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Cardiovascular effects of severe late-onset preeclampsia are reversed within six months postpartum

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ABSTRACT

Objectives: Preeclampsia (PE) is a common pregnancy-related disorder associated with cardiovascular long-term disease. Eighty percent are late-onset PE, occurring after 34 gestational weeks, and can present with severe symptoms. Magnitude and reversibility rate of maternal cardiovascular changes after severe late-onset PE have not been characterized. This study therefore evaluated longitudinal dynamics of maternal cardiovascular changes after severe late-onset PE.

Study design: Six previously normotensive women with severe late-onset PE and eight pregnant controls were included. Severe PE was defined as systolic blood pressure (SBP) ≥ 160 mmHg or diastolic blood pressure (DBP) ≥ 110 mmHg and proteinuria with/without evidence of end-organ dysfunction, or SBP ≥ 140 mmHg or DBP ≥ 90 mmHg with/without proteinuria and with evidence of end-organ dysfunction. Cardiovascular function was assessed by magnetic resonance imaging at 1–3 days, one week and six months postpartum.

Results: Left ventricular mass at 1–3 days postpartum was higher after severe late-onset PE (57 g/m^2) compared to after normal pregnancy (48 g/m^2; p = 0.01). Pulse wave velocity (PWV) decreased between 1 and 3 days and six months postpartum after PE (6.1 to 5.0 m/s; p = 0.028). There was no difference in PWV 1–3 days postpartum after severe PE compared after normal pregnancy (6.1 versus 5.6 m/s; p = 0.175). Blood pressure normalized within six months in all but one patient.

Conclusions: Cardiac effects after severe late-onset PE were small and transient. This indicates that left ventricular hypertrophy after severe late-onset PE may be a secondary physiologic response to increased peripheral resistance in PE. Vascular mechanisms rather than persistent cardiac hypertrophy postpartum may be the culprit for increased long-term cardiovascular risk after PE.

1. Introduction

Preeclampsia (PE) affects 3–8% of pregnancies and is a leading cause of maternal and perinatal morbidity and mortality worldwide [1]. Preeclampsia is a heterogeneous disease and may present in varying forms with varying degree of severity. Early-onset PE, manifesting before 34 gestational weeks, is particularly associated with higher maternal [2–4] and perinatal [2,5] morbidity and mortality as well as higher rate of fetal growth restriction [6,7] as compared to late-onset PE. Severe late-onset (after 34 gestational weeks) PE is however less studied and its effects on maternal cardiovascular dynamics early after delivery remain unclear.

The cure for PE is delivery of the placenta, supporting the crucial etiological role of the placenta in the development of PE [8]. Maternal effects of PE do however not cease with the birth of the infant and the delivery of the placenta. Women with pregnancy complicated by PE have an increased lifetime risk of hypertension and cardiovascular disease [9]. Mechanisms may be related to a higher rate of metabolic syndrome in women with a history of PE [10] and the persistence of abnormal endothelial function postpartum [11]. An echocardiography study has shown PE to be associated with global diastolic dysfunction, increased left ventricular mass and increased cardiac work index, suggesting that women with PE display abnormal cardiac adaption to pregnancy [12]. Although these changes mainly seem transient and

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revert to normal after delivery, especially early-onset PE may lead to persistent changes present months or years postpartum, predictive for development of hypertension [13,14]. These changes may be related to early gestational age at onset of maternal disease. However, the severity of PE may depend on how different organ systems indirectly are affected by the general endothelial damage, i.e. blood pressure elevation, central nervous system dysfunction, hepatic and renal abnormalities, pulmonary edema and thrombocytopenia. Severe late-onset PE may thus lead to persistent changes in the vascular bed as well as the maternal cardiac structure and function due to overall decreased function of these organs, despite onset after 34 gestational weeks.

The aim of the study was therefore to investigate the dynamics of structural and functional changes of the maternal heart within six months postpartum in women with severe late-onset PE compared to uncomplicated pregnancies.

2. Methods

2.1. Study population

The Regional Ethical Review Board approved the study (2013/551; 19 September 2013) and participants provided written informed consent before participating. This prospective cohort study was carried out at Skåne University Hospital and subjects were included between October 2014 and March 2017. Women with severe late-onset (after 34 gestational weeks) PE and healthy women with uncomplicated singleton pregnancy were recruited at the prenatal obstetric clinics. Exclusion criteria were previous cardiovascular disease other than preeclampsia, or cardiac surgery, smoking, multiple gestation, thyroid disease, pregestational diabetes mellitus or gestational diabetes, gestational hypertension, and/or implants or other contraindications to CMR.

Preeclampsia was classified according to the International Society for the Study of Hypertension in Pregnancy guidelines [15]. Severity of PE was defined according to criteria by the American College of Obstetricians and Gynecologists Task Force on Hypertension in Pregnancy [16]. Severe PE was thus defined as presence of one or more of the following criteria: blood pressure elevation $\geq$160 mmHg systolic blood pressure or $\geq$110 mmHg diastolic blood pressure, elevated liver transaminases to twice above normal in blood, new-onset cerebral or visual disturbances, thrombocytopenia with platelet count $< 100 \times 10^9$/L, renal dysfunction defined as serum creatinine concentration $>$ 97 μmol/L or a doubling of serum creatinine concentration in the absence of other renal disease, and/or pulmonary edema.

Blood samples and resting brachial blood pressure measurements were performed according to clinical routine. Blood pressure was also acquired in conjunction with CMR. Cardiac magnetic resonance imaging was performed at three time points postpartum: one to three days, one week, and six months postpartum. Medication was assessed through patient records.

3. Cardiac magnetic resonance imaging

All participants underwent CMR imaging without contrast agent using either a 1.5T Philips Achieva (Best, the Netherlands) or a Siemens Aera (Erlangen, Germany). For quantification of ventricular volumes, cine images were acquired in the standard projections, i.e. short-axis and 2-, 3- and 4-chamber long-axis views. The cine images were acquired using a balanced steady state free precession (bSSFP) sequence. Typical parameters were: slice thickness = 8 mm; field of view = 320 mm; flip angle = 60°; TR/TE = 4/2ms; in-plane resolution = 1.1 × 1.1 mm.

Phase-contrast quantitative flow data were acquired in the ascending aorta at the level of the pulmonary trunk and in the aorta at the level of the diaphragm, using a standard non-breath hold 2D gradient recalled echo with retrospective ECG gating. Typical parameters were TR/TE = 20/3ms; flip angle = 20°; slice thickness = 8 mm; in-plane resolution 1.3 × 1.3 mm and acquisition time 2 min.

A stack of oblique sagittal anatomical images covering the thoracic aorta was acquired to measure the length of the centreline of the aorta between flow planes, which was used for calculation of pulse wave velocity.

4. Cardiac magnetic resonance image analysis

4.1. Ventricular volumes

Left and right ventricular (LV and RV) volumes were measured by manual delineation in the short-axis cine images covering the left and right ventricles. End-diastole and end-systole were identified as the time frames with maximum and minimum left intraventricular volumes respectively. Left and right ventricular end-diastolic volume (EDV) and end-systolic volume (ESV) were calculated as the sum of all slice volumes at end-diastole and end-systole respectively. Left ventricular mass (LVM) was calculated as left ventricular wall volume multiplied by left ventricular myocardial density (1.05 g/ml). Stroke volume (SV) was calculated as the difference between EDV and ESV, and ejection fraction (EF) as SV divided by EDV. All parameters except EF were indexed to body surface area to obtain EDV index (EDVi), ESV index (ESVi), SV index (SVi), and LVM index (LVMi).

5. Aortic flow and pulse wave velocity

Flow curves were obtained from the ascending aorta and the descending aorta at the level of the diaphragm by manual delineation in the phase-contrast quantitative flow images. Cardiac output was obtained by multiplying ascending aortic flow with heart rate. Cardiac index (CI) was obtained by normalizing cardiac output to body surface area.

Pulse wave velocity between the flow planes of the ascending aorta and the aorta at the level of the diaphragm was calculated as the distance between the planes divided by the transit time of the flow curve from the ascending aorta to the aorta at the level of the diaphragm. The distance between the flow planes was measured by tracing the centreline of the aorta in the oblique sagittal anatomical image stack covering the aorta. Flow-curve transit time between the flow planes was calculated as the difference between tangent line intersections at the point of maximum upslope with the time axis for each flow curve respectively.

5.1. Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics for Macintosh 25 (IBM Corporation, Armonk, NY). Power analysis was conducted to determine the needed sample size using the Sealed Envelope Power Calculator [17] and was based on maternal data from a previous study during the third trimester of pregnancy with left ventricular mass (LVM) by CMR being 179 ± 5 g [18]. With 80% power and $\alpha = 0.05$ five women in each group were required with the assumption that mean LVM was 5% higher in women with preeclampsia. Kruskal-Wallis H was used to determine statistically significant differences between groups and the Wilcoxon signed-rank test was used to compare repeated measurements in the same group at different time points. Differences were considered significant if $p < 0.05$.

6. Results

Pregnant women with severe late-onset PE and healthy pregnant women were approached for inclusion between October 2014 and March 2017. Six women with severe late-onset PE and eight women with uncomplicated pregnancy were ultimately included in the current study. Due to their general condition, one woman with PE did not undergo CMR one week after delivery and one woman with

Table 1
Maternal baseline, fetal and pregnancy characteristics.

		Normal pregnancy (n = 8)	Preeclampsia (n = 6)	p-value
Maternal age (years)		29 (20–41)	29 (23–36)	0.948
Body mass index (one to three days)		25 (23–34)	28 (22–31)	0.568
Body mass index (one week)		25 (25–32)	28 (25–33)	0.380
Body mass index (six months)		23 (20–33)	25 (20–29)	0.366
Gestational age at delivery (weeks)		39.4 (37.7–42.1)	37.4 (35.6–38.0)	0.013
Birthweight (g)		3,450 (2,694–4,086)	3,054 (2,565–3,616)	0.438
Fetal sex	Male	5	4	
	Female	3	2	
Parity	0	4	4	
	1	3	2	
	2	1	0	
Previous preeclampsia		0	1	
Severe hypertension (systolic ≥ 160 and/or diastolic ≥ 110)		0	6	
Mean arterial pressure 1–3 days after delivery		83 (77–100)	110 (90–115)	0.019
Mean arterial pressure 1 week after delivery		85 (80–90)	99 (70–113)	0.190
Mean arterial pressure 6 months after delivery		80 (77–90)	86 (64–103)	0.421
End-organ dysfunction		0	5	
Gestational age at diagnosis of preeclampsia (weeks)		–	37 (34.7–37.1)	
Birthweight < 10th percentile	no	7	6	
	yes	1	0	

Values are expressed as median (range) or n.

uncomplicated pregnancy did not undergo CMR one to three days after delivery. Baseline characteristics of the study population are shown in Table 1.

There was no statistically significant difference between the two groups with respect to maternal age and body mass index (BMI). Gestational age at delivery was significantly higher after uncomplicated pregnancy compared to pregnancy complicated by PE (39.4 gestational weeks versus 37.4; p = 0.013). Although median birthweight after pregnancy complicated by PE was 88% (3,054 g) of birthweight after uncomplicated pregnancy (3,450 g), the difference was not statistically significant (p = 0.48). One study participant with uncomplicated pregnancy gave birth to a small for gestational age (SGA) infant. All other infants were either appropriate for gestational age (AGA) or large for gestational age (LGA).

Median gestational age for diagnosis of severe late-onset PE was 37 gestational weeks. Severe hypertension, in accordance with the statement from the ISSHP for the definition of severe preeclampsia [19], necessitating admission to the prenatal obstetric clinic for further evaluation was present in all subjects with PE. One woman was classified as having severe PE due exclusively to severe hypertension without any accompanying end-organ dysfunction. The other five women with severe PE developed end-organ dysfunction. In all but one patient blood pressure returned to normal within six months after delivery. The patient in whom blood pressure was still elevated had been diagnosed with autosomal dominant polycystic kidney disease before pregnancy. At inclusion this patient however had normal blood pressure and normal kidney function. This subject developed severe PE with abnormal liver function and severe hypertension. Further, due to remained elevated blood pressure during follow-up antihypertensive therapy in the form of nifedipine was continued. Among the remaining patients three participants with pregnancy complicated by PE received antihypertensive treatment during the first CMR examination performed one to three days postpartum; one patient received metoprolol in combination with nifedipine and two patients received enalapril. These three subjects were relieved of antihypertensive treatment before the first follow-up examination at one week after delivery. No other subject received antihypertensive treatment after delivery.

Cardiovascular magnetic resonance data are presented in Table 2. Left ventricular mass index was higher in women with severe late-onset PE (57 g/m^2) at one to three days after delivery compared with women with uncomplicated pregnancy (48 g/m^2; p = 0.01). Between one to three days after delivery and six months after delivery LVMi in women with PE decreased by 19% (57 g/m^2 versus 48 g/m^2; p = 0.028). At six months after delivery there was no difference in LVMi between patients and controls (Fig. 1).

Pulse wave velocity (PWV) one to three days after delivery was similar between women with PE and controls (6.1 m/s versus 5.6 m/s; p = 0.175) (Fig. 1). Pulse wave velocity however decreased in women with PE between one to three days postpartum (6.1 m/s) and six months postpartum (5.0 m/s; p = 0.043). There was no change over time in PWV in women with uncomplicated pregnancy (5.6 m/s versus 5.2 m/s; p = 0.138) and no difference in PWV between women with PE and controls at six months postpartum (5.0 m/s versus 5.2 m/s; p > 0.999).

There were no differences between women with PE and controls one to three days postpartum in cardiac index, left ventricular end systolic volume index, left ventricular end diastolic volume index, left ventricular ejection fraction, right ventricular end systolic volume index, right ventricular end diastolic volume index or right ventricular ejection fraction (Fig. 2).

7. Discussion

Cardiac effects after severe late-onset preeclampsia with normalized

Table 2
Maternal cardiovascular structure and function one to three days, one week and six months postpartum.

	One to three days postpartum			One week postpartum			Six months postpartum		
	Normal pregnancy	Preeclampsia	p-value	Normal pregnancy	Preeclampsia	p-value	Normal pregnancy	Preeclampsia	p-value
LVMi (g/m^2)	48 (44–57)	57 (53–68)	**0.010**	50 (44–61)	55 (50–73)	0.143	46 (39–51)	48 (45–53)	0.302
LVEDVi (ml/m^2)	94 (79–114)	89 (81–124)	0.668	97 (78–132)	86 (78–134)	0.884	89 (79–109)	85 (72–101)	0.439
LVESVi (ml/m^2)	40 (31–48)	38 (28–58)	0.886	47 (35–61)	39 (31–60)	0.464	36 (29–46)	35 (26–40)	0.519
LVEF (%)	60 (57–62)	57 (53–65)	0.199	53 (48–62)	57 (50–63)	0.242	59 (54–66)	61 (54–65)	0.606
RVEDVi (ml/m^2)	96 (82–126)	92 (83–118)	0.475	93 (75–133)	89 (84–129)	0.884	89 (74–110)	87 (81–114)	0.699
RVESVi (ml/m^2)	45 (33–62)	41 (34–53)	0.391	48 (36–68)	43 (36–60)	0.661	37 (31–55)	36 (34–48)	0.796
RVEF (%)	53 (51–60)	58 (54–60)	0.153	53 (43–59)	53 (49–58)	0.661	57 (50–64)	58 (51–61)	0.606
CI (l/min/m^2)	3.5 (2.8–4.3)	3.5 (2.9–4.6)	0.631	3.2 (2.5–3.8)	2.9 (2.8–4.9)	0.770	2.9 (2.6–3.8)	3 (2.7–3.2)	0.796
PWV (m/s)	5.6 (5.0–6.2)	6.1 (5.4–6.3)	0.175	5.1 (4.7–6.9)	6.1 (4.9–7.3)	0.144	5.2 (4.1–5.6)	5 (4.3–5.9)	> 0.999

Values are expressed as median (range).
LVMi, left ventricular mass index; LVEDVi, left ventricular end diastolic volume index; LVESVi, left ventricular end systolic volume index; LVEF, left ventricular ejection fraction; RVEDVi, right ventricular end diastolic volume index; RVESVi, right ventricular end systolic volume index; RVEF, right ventricular ejection fraction; CI, cardiac index; PWV, pulse wave velocity.

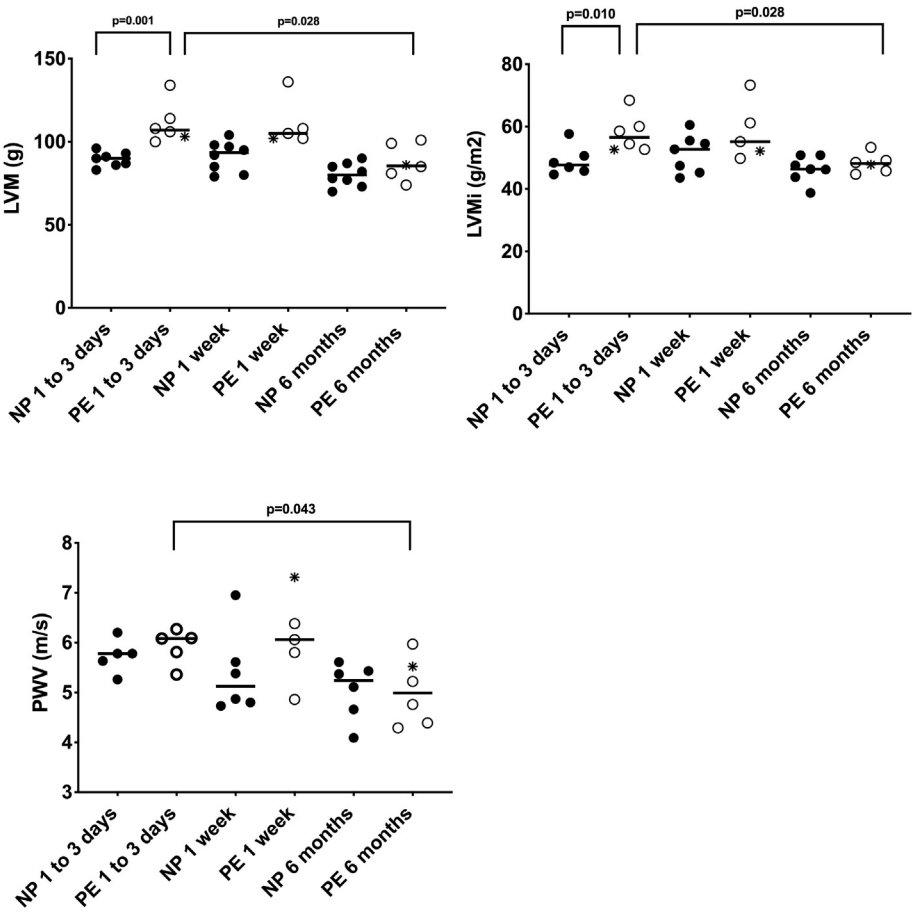

Fig. 1. Maternal cardiovascular changes after pregnancy complicated by severe late-onset preeclampsia (PE; open circles) and after normal pregnancy (NP; closed circles) for left ventricular mass (LVM; **top left**), LVM indexed to body surface area (LVMi; **top right**) and pulse wave velocity (PWV; **bottom**). Left ventricular mass was higher at one to three days postpartum after severe late-onset PE compared to after normal pregnancy, and decreased between one to three days and six months after delivery. Pulse wave velocity decreased between one to three days and six months postpartum after pregnancy complicated by preeclampsia. The patient with autosomal dominant polycystic kidney disease is marked with *.

blood pressure at six months were small and transient. The results indicate that left ventricular hypertrophy after severe late-onset PE may be a secondary physiologic response to increased peripheral resistance in PE. Vascular mechanisms rather than persistent cardiac hypertrophy postpartum may thus be the culprit for increased long-term cardiovascular risk after preeclampsia.

The rapid resolution of left ventricular hypertrophy after delivery suggests that mechanisms other than structural cardiac changes may explain the association between PE and increased risk for future cardiovascular disease. A possible underlying mechanism may be the imbalance of pro-angiogenic and antiangiogenic factors such as soluble fms-like tyrosine kinase-1 and placental growth factor as seen in preeclampsia compared to healthy controls. In particular, placental growth factor levels after 22 weeks of gestation are lower in women who develop late-onset PE, especially in its more severe form, compared to women with uncomplicated pregnancy [20]. Furthermore, recent evidence suggests that low levels of placental growth factor in mid-pregnancy are associated with increased systolic blood pressure nine years after delivery, even in women with an otherwise uncomplicated pregnancy [21]. According to another hypothesis, persistent endothelial regulatory changes as an end-result of release of placental syncytiotrophoblast extracellular vesicles and free fetal hemoglobin into maternal circulation in preeclamptic pregnancy may also in part explain vascular alteration that may drive development of future cardiovascular disease. This hypothesis is supported by a study that showed placental syncytiotrophoblast extracellular vesicles to be included into coronary artery endothelial cells, which causes microRNA-mediated alterations in gene expression and may contribute to oxidative stress [22,23].

In the present study women were evaluated using CMR imaging, which accurately quantifies cardiac volumes and function [24], blood flow [25] and thoracic pulse wave velocity [26]. On the contrary, transthoracic echocardiography is based on geometric assumptions that may introduce volume measurement errors, particularly when evaluating the maternal heart during pregnancy. In a recent study, echocardiography underestimated cardiac volumes and mass during the peripartum period as compared to CMR [18]. Further, considering the difference in sample size needed for similar power using echocardiography and CMR [27], the application of CMR in the current study is a key strength allowing for more precise evaluation of cardiovascular effects after PE.

This study included a well-controlled population of women with pregnancy complicated by severe late-onset PE. Few studies have focused on the cardiovascular characteristics associated with severe PE. Vaught et al. [28] showed in severe PE short-term cardiac effects by echocardiography to be higher right ventricular systolic pressure, higher rates of abnormal diastolic function, decreased global right ventricular longitudinal systolic strain and increased left-sided chamber remodeling. That study however investigated early-onset PE, whereas the current study adds knowledge as it mainly describes a population of severe late-onset PE. Further, the current study also assessed cardiovascular function longitudinally over a longer interval postpartum. A previous study of maternal cardiovascular effects by PE using CMR showed no difference in systolic or diastolic cardiac function or left ventricular mass between women with and without PE [29]. Those women were however evaluated at a median time of 95 and 101 months after delivery, whereas the results of the current study suggest that cardiac effects after PE are resolved already 6 months after delivery.

Although late-onset PE becomes clinically apparent late in pregnancy, the maternal cardiovascular system undergoes significant changes also in an early preclinical phase. Increased arterial stiffness in

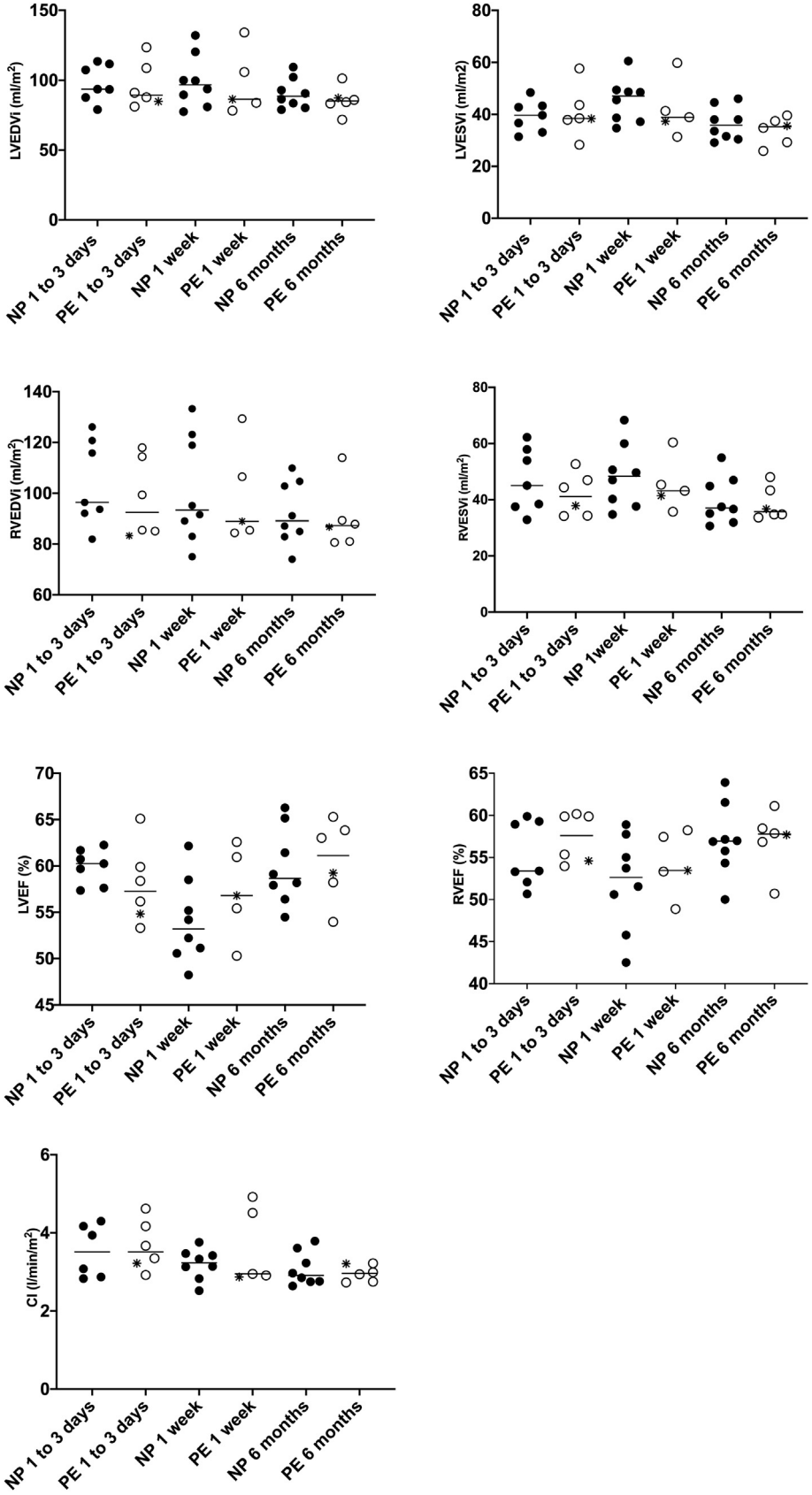

Fig. 2. Maternal cardiovascular changes after pregnancy complicated by severe late-onset preeclampsia (PE; open circles) and after normal pregnancy (NP; closed circles). No significant differences were found between groups or between time points. LVEDVi, left ventricular end diastolic volume index; LVESVi, left ventricular end systolic volume index; LVEF, left ventricular ejection fraction; RVEDVi, right ventricular end diastolic volume index; RVESVi, right ventricular end systolic volume index; RVEF, right ventricular ejection fraction; CI, cardiac index.

PE compared to normal pregnancy has been shown as early as the first trimester [30]. Women with late-onset PE also show abnormal cardiac remodeling in the preclinical phase of PE [31,32], presumably in response to higher midgestational mean arterial pressure associated with PE. It may therefore be assumed that the increase in LVMi found in the current study one to three days after delivery in women with severe late-onset PE is predominantly due to increased afterload. Further increase in afterload is plausible during the clinical phase of PE when the woman develops severe hypertension. However, the deleterious effects of the late increase in afterload during the clinical phase of PE are limited due to the prompt delivery of the fetus and placenta. This may explain the discrepancy between severity of PE and small magnitude of cardiovascular changes. Furthermore, the changes in systemic arterial properties associated with PE are resolved after delivery, which was reflected in the current study as normalization of LVMi, blood pressure and decrease in PWV in women with PE within six months after delivery. Therefore, future studies ought to assess maternal cardiovascular function before gestation and in early stages of pregnancy in order to clarify whether cardiovascular changes exist already before pregnancy predetermining the evolution of PE, develop in a preclinical phase of the disease or are the direct result of clinical deterioration during the late stage of PE.

The current results are partially consistent with previous findings. Melchiorre et al. [12] showed that women at term gestation with pregnancy complicated by PE had increased LVMi compared with women with uncomplicated pregnancy using echocardiography. In another study by Melchiorre et al. [14], persistently altered left ventricular geometry was found in 19% of women with term PE one year postpartum. Altered left ventricular geometry was in that study defined as relative wall thickness higher than 0.42 or LVMi higher than 95 g/m^2. The current study further elucidates the dynamics of decrease in the initially increased LVMi in women with severe late-onset PE. Furthermore, it also shows that left ventricular hypertrophy resolves faster and more extensively than previously reported. The well-defined population of late-onset severe PE in the current study provides further support for the hypothesis that late-onset PE is associated with fast reversible left ventricular changes even among patients with severe PE.

In the current study, cardiac index was not different between groups. A possible explanation for this may be that the groups were comparable in terms of fetal growth. All included women with severe late-onset PE gave birth to either an AGA or LGA infant. Fetal growth and maternal hemodynamics are interrelated, so that fetal growth restriction is associated with lower maternal cardiac output compared to normotensive women with an AGA fetus [33]. Furthermore, recent evidence supports the hypothesis that the maternal hemodynamic characteristics in women with PE are related to fetal growth and not necessarily to gestational age at disease onset [34,35]. Current findings are in accordance with a recent study by Ferrazzi et al. [34] reporting no differences in cardiac index between PE and normotensive pregnancy, irrespective of gestational age at disease onset, as long as fetal growth is normal. Ferrazzi et al. further showed that women with PE and AGA fetuses have lower total vascular resistance compared to women with PE and SGA fetuses, irrespective of gestational age at disease onset. Furthermore, Tay et al. [35] showed that women with pregnancy complicated by PE and fetal growth restriction had higher peripheral vascular resistance compared to women with uncomplicated pregnancy, while women with PE but without fetal growth restriction had lower peripheral vascular resistance compared to women with uncomplicated pregnancy. It may thus be hypothesized that PE with normal fetal growth irrespective of gestational age at disease onset or severe features is characterized by hemodynamic features that may trigger less prominent left ventricular changes and resolve faster after delivery compared to PE with abnormal fetal growth. Further work is however required to establish this.

The current study showed no significant difference in pulse wave velocity directly after delivery between women after severe late-onset PE and women after uncomplicated pregnancy. Pulse wave velocity did however decrease in women with PE during follow-up from 6.1 m/s to 5.0 m/s. This change over time indicates that a difference in vascular function may exist between groups late in pregnancy and after delivery, albeit not statistically significant in the current study, likely due to the low number of included cases. Preeclampsia is associated with a 1 m/s increase in carotid-femoral pulse wave velocity compared to normotensive pregnancy [36]. This is comparable to the PWV decrease shown in the current study during the follow-up period. Estensen et al. [37] reported persistently stiffer systemic arteries in women with PE also at six months postpartum compared with uncomplicated pregnancy. As gestational age was similar between studies, the differences in results may be due to methodologies applied for measuring arterial stiffness. Whereas the previous study used total arterial compliance and characteristic impedance the current study directly measured PWV [38] as recommended by the American Heart Association [39]. Regardless of the method used, arterial stiffness measures also depend on blood pressure [40], which was increased in patients with PE one to three days postpartum and normalizes during the follow-up period in the current study. Blood pressure reduction after delivery unloads the aortic wall, which presumably leads to reduced PWV that may explain the decrease in PWV found in women with PE.

8. Limitations

The results of the present study should be viewed in the light of some limitations where the major limitation is the small sample size. This was due to the low incidence of severe late-onset PE [41,42]. To increase inclusion of a well-defined group of women with severe late-onset PE a multi-center study approach will be necessary.

9. Conclusions

Cardiac effects after severe late-onset PE with normalized blood pressure at six months are small and transient. This indicates that left ventricular hypertrophy after severe late-onset PE may be a secondary physiologic response to increased peripheral resistance in PE. Vascular mechanisms rather than persistent cardiac hypertrophy postpartum may be the culprit for increased long-term cardiovascular risk after preeclampsia.

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Author contributions

EH had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of data analyses. HA, SRH and EH contributed substantially to the study design. GK and DS drafted the manuscript. GK, DS, KSE, and EH analysed data. GK, DS, KSE, HA, SRH and EH interpreted data. All authors revised the manuscript critically for important intellectual content, have provided final approval of the version to be published, and have agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Corrigendum to "Cardiovascular effects of severe late-onset preeclampsia are reversed within six months postpartum" [Preg. Hypertens. 19 (2020) 18–24]

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The second author Daniel Salehi has changed last name to Ryd and would like to have his name updated to Daniel Ryd. No changes to content of paper.

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