Received: 5 June 2025 | Revised: 29 August 2025 | Accepted: 10 September 2025

DOI: 10.1111/aogs.70059

ORIGINAL RESEARCH

Ophthalmic artery Doppler and carotid intima-media thickness 3–6 years postpartum in women with and without a history of placental insufficiency

Pablo Garcia-Manau[1,2,3,4] | Judit Platero[1,3,5] | Noah Costa[5,6] | Zoraida Garcia[5,6] | Carmen Garrido-Giménez[1,3,5,6] | Claudia Pellicer[1] | Johana Ullmo[1,3,5] | Madalina Nan[7,8] | Josefina Mora[6,7,8] | Alvaro Garcia-Osuna[7,8] | Olga Sánchez-Garcia[5,6] | Mariona Jordi[1] | Marta Choliz[1] | Mónica Cruz-Lemini[1,3,5,6] | Cristina Trilla[1,3,5,6] | Carla Dominguez-Gallardo[1,3,5] | Elisa Llurba[1,3,5,6]

[1]Department of Obstetrics and Gynecology, Maternal-Fetal Medicine Unit, Hospital de la Santa Creu i Sant Pau, Universitat Autònoma de Barcelona, Barcelona, Spain

[2]Nephrology Research Group, Institut de Recerca (IR SANT PAU), Barcelona, Spain

[3]Departament de Pediatria, Obstetrícia i Ginecologia i de Medicina Preventiva i Salut Pública, Universitat Autònoma de Barcelona, Bellaterra, Spain

[4]Primary Care Interventions to Prevent Maternal and Child Chronic Diseases of Perinatal and Developmental Origin Network (RICORS-SAMID, RD21/0012/0019), Instituto de Salud Carlos III, Madrid, Spain

[5]Women and Perinatal Health Research Group, Institut de Recerca (IR SANT PAU), Barcelona, Spain

[6]Spanish Network in Maternal, Neonatal, Child and Developmental Health Research (RICORS-SAMID, RD24/0013/0001) and Primary Care Interventions to Prevent Maternal and Child Chronic Diseases of Perinatal and Developmental Origin Network (RICORS-SAMID, RD21/0012/0001), Instituto de Salud Carlos III, Madrid, Spain

Abstract

Introduction: Preeclampsia and fetal growth restriction, which are clinical presentations of placental dysfunction, are frequently associated with angiogenic imbalance during pregnancy and increased long-term cardiovascular risk. Whether this risk is driven by the pre-pregnancy risk factors, clinical disease, or by an elevated sFlt-1/PlGF ratio remains unclear. This study aimed to assess the association between vascular assessments (ophthalmic artery Doppler and carotid intima-media thickness) 3–6 years postpartum and a history of preeclampsia and fetal growth restriction, and to evaluate if associations were impacted by an angiogenic imbalance during pregnancy.

Material and Methods: This was a cross-sectional study, which included individuals prospectively recruited during their index pregnancy between 2018 and 2021 and re-evaluated 3–6 years postpartum. Preeclampsia, fetal growth restriction, and sFlt-1/PlGF values were defined from pregnancy data. Postpartum assessment included ophthalmic artery Doppler and carotid intima-media thickness performed by a single operator. Multivariable linear regression models assessed associations between placental dysfunction, angiogenic imbalance, and vascular parameters, adjusting for maternal covariates.

Results: 354 participants were included, 148 with and 206 without a history of preeclampsia or fetal growth restriction. Both placental dysfunction and angiogenic imbalance during pregnancy were independently associated with a significantly higher

Abbreviations: CIMT, carotid intima-media thickness; FGR, fetal growth restriction; OA-PI, ophthalmic artery pulsatility index; OA-PSV ratio, ophthalmic artery peak systolic velocity ratio; OA-PSV1, ophthalmic artery first systolic velocity peak; OA-PSV2, ophthalmic artery second systolic velocity peak; PE, preeclampsia; PlGF, placental growth factor; sFlt-1, soluble fms-like tyrosine kinase-1.

Pablo Garcia-Manau and Judit Platero contributed equally.

[7]Department of Clinical Biochemistry, Hospital de la Santa Creu i Sant Pau, Institut d'Investigació Biomèdica Sant Pau (IIB Sant Pau), Barcelona, Spain

[8]Department of Biochemistry and Molecular Biology, Facultat de Medicina, Universitat Autònoma de Barcelona, Barcelona, Spain

Correspondence
Pablo Garcia-Manau, Department of Obstetrics and Gynecology, Maternal-Fetal Medicine Unit, Hospital de la Santa Creu i Sant Pau, Universitat Autònoma de Barcelona, Sant Quintí 89, 08025, Barcelona, Catalonia, Spain.
Email: pgarciamanau@gmail.com

Funding information
Instituto de Salud Carlos III, Grant/Award Number: PI22/00462; Spanish Clinical Research Network, Grant/Award Number: PT13/0002/0028

ophthalmic artery peak systolic velocity ratio 3–6 years postpartum. Participants with a history of placental dysfunction showed higher values compared to those without [0.75 (0.67–0.81) vs. 0.69 (0.63–0.78), $p=0.03$], as did those with an elevated sFlt-1/PlGF ratio during pregnancy [0.76 (0.66–0.82) vs. 0.70 (0.64–0.78), $p=0.03$]. The highest values were observed in women who had experienced both conditions. When preeclampsia and fetal growth restriction were analyzed separately, the association remained significant for preeclampsia, whereas in the fetal growth restriction group, a significant difference was observed only in the right eye. No statistically significant differences were observed in carotid intima-media thickness.

Conclusions: Both a history of angiogenic imbalance and a clinical placental dysfunction presentation (particularly preeclampsia) during pregnancy were associated with increased ophthalmic artery peak systolic velocity ratio 3–6 years postpartum, whereas carotid intima-media thickness did not differ between the study groups.

KEYWORDS
angiogenic factors, cardiovascular, fetal growth restriction, ophthalmic artery, PlGF, preeclampsia, sFlt-1

1 | INTRODUCTION

Placental insufficiency is a pathological condition characterized by impaired placental perfusion.[1] This dysfunction often presents as preeclampsia (PE) or fetal growth restriction (FGR) but may also lead to other major obstetric complications, including stillbirth, preterm birth, and placental abruption.[1,2] This condition is the leading cause of maternal admission to intensive care units during pregnancy, contributing to significant healthcare costs.[3,4] The underlying mechanisms of placental insufficiency remain incompletely understood, though syncytiotrophoblast stress is considered the pathophysiological hallmark.[5,6] This stress may arise from inadequate placentation early in pregnancy, ischemia–reperfusion injury, or progressive villous crowding in late gestation. This cellular stress triggers the release of multiple factors into the maternal circulation, including an excess of antiangiogenic proteins such as soluble fms-like tyrosine kinase-1 (sFlt-1) and reduced levels of proangiogenic placental growth factor (PlGF), resulting in an elevated sFlt-1/PlGF ratio.[5–7] This imbalance triggers vasoconstriction and increased endothelial vascular permeability and is a direct reflection of syncytiotrophoblast cellular stress, which contributes to maternal and fetal compromise.[2,5,6] Notably, this dysregulation can be detected weeks before the appearance of clinical symptoms.[7,8]

Although placental insufficiency is considered a pregnancy-specific disorder, its impact extends far beyond delivery. It is well established that PE and FGR are significant risk factors for long-term cardiovascular disease, with myocardial dysfunction and adverse cardiac remodeling observed years after the affected pregnancy.[9,10] Angiogenic imbalance has also been linked to an increased long-term cardiovascular risk, with evidence suggesting that elevated sFlt-1/PlGF values during pregnancy are associated with a higher cardiovascular risk up to 12 years postpartum.[11,12] However, the relationship between angiogenic imbalance, its clinical manifestations such as PE and FGR, and other cardiovascular risk factors such as hypertension, in contributing to long-term cardiovascular impairment remains poorly understood. It is unclear whether the increased long-term cardiovascular risk is a consequence of PE itself or is largely driven by other preexisting cardiovascular risk factors.

Key message

Women with both preeclampsia and angiogenic imbalance during pregnancy show a higher ophthalmic artery systolic velocity ratio 3–6 years postpartum. The combination of clinical disease and an abnormal angiogenic profile may better identify individuals at higher long-term cardiovascular risk.

The aim of this study was to assess the impact of placental dysfunction (either PE or FGR) and angiogenic imbalance during pregnancy on ophthalmic artery Doppler and carotid intima-media thickness (CIMT) 3–6 years postpartum.

2 | MATERIAL AND METHODS

This was a cross-sectional study conducted at Hospital de la Santa Creu i Sant Pau between August 2023 and February 2025, including individuals who had been prospectively recruited during their index pregnancy as part of three previous studies conducted between 2018 and 2021 (EUROPE, ANGIOCOR, and BiSC).[13–15] In those studies, clinical data on maternal history and pregnancy complications were collected. Serum concentrations of PlGF and sFlt-1 (pg/mL)

were measured during pregnancy using fully automated Elecsys® assays on an electrochemiluminescence immunoassay platform (cobas e analyzers; Roche Diagnostics, Penzberg, Germany), regardless of whether or not the participants developed any clinical manifestations of placental insufficiency, as specified in the protocols of the three studies. However, the sFlt-1/PlGF ratio could not be obtained systematically in every case. When available, sFlt-1/PlGF ratio values were classified into two categories (<38 and ≥38) in order to simplify the analysis, as 38 is the threshold commonly used to define abnormal angiogenic status in the context of PE.[8] PE was defined, according to the American College of Obstetricians and Gynecologists, as new-onset hypertension or worsening of preexisting hypertension during pregnancy, accompanied by proteinuria (protein/creatinine ratio of 0.3 mg/dL or more or dipstick reading of 2+ if quantitative method was not available) or evidence of maternal organ dysfunction, either clinical or laboratory-based. Organ dysfunction criteria included: thrombocytopenia (platelet count $<100\times10^9$/L), renal insufficiency (serum creatinine ≥1.1 mg/dL or a doubling of baseline values in the absence of underlying renal disease), hepatic dysfunction (elevated liver transaminases to twice normal concentration), epigastric or right upper quadrant pain unresponsive to analgesia, pulmonary edema, new-onset headache unresponsive to treatment and not explained by alternative diagnoses, or visual disturbances such as blurred vision or photopsia.[16] FGR was defined as an estimated fetal weight below the 3rd centile or between the 3rd and 10th centiles with any fetomaternal Doppler abnormality, including uterine arteries, umbilical artery, middle cerebral artery, or cerebroplacental ratio.[17] All cases diagnosed with PE or FGR were cross-checked to confirm the diagnosis.

Participants were re-assessed between 3 and 6 years after their index pregnancy, after providing written informed consent approved by the Ethics Committee of the same institution (IIBSP-MOM-2022-87) on 19 July 2023. Maternal demographic characteristics and medical history were recorded. Diet and physical activity were evaluated using the REGICOR questionnaires, both validated in the Spanish population.[18,19] The assessment included arterial blood pressure measurement and the evaluation of CIMT and ophthalmic artery Doppler using an Affiniti 70G ultrasound system (Philips Healthcare, Andover, MA, USA) with a 7–12 MHz linear array transducer, with participants in the supine position. All measurements were performed by the same researcher to minimize inter-observer variability.

Blood pressure was measured once in a single arm, with the participant in a seated position, after a 5-min rest period, using an automated sphygmomanometer. For CIMT assessment, as the ultrasound system did not support semi-automated measurements, manual measurements were obtained from the far wall at 1 cm, 1.5 cm, and 2 cm proximal to the carotid bulb. Mean values for the right and left common carotid arteries were calculated from three consecutive cardiac cycles.[20] For ophthalmic artery Doppler evaluation, the transducer was placed transversely over the participant's closed upper eyelid. Color flow was used to identify the ophthalmic artery, which is found superior and medial to the hypoechoic band representing the optic nerve.[21] Pulsed-wave Doppler was then used to record three to five similar waveforms. The insonation angle was maintained at <20°, with a sample gate size of 2 mm, depth set between 3.0 and 4.5 cm, a high-pass filter at 50 Hz, and a pulse repetition frequency of 125 kHz.[22] The analysis included four Doppler indices: the first and second systolic velocity peaks (OA-PSV1 and OA-PSV2), the pulsatility index (OA-PI), and the ratio between the second and first peaks (OA-PSV ratio). The ultrasound system automatically provided the first systolic peak and the pulsatility index, while the second systolic peak was manually measured. The OA-PSV ratio was calculated based on these measurements.[23]

This study was designed as a cross-sectional follow-up of previously recruited participants from prospective pregnancy cohorts, and all eligible individuals were invited to participate in order to maximize representativeness and statistical power. Descriptive data were presented as median and interquartile range (IQR) for continuous variables and as numbers and percentages for categorical variables. Normality was assessed using the Shapiro–Wilk test. Group comparisons were conducted using the Mann–Whitney *U*-test or Student's *t*-test for quantitative variables, while the chi-square test or Fisher's exact test was used for categorical variables, as appropriate. To assess the association between previous PE or FGR and ophthalmic artery Doppler or CIMT parameters, univariable and multivariable linear regression models were performed. Multivariable models were adjusted for clinically relevant covariates identified a priori based on existing literature and biological plausibility, rather than solely on statistical significance in univariable analyses. This approach aimed to account for most potential confounding factors. The selected covariates included maternal age, body mass index, smoking status, race/ethnicity, parity, mean arterial blood pressure, diabetes mellitus, autoimmune disease, dyslipidemia, and menopause. This strategy ensures consistency across models and reduces the risk of residual confounding. Results were expressed as coefficients with standard errors (SE), 95% confidence intervals (CI), and *p*-values. To explore the interaction between clinical history of placental dysfunction and angiogenic imbalance, we performed a multivariate linear regression model using mean OA-PSV ratio as the dependent variable. The main predictor was a four-category variable combining clinical history of placental dysfunction (PE or FGR vs. none) and angiogenic profile (sFlt-1/PlGF ≥38 vs. <38) with the group of individuals without placental dysfunction and with a normal angiogenic profile used as the reference. The model was adjusted for the same covariates. All statistical analyses were performed using the Jamovi software (The Jamovi Project, Version 2.3, https://www.jamovi.org). A two-sided *p*-value <0.05 was considered statistically significant. The study was conducted in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.

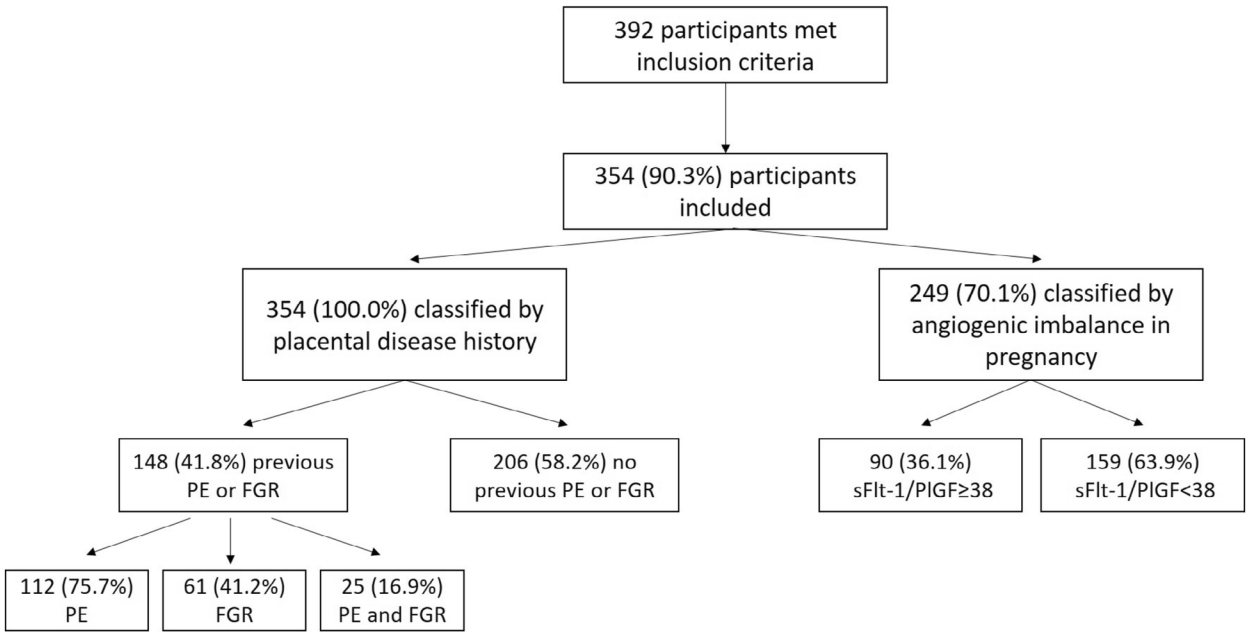

FIGURE 1 Flowchart. PE, preeclampsia; FGR, fetal growth restriction; PlGF, placental growth factor; sFlt-1, soluble fms-like tyrosine kinase-1.

3 | RESULTS

During the study period, 394 participants were included. Among them, 148 (41.8%) had a history of previous PE or FGR, while 206 (58.2%) did not. (Figure 1) No significant differences were observed in baseline characteristics, diet, or physical exercise, except for race, arterial blood pressure values, the rate of current chronic hypertension, gestational age at delivery, and sFlt-1/PlGF values during pregnancy. Further details are provided in Table 1.

Multivariable logistic regression analysis showed that a history of placental dysfunction was significantly associated with a higher mean OA-PSV ratio compared to those without a history of PE or FGR [0.75 (0.67–0.81) vs. 0.69 (0.63–0.78), $p=0.03$]. This difference was mainly driven by higher OA-PSV ratio values in the right eye ($p=0.01$), whereas no significant difference was observed in the left eye. No significant differences were found in OA-PI, OA-PSV1, or OA-PSV2 in either eye. Similarly, no differences were observed in right, left, or mean CIMT between groups. More details are provided in Table 2.

Participants were also classified according to angiogenic imbalance during gestation (≥38 or <38). sFlt-1 and PlGF values were available for 249 (70.1%) participants. Of these, 159 individuals (63.9%) had a normal angiogenic profile (sFlt-1/PlGF <38), while 90 (36.1%) showed abnormal angiogenic values (sFlt-1/PlGF ≥38). (Figure 1) According to this classification, baseline characteristics differed between groups in BMI, parity, arterial blood pressure values, and the rates of current and previous chronic hypertension and gestational age at delivery. Gestational age at sFlt-1/PlGF determination also differed between groups. No other significant differences were observed between groups. (Table 3) Multivariable linear regression showed that an abnormal angiogenic profile was associated with a significantly higher mean OA-PSV ratio compared to those with a normal profile [0.76 (0.66–0.82) vs. 0.70 (0.64–0.78), $p=0.03$]. This increase was mainly driven by higher OA-PSV ratio values in the right eye, which showed a statistically significant difference between groups ($p=0.02$), whereas no differences were observed in the left eye, although a trend was noted ($p=0.05$). No significant differences were found for other ophthalmic artery Doppler indices or CIMT measurements. More details are provided in Table 4.

After analyzing the interaction between the clinical history of placental dysfunction and angiogenic imbalance, individuals with both a history of placental dysfunction and an abnormal angiogenic profile during pregnancy showed significantly higher OA-PSV ratio values compared to the reference group ($\beta=0.04$, 95% CI [0.01–0.08], $p<0.01$). In contrast, no significant differences were observed among those with only a history of placental dysfunction or only an abnormal sFlt-1/PlGF value during gestation (Table 5 and Figure 2).

Supplementary analyses were also performed to explore the associations separately for PE and FGR. For PE, findings were consistent with the main results: individuals with a history of PE had a significantly higher mean OA-PSV ratio compared with those without PE [0.75 (0.68–0.83) vs. 0.70 (0.63–0.78), $p=0.04$]. For FGR, no statistically significant differences were observed in the mean OA-PSV ratio [0.74 (0.67–0.80) vs. 0.71 (0.63–0.80), $p=0.27$]. However, OA-PSV ratio values in the right eye were significantly higher in participants with a history of FGR compared with those without [0.76 (0.66–0.81) vs. 0.71 (0.62–0.80), $p=0.04$]. No relevant differences were found in CIMT measurements in either group. More details can be found in Tables S1–S4.

TABLE 1 Baseline characteristics of study population.

	Previous FGR[a]/PE[b] (*n* = 148)	No previous FGR[a]/PE[b] (*n* = 206)	*p*
Follow-up interval, years	5.16 (4.58–5.75)	5.15 (4.87–5.41)	0.30
Age at inclusion, years	41.8 (37.8–45.4)	40.7 (37.3–44.5)	0.18
Systolic blood pressure, mmHg	122 (113–132)	111 (103–121)	<0.01
Diastolic blood pressure, mmHg	78 (71–83)	73 (67–80)	<0.01
Mean arterial pressure, mmHg	92.0 (85.3–99.7)	85.3 (79.0–93.3)	<0.01
Body mass index, kg/m^2	26.1 (23.1–31.2)	25.4 (22.9–29.9)	0.17
Race or ethnic group[c]			<0.05
Black	7 (4.7)	9 (4.4)	
East Asian	2 (1.3)	1 (0.5)	
Latin American	39 (26.2)	40 (19.4)	
Mixed race	2 (1.3)	2 (1.0)	
South Asian	5 (3.4)	0	
White	94 (63.1)	154 (74.8)	
Primiparous	63 (43.6)	83 (40.3)	0.71
Previous spontaneous pregnancy loss	34 (22.8)	56 (27.2)	0.35
Chronic hypertension	28 (18.8)	16 (7.8)	<0.01
Type 1 or 2 diabetes mellitus	6 (4.0)	5 (2.4)	0.39
Antiphospholipid syndrome	0	2 (1.0)	0.23
Autoimmune disease	4 (2.7)	10 (4.9)	0.30
Dyslipidemia	15 (10.1)	14 (6.8)	0.27
Menopause	10 (6.7)	8 (3.9)	0.22
Current cigarette smoking	16 (10.7)	24 (11.7)	0.34
"Regicor" diet score	24.0 (21.0–26.0)	24.0 (22.0–27.0)	0.25
"Regicor" physical exercise score (MET's/week)	2768.0 (1664.0–4442.0)	3107.0 (1751.0–4569.0)	0.55
sFlt-1 during pregnancy	6446.0 (3035.0–9963.0)	2881.0 (1937.0–4724.0)	<0.01
PlGF during pregnancy	127.0 (60.5–221.0)	266 (156–599)	<0.01
sFlt-1/PlGF during pregnancy	58.2 (13.6–145.0)	10.2 (3.8–26.1)	<0.01
Gestational age at sFlt-1/PlGF determination, weeks	36.2 (34.2–37.5)	35.0 (32.5–38.3)	0.25
Chronic hypertension before pregnancy	13 (8.7)	9 (4.4)	0.09
Gestational age at delivery, weeks	37.6 (36.2–28.9)	39.8 (38.8–40.6)	<0.01
Previous FGR[a]	61 (40.9)	0	<0.01
Delivery <32 weeks	7 (11.5)	0	<0.01
Delivery <37 weeks	25 (41.0)	0	<0.01
Delivery ≥37 weeks	36 (59.0)	0	<0.01
Previous PE[b]	112 (75.2)	0	<0.01
Delivery <34 weeks	12 (10.7)	0	<0.01
Delivery <37 weeks	39 (34.8)	0	<0.01
Delivery ≥37 weeks	73 (65.2)	0	<0.01
sFlt-1/PlGF <38	48/116 (41.4)	111/133 (83.5)	<0.01

Note: Data are the number of events (%) or median (IQR).

Abbreviations: FGR, fetal growth restriction; MET, metabolic equivalent of task; PE, preeclampsia; PlGF, placental growth factor; sFlt-1, soluble fms-like tyrosine kinase-1.

[a]FGR was determined based on Figueras/Gratacos diagnostic criteria.

[b]PE was diagnosed using ACOG criteria.

[c]Race and ethnicity were self-reported by participants from predefined categories.

TABLE 2 Ophthalmic artery Doppler and carotid intima-media thickness in both groups, regardless of sFlt-1/PlGF.

	Previous FGR[a]/PE[b] ($n=148$)	No previous FGR[a]/PE[b] ($n=206$)	Adjusted p[c]
Mean OA-PI	1.64 (1.44–1.89)	1.72 (1.48–1.94)	0.90
Mean OA-PSV ratio	0.75 (0.67–0.81)	0.69 (0.63–0.78)	0.03
Right eye			
OA-PI	1.71 (1.48–1.95)	1.71 (1.51–1.98)	0.99
OA-PSV1, cm/s	30.9 (23.1–35.9)	31.5 (26.8–37.1)	0.07
OA-PSV2, cm/s	22.2 (16.7–26.8)	21.6 (17.3–26.0)	0.70
OA-PSV ratio	0.74 (0.66–0.85)	0.69 (0.60–0.79)	0.01
Left eye			
OA-PI	1.62 (1.39–1.88)	1.70 (1.46–1.94)	0.90
OA-PSV1, cm/s	31.0 (25.2–37.2)	33.6 (27.5–39.3)	0.22
OA-PSV2, cm/s	23.8 (17.6–28.8)	23.3 (19.4–28.0)	0.94
OA-PSV ratio	0.75 (0.67–0.83)	0.70 (0.64–0.79)	0.11
Right CIMT, mm	0.542 (0.480–0.607)	0.518 (0.462–0.574)	0.96
Left CIMT, mm	0.556 (0.497–0.639)	0.534 (0.475–0.606)	0.96
Mean CIMT, mm	0.556 (0.503–0.607)	0.523 (0.484–0.573)	0.97

Note: Data are median (IQR).

Abbreviations: CIMT, carotid intima-media thickness; OA-PI, ophthalmic artery pulsatility index; OA-PSV, ophthalmic artery peak systolic velocity ratio; OA-PSV1, ophthalmic artery first systolic velocity peak; OA-PSV2, ophthalmic artery second systolic velocity peak.

[a]FGR was determined based on Figueras and Gratacos diagnostic criteria.

[b]PE was diagnosed using ACOG criteria.

[c]Adjusted for maternal age, BMI, mean arterial pressure, race or ethnic group, parity, diabetes mellitus, menopause, autoimmune disease, dyslipidemia, and current cigarette smoking.

4 | DISCUSSION

Both angiogenic imbalance and a history of placental dysfunction during pregnancy are associated with a higher OA-PSV ratio 3–6 years postpartum, reflecting increased peripheral vascular resistance. This association was particularly evident among individuals who experienced clinically manifest placental dysfunction (PE or FGR) in the presence of an abnormal angiogenic profile, suggesting that the presence of clinical manifestations of placental dysfunction may be a key determinant of a worse long-term cardiovascular profile. By contrast, neither angiogenic imbalance nor the development of PE or FGR during pregnancy was associated with increased CIMT 3–6 years postpartum.

Ophthalmic artery Doppler serves as a window to the cerebral vasculature, and its impairment is considered an indirect marker of increased peripheral vascular resistance.[22,24] Several studies have demonstrated that ophthalmic artery Doppler can accurately predict PE at various gestational ages, including the first trimester.[23,25–27] Moreover, in women with new-onset hypertension during pregnancy, the OA-PSV ratio and the sFlt-1/PlGF ratio have shown similar, albeit modest, performance in predicting adverse outcomes and delivery within 1 week.[28] However, few studies have instigated whether ophthalmic artery Doppler abnormalities persist in the long term after pregnancy in individuals who develop PE or FGR during gestation. Previous studies have reported abnormal OA-PSV ratio values in the immediate postpartum period and up to 6–9 weeks after delivery in individuals with a history of hypertensive disorders of pregnancy compared to those with normotensive pregnancies.[29,30] Another prospective study evaluated cardiovascular alterations in individuals with and without hypertensive disorders of pregnancy, showing that at two years postpartum, those who had experienced PE or gestational hypertension showed higher OA-PSV ratio values than normotensive controls.[31] However, these studies did not assess whether angiogenic imbalance was associated with long-term cardiovascular impairment, nor did they explore its relationship with the clinical manifestations of placental insufficiency, such as PE and FGR.

Individuals who experience PE are at increased risk of developing atherosclerosis later in life. Previous studies have evaluated CIMT in individuals with a history of PE at various time points postpartum. A case–control study found no increase in CIMT at five years postpartum in individuals with a history of early-onset PE compared to normotensive pregnancies.[32] In contrast, another study reported greater CIMT values at ten years postpartum among individuals with a history of hypertensive disorders of pregnancy.[11] An abnormal angiogenic imbalance during pregnancy has also been correlated by our group with higher CIMT 12 years postpartum in individuals with a history of PE.[12] In our study, conducted from 3 to 6 years after delivery, no differences in CIMT were observed according to the presence or absence of placental dysfunction, nor in relation to angiogenic imbalance. This may reflect a transient and potentially reversible vascular adaptation, or alternatively, that vascular changes may not yet be detectable at this stage.

TABLE 3 Baseline characteristics of study population according to sFlt-1/PlGF ≥ or <38.

	sFlt-1/PlGF ≥38 (*n* = 90)	sFlt-1/PlGF <38 (*n* = 159)	*p*
Follow-up interval, years	5.13 (4.36–5.74)	5.07 (4.28–5.46)	0.12
Age at inclusion, years	41.6 (37.7–44.6)	41.3 (37.3–44.9)	0.87
Systolic blood pressure, mmHg	123 (113–131)	115 (105–124)	<0.01
Diastolic blood pressure, mmHg	78 (72–83)	73 (67–82)	0.01
Mean arterial pressure, mmHg	92.7 (87.0–98.7)	87.0 (79.5–95.7)	<0.01
Body mass index, kg/m^2	28.2 (24.4–32.7)	25.5 (22.7–30.9)	0.02
Race or ethnic group[a]			0.31
Black	2 (2.2)	9 (5.7)	
East Asian	0	2 (1.3)	
Latin American	28 (31.1)	32 (20.1)	
Mixed race	1 (1.1)	2 (1.3)	
South Asian	2 (2.2)	3 (1.9)	
White	57 (63.3)	111 (69.8)	
Primiparous	47 (52.2)	59 (37.1)	0.02
Previous spontaneous pregnancy loss	21 (23.3)	39 (24.5)	0.83
Chronic hypertension	21 (21.3)	18 (11.3)	0.01
Type 1 or 2 diabetes mellitus	5 (5.6)	4 (2.5)	0.22
Antiphospholipid syndrome	0	2 (1.3)	0.29
Autoimmune disease	2 (2.2)	8 (5.0)	0.28
Dyslipidemia	9 (1.0)	13 (8.2)	0.63
Menopause	5 (5.6)	9 (5.7)	0.97
Current cigarette smoking	20 (22.2)	32 (20.1)	0.08
"Regicor" diet score	23.0 (21.0–25.0)	24.0 (22.0–26.0)	0.26
"Regicor" physical exercise score (MET's/week)	3169.0 (1993.0–4392.0)	2732.0 (1571.0–4707.0)	0.51
sFlt-1 during pregnancy	8442.0 (6511.0–10866.0)	2650.0 (1921.0–3569.0)	<0.01
PlGF during pregnancy	78.0 (55.0–121.0)	301.0 (197.0–572.0)	<0.01
sFlt-1/PlGF during pregnancy	86.5 (59.2–207)	8.3 (4.1–18.9)	<0.01
Gestational age at sFlt-1/PlGF determination	37.0 (34.8–38.2)	34.9 (32.5–37.5)	<0.01
Chronic hypertension before pregnancy	12 (13.3)	9 (5.7)	0.04
Gestational age at delivery, weeks	37.3 (35.0–38.6)	39.3 (37.9–40.5)	<0.01
Previous FGR[b]	28 (31.1)	28 (17.6)	0.01
Delivery <32 weeks	7 (25.0)	0	<0.01
Delivery <37 weeks	19 (67.9)	1 (3.6)	<0.01
Delivery ≥37 weeks	9 (32.1)	27 (96.4)	<0.01
Previous PE[c]	56 (62.2)	24 (15.1)	<0.01
Delivery <34 weeks	11 (10.7)	0	<0.01
Delivery <37 weeks	30 (34.8)	1 (4.2)	0.13
Delivery ≥37 weeks	26 (65.2)	23 (95.8)	0.13

Note: Data are number of events (%) or median (IQR).

Abbreviations: FGR, fetal growth restriction; MET, metabolic equivalent of task; PE, preeclampsia; PlGF, placental growth factor; sFlt-1, soluble fms-like tyrosine kinase-1.

[a]Race and ethnicity were self-reported by participants from predefined categories.

[b]FGR was determined based on Figueras and Gratacos diagnostic criteria.

[c]PE was diagnosed using ACOG criteria.

This study has important clinical implications, as our findings suggest that although both placental insufficiency and angiogenic imbalance are associated with increased peripheral vascular resistance, the key determinant of long-term vascular impact appears to be the development of clinical manifestations of the disease, particularly PE. It is possible that, in the presence of

TABLE 4 Ophthalmic artery Doppler and carotid intima-media thickness according to sFlt-1/PlGF ≥ or <38, regardless of previous FGR or PE.

	sFlt-1/PlGF ≥38 (*n* = 90)	sFlt-1/PlGF <38 (*n* = 159)	Adjusted *p*[a]
Mean OA-PI	1.59 (1.42–1.97)	1.73 (1.51–1.92)	0.54
Mean OA-PSV ratio	0.76 (0.66–0.82)	0.70 (0.64–0.78)	0.03
Right eye			
OA-PI	1.69 (1.42–1.99)	1.73 (1.52–1.98)	0.73
OA-PSV1, cm/s	30.3 (22.9–35.7)	31.1 (24.1–36.7)	0.52
OA-PSV2, cm/s	21.9 (16.8–26.2)	21.1 (16.5–25.9)	0.66
OA-PSV ratio	0.76 (0.65–0.85)	0.70 (0.62–0.79)	0.02
Left eye			
OA-PI	1.59 (1.34–1.90)	1.72 (1.43–1.90)	0.48
OA-PSV1, cm/s	31.5 (24.7–37.9)	31.9 (26.1–38.0)	0.42
OA-PSV2, cm/s	24.0 (17.4–28.7)	23.1 (18.8–26.9)	0.88
OA-PSV ratio	0.76 (0.66–0.83)	0.71 (0.65–0.80)	0.05
Right CIMT, mm	0.538 (0.479–0.606)	0.522 (0.464–0.580)	0.41
Left CIMT, mm	0.576 (0.519–0.656)	0.536 (0.476–0.605)	0.42
Mean CIMT, mm	0.563 (0.511–0.623)	0.530 (0.491–0.573)	0.41

Note: Data are median (IQR).

Abbreviations: CIMT, carotid intima-media thickness; OA-PI, ophthalmic artery pulsatility index; OA-PSV, ophthalmic artery peak systolic velocity ratio; OA-PSV1, ophthalmic artery first systolic velocity peak; OA-PSV2, ophthalmic artery second systolic velocity peak; PlGF, placental growth factor; sFlt-1, soluble fms-like tyrosine kinase-1.

[a]Adjusted for: maternal age, BMI, mean arterial pressure, race or ethnic group, parity, diabetes mellitus, menopause, autoimmune disease, dyslipidemia, and current cigarette smoking.

a similar degree of angiogenic imbalance, those individuals whose cardiovascular system is unable to adequately compensate during pregnancy—manifesting as clinical disease—may reflect an intrinsically less resilient vascular phenotype. This underlying susceptibility could help explain the higher rates of hypertension and the increased ophthalmic vascular indices observed years later. In contrast, participants with either an isolated history of placental dysfunction or an abnormal angiogenic profile alone did not show significant differences in OA-PSV ratio. While slightly higher OA-PSV values were observed in these subgroups—especially in those with clinical disease but normal angiogenic ratio—these differences were not statistically significant, and the wide confidence intervals suggest potential heterogeneity in vascular response or limited power to detect more subtle effects.

This study has several strengths, as it evaluates cardiovascular markers from 3 to 6 years postpartum in a cohort with well-documented clinical and biochemical data from pregnancy, allowing for robust long-term associations. Secondly, unlike previous studies that focused solely on clinical diagnoses or angiogenic markers, this study integrates both, enabling a more nuanced understanding of their independent and combined effects on long-term vascular health. Thirdly, the proportion of early- and late-onset PE and FGR in our cohort is similar to that observed in the general population, reinforcing the representativeness of our sample and the generalizability of the results. Fourthly, all vascular assessments were performed by the same trained investigator using a standardized protocol, minimizing inter-observer variability and enhancing internal validity. Finally, our multivariable analyses were adjusted for a comprehensive set of clinically relevant covariates, ensuring consistency across models and reducing the risk of residual confounding. We acknowledge some limitations. Firstly, CIMT measurements were performed manually rather than using a semi-automated method. However, previous studies have demonstrated that differences between the two approaches are minimal, and this fact seems unlikely to affect the validity of our results.[33] Secondly, the gestational age at the time of angiogenic biomarker assessment differed between groups. Nevertheless, the cut-off used (sFlt-1/PlGF ≥38) reflects thresholds already established in clinical practice and is considered valid across all gestational ages, reducing the relevance of this variability. Another limitation is that angiogenic biomarker results were not concealed from clinicians during pregnancy, which may have influenced clinical management and, consequently, the development or prevention of clinical manifestations of placental dysfunction. Moreover, the examiner performing vascular assessments had access to participants' index pregnancy data and was therefore not fully blinded to their pregnancy history. However, this information was not reviewed during the examinations, and all measurements were performed using standardized protocols to minimize the risk of observer bias. Fourthly, because participants were recruited from prior prospective studies, there may be a selection bias favoring individuals more likely to attend long-term follow-up assessments, potentially limiting the generalizability of the

TABLE 5 Multivariate linear regression model for the association between combined placental dysfunction history and angiogenic imbalance during pregnancy with ophthalmic artery peak systolic velocity ratio.

Predictor category	Coefficient β (95% CI)	Adjusted *p*[a]
Placental dysfunction[b] + sFlt-1/PlGF ≥38	0.04 (0.01–0.08)	<0.01
Placental dysfunction[b] + sFlt-1/PlGF <38	0.03 (−0.01 to 0.07)	0.09
No placental dysfunction[b] + sFlt-1/PlGF ≥38	0.03 (−0.02 to 0.08)	0.25

Note: Individuals without placental dysfunction and with a normal angiogenic profile used as the reference.

Abbreviations: PlGF, placental growth factor; sFlt-1, soluble fms-like tyrosine kinase-1.

[a]Adjusted for: maternal age, BMI, mean arterial pressure, race or ethnic group, parity, diabetes mellitus, menopause, autoimmune disease, dyslipidemia, and current cigarette smoking.

[b]Placental dysfunction was considered either a history of preeclampsia or fetal growth restriction.

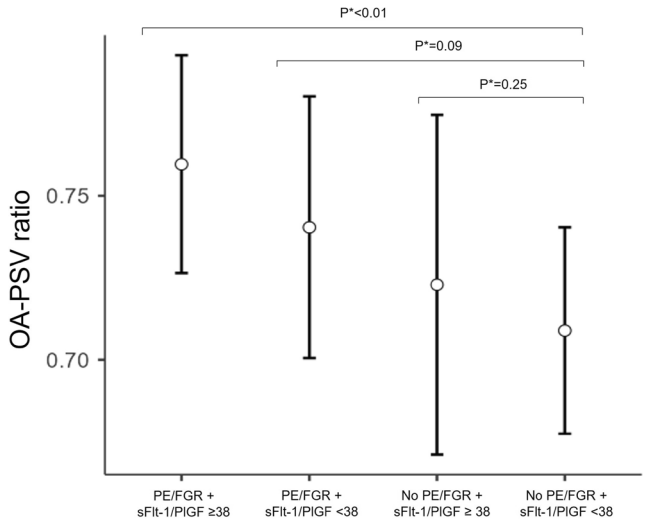

FIGURE 2 Adjusted OA-PSV ratio by clinical history of placental dysfunction and angiogenic profile. Estimated marginal means of ophthalmic artery peak systolic velocity ratio obtained from an adjusted multivariate linear regression model. Groups are defined according to the presence of a history of placental dysfunction (PE or FGR) and sFlt-1/PlGF ratio (≥38 vs. <38). Error bars indicate 95% confidence intervals. *Compared with individuals with no PE/FGR + sFlt-1/PlGF <38. OA-PSV, ophthalmic artery peak systolic velocity ratio; PlGF, placental growth factor; sFlt-1, soluble fms-like tyrosine kinase-1.

findings. Fifthly, the results may not be applicable to other definitions of PE or FGR. Moreover, although the proportion of early- and late-onset PE and FGR in our cohort is similar to that observed in the general population, the small number of early-onset cases limits our ability to explore potential differences in vascular findings between early- and late-onset disease. Sixthly, women who had an additional pregnancy between the index gestation and the follow-up were not excluded; however, none of these subsequent pregnancies were complicated by PE or FGR. We cannot fully rule out the possibility that women in the PE/FGR group had experienced these conditions in previous pregnancies, as many delivered elsewhere and complete medical records were not available. Finally, it is possible that other cardiovascular risk factors not captured in this study may have contributed to the observed outcomes and acted as potential confounders. While adjustments were made for key variables, unmeasured factors—such as socioeconomic status, genetic predisposition, psychosocial stress, fasting glucose, lipid profile, and complete metabolic syndrome criteria—could influence long-term vascular health and modify the associations observed. In addition, we cannot determine whether aspirin use during pregnancy had a role in shaping future cardiovascular risk since there were no untreated participants at high risk for PE. Despite these limitations, this study provides valuable insights into the long-term vascular impact of placental dysfunction and angiogenic imbalance. Future research should aim to validate these findings in larger and more diverse populations and investigate potential interventions during or after pregnancy to mitigate the long-term cardiovascular consequences in affected individuals. In addition, longitudinal studies with assessment of baseline cardiovascular function prior to pregnancy are needed to better elucidate whether pregnancy complications exacerbate preexisting vascular dysfunction or introduce new changes that may contribute to an increased risk of future cardiovascular disease.

5 | CONCLUSION

In conclusion, both angiogenic imbalance and a history of placental dysfunction during pregnancy are associated with increased OA-PSV ratio 3–6 years postpartum, with this relationship being especially significant in cases where clinical disease (particularly PE) develops. Future studies should explore whether elective delivery based on elevated sFlt-1/PlGF ratio, before clinical manifestations such as PE appear, may help improve long-term cardiovascular outcomes without worsening neonatal outcomes.

AUTHOR CONTRIBUTIONS

Conceptualisation: Pablo Garcia-Manau, Judit Platero, and Elisa LLurba. Methodology: Pablo Garcia-Manau. Data collection: Judit Platero, Pablo Garcia-Manau, Noah Costa, Claudia Pellicer, Madalina Nan, Josefina Mora, Alvaro Garcia-Osuna, and Johana Ullmo. Statistical analysis: Pablo Garcia-Manau. Data interpretation: Pablo Garcia-Manau, Judit Platero, and Elisa LLurba. Drafting of the article: Pablo Garcia-Manau and Judit Platero. Article review and editing: All authors.

ACKNOWLEDGMENTS

We thank Judit Solà Roca for statistical assessment.

FUNDING INFORMATION

This work was supported by public funds obtained in competitive calls with peer review (grant PI22/00462, Instituto de Salud Carlos III, Madrid, Spain), the Spanish Clinical Research and Clinical Trials Platform, SCReN (Spanish Clinical Research Network), funded by the ISCIII-General Subdirectorate for Evaluation and Promotion of Research, through project PT13/0002/0028, integrated in the 2013–2016 R+D+I State Plan and co-financed by and the European Regional Development Fund (FEDER); the Primary Care Interventions to Prevent Maternal and Child Chronic Diseases of Perinatal and Developmental Origin Network (RICORS-SAMID, RD21/0012/0001, Instituto de Salud Carlos III, Madrid, Spain), funded by the Recovery, Transformation and Resilience Plan 2017–2020, ISCIII, and by the European Union—Next Generation EU and by the Spanish Network in Maternal, Neonatal, Child and Developmental Health Research (RICORS-SAMID, RD24/0013/0001) Instituto de Salud Carlos III, Madrid, Spain, and co-financed by the European Regional Development Fund (FEDER) founds 2021–2027. Funding sources were not involved in study design, collection, analysis and interpretation of data, or in the writing of this manuscript.

CONFLICT OF INTEREST STATEMENT

PG-M and ELL declared receipt of lecture fees and fees from Roche Diagnostics. ELL declared receipt of consulting fees from Roche Diagnostics. The other authors declare no competing interests.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

The study was approved by the Ethics Committee of the Hospital de la Santa Creu i Sant Pau (IIBSP-MOM-2022-87) on 19 July 2023.

ORCID

Pablo Garcia-Manau https://orcid.org/0000-0002-2415-1626
Carmen Garrido-Giménez https://orcid.org/0000-0003-2180-1715
Cristina Trilla https://orcid.org/0000-0002-5650-1790
Carla Dominguez-Gallardo https://orcid.org/0000-0002-5365-1005
Elisa Llurba https://orcid.org/0000-0003-4048-6407

REFERENCES

1. Gagnon R. Placental insufficiency and its consequences. *Eur J Obstet Gynecol Reprod Biol*. 2003;110(Suppl 1):S99-S107. doi:10.1016/s0301-2115(03)00179-9
2. Kwiatkowski S, Bednarek-Jędrzejek M, Kwiatkowska E, Cymbaluk-Płoska A, Torbè A. Diagnosis of placental insufficiency independently of clinical presentations using sFlt-1/PLGF ratio, including SGA patients. *Pregnancy Hypertens*. 2021;25:244-248. doi:10.1016/j.preghy.2021.07.245
3. Magee LA, Nicolaides KH, von Dadelszen P. Preeclampsia. *N Engl J Med*. 2022;386(19):1817-1832. doi:10.1056/NEJMra2109523
4. Rana S, Lemoine E, Granger JP, Karumanchi SA. Preeclampsia. *Circ Res*. 2019;124(7):1094-1112. doi:10.1161/CIRCRESAHA.118.313276
5. Redman CW, Staff AC. Preeclampsia, biomarkers, syncytiotrophoblast stress, and placental capacity. *Am J Obstet Gynecol*. 2015;213(4 Suppl):S9.e1-S9.11.
6. Redman CWG, Staff AC, Roberts JM. Syncytiotrophoblast stress in preeclampsia: the convergence point for multiple pathways. *Am J Obstet Gynecol*. 2022;226(2S):S907-S927.
7. Levine RJ, Maynard SE, Qian C, et al. Circulating angiogenic factors and the risk of preeclampsia. *N Engl J Med*. 2004;350(7):672-683. doi:10.1056/NEJMoa031884
8. Stepan H, Herraiz I, Schlembach D, et al. Implementation of the sFlt-1/PlGF ratio for prediction and diagnosis of pre-eclampsia in singleton pregnancy: implications for clinical practice. *Ultrasound Obstet Gynecol*. 2015;45(3):241-246. doi:10.1002/uog.14799
9. Park K, Minissian MB, Wei J, Saade GR, Smith GN. Contemporary clinical updates on the prevention of future cardiovascular disease in women who experience adverse pregnancy outcomes. *Clin Cardiol*. 2020;43(6):553-559. doi:10.1002/clc.23374
10. Staff AC, Costa ML, Dechend R, Jacobsen DP, Sugulle M. Hypertensive disorders of pregnancy and long-term maternal cardiovascular risk: bridging epidemiological knowledge into personalized postpartum care and follow-up. *Pregnancy Hypertens*. 2024;36:101127. doi:10.1016/j.preghy.2024.101127
11. Benschop L, Schalekamp-Timmermans S, Broere-Brown ZA, et al. Placental growth factor as an indicator of maternal cardiovascular risk after pregnancy. *Circulation*. 2019;139(14):1698-1709. doi:10.1161/CIRCULATIONAHA.118.036632
12. Garrido-Gimenez C, Mendoza M, Cruz-Lemini M, et al. Angiogenic factors and long-term cardiovascular risk in women that developed preeclampsia during pregnancy. *Hypertension*. 2020;76(6):1808-1816. doi:10.1161/HYPERTENSIONAHA.120.15830
13. Dadvand P, Gascon M, Bustamante M, et al. Cohort profile: Barcelona life study cohort (BiSC). *Int J Epidemiol*. 2024;53(3):dyae063. doi:10.1093/ije/dyae063
14. Ullmo J, Cruz-Lemini M, Sánchez-García O, et al. Cardiac dysfunction and remodeling regulated by anti-angiogenic environment in patients with preeclampsia: the ANGIOCOR prospective cohort study protocol. *BMC Pregnancy Childbirth*. 2021;21:816. doi:10.1186/s12884-021-04263-w
15. Fundació Institut de Recerca de l'Hospital de la Santa Creu i Sant Pau. *Randomizated Open-Label Control Trial to Evaluate If the Incorporation of sFlt1/PlGF Ratio in the Diagnosis and Classification of PE Improves Maternal and Perinatal Outcomes in Women With the Suspicion of the Disease (EuroPE Study)*. clinicaltrials.gov; 2023. Accessed May 4, 2025. https://clinicaltrials.gov/study/NCT03231657
16. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' task force on hypertension in pregnancy. *Obstet Gynecol*. 2013;122(5):1122-1131. doi:10.1097/01.AOG.0000437382.03963.88
17. Figueras F, Gratacos E. An integrated approach to fetal growth restriction. *Best Pract Res Clin Obstet Gynaecol*. 2017;38:48-58. doi:10.1016/j.bpobgyn.2016.10.006
18. Molina L, Sarmiento M, Peñafiel J, et al. Validation of the Regicor short physical activity questionnaire for the adult population. *PLoS One*. 2017;12(1):e0168148. doi:10.1371/journal.pone.0168148
19. Schröder H, Benitez Arciniega A, Soler C, et al. Validity of two short screeners for diet quality in time-limited settings. *Public Health Nutr*. 2012;15(4):618-626. doi:10.1017/S1368980011001923
20. Gepner AD, Keevil JG, Wyman RA, et al. Use of carotid intima-media thickness and vascular age to modify cardiovascular risk prediction.

J Am Soc Echocardiogr. 2006;19(9):1170-1174. doi:10.1016/j.echo.2006.04.009
21. Erickson SJ, Hendrix LE, Massaro BM, et al. Color doppler flow imaging of the normal and abnormal orbit. *Radiology*. 1989;173(2):511-516. doi:10.1148/radiology.173.2.2678264
22. Kane SC, Brennecke SP, da Silva Costa F. Ophthalmic artery doppler analysis: a window into the cerebrovasculature of women with pre-eclampsia. *Ultrasound Obstet Gynecol*. 2017;49(1):15-21. doi:10.1002/uog.17209
23. Sarno M, Wright A, Vieira N, Sapantzoglou I, Charakida M, Nicolaides KH. Ophthalmic artery doppler in prediction of pre-eclampsia at 35-37 weeks' gestation. *Ultrasound Obstet Gynecol*. 2020;56(5):717-724. doi:10.1002/uog.22184
24. Gonser M, Vonzun L, Ochsenbein-Kölble N. Ophthalmic artery doppler in prediction of pre-eclampsia: insights from hemodynamic considerations. *Ultrasound Obstet Gynecol*. 2021;58(1):145-147. doi:10.1002/uog.23665
25. Gana N, Sarno M, Vieira N, Wright A, Charakida M, Nicolaides KH. Ophthalmic artery doppler at 11-13 weeks' gestation in prediction of pre-eclampsia. *Ultrasound Obstet Gynecol*. 2022;59(6):731-736. doi:10.1002/uog.24914
26. Lau KGY, Wright A, Kountouris E, Nicolaides KH, Kametas NA. Ophthalmic artery peak systolic velocity ratio distinguishes pre-eclampsia from chronic and gestational hypertension: a prospective cohort study. *BJOG*. 2022;129(8):1386-1393. doi:10.1111/1471-0528.17061
27. de Melo PFMV, Roever L, Mendonça TMS, da Silva Costa F, Rolnik DL, Diniz ALD. Ophthalmic artery doppler in the complementary diagnosis of preeclampsia: a systematic review and meta-analysis. *BMC Pregnancy Childbirth*. 2023;23(1):343. doi:10.1186/s12884-023-05656-9
28. Lau KGY, Kountouris E, Salazar-Rios L, Nicolaides KH, Kametas NA. Prediction of adverse outcome by ophthalmic artery doppler and angiogenic markers in pregnancies with new onset hypertension. *Pregnancy Hypertens*. 2023;34:110-115. doi:10.1016/j.preghy.2023.10.001
29. Gy Lau K, Bednorz M, Parisi N, Nicolaides KH, Kametas NA. Ophthalmic artery doppler in women with hypertensive disorders of pregnancy: relationship to blood pressure control and renal dysfunction at 6-9 weeks postnatally. *Ultrasound Obstet Gynecol*. 2024;63(6):738-745. doi:10.1002/uog.27563
30. Alves Borges JH, Goes DA, de Araújo LB, Dos Santos MC, Debs Diniz AL. Prospective study of the hemodynamic behavior of ophthalmic arteries in postpartum preeclamptic women: a doppler evaluation. *Hypertens Pregnancy*. 2016;35(1):100-111. doi:10.3109/10641955.2015.1116553
31. Dimopoulou S, Neculcea D, Papastefanou I, Galan A, Nicolaides KH, Charakida M. Long-term cardiovascular assessment of women with previous pregnancy complicated by hypertensive disorder. *Ultrasound Obstet Gynecol*. 2024;64(3):308-313. doi:10.1002/uog.27632
32. Blaauw J, Souwer ETD, Coffeng SM, et al. Follow up of intima-media thickness after severe early-onset preeclampsia. *Acta Obstet Gynecol Scand*. 2014;93(12):1309-1316. doi:10.1111/aogs.12499
33. Mac Ananey O, Mellotte G, Maher V. Comparison of semi-automated and manual measurements of carotid intima-media thickening. *Biomed Res Int*. 2014;2014:531389. doi:10.1155/2014/531389

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Garcia-Manau P, Platero J, Costa N, et al. Ophthalmic artery Doppler and carotid intima-media thickness 3–6 years postpartum in women with and without a history of placental insufficiency. *Acta Obstet Gynecol Scand*. 2026;105:94-104. doi:10.1111/aogs.70059