OBSTETRICS

Maternal cardiac parameters can help in differentiating the clinical profile of preeclampsia and in predicting progression from mild to severe forms

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BACKGROUND: A primary role of maternal heart dysfunction in the pathophysiology of preeclampsia had been previously advocated although if contradictory results have been reported.

OBJECTIVES: The objectives of the study were to describe maternal hemodynamic parameters according to 2 main preeclampsia phenotypes and to investigate whether cardiac findings may be helpful in characterizing the severity and the progression of the disease.

STUDY DESIGN: This was a prospective cohort study. We used an ultrasonic cardiac output monitor system to compare the hemodynamic parameters of women with preeclampsia with a group of healthy normotensive women enrolled as controls with a ratio of 1:2. Cardiac output, systemic vascular resistance, and stroke volume were compared among controls and preeclamptic women who were grouped in accordance to the following characteristics: early preeclampsia (<34 weeks' gestation) vs late preeclampsia onset (≥34 weeks' gestation); preeclampsia associated with appropriate for gestational age or small-for-gestational-age newborns. Hemodynamic characteristics were also compared between preeclamptic women with a mild form vs those who progressed toward a severe form.

RESULTS: A total of 38 preeclamptic women and 61 normotensive women were included in the study. Both cases of preeclampsia associated with small-for-gestational-age neonates as those with normal-sized ones showed higher systemic vascular resistance compared with the control group (respectively, 1580.6 ± 483.2 vs 1479.1 ± 433.3 vs 1105.3 ± 293.1; $P < .0001$), while a lower cardiac output was reported only for preeclamptic women with small-for-gestational-age neonates compared with controls (5.7 ± 1.5 vs 6.5 ± 1.3; $P = .02$). Maternal cardiac parameters were comparable between these 2 groups of preeclamptic women (small-for-gestational-age vs appropriate-for-gestational-age preeclampsia) with the exception of a lower stroke volume in the former one (64.8 ± 24.4 vs 75.2 ± 17.8; $P = .04$). Similarly, women with both early and late preeclampsia showed higher systemic vascular resistance compared with controls (1559.5 ± 528.3 vs 1488.5 ± 292.9 vs 1105.3 ± 293.1, respectively; $P < .001$), while a lower cardiac output was noted only in the early-onset group compared with controls (5.5 ± 1.2 $P = .02$). Maternal cardiac findings were similar between women with early vs late-onset preeclampsia. Hemodynamic parameters are significantly different between those women with mild preeclampsia who remained stable compared with those who progressed toward a severe disease. Cardiac output Z-score, systemic vascular resistance Z-score, and uterine arteries' pulsatility index Z-score showed similar sensitivity (80% vs 75% vs 80%, respectively) and specificity (73% vs. 73% vs 74%, respectively), while the association of systemic vascular resistance Z-score and uterine arteries pulsatility index Z-score showed a sensitivity of 95% and a specificity of 80% (area under the curve, 0.90) in predicting evolution toward severe forms.

CONCLUSION: Evaluation of maternal cardiovascular system could help clinician in defining a subset of preeclamptic patients with more profound placental impairment and might predict the likelihood of progression toward a severe condition in cases with a mild preeclampsia at clinical onset.

Key words: cardiac output, fetal growth restriction, maternal hemodynamic, preeclampsia, systemic vascular resistance, ultrasonic cardiac output monitor, uterine arteries

Preeclampsia is a leading cause of maternal and perinatal complications, being also associated with a higher risk of women cardiovascular disease in the long term.[1–5] In the last decade, many studies supported the hypothesis of the existence of 2 main types of preeclampsia: an early-onset type frequently associated with fetal growth restriction and with abnormal placentation, and a late-onset one characterized by normal fetal growth and triggered by metabolic or inflammatory maternal factors or by villus overcrowding.[6–12]

Given the availability of noninvasive cardiovascular monitoring devices (ie, Ultrasound Cardiac Output Monitor, USCOM 1A Ltd, Sydney, New South Wales, Australia; NICOM Cheetah Medical, Inc, Wilmington, DE; NICaS, NI Medical, Petach Tikva, Israel), the evaluation of maternal cardiovascular system has been increasingly used in the assessment of women affected by hypertensive disorders of pregnancy. The use of these devices has been validated in the obstetric population despite the maternal hemodynamic changes caused by pregnancy and a good agreement between these tools and the standard 2-dimensional echocardiography.[13–17]

Based on maternal cardiovascular parameters, different hemodynamic patterns have been described for cases of preeclampsia associated with normal-sized fetuses compared with those coexisting with fetal growth restriction.[9,10,12,18,19] More specifically, in the

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AJOG at a Glance

Why was this study conducted?

This study was conducted to assess maternal hemodynamic parameters in different types of preeclampsia.

Key findings

Cardiac output, systemic vascular resistance, and pulsatility index of uterine arteries are significantly different between those women with mild preeclampsia who remained stable compared with those who progressed toward a severe disease.

What does this add to what is known?

In women admitted with mild preeclampsia, maternal cardiac assessment by means of a noninvasive monitoring system predict the progression toward a severe form.

former group, higher cardiac output and lower peripheral vascular resistance have been noted compared with healthy control pregnancies; conversely, those with both preeclampsia and fetal growth restriction have lower cardiac output and higher peripheral vascular resistance. These changes do not seem be related to gestational age of onset.[20–23]

Less in known about the association between maternal hemodynamic status and the severity or the progression of the disease.

The aim of this study is 2-fold: to describe maternal hemodynamic parameters according to the 2 main preeclampsia phenotypes and to investigate whether cardiac findings may be helpful in characterizing the severity and the progression of the disease.

Materials and Methods

Study design and study population

This was a prospective cohort study including women admitted to our tertiary care center between January 2017and August 2018 with a diagnosis of preeclampsia according to the classification of the Working Group on High Blood Pressure in Pregnancy.[24]

Data from healthy women with uncomplicated pregnancies recruited during antenatal visits or third-trimester standard ultrasound examinations were selected as controls with a ratio of 1:2.

Demographic characteristics, pregnancy, and neonatal outcome were retrieved from hospital obstetric and neonatal records. Birthweight Z-scores were calculated using local references ranges.[25]

Exclusion criteria were: gestational age of less than 24 weeks, multiple pregnancies, preexisting chronic hypertension or kidney disease, cardiac disease, fetal congenital or chromosomal anomalies, or intrauterine fetal demise.

Gestational age was calculated from crown-rump length measure at 11^{+0} to 13^{+6} weeks' gestation or head circumference if the first ultrasound scan was performed after 14 weeks.

Preeclampsia was defined as high blood pressure ($\geq$140/90 mm Hg) occurring after 20 weeks of gestation associated with proteinuria ($\geq$300 mg per 24 hours or a protein/creatinine ratio $\geq$0.3 mg/dL). The presence of severe disease was defined by the occurrence of one of the following characteristics:

- Systemic blood pressure of 160 mm Hg or higher, or diastolic blood pressure of 110 mm Hg or higher on 2 occasion at least 4 hours apart while the patient is on rest (unless antihypertensive therapy is initiated before this time).
- Thrombocytopenia (platelet count <100.000/mL).
- Impaired liver function (elevated blood levels of liver transaminases to twice the normal concentration.
- New development of renal insufficiency.
- Pulmonary edema.
- New-onset cerebral or visual disturbances.

Preeclampsia was classified as early when clinical onset was <34 weeks of gestation or late when clinical onset was $\geq$ 34 weeks of gestation.

Small for gestational Age (SGA) was defined as birthweight <10th centile according to the national charts.[25] Preterm delivery was defined as <37 weeks' gestation, while term delivery was defined as $\geq$37 weeks' gestation. This study was approved by the local ethical committee.

Management

Upon hospital admission, all preeclamptic women underwent central hemodynamic assessment by means of USCOM (Ultrasound Cardiac Output Monitor; USCOM Ltd), a noninvasive device using continuous wave Doppler to obtain velocity time integrals of transaortic or transpulmonary blood flow. Information about cardiac output (CO), stroke volume (SV), and systemic vascular resistance (SVR) are indirectly obtained through an algorithm combining velocity time integrals, anthropometric parameters (height and weight), and blood pressure values. CO was also analyzed after normalization for the body surface area as the cardiac index.

The normotensive patients selected as controls were submitted to a single USCOM examination along their antenatal care.

Measurements were obtained under standardized conditions for the entire cohort. The USCOM probe was placed in the suprasternal notch to obtain a minimum of 3 consecutive Doppler profiles with the patient in a semirecumbent position.

Because CO and SVR change with gestational age and maternal characteristics (maternal age, height, weight, smoke), they were expressed as a Z-score using reference ranges of maternal central hemodynamic parameters during pregnancy.[26]

Systolic and diastolic blood pressures were recorded with an automated device (Omron M-7; OMRON Healthcare Europe BV, Hoofddorp, The

TABLE 1
Maternal characteristics, pregnancy outcome, and hemodynamic parameters of preeclamptic women based on the association with AGA or SGA newborns

Variable	Control (n = 61)	PE-AGA (n = 17)	PE-SGA (n = 21)	*p* value	*p* value for between-group comparison		
					PE-AGA vs control	PE-SGA vs control	PE-AGA vs PE-SGA
Maternal age, y	32.0 ± 5.0	32.9 ± 7.5	35.5 ± 5.8	.03	.47	.008	.14
BMI, kg/m^2	26.9 ± 4.6	29.9 ± 7.2	25.2 ± 8.3	.22	.13	.60	.10
Gestational age at examination, wks	36.5 ± 0.8	36.1 ± 1.9	33.5 ± 3.2	< .001	.29	< .0001	.02
Gestational age at delivery, wks	39.7 ± 1.1	37.0 ± 2.0	35.4 ± 2.2	< .0001	< .0001	< .0001	.56
Birthweight, g	3532.4 ± 468.7	2883.4 ± 483.2	1836.2 ± 468.1	< .0001	< .0001	< .0001	< .0001
Birtweight (Z-score)	0.5 ± 0.9	0.1 ± 0.5	−1.5 ± 1.3	< .0001	.07	< .0001	< .0001
Heart rate, bpm	85.4 ± 15.2	85.0 ± 17.6	88.5 ± 27.0	.78	.92	.52	.65
Cardiac output, L/min	6.5 ± 1.3	5.9 ± 1.6	5.7 ± 1.5	.04	.20	.02	.43
Cardiac output (Z-score)	−0.2 ± 1.0	−0.7 ± 1.4	−0.8 ± 1.2	.05	.07	.04	.94
Systemic vascular resistance, dynes/s per cm^{-5}	1105.3 ± 293.1	1479.1 ± 433.3	1580.6 ± 483.2	< .0001	< .0001	< .0001	.63
Systemic vascular resistance (Z-score)	−0.02 ± 1.2	1.4 ± 1.0	1.5 ± 1.2	< .0001	< .0001	< .0001	.95
Stroke volume, mL	82.0 ± 24.9	75.2 ± 17.8	64.8 ± 24.4	.03	.96	.009	.04
Uterine arteries PI (Z-score)	NA	−0.1±1.6	1.8±1.6	NA	NA	NA	< .001

Data are expressed as mean ± SD or number and (percentage).

AGA, appropriate for gestation age; BMI, body mass index; *NA*, not available; *PE*, preeclampsia; *PI*, pulsatility index; *SGA*, appropriate for gestation age.

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Netherlands), which has been validated in pregnancy, following recommendations from the European Society of Hypertension.[27]

Uteroplacental hemodynamic assessment was performed measuring the pulsatility index (PI) of uterine arteries according a standardized technique. Using color Doppler, 3 consecutive waveforms of uterine arteries at the level of the cross-over of the external iliac artery were obtained, and the mean of the right and left PI was calculated and converted into percentiles to adjust for gestational weeks.

According to local protocol and national guidelines, women with mild preeclampsia are delivered at 37 gestational weeks; in the presence of severe disease, delivery is carried out after maternal stabilization and antenatal corticosteroids administration or soon after hospital admission for cases at late-onset occurrence (≥34 weeks of gestation).[24,25,28]

Outcome

A comparison of demographics, clinical characteristics, hemodynamic measurements, and pregnancy outcomes was performed between preeclamptic women and controls.

The primary outcome of the study was to compare hemodynamic findings (CO, SVR, SV) at diagnosis among controls and women with preeclampsia who were grouped in accordance to the following characteristics:

- Early preeclampsia (<34 weeks' gestation) vs late preeclampsia (≥34 weeks' gestation) onset.
- Preeclampsia associated with appropriate for gestational age (AGA) or SGA newborns.

The secondary outcome of this study was to compare hemodynamic findings between women with stable mild preeclampsia and preeclampsia with progression toward severe forms and to assess whether hemodynamic parameters at diagnosis could predict the progression of the disease.

The results of hemodynamic investigation were concealed to the attending physician because they were collected only for research purpose and did not modify the clinical management.

Statistical analysis

Statistical analysis was performed using Statistical Package for Social Sciences

TABLE 2
Maternal characteristics, pregnancy outcome, and hemodynamic parameters of preeclamptic women according to the onset of disease: early (<34 weeks' gestation) or late (≥34 weeks' gestation)

Variable	Control (n = 61)	Late-onset PE (n = 25)	Early-onset PE (n = 13)	*p* value	*p* value for between-group comparison		
					Early-onset PE vs control	Late-onset PE vs control	Early- vs late-onset PE
Maternal age, y	32.0 ± 5.0	32.3 ± 6.2	38.2 ± 5.8	.01	.003	.28	.039
BMI, kg/m^2	26.9 ± 4.6	29.7 ± 7.1	23.2 ± 8.3	.13	.26	.17	.06
Gestational age at examination, wks	36.5 ± 0.8	36.4 ± 1.3	31.3 ± 2.3	< .0001	< .0001	.24	< .0001
Gestational age at delivery, wks	39.7 ± 1.1	37.2 ± 1.0	34.0 ± 2.0	< .0001	< .0001	< .0001	.004
Birthweight, g	3532.4 ± 468.7	2656.9 ± 534.2	1627.3 ± 457.0	< .0001	< .0001	< .0001	.001
Birthweight (Z-score)	0.5 ± 0.9	−0.6 ± 1.2	−1.1 ± 1.7	< .0001	< .0001	< .0001	.33
Heart rate, bpm	85.4 ± 15.2	89.9 ± 25.3	81.2 ± 17.2	.35	.37	.31	.27
Cardiac output, L/min	6.5 ± 1.3	5.9 ± 1.6	5.5 ± 1.2	.037	.02	.12	.29
Cardiac output (Z-score)	−0.2 ± 1.0	−0.6 ± 1.4	−1.0 ± 1.0	.03	.01	.12	.23
Systemic vascular resistance, dynes/s per cm^{-5}	1105.3 ± 293.1	1488.5 ± 292.9	1559.5 ± 528.3	< .0001	< .0001	< .0001	.73
systemic vascular resistance (Z-score)	−0.02 ± 1.2	1.4 ± 1.3	1.6 ± 0.8	< .0001	< .0001	< .0001	.34
Stroke volume, mL	82.0 ± 24.9	72.2 ± 26.0	68.0 ± 20.2	.20	.09	.32	.77
Uterine arteries PI (Z-score)	NA	0.6 ± 1.6	1.8 ± 1.8	NA	NA	NA	.04

Data are expressed as mean ± SD or number and (percentage).

BMI, body mass index; *NA*, not available; *PE*, preeclampsia; *PI*, pulsatility index.

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version 22 (IBM Inc, Armonk, NY). Data were displayed as mean ± SD or as number (percentage). Categorical variables were compared using the χ^2 or Fisher exact test. Between-group comparison of continuous variables was undertaken using a Student *t* test and the Mann-Whitney nonparametric equivalent test.

Two-sided *P* values were calculated and values of $P < .05$ were considered as statistically significant. Comparisons between 2 or more groups were performed using Kruskal-Wallis test. Binomial logistic regression including all covariates significantly different at univariate analysis was used to assess the predictors of progression towards severe forms and receiver-operating characteristic curves for associated predictors were calculated. The study was performed following the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.[29]

Results

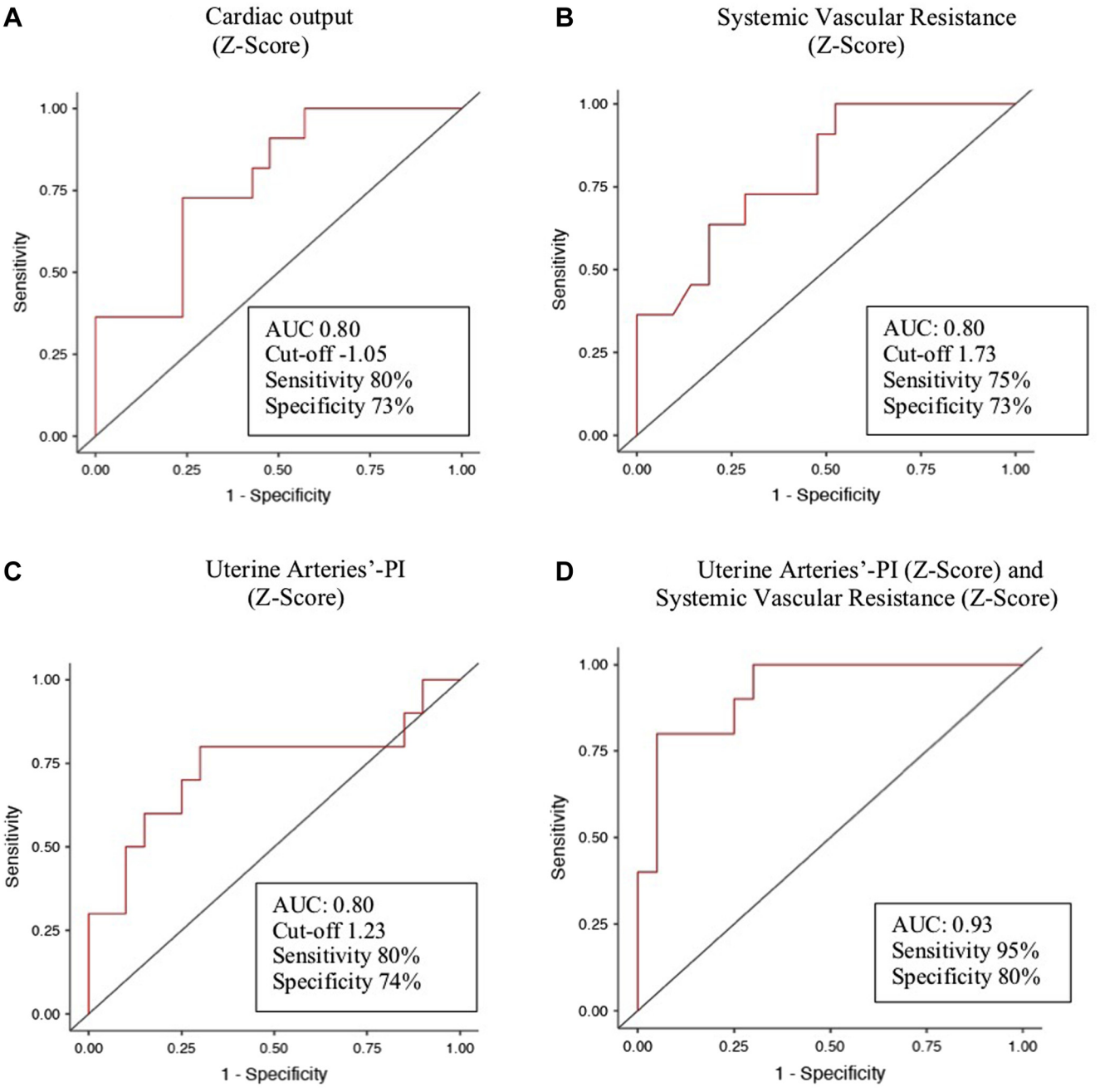
Over the study period, 38 preeclamptic women were included in the present study. Seventy-six normotensive women with uncomplicated pregnancies underwent USCOM evaluation during pregnancy; 11 of them were excluded because the neonatal weight was subsequently found to be <10th percentile; 4 women were excluded because they developed hypertension during the postpartum period. Ultimately, a total of 61 women were included in the present study as controls.

Patients with preeclampsia were divided into 2 groups based, respectively, either on the association with SGA newborns or on the gestational age at onset of disease. The clinical characteristics and USCOM findings of the 2 subgroups of preeclampsia and controls are summarized in Tables 1 and 2. A lower CO, CO Z-Score, and SV was noted in women with preeclampsia and SGA compared with normotensive controls. Both women with preeclampsia and SGA newborns and those with preeclampsia and AGA newborns showed significantly higher SVR and SVR Z-score compared with controls (Table 1).

No difference regarding these hemodynamic parameters was found comparing preeclamptic women with AGA and SGA newborns with the exception of a lower SV in the latter group ($P = .04$) (Table 1).

Compared with controls, women with early- and late-onset preeclampsia had significantly higher SVR and SVR Z-score, while a lower CO, CO Z-core, and SV were noted only in the former group.

FIGURE
Receiver operating characteristic curves



AUC=Area Under the Cureve

Receiver operating characteristic curve of cardiac output Z-score **(A)**, systemic vascular resistance Z-score **(B)**, uterine arteries PI Z-score **(C)**, and uterine arteries PI plus systemic vascular resistance Z-score **(D)** for the prediction of progression toward severe preeclampsia.

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No difference regarding these hemodynamic parameters was found comparing cases of early vs late preeclampsia (Table 2).

At admission, only 3 women of our study group fulfilled the criteria of severity. Among the 35 remaining cases of mild preeclampsia, 11 patients developed a severe form in a mean interval of 2.31 ± 2.33 weeks (10 before and 1 the day after delivery). As shown in Table 3, the following parameters were

TABLE 3
Maternal characteristics, pregnancy outcome, and hemodynamic parameters recorded at preeclampsia onset between women with a stable disease (mild PE) and women subsequently developing a severe disease (progression to severe)

Variables	Stable mild PE (n = 24)	Progression to severe PE (n = 11)	*p* value
Maternal age, y	34.8 ± 5.7	32.9 ± 8.5	.56
BMI, kg/m^2	28.0 ± 9.3	27.4 ± 4.9	.86
Gestational age at onset, wks	35.7 ± 2.3	33.1 ± 3.7	.02
Gestational age at delivery, wks	36.8 ± 1.6	35.4 ± 1.4	.05
Birthweight, g	2490.5 ± 692.7	2070.0 ± 619.2	.09
Birthweight (Z-score)	−0.7 ± 1.5	−0.9 ± 1.1	.65
Small for gestational age	11 (45.8%)	8 (72.7%)	.13
Heart rate, bpm	89.2 ± 26.5	79.5 ± 14.8	.26
Cardiac output (Z-score)	−0.3 ± 1.1	−1.6 ± 1.1	.004
Systemic vascular resistance (Z-score)	1.1 ± 0.9	2.3 ± 1.0	.001
Stroke volume, mL	72.6 ± 24.7	62.5 ± 16.6	.22
Uterine arteries PI (Z-score)	0.4 ± 1.4	1.7 ± 1.6	.03

Data are expressed as mean ± SD or number and (percentage).

BMI, body mass index; *PE*, preeclampsia; *PI*, pulsatility index.

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significantly different upon the admission between the 24 cases who remained mild vs those 11 who became severe: GA at onset, CO Z-score, SVR Z-score and uterine arteries PI (Table 3).

Binomial logistic regression including both central (CO Z-score, SVR Z-score) and peripheral (uterine arteries PI Z-score) hemodynamic parameters and gestational age at onset demonstrated that uterine arteries PI Z-score and SVR Z-score are main and independent predictors of evolution toward severe preeclampsia (Table 4).

CO Z-score, SVR Z-score, and uterine arteries PI Z-score showed similar sensitivity (80% vs 75% vs 80%, respectively) and specificity (73% vs 73% vs 74%, respectively), while the association of SVR Z-score and uterine arteries PI Z-score showed a sensitivity of 95% and a specificity of 80% (area under the curve, 0.90) in predicting evolution toward a severe disease (Figure).

TABLE 4
Association of uterine arteries pulsatility index and systemic vascular resistance with evolution toward severe preeclampsia by binomial logistic regression (forward stepwise method)

Predictor	Estimate	SE	Z	p value	Odds ratio	95% confidence interval	
						Lower	Upper
Uterine arteries PI (Z-score)	1.7	0.7	2.4	.02	5.5	1.4	22.1
Systemic vascular resistance (Z-score)	2.9	1.2	2.4	.02	17.2	1.7	176.2

PI, pulsatility index; *SVR*, systemic vascular resistance.

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Comment

Principal findings

Our study confirmed the existence of different hemodynamic patterns among women who develop preeclampsia compared with normotensive pregnancies.

Interestingly, lower CO in respect of controls was noted when preeclampsia was associated with SGA neonates or was diagnosed before 34 weeks, while CO was similar between normotensive and preeclamptic women with normal-sized neonates or with late occurrence (at or after 34 weeks); On the other hand, maternal cardiac parameters were comparable between women with early vs late-onset preeclampsia and between preeclamptic with SGA vs AGA neonates with the exception a lower stroke volume in those with SGA neonates.

Furthermore, women with both early and late preeclampsia showed higher SVR compared with controls.

Finally, we found that the maternal cardiac findings and Uterine Doppler were significantly different between those women with mild preeclampsia who remained stable compared with those who progressed towards a severe disease. In particular, cases of mild preeclampsia which became severe were characterized by lower CO, and higher SVR and PI of uterine arteries, independently from timing at diagnosis and association with SGA neonates.

Results

Our data seem to support the concept that preeclampsia is associated and possibly induced by maternal cardiac maladaptation to pregnancy.[21–23,30,31] In fact, we found a different hemodynamic profile in women who developed either type of preeclampsia (early or late; associated or not with SGA neonates) compared with normotensive women.

The new and most interesting finding was that prioritizing features of severe disease allows to underline different

hemodynamic patterns within preeclamptic women, while this difference is not figured out focusing on the classification of preeclampsia according to fetal smallness or with the gestational age at onset, However, although no significant difference was noted among the 2 subsets of preeclamptic women, the cardiac profile of the women with preeclampsia and SGA or early preeclampsia seems characterized by a slightly lower cardiac output and higher SVR compared, respectively, with AGA preeclampsia or a late-onset one.

This observation seems in accordance with the more recent vision on the dual pathophysiology of preeclampsia that is considered to be distinguishable in 2 separate entities: one triggered by severe placental dysfunction, which is commonly associated with fetal growth restriction or SGA neonates and has mostly (but not necessarily) a preterm onset; the other favored by metabolic factors that arise closer to term and are not associated with fetal growth impairment.[9,10,12,32−34]

Clinical implications

A primary role of maternal heart dysfunction in the pathophysiology of preeclampsia had been previously proposed, although if, in some cases, contradictory results have been reported.[30,32,33,34]

Valensise et al[9] described the existence of 2 different types of preeclampsia (early vs late) mostly based on the onset of disease and associated with different hemodynamic findings. Early preeclampsia was characterized by higher uterine arteries PI, higher SVR, and lower CO; on the contrary, normal SVR and normal uterine arteries PI together with higher CO characterized the late onset of disease.[35,36]

Subsequent studies on maternal cardiac remodeling suggested a common pathogenesis of preeclampsia when presenting with an early onset and when associated with SGA neonates.[32−34] As confirmed by the present study, these phenotypes are both characterized by a high resistance/low hemodynamic status because of an increased systemic afterload and a contracted circulating volume (SV); on the other hand, women with late-onset preeclampsia, associated with an AGA fetus display a high SVR/unchanged CO state compared with controls.[30,33,34]

More recently, focusing on the association with SGA neonates, Ferrazzi et al[23] demonstrated that preeclampsia with placental insufficiency is characterized by low CO and high SVR, independently from the gestational age at onset of hypertension disorders. They also found significantly different cardiac findings between women with hypertensive disorders associated or not with SGA neonates, but of note, in this study women with both gestational hypertension and preeclampsia have been put into the same group, while in our own study, cases of isolated hypertension have been excluded.

Similar findings were reported by Tay et al,[21] who demonstrated that hemodynamic characteristics of preeclampsia are unrelated to gestational age at onset but strongly associated with the presence or absence of fetal growth restriction. In this latter study, when preeclampsia was not associated with impaired fetal growth, CO was demonstrated to be higher and SVR lower compared with the control group. This observation seems to be in contrast with our own findings. However, it should be noted that cardiac indices were not corrected for maternal anthropometric characteristics, although these varied considerably across the study groups.[37]

Research implications

Based on our results and on recent evidences, we envisage that evaluation of maternal cardiovascular system could help clinician in defining a subset of preeclamptic patients who have a higher risk of pregnancy complications. In particular, the assessment of SVR by noninvasive monitoring devices together with the Doppler interrogation of uterine arteries PI seems to characterize those cases with more profound placental impairment and might predict the likelihood of progression toward a severe condition in cases with a mild preeclampsia at clinical onset.[36,38−40]

Furthermore, although preeclampsia is still defined as a unique disease, interrogation of maternal cardiovascular system can help clinician in providing the best targeted therapy tailored on maternal hemodynamic status.[41−44]

The presence of features of severe preeclampsia still represents one of the leading indications to preterm iatrogenic delivery in women with preeclampsia.[45] For the first time, we have correlated both central and peripheral hemodynamic parameters with the clinical severity of the disease, using them in terms of predictivity and demonstrating an a priori different cardiovascular state in women who will subsequently develop a severe form requiring indicated delivery.

Recently the use of angiogenic factors (soluble fms-like tyrosine kinase/placental growth factor; vascular endothelial growth factor receptor) has been widely proposed to predict the occurrence of severe preeclampsia in women at risk for hypertensive disorders of pregnancy.[46−53] In our opinion, cardiovascular parameters could represent, together with angiogenic factors, a reliable admission test to identify those women at higher risk of evolution toward a severe form of preeclampsia.

Strengths and limitations

The main limitation of our study was the small number of preeclamptic women included, which is, however, comparable with previous works on the same subject. Maternal hemodynamic parameters were investigated only at the admission, so we are not able to draw conclusions about their longitudinal changes in relation to the clinical course of the condition and to the effect of antihypertensive medications. Furthermore, the stratification of preeclampsia according to birthweight <10 percentile rather than to estimated fetal growth and Doppler findings can be considered as a limitation, although we retain that the neonatal smallness would be a robust proxy of placental insufficiency in women with preeclampsia.

One of the strengths of our study was to have obtained a Z-score for all the hemodynamic measurements (CO,

SVR) by means of a calculator that adjusts for those demographic (ie, maternal age, height, weight) and anthropometric characteristics influencing cardiovascular parameters.[26,37]

Conclusions

In conclusion, based on our data, maternal cardiac dysfunction is confirmed to play a key role in the pathophysiology of preeclampsia in its various forms and seems to predict the progression from mild to severe condition. These observations, if confirmed by larger prospective studies, are expected to alter the current classification and management of hypertensive disorders of pregnancy. ■

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