Current Science
CS 6 (4), 6499-6515 (2026)
Received 20 June 2026 | **Accepted 13 July** 2026 | **Online Available 17 July** 2026
https://doi.org/10.52845/CS/2026-6-4-8

Current Science

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OPEN ACCESS

ISSN(O)2795-8639

Original Article

Investigate Placental Vascular Impedance Is Associated with Maternal Cardiac Performance and Remodeling in Pregnancy

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Abstract:

Objectives: This study aimed to evaluate the relationship between the placental pulsatility index (PPI) and maternal cardiovascular adaptation, specifically assessing cardiac geometry, diastolic/systolic function, and global hemodynamics.

Methods: In this cross-sectional study of 389 singleton pregnancies (May 2024–April 2025), concurrent Doppler-derived PPI and comprehensive transthoracic echocardiography were performed. Pearson correlations were used to analyze the link between PPI and cardiac indices.

Results: Elevated PPI was significantly associated with attenuated physiological eccentric remodeling, evidenced by inverse correlations with LV end-diastolic volume ($r = -0.125$, $p = 0.024$) and interventricular septal thickness ($r = -0.139$, $p = 0.012$). PPI showed robust positive correlations with diastolic parameters, such as the mitral E/A ratio ($r = 0.227$, $p < 0.001$) and septal e'/a' ratio ($r = 0.254$, $p < 0.001$). Furthermore, higher PPI correlated with decreased cardiac output ($r = -0.237$, $p < 0.001$), while conventional systolic indices remained largely stable.

Conclusions: Increased placental vascular resistance is linked to detectable alterations in maternal diastolic function and ventricular geometry. Diastolic parameters appear more sensitive to placental impedance, suggesting their potential value in antenatal cardiovascular surveillance.

Keywords: Placental Pulsatility Index(PPI), Maternal Cardiovascular Adaptation, Uteroplacental Hemodynamics, Fetoplacental Vascular Impedance, Echocardiographic Structural Remodeling

Introduction

Human placentation is a highly coordinated and tightly regulated biological process that depends on complex interactions between the developing placenta and maternal physiological systems. Successful pregnancy requires extensive maternal adaptation across cardiovascular systems, to ensure adequate uteroplacental perfusion and fetal development[1-3].

During early gestation, extra-villous trophoblasts invade the maternal spiral arteries, resulting in

their transient occlusion and the establishment of a physiologically hypoxic intrauterine environment that is essential for normal placental morphogenesis. This is followed by progressive spiral artery remodeling, characterized by the loss of vascular smooth muscle and elastic components, ultimately transforming these vessels into low-resistance, high-capacitance conduits. The establishment of an effective uteroplacental circulation is a gradual process and is generally not completed until after approximately 14 weeks of gestation[4, 5]. Inadequate trophoblastic invasion or incomplete vascular remodeling represents a key pathological feature of placental dysfunction and is strongly associated with major obstetric complications, including preeclampsia and fetal growth restriction[6, 7].

Doppler ultrasonography is a well-established and indispensable modality for the evaluation of placental perfusion and function. Nevertheless, conventional Doppler indices, including uterine artery and umbilical artery pulsatility indices, provide valuable information regarding maternal and fetal vascular resistance, respectively[7-11]. conventional Doppler indices predominantly reflect discrete components of the fetoplacental and uteroplacental circulations, and thus may not adequately represent the complex and integrated hemodynamic interplay within the placenta. To address this limitation, Gudmundsson et al. proposed the placental pulsatility index (PPI) as a novel Doppler-derived parameter that simultaneously incorporates vascular impedance from both the maternal and fetal compartments of the placental circulation. By integrating these hemodynamic components, PPI enables a more comprehensive assessment of placental vascular resistance and overall circulatory status. Their findings demonstrated that incorporation of PPI enhances the predictive sensitivity for adverse pregnancy outcomes compared with conventional Doppler indices alone[12].

Subsequent investigations by Todumrong et al. further evaluated the clinical applicability of PPI in high-risk pregnancies during the second trimester, demonstrating that elevated PPI values are significantly associated with adverse outcomes, including small for gestational age (SGA), fetal growth restriction (FGR), and adverse perinatal events. Collectively, these studies underscore the potential of PPI as an integrative and clinically valuable biomarker for assessing placental function and facilitating risk stratification in pregnancy[13].

The maternal cardiovascular system undergoes substantial physiological remodeling during pregnancy, characterized by marked increases in plasma volume, cardiac output, and heart rate, alongside a concomitant reduction in systemic vascular resistance[2, 3]. These hemodynamic adaptations are initiated early in gestation and generally peak during the second trimester[14], facilitating adequate oxygen and nutrient delivery to support fetal growth and development[15]. Failure to appropriately establish or sustain these adaptive changes has been associated with adverse pregnancy outcomes, including hypertensive disorders and placental insufficiency[16]. Emerging evidence further indicates that placental vascular resistance is closely linked to maternal cardiovascular function. Specifically, studies have demonstrated significant associations between uteroplacental and fetoplacental Doppler indices and maternal cardiac parameters, such as cardiac output, systemic vascular resistance, and ventricular performance. Collectively, these findings support the concept of a dynamic “placenta–heart axis,” wherein placental development and maternal cardiovascular adaptation are interdependent processes that co-evolve throughout gestation[1, 17-19].

Despite increasing recognition of the complex interplay between placental and maternal cardiovascular systems, the relationship between

placental vascular resistance and maternal cardiac adaptation remains incompletely understood. In particular, it remains unclear whether gestational changes in placental impedance differentially influence regional myocardial function as opposed to global cardiac performance. Accordingly, the present study aimed to investigate the associations between the placental pulsatility index and maternal cardiac function across gestation, with a specific focus on identifying stage-dependent patterns of cardiovascular adaptation. We hypothesized that increasing placental vascular resistance would be associated with a progressive transition from regional myocardial alterations to global hemodynamic adaptation, reflecting a dynamic and evolving interaction within the placenta–heart axis.

Materials and Methods

Ethical Approval and Participant Consent

The Medical Research Ethics Review Committee of Yichun Maternal and Child Health Hospital, Jiangxi, China approved this study (Approval No. 2025004-LW004). In all research procedures involving human subjects, institutional ethical guidelines and the principles of the latest revision of the Declaration of Helsinki were strictly followed. We anonymized all participant data before performing statistical analysis in order to protect participant confidentiality. Each participant gave written informed consent before enrolling in the study.

Study Population and Setting

During May 2024 and April 2025, retrospective data were obtained from 389 pregnant women with singletons underwent prenatal ultrasounds at Yichun Maternal & Child Health Hospital for fetal prenatal screenings. Based on crown-rump length measurements obtained during first-trimester sonographic assessments (8-14 weeks of gestation), gestational age (GA) was determined[20]. Eligible participants were limited to women with singleton pregnancies in whom no maternal comorbidities or fetal abnormalities were identified. Participants were excluded if there was any history of chromosomal abnormalities, major fetal structural anomalies, or maternal medical complications.

The prenatal ultrasound evaluations were conducted using a Voluson E10 ultrasound system (General Electric Medical Systems, Milwaukee, WI, USA) equipped with a C2-9-D multifrequency transabdominal transducer (XDclear Wide Band Convex Probe). Fetal anatomical ultrasounds and biometric measurements were conducted in accordance with the Standards of Practice of the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) and the American Institute of Ultrasound in Medicine (AIUM)[21, 22].

Maternal Cardiac Function Assessment

All participants underwent comprehensive transthoracic echocardiographic examination performed on the Philips Affiniti 70 ultrasound platform (Koninklijke Philips N.V., The Netherlands), utilizing an S5-1 broadband sector-array transducer. All imaging was conducted with participants positioned in the standard left lateral decubitus position, in strict accordance with the recommended protocols and technical specifications established by the American Society of Echocardiography (ASE) [23].

All echocardiographic measurements were acquired from standardized acoustic windows in strict accordance with current imaging guidelines. From the parasternal left ventricular long-axis view, the following left ventricular (LV) linear dimensions were systematically obtained: LV end-diastolic internal diameter (LVIDd), LV end-systolic internal diameter (LVIDs), interventricular septal thickness at end-diastole (IVSd) and end-systole (IVSs), and LV posterior wall thickness at end-diastole (LVPWd) and end-systole (LVPWs). The aortic annulus diameter

(AO annulus) was additionally measured from this view. M-mode echocardiography was subsequently employed to derive the following LV functional parameters: end-diastolic volume (EDV), end-systolic volume (ESV), ejection fraction (LV EF), fractional shortening (LV FS), stroke volume (SV), and cardiac output (CO).

From the great-vessel short-axis view, the pulmonary artery annulus diameter (PA annulus) was obtained. Pulsed-wave Doppler interrogation of the main pulmonary artery was performed to record peak systolic velocity (PA pSV), mean velocity (PA mV), peak pressure gradient (PA pPG), and mean pressure gradient (PA mPG).

From the apical four-chamber view, linear chamber dimensions were systematically acquired, encompassing the superior–inferior and mediolateral diameters of the left atrium (LAVD and LATD) and right atrium (RAVD and RATD), as well as the longitudinal and transverse diameters of the left ventricle (LVLD and LVTD). Right ventricular transverse diameter (RVTD), mitral annulus diameter (MV annulus), and tricuspid annulus diameter (TV annulus) were additionally recorded from this view. Pulsed-wave Doppler was applied to measure early (MVE) and late (MVA) diastolic transmitral inflow velocities, from which the mitral E/A ratio was subsequently derived as an index of LV diastolic filling.

Tissue Doppler imaging (TDI) was employed to assess early (e′) and late (a′) diastolic myocardial velocities at both the interventricular septum (IVS e′ and IVS a′) and the lateral mitral annulus (LW e′ and LW a′). The LV E/e′ ratio was thereafter calculated to estimate LV filling pressure, evaluate myocardial compliance, and serve as a validated index of LV diastolic relaxation.

From the apical five-chamber view, pulsed-wave Doppler interrogation of the ascending aorta was performed to obtain systolic flow indices, including peak systolic velocity (AO pSV), mean velocity (AO mV), peak pressure gradient (AO pPG), and mean pressure gradient (AO mPG).

All Doppler acquisitions were performed during periods of calm, quiet respiration to minimize respiratory-induced hemodynamic variability. For each parameter, three consecutive technically adequate and hemodynamically stable waveforms were selected, and the mean of the three measurements was recorded as the representative value. The majority of Doppler-derived indices were automatically computed by the built-in software of the ultrasound platform upon accurate manual tracing of the Doppler waveform envelope, thereby ensuring methodological consistency and minimizing the potential for operator-dependent computational error.

All ultrasound procedures were performed in adherence to the "as low as reasonably achievable" (ALARA) principle[24] to ensure safety. All scans and measurements were performed by one experienced, board-certified sonographer of seniority with more than a decade of clinical practice. Intra-observer reliability was assessed using reliability statistics, based on repeated measurements conducted by the same examiner. The formal assessment of intra-observer reliability was performed through a reproducibility analysis of 20 randomly selected aortic diameter measurements obtained during maternal echocardiographic examinations. This analysis provided a quantitative evaluation of measurement consistency and minimized potential observer-related variability. Two independent repeated measurements were acquired by the same experienced examiner under identical conditions to evaluate intra-observer consistency.

Statistical Analysis

All statistical analyses were performed using SPSS version 27.0 (IBM Corp., Armonk, NY, USA). Continuous variables are presented as mean ± standard deviation (SD). Intraobserver

consistency was evaluated using Cochran's Q test. The association between placental pulsatility index (PPI) and maternal echocardiographic parameters was assessed using the Pearson product–moment correlation coefficient. Nonparametric tests were applied for variables that did not conform to a normal distribution. A two-tailed P value <0.05 was considered statistically significant.

Result

Study Population

A total of 389 healthy pregnant women were included in the present study. Among the analyzed singleton pregnancies, 8 cases (2.1%) were conceived via in vitro fertilization (IVF), whereas the majority, 381 cases (97.9%), resulted from spontaneous conception. The median maternal age was 29.0 years (range: 18–45 years). At the time of ultrasound assessment, the median gestational age was 27+2 weeks (range: 14+0 to 40+2 weeks). The median placental pulsatility index (PPI) was 0.96, with values ranging from 0.53 to 2.26.

Assessment of Measurement Repeatability

The analysis demonstrated excellent internal consistency, as evidenced by a Cronbach's alpha coefficient of 1.000, indicating near-perfect agreement between successive measurements obtained by the same observer. Cochran's Q test was subsequently applied to determine whether statistically significant systematic differences existed among the repeated measurements across participants. The results revealed no statistically significant discrepancy between the paired measurements (Cochran's Q = 0.250, p = 0.617), confirming the stability, precision, and reproducibility of the echocardiographic acquisition protocol. The absolute measurement differences ranged from −0.02 to 0.01 cm, with a mean difference of 0.0010 cm and a standard deviation of 0.00912 cm, collectively reflecting a negligible degree of intra-observer variability.

Left Ventricular Systolic Function and Hemodynamics

PPI demonstrated a modest association with left ventricular ejection fraction (EF) (r = 0.109, P = 0.050) and a moderate inverse correlation with cardiac output (CO) (r = −0.237, P < 0.001). No significant associations were identified between PPI and fractional shortening (FS) or stroke volume (SV). Overall, these results indicate limited and inconsistent relationships between PPI and conventional indices of LV systolic performance. (Table1)

Table 1 Correlations between placental pulsatility index (PPI) and Left Ventricular Systolic Function and Hemodynamics

	PPI	FS	EF	SV	Cardiac Output
PPI	1	.093	.109*	-.065	-.237**
FS		1	.918**	.462**	.404**
EF			1	.409**	.357**
SV				1	.851**
Cardiac Output					1

*p < 0.05 and **p < 0.01

LV FS: Left Ventricular Fractional Shortening; LV EF: Left Ventricular Ejection Fraction; SV: Stroke Volume; CO: Cardiac Output

Left Ventricular Diastolic Function and Hemodynamics

In contrast, PPI was more consistently associated with parameters of LV diastolic function. Significant positive correlations were observed with early transmitral inflow velocity (E) (r = 0.125, P = 0.024) and the E/A ratio (r = 0.227, P < 0.001). Tissue Doppler analysis further demonstrated positive correlations between PPI and interventricular septal E/A ratio (r = 0.254, P < 0.001) as well as lateral e′ velocity (r = 0.162, P = 0.003). Conversely, PPI was negatively correlated with septal a′ velocity (r = −0.181, P = 0.001) and lateral a′ velocity (r = −0.161, P = 0.004). These findings indicate that elevated PPI is primarily associated with alterations in maternal LV diastolic function. (Table2).

Table 2. Correlations between placental pulsatility index (PPI) and Left Ventricular Diastolic Function and Hemodynamics

	PPI	MV E	MV A	MV E/A ratio	IVS e′	IVS a′	IVS e′/a′ ratio	LW e′	LW a′	LW e′/a′ ratio	LV E/e′ ratio
PPI	1	.125*	-0.104	.227**	0.098	-.181**	.254**	.162**	-.161**	.193**	-0.049
MV E		1	.453**	.427**	.229**	0.050	.116*	.237**	0.072	0.089	.567**
MV A			1	-.592**	0.038	.463**	-.350**	-0.014	.244**	-.183**	.377**
MV E/A ratio				1	.196**	-.424**	.497**	.231**	-.169**	.258**	.159**
IVS e′					1	.178**	.509**	.417**	.102*	.184**	-.143**
IVS a′						1	-.709**	-0.098	.453**	-.383**	.111*
IVS e′/a′ ratio							1	.352**	-.311**	.454**	-.179**
LW e′								1	0.023	.574**	-.608**
LW a′									1	-.733**	0.024
LW e′/a′ ratio										1	-.375**
LV E/e′ ratio											1

*p < 0.05 and **p < 0.01

MVE: Mitral valve peak velocity of the early diastolic filling wave; MVA: Mitral valve peak velocity of the atrial contraction wave; IVS e′: Tissue Doppler of early diastolic velocities of the interventricular septal; IVS a′: Tissue Doppler of late diastolic velocities of the interventricular septal; LW e′: Tissue Doppler of early diastolic velocities of the Lateral Wall; LW a′: Tissue Doppler of late diastolic velocities of the Lateral Wall; LV E/e′ ratio: Left Ventricular E/e′ Ratio

Ascending Aorta and Main Pulmonary Artery Hemodynamics

PPI was not significantly associated with most aortic or pulmonary flow parameters, including peak systolic velocities and pressure gradients. However, weak positive correlations were observed with aortic and pulmonary artery velocity–time integrals. With respect to valvular annular dimensions, PPI demonstrated a modest inverse correlation with mitral annular diameter (r = −0.110, P = 0.048) and a more pronounced negative correlation with pulmonary artery annular diameter (r = −0.204, P < 0.001), whereas no significant association was identified with the aortic annulus. Collectively, these findings suggest minimal involvement of large-vessel hemodynamics in the relationship between PPI and maternal cardiovascular adaptation. (Table3).

Table 3 Correlations between placental pulsatility index (PPI) and Outflow tract hemodynamics

	AO pSV	AO mV	AO pPG	AO mPG	AO VTI	PA pSV	PA mV	PA pPG	PA mPG	PA VTI
PPI	1 -0.080	-0.089	-0.091	-0.100	.126*	-0.024	-0.040	-0.011	-0.022	.110*
AO pSV	1	.875**	.985**	.893**	.704**	.474**	.421**	.467**	.417**	.357**
AO mV		1	.867**	.959**	.646**	.471**	.471**	.469**	.467**	.352**
AO pPG			1	.898**	.681**	.493**	.439**	.482**	.436**	.364**
AO mPG				1	.640**	.472**	.462**	.471**	.468**	.364**
AO VTI					1	.283**	.246**	.256**	.246**	.395**
PA pSV						1	.884**	.972**	.864**	.713**
PA mV							1	.866**	.898**	.696**
PA pPG								1	.857**	.690**
PA mPG									1	.645**
PA VTI										1

*p < 0.05 and **p < 0.01

AO pSV: Ascending Aorta Peak Systolic Velocity; AO mV: Ascending Aorta Mean Velocity; AO pPG: Ascending Aorta Peak Pressure Gradient; AO mPG: Ascending Aorta Mean Pressure Gradient; AO VTI: Ascending Aorta Velocity Time Integral; PA pSV: Main pulmonary artery Peak Systolic Velocity; PA mV: Main pulmonary artery Mean Velocity; PA pPG: Main pulmonary artery Peak Pressure Gradient; PA mPG: Main pulmonary artery Mean Pressure Gradient; PA VTI: Main pulmonary artery Velocity Time Integral

Left Ventricular Morphologic Remodeling

Pearson correlation analysis demonstrated that the placental pulsatility index (PPI) was significantly associated with indices of left ventricular (LV) structural remodeling, although correlations were generally weak. PPI showed significant inverse correlations with interventricular septal thickness in diastole (IVSd) ($r = -0.139$, $P = 0.012$), LV internal diameter in diastole (LVIDd) ($r = -0.134$, $P = 0.016$), and LV internal diameter in systole (LVIDs) ($r = -0.123$, $P = 0.026$). Similarly, LV volumetric indices, including end-diastolic volume (EDV) ($r = -0.126$, $P = 0.024$) and end-systolic volume (ESV) ($r = -0.181$, $P = 0.001$), were inversely correlated with PPI. No significant associations were observed with left ventricular posterior wall thickness, interventricular septal-to-posterior wall ratio, or atrial dimensions. These findings suggest that higher PPI is associated with modest reductions in LV chamber size and volume. (Table4 & Table5).

Table 4 Correlations between placental pulsatility index (PPI) and maternal cardiac structural parameters (1)

	PPI	IVSd	IVSs	LVIDd	LVIDs	LVPWd	LVPWs	EDV	ESV	IVS/LVPW	IVS%
PPI	1	-.139*	-0.094	-.134*	-.123*	-0.034	-0.024	-.125*	-.181**	-0.047	0.046
IVSd		1	.480**	-0.047	-0.077	.218**	.285**	-0.058	0.015	.129*	-.543**
IVSs			1	0.084	-.115*	.246**	.316**	.106*	-0.071	0.043	.454**
LVIDd				1	.621**	-0.023	.116*	.884**	.712**	0.019	.133**

LVIDs	1	-0.020	-.107*	.624**	.880**	0.042	-0.046
LVPWd		1	.394**	-0.009	-0.002	-0.011	0.023
LVPWs			1	.104*	-0.065	0.030	0.015
EDV				1	.733**	-.260**	.160**
ESV					1	0.051	-0.082
IVS/LVPW						1	-0.068
IVS%							1

*p < 0.05 and **p < 0.01

IVSd: Interventricular Septal Thickness in Diastole; IVSs: Interventricular Septal Thickness in Systole; LVIDd: Left VentricularInternal Diameter in Diastole; LVIDs: Left Ventricular Internal Diameter in Systole; LVPWd: Left Ventricular Posterior Wall Thickness in Diastole; IVPWs: Left Ventricular Posterior Wall Thickness in Systole; EDV: Left Ventricular End-Diastolic Volume; ESV: Left Ventricular End-Systolic Volume; IVS/LVPW: Interventricular Septum to Left Ventricular Posterior Wall Ratio; IVS%: Interventricular Septal Thickness Percentage

Table 5 Correlations between placental pulsatility index (PPI) and maternal cardiac structural parameters (2)

	PPI	LAVD	LATD	RAVD	RATD	LVLD	LVTD	RVLD	RVTD	MV Annulus	TV Annulus	AO Annulus	PA Annulus
PPI	1	-.015	-.012	-.099	-.028	0.044	0.073	0.095	0.097	-.110*	-0.053	.133*	-.204**
LAVD		1	.482**	.693**	.490**	-0.019	.585**	.585**	.556**	-0.002	-0.006	0.098	.242**
LATD			1	.469**	.521**	-0.008	.356**	.345**	.391**	0.000	-0.006	0.071	.145**
RAVD				1	.364**	-0.005	.415**	.406**	.417**	0.012	0.015	.122*	.284**
RATD					1	0.013	.359**	.350**	.419**	0.000	0.018	0.046	.199**
LVLD						1	0.022	0.061	0.001	-0.011	-0.004	0.041	0.058
LVTD							1	.533**	.593**	-0.040	-0.057	.173**	.203**
RVLD								1	.557**	0.024	0.022	0.087	.222**
RVTD									1	0.024	0.033	.156**	.165**
MV Annulus										1	.985**	0.046	0.091
TV Annulus											1	0.040	.108*
AO Annulus												1	-0.060
PA Annulus													1

*p < 0.05 and **p < 0.01

LAVD: Left Atrial Vertical Diameter; LATD: Left Atrial Transverse Diameter; RAVD: Right Atrial Vertical Diameter; RATD:

Right Atrial Transverse Diameter; LVLD: Left Ventricular Length Diameter; LATD: Left Ventricular Transverse Diameter;
RVLD: Right Ventricular Length Diameter; RVTD: Right Ventricular Transverse Diameter; MV Annulus: Mitral Valve Annulus Diameter; TV Annulus: Tricuspid Valve Annulus Diameter; AO Annulus: Aortic Valve Annulus; PA Annulus: Pulmonary Valve Annulus Diameter

Discussion

Overview

The present investigation examines associations between the Placental Pulsatility Index (PPI) and a broad range of maternal echocardiographic parameters in 389 singleton pregnancies. PPI combines umbilical and uterine artery pulsatility indices into a single composite measure of total uteroplacental resistance, capturing both fetoplacental and maternal vascular contributions simultaneously. This integrative approach was motivated by evidence that neither index alone adequately represents the hemodynamic burden at the maternal–fetal interface[12].

Normal pregnancy imposes a sustained and substantial cardiovascular load. Cardiac output rises considerably from early gestation, initially through increases in stroke volume and later through a rise in heart rate, while systemic vascular resistance falls in response to nitric oxide, prostacyclin, relaxin, and placenta-derived angiogenic factors including PlGF[25, 26]. Serial echocardiographic studies have documented progressive eccentric left ventricular remodeling then expanding chamber dimensions, rising end-diastolic volumes, and increasing stroke volume driven by plasma volume expansion and reduced afterload[2, 27]. Against this background, PPI indexes the hemodynamic state at the placental interface, and deviations in its value are expected to track, and potentially shape, the trajectory of maternal cardiac adaptation throughout gestation[15, 17, 28].

PPI and Cardiac Output

The most direct hemodynamic finding was a significant inverse relationship between PPI and maternal cardiac output ($r = -0.237$, $p < 0.001$). This is not unexpected given the known physiology: as uteroplacental resistance declines in normal pregnancy, effective cardiac afterload falls and output rises to meet the demands of the growing fetal-placental unit. Where resistance remains relatively elevated, that output augmentation is proportionally blunted.

Several independent groups have documented this relationship across different clinical contexts. Tay et al. showed, in a study spanning normotensive, preeclamptic, and FGR pregnancies, that uterine artery pulsatility index correlated negatively with cardiac output and positively with peripheral vascular resistance, and these associations held irrespective of hypertensive status[18]. Maseliene et al. reported similar findings in a prospective echocardiographic study of normotensive and hypertensive pregnancies, noting that both uterine and umbilical pulsatility indices rose in tandem with falling cardiac output[29]. A meta-analysis of normotensive and hypertensive pregnancies likewise confirmed that peripheral vascular resistance and cardiac output move in opposing directions as uteroplacental impedance shifts[14]. Papastefanou et al. further argued, on the basis of a large mid-gestation cohort, that placental Doppler variables were stronger determinants of birthweight than maternal cardiac output in itself[30], placing the placental vascular bed upstream in the maternal–fetal hemodynamic hierarchy.

The present findings extend this relationship between PPI and fetal output across the entire gestational spectrum in uncomplicated pregnancies, indicating that it represents a

physiological continuum rather than a threshold phenomenon limited to overt clinical pathology. Even within the normal range, higher PPI values may reflect a comparatively less complete maternal cardiovascular adaptation to the hemodynamic demands of pregnancy.

Diastolic Function

The diastolic findings were the most consistent in the dataset, with significant associations observed across transmitral Doppler, septal TDI, and lateral TDI, three methodologically distinct assessments of left ventricular filling. Higher PPI was associated with higher mitral E/A ratio ($r = 0.227$, $p < 0.001$), higher septal e'/a' ($r = 0.254$, $p < 0.001$), and higher lateral e'/a' ($r = 0.193$, $p < 0.001$), alongside reductions in late diastolic annular velocities (a') at both septal and lateral sites. The coherence of this pattern across independent measurement modalities strengthens confidence that the relationship is real rather than a statistical artifact.

Physiologically, these findings point to a reduced atrial contribution to late diastolic filling in women with higher placental impedance. Bamfo et al. documented that septal and lateral a' velocities rise across normal gestation, reflecting the increasing role of atrial systole in augmenting ventricular filling as pregnancy progresses[31]; the attenuated a' values in higher-PPI pregnancies represent a departure from that trajectory. Fok et al. similarly demonstrated that Em/Am ratios fall progressively with advancing gestational age in normal pregnancy, indicating a shifting balance between early and late diastolic filling components [32]. Valensise et al. offered relevant longitudinal evidence: in normotensive primigravidae followed across the first two trimesters, isovolumetric relaxation time correlated inversely with uterine artery resistance index, suggesting that falling placental impedance and improving myocardial relaxation are temporally coupled[33]. The present cross-sectional findings are consistent with this temporal framework, suggesting that, at any given gestational age, women with higher PPI exhibit a diastolic profile that departs modestly yet consistently from the expected pattern of cardiovascular adaptation.

The E/e′ ratio, the most widely used noninvasive surrogate of left ventricular filling pressure, was not significantly associated with PPI ($r = −0.049$, $p = 0.380$), despite significant associations between PPI and each of its individual components, E and e′[34, 35]. Since both numerator and denominator co-varied proportionally across the PPI range, their ratio remained stable, arguing against any meaningful elevation of filling pressure. This reframes the observed diastolic changes as adaptive modulation of filling dynamics rather than early diastolic dysfunction. The recognized limitations of E/e′ in pregnant populations may also explain its relative insensitivity in the present study, as both E and e′ undergo non-linear gestational changes that can diminish the ratio's ability to discriminate subtle differences in diastolic function[36, 37]. The maternal ventricle appears to recalibrate its filling strategy in response to PPI-related loading changes while preserving filling pressure homeostasis. Whether this recalibration becomes insufficient at higher levels of placental impedance, as seen in preeclampsia or severe FGR, is a question the present data cannot answer but one that warrants prospective investigation.

Mechanistically, the diastolic sensitivity to PPI likely reflects PPI's influence on ventricular loading conditions. Elevated placental resistance modestly reduces effective preload and alters afterload dynamics, to which diastolic parameters are particularly sensitive. PlGF, whose secretion declines with placental dysfunction, is a key modulator of systemic resistance and cardiac afterload[38, 39]; its relative reduction may shift ventricular filling patterns even in pregnancies that remain clinically uncomplicated.

Systolic Function and Outflow Hemodynamics

In contrast to the diastolic domain, associations between PPI and systolic parameters were weaker and less consistent. Ejection fraction (Teichholz method) showed only a borderline correlation with PPI (r = 0.109, p = 0.050), and aortic peak velocity, mean velocity, and transvalvular gradients were not significantly associated. This is consistent with prior evidence that global left ventricular systolic performance is robustly maintained during pregnancy even when placental and hemodynamic indices are perturbed[25, 27, 40]. Garcia-Gonzalez et al., in a large cohort of uncomplicated pregnancies at 35–37 weeks, demonstrated that PlGF was the dominant predictor of maternal hemodynamic indices, with placental function more closely linked to cardiac output and peripheral resistance than to intrinsic systolic contractility[38]; the present findings align with that hierarchy.

Notably, the only outflow variable associated with PPI was the velocity–time integral (VTI) in both the aortic and pulmonary tracts. Because VTI serves as a surrogate of stroke volume, this finding suggests that PPI is more closely related to total forward flow per beat than to instantaneous velocity or pressure generation.[35]. The dissociation between VTI and pressure-velocity indices suggests that PPI modulates stroke volume through preload-dependent mechanisms: when placental resistance is higher and venous return is relatively attenuated, the heart ejects a somewhat smaller volume per beat without altering intrinsic ejection mechanics. This is consistent with the concept that maternal hemodynamic adaptation to placental resistance operates primarily through volume and loading adjustments rather than changes in myocardial contractility[3, 17].

Cardiac Structural Associations

PPI was inversely associated with several structural parameters of the left ventricle: interventricular septal thickness in diastole (r = −0.139, p = 0.012), LV internal diameter in diastole (r = −0.134, p = 0.016), LV internal diameter in systole (r = −0.123, p = 0.026), end-diastolic volume (r = −0.125, p = 0.024), and end-systolic volume (r = −0.181, p = 0.001). These findings point toward less marked eccentric remodeling in pregnancies with higher placental resistance, consistent with the interpretation that PPI-related preload attenuation limits the volume-driven chamber expansion that characterizes normal gestational adaptation[28, 41]. The inverse association with IVSd further suggests that indices of ventricular wall thickness, which are largely influenced by pressure and volume loading conditions, remain sensitive to variations in placental impedance even among women with otherwise uncomplicated pregnancies[42].

The valvular annular findings added an unexpected layer of complexity. Pulmonary artery annulus diameter showed the strongest negative correlation with PPI of any structural variable (r = −0.204, p < 0.001), and mitral annulus diameter was also inversely associated (r = −0.110, p = 0.048). Aortic annulus diameter, by contrast, showed a positive association (r = 0.133, p = 0.017). The divergence between pulmonary and aortic directions likely reflects circuit-specific loading dynamics: the pulmonary circulation normally undergoes marked resistance reduction in gestation[27], and blunted PA annular expansion at higher PPI values may indicate attenuated right-sided volume adaptation. The positive aortic annulus association is harder to interpret but may reflect compensatory remodeling of systemic outflow geometry in the context of preserved left ventricular function despite attenuated volume loading. Whether these annular differences carry functional significance or represent geometric variation warrants dedicated investigation.

Clinical Relevance

Taken together, these findings have a reasonably clear practical implication: diastolic assessment is more informative than systolic measurement when evaluating maternal cardiovascular

adaptation to placental vascular disease. Ejection fraction was essentially flat across the PPI range; transmitral and TDI-derived diastolic indices were not. For clinical protocols that currently rely on EF as the primary cardiac endpoint in at-risk pregnancies, this suggests a gap that could be addressed by adding E/A ratio and tissue Doppler annular velocities to the standard assessment.

The preservation of E/e' ratios across the PPI range in this uncomplicated cohort implies that the diastolic changes observed represent physiological adaptation rather than early cardiac decompensation. However, it does not preclude filling pressure elevation when placental dysfunction is more severe preeclampsia and FGR may represent a continuum from the subtle changes seen here to overt diastolic impairment. Prospective studies with outcome data are needed to determine whether specific PPI or diastolic thresholds predict subsequent maternal cardiovascular deterioration.

Strengths and Limitations

The cohort of 389 singleton pregnancies spanning 14 to 40 weeks of gestation provided adequate statistical power for correlation analyses and enabled examination of associations across the full gestational spectrum. Echocardiography was performed according to ASE guidelines and encompassed a comprehensive multidomain parameter set. The use of PPI as a composite Doppler index rather than individual vessel pulsatility indices strengthens the physiological interpretability of the findings. Rigorous exclusion criteria minimized confounding from maternal comorbidities and fetal structural pathology.

The primary limitation is the cross-sectional nature of the study, which assesses participants at a single time point and therefore cannot establish temporal sequence or causal inference. Consequently, it remains unclear whether increased placental impedance precedes changes in maternal cardiac structure and function or develops as a consequence of them. Pearson correlation was the sole analytical method; no adjustment was made for gestational age, BMI, parity, or other established covariates of both echocardiographic and Doppler parameters, and residual confounding cannot be excluded. The single-center design within a Chinese tertiary institution limits generalizability to other ethnic and healthcare settings. Inter-observer reliability was not formally quantified. Finally, the absence of perinatal outcome data precluded any assessment of the prognostic significance of the observed associations. Multicentre longitudinal studies with serial echocardiographic assessments and linked pregnancy outcomes are needed before these findings can inform clinical practice.

Conclusion

PPI associates with maternal cardiac function across multiple echocardiographic domains, with the strongest and most consistent signal in diastolic parameters. Systolic indices show limited sensitivity to variation in placental vascular resistance within an uncomplicated pregnancy cohort. The diastolic changes appear to reflect adaptive modulation of ventricular filling in response to altered loading conditions rather than pathological dysfunction, given the preservation of filling pressure estimates across the PPI range. Structurally, higher PPI tracks with attenuation of the physiological eccentric remodeling that characterizes normal gestation. Collectively, these observations support a quantitative maternal–placental hemodynamic relationship that is present throughout uncomplicated pregnancy and may become clinically relevant when placental resistance is more substantially elevated. Whether incorporating PPI into diastolic function assessment can enhance the early identification of pregnancies at risk for maternal cardiovascular maladaptation warrants prospective investigation.

Article Information

Acknowledgments

We acknowledge support from the Funding: Jiangxi Provincial Health Commission Research Project (No. 202611564). Our work is supported by the Department of ultrasound and the Department of obstetrics and gynecology partnership Yichun Maternal & Child Health Hospital, Jiangxi, China, and funding from the Jiangxi Provincial Health Commission Research Project funding scheme.

Funding

Jiangxi Provincial Health Commission Research Project (No. 202611564)

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Data Availability Statement

Data is available from the corresponding author upon reasonable request, with appropriate regulatory approvals. All data relevant to the study was included in the article.

Declarations

Ethics approval and consent to participate

This study was approved by the Medical Research Ethics Review Committee of Yichun Maternal and Child Health Hospital, Jiangxi Province, China (Approval No. 2025004-LW004). Written informed consent was obtained from all participants prior to inclusion. In accordance with institutional protocols, all patients routinely provide written authorization permitting the use of their clinical data for research purposes as part of standard medical practice.

Consent for Publication

Written informed consent was obtained from the patient for the publication of all associated data. The patient was fully informed that any personally identifiable information would be anonymized to ensure confidentiality and privacy.

Conflict of interest declaration:

All authors declare that he does not have any competing interests.

AI Statement

The manuscript underwent linguistic refinement using ChatGPT(free web version) to improve English spelling, grammar, and sentence structure. All revisions were carefully reviewed and validated by the authors to ensure accuracy, clarity, and preservation of the original scientific content.

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