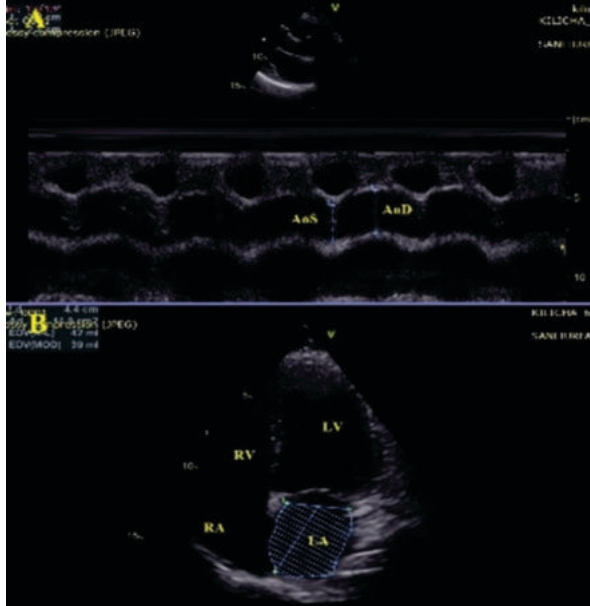


Fig 1. AoD and AoS measurements from parasternal long axis view (A) and LAV calculation from apical 4-chamber view (B).

Abbreviations: AoS: aortic systolic diameter; AoD: aortic diastolic diameter; LA: left atrium; LV: left ventricle; RA: right atrium; RV: right ventricle

* Informed consent was obtained from the 32nd patient for sharing picture.

Statistical Analysis

The SPSS for Windows software package (ver. 20.0; SPSS Inc., Chicago, IL, USA) was used for the statistical analysis. Categorical variables are presented as counts and percentages. Continuous variables were evaluated for normal distribution by using the Kolmogorov-Smirnov test and presented as mean ± standard deviation or median with interquartile range. To assess the differentiation between the groups, Student's t-test was used for normally distributed variables. The Pearson correlation test was used for correlation analysis between Ao strain, left atrial volume indexes, and other variables. A p-value less than 0.5 was considered statistically significant.

RESULTS

A total of 51 preeclampsia patients (PE group) and 39 healthy pregnant controls (HP group) were enrolled in the study. At the examination of all pregnant women, the mean gestational age was 35.1 ± 3.3 weeks in the PE group, and 36.9 ± 3.1 weeks in the HP group ($p: 0.284$). Significant proteinuria (>300 mg/24-hour urine collection) was observed in hypertensive pregnant preeclampsia patients. No significant proteinuria was found in the HP group. Maternal age, number of gestations, and body surface area were similar between study groups. Blood pressure, heart rate, and pulse pressure were significantly higher in the PE group compared with the HP group. The baseline demographic, clinical, and laboratory characteristics of the patient and control groups are summarized in Table 1.

When analyzing ascending aorta diameters and measured parameters, AoD, AoS, and Ao strain were significantly higher in the PE group ($p < 0.05$ for all), while the Ao stiffness index was lower ($p: 0.009$). There was no significant difference between the groups in terms of Ao compliance, Ao distensibility, or elastic modulus. LVESD,

interventricular septum and posterior wall thickness were higher in the PE group ($p < 0.05$ for all). LVMI, mitral E, mitral A, mitral E/Em, deceleration time, and myocardial performance index were significantly higher in the PE group ($p < 0.05$ for all) (Table 2).

According to the 2D and tissue Doppler echocardiographic evaluation, the mitral lateral Em value was lower in the PE group ($p: 0.006$), while there were no significant differences between the groups in terms of other LV filling parameters. The PE group showed higher values of the LA maximum LAV index (LAVImax), minimum LAV index (LAVImin), and presystolic LAV index (LAVIp) compared with the HP group ($p < 0.001$ for all) (Table 3).

Ascending Ao Strain value was positively correlated with LAVImax ($r: 0.254$, $p: 0.016$), LAVImin ($r: 0.385$, $p: 0.001$), and LAVIp ($r: 0.265$, $p: 0.011$) (Fig 2). Other positively and negatively correlated parameters are presented in Table 4.

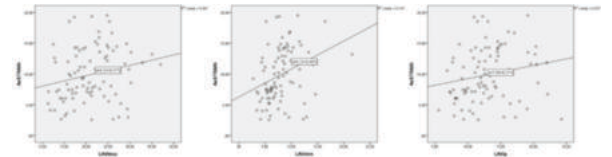


Fig 2. Pearson's Correlation Analyses Between AO Strain And Other Parameters

Abbreviations: Ao: aorta; LAVI: left atrial volume index

DISCUSSION

The main findings of our study can be summarized in a few sentences. A greater increase in ascending Ao diameters was observed in pregnant women with PE compared with HP controls. Ao strain and Ao stiffness index values were significantly impaired in the PE patients. Moreover, the PE group showed a significant impairment in the LAV indexes compared with the HP group. LVMI and LV wall thickness were increased in the PE group. Mitral E, mitral A, mitral E/Em, deceleration time, and myocardial performance index were significantly higher in the PE group. Additionally, the ascending Ao strain value was positively correlated with LAV indexes.

A pregnancy-specific disorder PE is one of the major causes of maternal and perinatal morbidity and mortality [16]. Uteroplacental blood flow alterations due to defective thromboplastic invasion and maternal inflammatory activation lead to vascular endothelial dysfunction in PE pathogenesis [17]. An impaired release of vascular endothelial factors causes an increase in small arterial resistance and impairs vascular smooth muscular relaxation, contributing to large artery stiffening [18-21]. Recent studies have shown a relationship between PE and cardiovascular events [22, 23]. Moreover, a study showed that the risk of death due to cardiovascular diseases was 6-8 times higher in those with PE and preterm birth compared to normotensives [22].

Cardiac output is increased during pregnancy. Compared to normotensive pregnant women, this increase may be more pronounced in PE patients, and as a result, there may be an increase in arterial stiffness parameters. A number of cardiac changes, such as abnormal systolic function, increased systemic vascular resistance, impaired diastolic functions, and LV global hypertrophy in PE patients, were demonstrated with echocardiography [24-27]. Similar to these previous studies and supporting these echocardiographic alterations, LVMI, mitral E, mitral A, mitral E/Em, deceleration time, and myocardial performance index were significantly higher in the PE group in our study. Recent studies evaluating LAV and LAVI found that patients with an increased LAV have a greater risk of cardiovascular disease than do patients with normal values [28]. Therefore, we aimed to investigate LAV in patients with PE. It is expected that there will be an increase in LAVI due to the natural effects of pregnancy in both groups. In a previous study, LAVI was higher in hypertensive pregnancy diseases [29]. In our study, there was a significant increase in LAVI in PE patients compared to healthy pregnant women, too. All these findings support the idea that LA functions may be impaired at a higher rate in patients with PE.

Arterial stiffness measurements and ascending aorta elastic properties have recently been studied in PE patients [5, 7-13]. In a study, Orabona et al. [11] showed that Ao compliance was found to be lowest in early-

onset PE (EOPE) patients and highest in late-onset PE (LOPE) patients compared to healthy controls. M-Mode Ao strain was found to be similar in healthy controls and LOPE patients and it was found to be lower in EOPE patients in this study [11]. In another study by Ciftci et al. [10], Ao strain was found to be lower in patients who had PE previously, compared to healthy controls. In the study of Orabona et al. [11], Ao distensibility was detected lowest in EOPE patients, and highest in LOPE patients; Ao stiffness index and Peterson's elastic modulus were highest in EOPE patients, and lowest in LOPE patients compared to healthy controls. In the study of Ciftci et al. [10], Ao distensibility was found to be lower, Ao stiffness index and Peterson's elastic modulus were higher in patients who had PE previously. Sciatti et al. [12], on the other hand, investigated the same aortic elastic parameters in Hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome patients and obtained findings similar to those of Orabona et al. In our study, Ao strain was higher and the Ao stiffness index was lower in PE group. Ao compliance, Ao distensibility, and elastic modulus did not differ between groups. But, in these studies, patients with previous PE or a history of PE were included. Additionally, the patients in the control group consisted of healthy individuals. Our study consisted of patients with new onset PE patients and healthy pregnant women at similar weeks.

In the correlation analyzes, we found that the parameters of LAVI max, LAVI min, LAV p, hemoglobin, and leucocyte were correlated with Ao strain. Also, Ao distensibility, Ao compliance, Ao stiffness index, and elastic modulus were correlated with Ao strain. This may indicate a relationship between ascending Ao elastic properties and LAV indexes. Further studies are needed on this subject.

Limitations

Our study has some limitations. Firstly, our study was single-centre and the number of cases was relatively small. Secondly, prenatal maternal hemodynamic status and postnatal follow-up the patients were not available, so it could not be excluded whether aortic elastic parameters were previously impaired. Finally, we only got the measurements from the ascending aorta. Measuring from different levels of the aorta could provide more precise information.

CONCLUSION

Aortic strain, aortic stiffness index, and LAV indexes were impaired in new onset hospitalized active preeclampsia patients. This study implies a close association between Ao strain, Ao stiffness index, and LAV indexes. Further studies with larger populations and subgroups classified according to the hemodynamic patterns in PE.

Competing Interest

The authors have no relevant financial or non-financial interests to disclose.

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Table-1: Demographic, Clinical, And Laboratory Findings Of The Preeclampsia And Normal Groups.

Variables	Preeclampsia group (n:51)	Healthy pregnant group (n:39)	p
Age (years)	29.04±3.75	28.03±3.57	0.197
Gestational age (weeks)	35.1±3.3	36.9±3.1	0.284
Number of gestations (n)	2.3±1.8	3.2±2.1	0.373
BMI (kg/m ²)	26.95±3.54	28.47±3.13	0.234
BSA (m ²)	1.85±0.18	1.82±0.20	0.382
SBP (mmHg)	138.56±13.20	117.06±7.75	0.038
DBP (mmHg)	85.62±7.89	70.64±6.89	<0.001
HR (beats/min)	89.43±12.16	76.08±10.2	<0.001
PP (mmHg)	52.94±9.42	46.41±5.49	<0.001
Hgb (g/dL)	13.41±1.31	14.39±1.48	0.981
Platelets (per µL)	244960.78±58910.91	247846.15±60786.74	0.822
Neutrophil (per µL)	4193.72±1066.57	4283.33±1177.11	0.710
Lymphocyte (per µL)	2109.02±598.56	2181.79±683.68	0.599
Creatinine (mg/dL)	0.76±0.14	0.72±0.14	0.782
24-hours proteinuria (g)	0.50±0.01	0.03±0.01	<0.001
ALT (U/L)	21.75±9.23	20.71±9.34	0.689
AST (U/L)	21.43±5.62	21.02±5.79	0.675

Abbreviations: BMI: body mass index; BSA: body surface area; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate; PP: pulse pressure; Hgb: haemoglobin; ALT: alanine transaminase; AST: aspartate transaminase

Bold fonts indicate a P value lesser than 0.05

Table-2: Echocardiography Findings Of The Preeclampsia And Normal Groups.

Variables	Preeclampsia group (n:51)	Healthy pregnant group (n:39)	P
AoDD (cm)	2.57±0.28	2.46±0.15	0.018
AoSD (cm)	2.89±0.29	2.69±0.14	<0.001
Ao Compliance (cm/mmHg)	0.06±0.02	0.05±0.02	0.052
Ao Strain (M-Mode, %)	10.95±4.47	8.42±3.85	0.005
Ao Distensibility (10 ⁻⁷ Pa ⁻¹)	496.77±250.13	418.60±263.46	0.158
Ao Stiffness Index	2.68±0.58	2.99±0.51	0.009
Peterson's Elastic modulus (Ep)	59.6±28.2	63.4±34.5	0.678
LA (mm)	33.9±2.6	33.0±3.3	0.205
LVEDD (mm)	46.9±4.1	45.8±4.4	0.198
LVEDS (mm)	29.5±3.7	27.5±3.6	0.013
LVEF (%)	65.3±4.6	67.6±5.4	0.324
IVS (mm)	11.8±1.6	9.7±1.2	0.004
PwD (mm)	11.5±1.4	9.3±1.2	0.002
SV (mL)	70.9±15.3	68.8±15.3	0.515
FS (%)	37.8±5.6	40.3±5.3	0.522
LV mass index (g/m ²)	138.8±29.8	100.9±19.7	0.040
Mitral E (m/s)	1.1±0.3	0.8±0.1	<0.001
Mitral A (m/s)	0.81±0.2	0.62±0.1	<0.001
Mitral E/A	1.33±0.3	1.30±0.3	0.615
Mitral E/Em	9.2±7.7	5.6±1.3	<0.001
DT (ms)	205.8±38.0	151.4±42.7	<0.001
MPI (%)	0.64±0.14	0.52±0.07	<0.001

Abbreviations:

AoDD: ascending aorta diastolic diameter; AoSD: ascending aorta systolic diameter; LA: left atrium; LVEDD: left ventricular end-diastolic diameter; LVEDS: left ventricular end systolic diameter; LVEF: left ventricular ejection fraction; IVS: interventricular septum; PwD: posterior wall; SV: Stroke volume; FS: fractional shortening; mitral E: early diastolic mitral flow velocities; mitral A: late diastolic mitral flow velocities; DT: mitral deceleration time; MPI: myocardial performance index Bold fonts indicate a P value lesser than 0.05

Table-3: Left Atrial 2D Tissue Doppler Findings And LA Volume Indexes Of The Preeclampsia And Normal Groups.

Variables	Preeclampsia group (n:51)	Healthy pregnant group (n:39)	p
LAT Em (m/s)	0.13±0.07	0.17±0.04	0.006
LAT Am (m/s)	0.12±0.01	0.11±0.03	0.371
LAT S (m/s)	0.12±0.03	0.16±0.02	0.144
SEP Em (m/s)	0.13±0.01	0.12±0.02	0.556
SEP Am (m/s)	0.10±0.02	0.09±0.02	0.090
SEP S (m/s)	0.10±0.02	0.11±0.02	0.076
LAVI max (cm ³ /mL)	22.9±5.1	18.2±4.9	<0.001
LAVI min (cm ³ /mL)	9.2±3.1	6.5±2.1	<0.001
LAVI p (cm ³ /mL)	14.3±4.0	11.1±2.9	<0.001

Abbreviations: LAT Em: mitral lateral e; LAT Am: mitral lateral a; LAT S: mitral lateral s; SEP Em: mitral septal e; SEP Am: mitral septal a; SEP S: mitral septal s; LAVI max: Left atrium maximum volume index; LAVI min: Left atrium minimum volume index; LAVI p: left atrium presystolic volume index

Bold fonts indicate a P value lesser than 0.05

Table-4: Pearson's Correlation Analyses Between Ao Strain And Other Parameters.

Variables	r	p
Ao Compliance	0.934	<0.001
Ao Distensibility	0.930	<0.001
Ao Stiffness Index	0.968	<0.001

Peterson's Elastic modulus	0.770	<0.001
LAVI max	0.254	0.016
LAVI min	0.385	0.001
LAVI p	0.265	0.011
Hgb	-0.254	0.016
Leukocyte	-0.213	0.044

Abbreviations: Ao: aorta; LAVI max: Left atrium maximum volume index; LAVI min: Left atrium minimum volume index; LAVI p: left atrium presystolic volume index, Hgb: haemoglobin
Bold fonts indicate a P value lesser than 0.05

REFERENCES

- Brown MA, Magee LA, Kenny LC, Karumanchi SA, McCarthy FP, Saito S, Hall DR, Warren CE, Adoyi G, Ishaku S; International Society for the Study of Hypertension in Pregnancy (ISSHP) (2018). The hypertensive disorders of pregnancy: ISSHP classification, diagnosis & management recommendations for international practice. *Pregnancy Hypertens.* 13:291-310. doi: 10.1016/j.preghy.2018.05.004.
- Leon LJ, McCarthy FP, Direk K, Gonzalez-Izquierdo A, Prieto-Merino D, Casas JP, Chappell L (2019). Preeclampsia and Cardiovascular Disease in a Large UK Pregnancy Cohort of Linked Electronic Health Records: A CALIBER Study. *Circulation.* 140:1050-1060. doi: 10.1161/CIRCULATIONAHA.118.038080.
- Easterling TR, Benedetti TJ, Schmucker BC, Millard SP (1990). Maternal hemodynamics in normal and preeclamptic pregnancies: a longitudinal study. *Obstet Gynecol.* 76(6):1061-1069.
- Bosio PM, McKenna PJ, Conroy R, O'Herlihy C (1999). Maternal central hemodynamics in hypertensive disorders of pregnancy. *Obstet Gynecol.* 94:978-984. doi: 10.1016/s0029-7844(99)00430-5.
- Yuan LJ, Duan YY, Xue D, Cao TS, Zhou N (2014). Ultrasound study of carotid and cardiac remodeling and cardiac-arterial coupling in normal pregnancy and preeclampsia: a case control study. *BMC Pregnancy Childbirth.* 14:113. doi: 10.1186/1471-2393-14-113.
- Güneş Y, Tuncer M, Yildirim M, Güntekin U, Gümrükçüoğlu HA, Sahin M (2008). A novel echocardiographic method for the prediction of coronary artery disease. *Med Sci Monit.* 14:MT42-46.
- Macedo ML, Luminoso D, Savvidou MD, McEniery CM, Nicolaides KH (2008). Maternal wave reflections and arterial stiffness in normal pregnancy as assessed by applanation tonometry. *Hypertension.* 51:1047-51. doi: 10.1161/HYPERTENSIONAHA.107.106062.
- Johansson MC, Barasa A, Basic C, Nyberg G, Schaefelberger M (2021). Increased arterial stiffness and reduced left ventricular long-axis function in patients recovered from peripartum cardiomyopathy. *Clin Physiol Funct Imaging.* 41:95-102. doi: 10.1111/cpf.12671.
- Torrado J, Farro I, Zócalo Y, Farro F, Sosa C, Scasso S, Alonso J, Bia D (2015). Preeclampsia Is Associated with Increased Central Aortic Pressure, Elastic Arteries Stiffness and Wave Reflections, and Resting and Recrutable Endothelial Dysfunction. *Int J Hypertens.* 2015:720683. doi: 10.1155/2015/720683.
- Cifici FC, Cifici O, Gullu H, Caliskan M, Uckuyu A, Ozcimen EE (2014). Does mild preeclampsia cause arterial stiffness and ventricular remodeling through inflammation? *Ginekolo Pol.* 85:900-907. doi: 10.17772/gp/1880.
- Orabona R, Sciatti E, Vizzardi E, Bonadei I, Valcamonico A, Metra M, Frusca T (2016). Elastic properties of ascending aorta in women with previous pregnancy complicated by early- or late-onset pre-eclampsia. *Ultrasound Obstet Gynecol.* 47:316-323. doi: 10.1002/uog.14838.
- Sciatti E, Orabona R, Prefumo F, Vizzardi E, Bonadei I, Valcamonico A, Metra M, Frusca T (2019). Elastic properties of ascending aorta and ventricular-arterial coupling in women with previous pregnancy complicated by HELLP syndrome. *J Hypertens.* 37:356-364. doi: 10.1097/HJH.0000000000001888.
- Dennehy N, Lees C (2022). Preeclampsia: Maternal cardiovascular function and optimising outcomes. *Early Hum Dev.* 174:105669. doi: 10.1016/j.earlhumdev.2022.105669.
- Lacombe F, Dart A, Dewar E, Jennings G, Cameron J, Laufer E (1992). Arterial elastic properties in man: a comparison of echo-Doppler indices of aortic stiffness. *Eur Heart J.* 13:1040-1045. doi: 10.1093/oxfordjournals.eurheartj.a060311.
- O'Rourke MF, Staessen JA, Vlachopoulos C, Duprez D, Plante GE (2002). Clinical applications of arterial stiffness; definitions and reference values. *Am J Hypertens.* 15:426-444. doi: 10.1016/s0895-7061(01)02319-6.
- Cunningham FG, Lindheimer MD (1992). Hypertension in pregnancy. *N Engl J Med.* 326:927-932. doi: 10.1056/NEJM199204023261405.
- Borzychowski AM, Sargent IL, Redman CW (2006). Inflammation and pre-eclampsia. *Semin Fetal Neonatal Med.* 11:309-316. doi: 10.1016/j.siny.2006.04.001.
- Kinlay S, Creager MA, Fukumoto M, Hikita H, Fang JC, Selwyn AP, Ganz P (2001). Endothelium-derived nitric oxide regulates arterial elasticity in human arteries in vivo. *Hypertension.* 38:1049-1053. doi: 10.1161/hy1101.095329.
- Elvan-Taspinar A, Franx A, Bots ML, Bruinse HW, Koomans HA (2004). Central hemodynamics of hypertensive disorders in pregnancy. *Am J Hypertens.* 17:941-946. doi: 10.1016/j.amjhyper.2004.05.018.
- Tihtonen KM, Kööbi T, Uotila JT (2006). Arterial stiffness in preeclamptic and chronic hypertensive pregnancies. *Eur J Obstet Gynecol Reprod Biol.* 128:180-186. doi: 10.1016/j.ejogrb.2005.12.026.
- Kaihura C, Savvidou MD, Anderson JM, McEniery CM, Nicolaides KH (2009). Maternal arterial stiffness in pregnancies affected by preeclampsia. *Am J Physiol Heart Circ Physiol.* 297:H759-764. doi: 10.1152/ajpheart.01106.2008.
- Irgens HU, Reisaeter L, Irgens LM, Lie RT (2001). Long term mortality of mothers and fathers after pre-eclampsia: population based cohort study. *BMJ.* 323:1213-1217. doi: 10.1136/bmj.323.7323.1213.
- Ray JG, Vermeulen MJ, Schull MJ, Redelmeier DA (2005). Cardiovascular health after maternal placental syndromes (CHAMPS): population-based retrospective cohort study. *Lancet.* 366:1797-1803. doi: 10.1016/S0140-6736(05)67726-4.
- Suzuki H, Watanabe Y, Arima H, Kobayashi K, Ohno Y, Kanno Y (2008). Short- and long-term prognosis of blood pressure and kidney disease in women with a past history of preeclampsia. *Clin Exp Nephrol.* 12:102-109. doi: 10.1007/s10157-007-0018-1.
- Hausvater A, Giannone T, Sandoval YH, Doonan RJ, Antonopoulos CN, Matsoukis IL, Petridou ET, Daskalopoulou SS (2012). The association between preeclampsia and arterial stiffness. *J Hypertens.* 30:17-33. doi: 10.1097/HJH.0b013e32834e4b0f.
- Noris M, Perico N, Remuzzi G (2005). Mechanisms of disease: Pre-eclampsia. *Nat Clin Pract Nephrol.* 1:98-114. doi: 10.1038/ncpneph0035.
- Roberts JM, Gammill HS (2005). Preeclampsia: recent insights. *Hypertension.* 46:1243-1249. doi: 10.1161/01.HYP.0000188408.49896.c5.
- Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, Picard MH, Roman MJ, Seward J, Shanewise JS, Solomon SD, Spencer KT, Sutton MS, Stewart WJ;

Chamber Quantification Writing Group; American Society of Echocardiography's Guidelines and Standards Committee; European Association of Echocardiography (2005). Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiogr.* 18:1440-1463. doi: 10.1016/j.echo.2005.10.005.

- Giorgione V, Melchiorre K, O'Driscoll J, Khalil A, Sharma R, Thilaganathan B (2022). Maternal echocardiographic changes in twin pregnancies with and without pre-eclampsia. *Ultrasound Obstet Gynecol.* 59:619-626. doi: 10.1002/uog.24852.