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Women with Preterm Birth Have Evidence of Subclinical Atherosclerosis a Decade After Delivery

Janet M. Catov, PhD, MS,[1,2] Gabrielle G. Snyder, MPH,[2] Bertha L. Bullen, PhD,[3] Emma J.M. Barinas-Mitchell, PhD,[2] and Claudia Holzman, PhD[3]

Abstract

Background: Women with preterm birth (PTB) have excess risk of cardiovascular disease (CVD) and metabolic dysregulation after delivery, but vascular mechanisms are poorly understood. We considered that women with PTB may have evidence of subclinical atherosclerosis after delivery, perhaps related to cardiometabolic risk factors.
Materials and Methods: The Pregnancy Outcomes and Community Health Moms (POUCHmoms) study followed women from pregnancy through 7 to 15 years after delivery ($n=678$). Women underwent B-mode ultrasound to measure the average intima-media thickness (IMT) across the common carotid, bulb, and internal carotid artery segments at follow-up ($n=605$). Linear regression estimated the overall and segment-specific difference in IMT between women with preterm and term births.
Results: Women were, on average, 38 years old (SD 5.7) at the follow-up visit. Those with a prior preterm versus term birth had thicker mean IMT (average of eight segments, 0.592 mm vs. 0.575, $p=0.04$). Differences persisted after accounting for age, race, smoking, and body mass index (difference = +0.018 mm, $p=0.019$) and were attenuated after adjustment for blood pressure, medication use, and total cholesterol (difference = +0.014, $p=0.052$). Thicker mean bulb IMT in women with PTB was robust to cardiovascular risk factor adjustments (fully adjusted difference = +0.033, $p=0.029$). Excluding cases of prepregnancy hypertension or preeclampsia did not change results.
Conclusions: Mechanisms leading to subclinical atherosclerosis may link PTB with future CVD. PTB differences in maternal vessel remodeling in the carotid bulb, an arterial segment more prone to early development of atherosclerosis, were independent of traditional risk factors suggesting that novel processes may be involved.

Keywords: preterm birth, atherosclerosis, cardiometabolic risk factors

Introduction

Women with preterm birth (PTB), defined as delivery occurring before 37 weeks' gestation, have excess risk of cardiovascular disease (CVD) and metabolic dysregulation after delivery,[1–4] but vascular mechanisms are poorly understood. Very few studies evaluate subclinical vascular features, and recent evidence suggests that the PTB-CVD association may not be due to shared risk factors such as blood pressure, lipids, and adiposity.[5] Further complicating these studies, PTB is a heterogeneous condition, with cases typically classified according to clinical circumstances as spontaneous (preterm labor or preterm premature rupture of membranes) and medically indicated (early C-section or labor induction due to maternal or fetal conditions). Despite concerns with this approach,[6–8] these clinical phenotypes are often represented as pathophysiologically distinct. And yet, there is compelling evidence that the epidemiologic outcomes,[2,4,9] metabolic changes,[10,11] and placental abnormalities in indicated and spontaneous PTBs overlap, and thus, vascular mechanisms may also be shared.[12,13]

Studying the postpregnancy vascular health of women following PTB may help elucidate pathways and relevant subtypes that mark excess CVD risk. Atherosclerotic vascular disease is a chronic, inflammatory fibroproliferative disease of the large and medium-sized arteries fueled by lipids.[14] The intima-media thickness (IMT) of the common carotid artery (CCA), the carotid bulb, and the internal carotid artery (ICA) have been used as markers of carotid atherosclerosis and are prognostic of cardiovascular events.[15–19] Our group has previously reported that women with PTB had thicker carotid IMT measured 8 years after delivery, but results were not

[1]Department of Obstetrics, Gynecology and Reproductive Sciences, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania.
[2]Department of Epidemiology, University of Pittsburgh Graduate School of Public Health, Pittsburgh, Pennsylvania.
[3]Department of Epidemiology and Biostatistics, Michigan State University, East Lansing, Michigan.

independent of traditional CVD risk factors.[20] We also related PTB to carotid IMT in a study that relied on maternal report of pregnancy features and, thus, were not reliably able to distinguish clinical subtypes of PTB.[21] Neither prior study examined carotid segment-specific changes, despite evidence that different carotid segments may carry differential CVD risk factor associations and risk prediction.

In a cohort recruited during pregnancy and followed up to 15 years after delivery, we considered that women with PTB would have evidence of subclinical atherosclerosis, explained, in part, by cardiometabolic risk factors. We also hypothesized that associations with the carotid bulb may be particularly strong in reproductive age women as this segment is most susceptible to atherogenesis and, thus, often the first to reflect atherosclerotic thickening.[22]

Materials and Methods

Designed to examine pathways leading to preterm delivery, the POUCH Study enrolled 3019 pregnant women from 1998 to 2004 in Michigan, United States. A subcohort of 1371 participants was created for in-depth pregnancy measures that was composed of all those delivering preterm (<37 weeks' gestation), those with higher risk of preterm delivery (African American race/ethnicity or those with elevated concentrations of maternal alpha-fetoprotein screening), and a random sample of those delivering at term (≥37 weeks' gestation). In all analyses sampling weights are used to account for this subcohort sampling strategy.

POUCHmoms was designed to examine early evidence of cardiovascular risk 7–15 years after the POUCH Study pregnancy. Women were invited to a one time follow-up visit, and 678 participated from 2011 to 2014 (Fig. 1). Women who attended the follow-up visit compared to those who did not were somewhat older, had higher levels of education, were less likely to have received Medicaid insurance at pregnancy, and were more likely to be of white or other race/ethnicity (all $p < 0.05$; Supplementary Table S1; Supplementary Data are available online at www.liebertpub.com/jwh). Frequency of PTB, hypertension in pregnancy, and prepregnancy body mass index (BMI) did not differ between those in the follow-up study compared to those not followed. All participating women provided written informed consent; the study was approved by the Michigan State University and University of Pittsburgh Institutional Review Boards. Of the women who attended the follow-up visit, 12 were excluded due to technical failures when measuring IMT. Another 61 women were excluded because they had incomplete IMT measures, for a final population of 605 included in the current analysis. Those with IMT measures were more likely to be of normal BMI and of white or other race/ethnicity compared to those without IMT measures (Supplementary Table S1).

Pregnancy features

Detailed pregnancy data were collected through structured interviews and medical record review at mid-pregnancy and after delivery. PTB included birth prior to 36 completed weeks' gestation. Gestational age was calculated from the last menstrual period (LMP) or from ultrasound (≤25 weeks' gestation) when this estimate differed from the LMP-based estimate by more than 2 weeks. Spontaneous PTBs were those following preterm labor or preterm premature rupture of membranes; medically indicated preterm deliveries were due to maternal or fetal indications. Hypertensive disorders were identified when explicitly diagnosed or when women met the diagnostic criteria in place during this time frame.[23] Preeclampsia and gestational hypertension were defined as blood pressure ≥140 mmHg systolic or 90 mmHg diastolic on two occasions after 20 weeks of gestation, with preeclampsia requiring presence of proteinuria. Chronic hypertension was defined as blood pressure ≥140 mmHg systolic or 90 mmHg diastolic prior to pregnancy or before 20 weeks' gestation. Gestational diabetes status was determined by a failed 3-hour glucose tolerance test, failed glucose screen (>190 mg/dL) accompanied by a fasting glucose >95 mg/dL, or diagnosis in the medical records. Prepregnancy BMI and smoking status during pregnancy were self-reported at, on average, 22.4 weeks' gestation.

Carotid ultrasound

At the cardiovascular follow-up visit 7–15 years after delivery, B-mode ultrasound images of the right and left distal

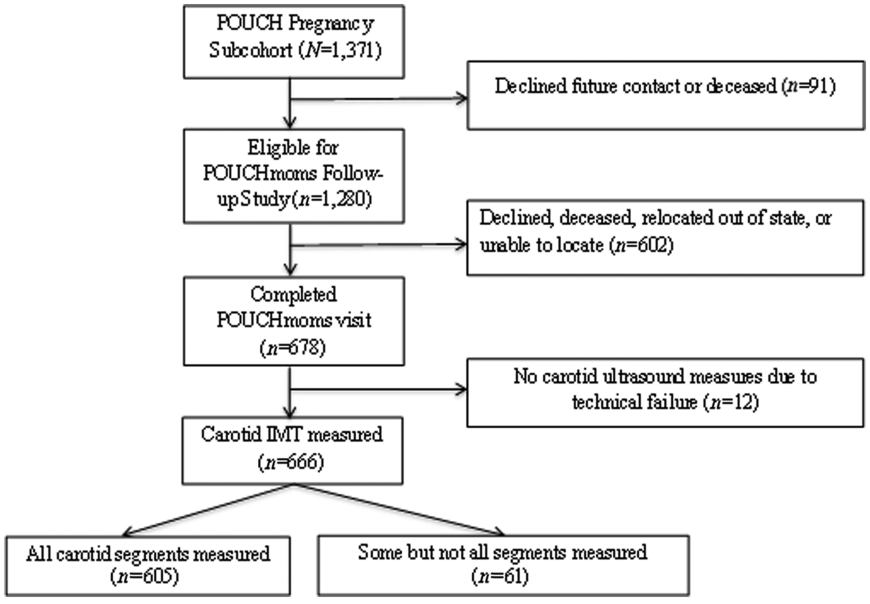

FIG. 1. Participants in POUCHmoms Study, 2011–2014. POUCHmoms, Pregnancy Outcomes and Community Health Moms.

Table 1. Maternal Characteristics at Pregnancy and 7–15 Years Later, According to Pregnancy Outcomes and Community Health Study Preterm Birth Status

	Term birth N = *459*	*Preterm birth* N = *146*	p[a]
POUCH pregnancy (1998–2004)			
Maternal age at POUCH delivery (years), mean(se)	26.8 (0.3)	26.4 (0.5)	0.465
Prepregnancy BMI (kg/m^2), mean(se)	27.0 (0.4)	26.2 (0.6)	0.307
African American, *n* (%)	176 (23.6)	39 (32.9)	0.002
Nulliparous before POUCH, *n* (%)	193 (43.8)	78 (54.0)	0.042
Hypertensive conditions, *n* (%)			0.004
None	420 (92.2)	120 (83.7)	
Gestational hypertension	20 (3.7)	6 (4.1)	
Preeclampsia	8 (1.9)	11 (7.4)	
Chronic hypertension	11 (2.2)	9 (4.8)	
Smoking during pregnancy, *n* (%)	76 (17.0)	34 (23.4)	0.110
Additional preterm births, *n* (%)	68 (12.9)	56 (39.5)	<0.0001
Small for gestational age, *n* (%)	59 (11.4)	12 (9.2)	0.095
Postpregnancy visit (2011–2014)			
Time to follow-up (years), mean(se)	11.0 (0.1)	11.1 (0.1)	0.504
Age (years), mean(se)	37.8 (0.3)	37.5 (0.5)	0.567
Years of regular smoking, mean(se)	5.8 (0.5)	6.9 (0.7)	0.209
Average leisure time physical activity (hours/week)	4.3 (0.3)	4.1 (0.4)	0.734
Diet quality	53.3 (0.5)	53.6 (1.0)	0.804
Smoking, *n* (%)	127 (27.1)	48 (34.2)	0.105
Insurance history, *n* (%)			0.071
Never on Medicaid	204 (51.4)	61 (40.0)	
Medicaid before POUCH only	86 (17.5)	28 (18.5)	
Medicaid after POUCH only	26 (4.5)	11 (8.0)	
Medicaid before/during and after POUCH	142 (26.6)	46 (33.5)	
Education, *n* (%)			0.429
<High school	35 (6.9)	13 (9.2)	
High school	61 (12.7)	18 (13.2)	
Vocational or some college	228 (49.2)	77 (53.5)	
≥College graduate	135 (31.2)	38 (24.1)	
Menopause, *n* (%)			0.054
No	418 (90.4)	121 (83.8)	
Yes (surgical and nonsurgical)	33 (7.4)	22 (14.2)	
Indeterminate	8 (2.2)	3 (2.0)	
Family history, *n* (%)			
Diabetes	173 (35.7)	64 (44.7)	0.150
Hypertension	304 (64.9)	105 (71.4)	0.354
Heart disease	118 (25.0)	48 (30.1)	0.519
Stroke	68 (14.5)	30 (21.8)	0.153
Gestational hypertension	77 (16.8)	26 (15.2)	0.669
Income, *n* (%)			0.108
<$20,000	119 (22.2)	39 (28.7)	
$20,000–<$50,000	152 (33.8)	49 (34.4)	
$50,000–<$90,000	105 (26.5)	26 (16.8)	
≥$90,000	74 (17.6)	31 (20.0)	
Statin use, *n* (%)	13 (3.2)	7 (4.4)	0.512
Antihypertensive medication use, *n* (%)	52 (10.1)	24 (16.8)	**0.039**
Body mass index (kg/m^2), mean(se)	30.9 (0.5)	29.8 (0.7)	0.199
Waist circumference (cm), mean(se)	90.1 (0.9)	88.4 (1.4)	0.288
Systolic blood pressure (mm Hg), mean(se)	114.2 (0.7)	115.2 (1.3)	0.475
Diastolic blood pressure (mm Hg), mean(se)	75.3 (0.6)	75.7 (1.0)	0.734
HDL cholesterol (mg/dL), mean(se)	54.7 (0.8)	55.0 (1.2)	0.857
LDL cholesterol (mg/dL), mean(se)	105.2 (1.5)	110.4 (2.8)	0.102
Triglycerides (mg/dL), median (IQR)	86.3 (64.7)	95.2 (66.4)	0.378
Total cholesterol (mg/dL), mean (se)	181.2 (1.8)	189.7 (3.8)	**0.045**

[a]Accounting for sampling weights; $N = 605$ except the following: $n = 604$ for insurance status; $n = 595$ for income; $n = 597$ for family history.

BMI, body mass index; HDL, high density lipoprotein; IQR, interquartile range; LDL, low density lipoprotein; POUCH, Pregnancy Outcomes and Community Health.

CCA, carotid bulb, and the first centimeter of the ICA were obtained in end diastole using the Terason t3000 Ultrasound System (Teratech Corp, Burlington, MA). Semiautomated edge-detection software (Artery Measurement System, Gothenburg, Sweden) was used to identify the lumen–intima and media–adventitia interfaces across 1 cm segments of the near and far walls of the CCA and the far wall of the bulb and ICA. IMT values across these eight sites were averaged to obtain mean average IMT. Site-specific mean IMT (CCA, bulb, ICA) was also evaluated. Reproducibility of the IMT measures was excellent, with an intra-class correlation coefficient between sonographers of ≥0.87 and between readers of 0.92.

Covariates

Race/ethnicity and age were reported during pregnancy. Other covariates were assessed at the follow-up visit, including education (<high school, high school, vocational or some college, ≥college), menopausal status (nonsurgical [no menstrual periods during the previous 12 months] and surgical [removal of both ovaries], or indeterminate), household income (<$20,000, $20,000–<$50,000, $50,000–<$90,000, ≥$90,000; missing for $n=10$), family history of chronic health conditions, smoking (during pregnancy and current), lipid lowering or antihypertensive medication use, and the gestational age at delivery of all births before and after the POUCH Study birth. These interval births were classified as preterm or term based on maternal recall and considered as covariates. Numbers were too small to separately evaluate the group with two or more PTBs ($n=56$). Insurance status was evaluated as Medicaid coverage during and/or after the POUCH Study pregnancy. Leisure physical activity was reported as hours/week using the Modifiable Activity Questionnaire,[24,25] and diet quality was assessed using the Block Food Frequency Questionnaire.[26] BMI (kg/m^2) was calculated from measured height and weight at the follow-up visit. Waist circumference was assessed in centimeters with a Gulick tape measure, taken at the peak of expiration.

Blood pressure was measured thrice at the follow-up visit *via* a standard research protocol using either a Panasonic EW3109W (Panasonic Corp, Newark NJ) or an Omron Hem-907 (Omron Healthcare, Inc.; Lake Forest, IL) with an appropriately sized cuff. Readings from both digital monitors were comparable and were similar to manual readings. BP was the mean of the second and third measurements. Fasting blood samples were collected at the follow-up visit. Total cholesterol, high-density lipoprotein (HDL)-cholesterol, and triglycerides were measured under standard enzymatic procedures[27–29] in the University of Pittsburgh Heinz Nutrition Laboratory. The coefficient of variation ranged from 1.3% to 6.5%. Low-density lipoprotein (LDL)-cholesterol was evaluated using the Friedewald calculation and measured directly when triglycerides were ≥400 mg/dL ($n=8$).[30]

Statistical analysis

Maternal characteristics during pregnancy and at the follow-up visit were compared according to PTB status using chi square or *t*-tests. Associations between PTB and mean carotid IMT were estimated in linear regression models adjusted for age, race/ethnicity, smoking, and BMI at the follow-up visit. Models were then further adjusted for cardiovascular risk factors known to impact IMT or that differed according to PTB status (systolic blood pressure, antihypertensive medication use, and total cholesterol). Models were replicated for carotid segment-specific IMT (CCA, bulb, and ICA). Sensitivity analysis replicated models after excluding women with chronic hypertension ($n=20$) or preeclampsia ($n=19$), the dominant maternal conditions leading to medically indicated PTB. All analyses were conducted in SAS version 9.4 (Cary, NC), and sampling weights were applied to derive estimates reflective of the original source cohort.

Results

Women with a PTB ($n=146$) were more likely to be of African American race/ethnicity, to have had prepregnancy hypertension or preeclampsia, to be primiparous during the POUCH Study, and to have had additional PTBs compared to women with term births (Table 1). At the follow-up visit 7–15 years after delivery (mean interval, 11 years) women with a prior PTB were more likely to be taking antihypertensive medication (16.8% vs. 10.1% $p=0.039$) and had modestly higher total cholesterol than women with term births (189.7 [SE 3.8] vs. 181.2 [1.8]; $p=0.045$).

Women with a preterm compared to term birth had thicker carotid IMT averaged across all eight segments (0.592 [0.01] vs. 0.575 [0.00], $p=0.04$; Table 2). Differences were most pronounced in the carotid bulb (0.629 [0.01] vs. 0.588 [0.01], $p=0.01$). Thicker IMT according to PTB status persisted after accounting for maternal age, race/ethnicity, smoking, and BMI (adjusted difference +0.018 [0.01], $p=0.019$; Table 3) and was attenuated after further adjusting for systolic blood pressure, antihypertensive medication use, and total cholesterol (adjusted difference +0.014 [0.01]; $p=0.052$). Differences in the carotid bulb persisted after accounting for maternal factors and traditional cardiometabolic risk factors (fully adjusted difference +0.033 [0.01]; $p=0.029$).

When evaluated according to PTB clinical circumstances, IMT averaged across all segments was most pronounced

Table 2. Carotid Intima-Media Thickness 7–15 Years After Pregnancy, According to Prior Preterm Birth Status

	Term (n = *459*)	*Preterm* (n = *146*)	p
Overall carotid IMT, mm (mean, se)	0.575 (0.00)	0.592 (0.01)	0.04
Common carotid IMT, mm (mean, se)	0.597 (0.00)	0.606 (0.01)	0.25
Carotid bulb IMT, mm (mean, se)	0.588 (0.01)	0.629 (0.01)	0.01
Internal carotid IMT, mm (mean, se)	0.516 (0.01)	0.529 (0.01)	0.30

$N=605$; accounting for sampling weights.
IMT, intima-media thickness.

Table 3. Difference in Carotid Intima-Media Thickness (mm) According to Preterm Birth and Clinical Subtypes; Women with Term Births Are the Referent

	All preterm births		*Clinical presentation*				*Gestational age at delivery*			
	Preterm (n = *146*)	p	*Spontaneous* (n = *97*)	p	*Indicated* (n = *49*)	p	*34-< 37 weeks* (n = *113*)	p	*<34 weeks* (n = *33*)	p
Model 1[a]										
Carotid IMT (all segments)	0.018 (0.01)	0.019	0.007 (0.01)	0.411	0.040 (0.01)	0.002	0.022 (0.01)	0.010	0.004 (0.01)	0.762
Common carotid IMT	0.010 (0.01)	0.144	–0.001 (0.01)	0.869	0.032 (0.01)	0.001	0.012 (0.01)	0.106	0.003 (0.01)	0.816
Carotid bulb IMT	0.039 (0.02)	0.013	0.030 (0.02)	0.081	0.056 (0.03)	0.044	0.044 (0.02)	0.014	0.021 (0.03)	0.415
Internal carotid IMT	0.013 (0.01)	0.265	0.002 (0.01)	0.908	0.037 (0.02)	0.061	0.020 (0.01)	0.134	–0.010 (0.02)	0.620
Model 2[a]										
Carotid IMT (all segments)	0.014 (0.01)	0.052	0.005 (0.01)	0.561	0.034 (0.01)	0.009	0.018 (0.01)	0.026	0.001 (0.01)	0.965
Common carotid IMT	0.007 (0.01)	0.300	–0.003 (0.01)	0.741	0.026 (0.01)	0.010	0.009 (0.01)	0.217	0.000 (0.01)	0.999
Carotid bulb IMT	0.033 (0.01)	0.029	0.024 (0.02)	0.138	0.050 (0.03)	0.075	0.038 (0.02)	0.028	0.014 (0.02)	0.554
Internal carotid	0.011 (0.01)	0.336	0.0003 (0.01)	0.980	0.034 (0.02)	0.101	0.018 (0.01)	0.171	–0.012 (0.02)	0.578

Model 1 adjusted for age, race/ethnicity, smoking, and BMI; Model 2 adjusted for factors in model 1 and systolic blood pressure, total cholesterol, and antihypertensive medication.
[a]All models account for cohort sampling weights.

Table 4. Difference in Carotid Intima-Media Thickness (mm) According to Subtypes of Preterm Excluding Women with Prepregnancy Hypertension or Preeclampsia

	All preterm births		*Clinical presentation*				*Gestational age at delivery*			
	Preterm (n = *126*)	p	*Spontaneous* (n = *91*)	p	*Indicated* (n = *35*)	p	*34-< 37 weeks* (n = *99*)	p	*<34 weeks* (n = *27*)	p
Carotid IMT (all segments)*	0.014 (0.01)	0.058	0.007 (0.01)	0.442	0.034 (0.01)	0.007	0.019 (0.01)	0.023	–0.002 (0.02)	0.890
Common carotid IMT	0.007 (0.01)	0.343	–0.003 (0.01)	0.722	0.031 (0.01)	0.009	0.010 (0.01)	0.182	–0.006 (0.01)	0.630
Carotid bulb IMT	0.031 (0.02)	0.034	0.029 (0.02)	0.093	0.038 (0.03)	0.126	0.035 (0.02)	0.037	0.019 (0.03)	0.486
Internal carotid IMT	0.012 (0.01)	0.329	0.003 (0.01)	0.838	0.036 (0.02)	0.107	0.019 (0.01)	0.158	–0.014 (0.02)	0.548

*Mean of the common, carotid bulb and internal carotid IMTs.

among women with medically indicated PTB (fully adjusted difference +0.034 [0.01], $p = 0.009$). It appeared that all carotid segments were affected in these women, although only the common carotid difference achieved statistical significance. In addition, those delivering preterm between 34 and <37 weeks had thicker overall IMT (fully adjusted difference +0.018 [0.01], $p = 0.026$); adjusted differences in the carotid bulb were particularly robust in this group (+0.038 [0.01], $p = 0.028$). Of note, differences were only modestly attenuated and remained statistically significant when women with chronic hypertension or preeclampsia were excluded from analysis (Table 4). Adjustment of models for self-reported PTBs that occurred before or after the POUCH Study pregnancy did not change any results. Results also were unaffected when postmenopausal women or those with indeterminate menopause status were excluded ($n = 66$).

Discussion

Our results from a prospective pregnancy cohort recruited at mid-gestation and followed 7–15 years after delivery indicate that subclinical atherosclerosis may be a mechanism linking PTB with future CVD. The more robust associations with the carotid bulb suggest that early evidence of atherosclerosis in women with PTBs may not be entirely explained by traditional cardiometabolic risk factors. PTBs delivered between 34 and <37 weeks gestation and those following medical indication are likely driving these associations. Results persisted after excluding cases of preeclampsia and chronic hypertension, suggesting that other maternal morbidity and mechanisms may underlie these associations.

Our results are in line with those reported by the few other studies of subclinical vascular factors assessed in women with a prior PTB and extend them in several ways. First, our community-based cohort was recruited at mid-pregnancy, and thus, we had precise PTB information (rather than self-reported) derived from a cohort reflective of a general obstetric population. While the crude differences in overall IMT according to PTB that we detected were of a similar magnitude compared to other studies, adjustment for maternal and traditional cardiometabolic risk factors yielded IMT differences that were almost twofold higher (0.014 compared to 0.008 and 0.007).[20,21] It is likely that the objective assessment of our pregnancy and postdelivery features enhanced the precision of our findings. In addition, the current study uniquely evaluated carotid segment-specific features that may be most relevant in reproductive age women and that may be more robustly linked to future cardiovascular events.[31] Importantly, the carotid bulb vessel wall thickening detected in the current study persisted after accounting for traditional cardiometabolic risk factors, chronic hypertension, and preeclampsia. This finding raises the possibility that early atherosclerosis in women with a prior PTB may be due to novel factors, and this possibility warrants further study.

Women with medically indicated PTBs had the most severe IMT, and this was not explained by chronic hypertension or preeclampsia. Thus, occult maternal morbidity that may affect placentation and fetal growth may explain our findings. Large record linkage studies have reported that maternal CVD risk is elevated in women with spontaneous PTB compared to term uncomplicated births.[1,3] Most women in our study were under 50 years of age (mean age 38 years), and thus, it is possible that longer follow-up of women with spontaneous PTB risk may reveal subclinical carotid vessel thickening.

Current guidelines for cardiovascular screening in women include history of hypertensive disorders of pregnancy and gestational diabetes as sex-specific risk markers.[32] Our results suggest that PTB may also be a pregnancy feature that can mark women at excess risk for CVD who may benefit from postpartum and ongoing primary care follow-up.

Our study must be considered in the context of limitations. Although large, our cohort is not entirely representative of the source cohort. In addition, enrolled women with IMT measurement were, in general, less obese than those excluded due to incomplete visualization of the entire carotid artery, and thus, our estimates may be biased toward the null. In addition, our study population was too young to determine if the subclinical atherosclerosis we detected may contribute to cardiovascular events. Longer follow-up is needed to identify if PTB is linked to IMT progression and CVD events. We also had small numbers in some subgroups, such as early PTB (<34 weeks, $n = 33$), and thus were limited in our ability to detect true associations. We also chose to focus on the POUCH Study PTB, as the clinical circumstances of other PTBs could not be reliably reported *via* maternal recall.[33] Future studies that can adjudicate these features are warranted. Strengths of our study include the prospective community cohort design, which enhances generalizability, and the comprehensive measurement of all carotid artery segments. We also collected pregnancy data prospectively and thus could relate precise pregnancy features to the maternal vascular profile a decade after delivery.

Conclusions

Our results indicate that subclinical atherosclerosis may be a mechanism linking PTB with future CVD. The more robust associations with the carotid bulb suggest that early evidence of atherosclerosis in women with PTBs is not entirely explained by traditional cardiometabolic risk factors. Women with PTB may identify a subset with accelerated progression to atherosclerotic coronary disease who may benefit from ongoing primary care surveillance after delivery.

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Author Disclosure Statement

No competing financial interests exist.

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Address correspondence to:
Janet M. Catov, PhD, MS
Department of Obstetrics, Gynecology and Reproductive Sciences
University of Pittsburgh School of Medicine
204 Craft Avenue
Suite A208
Pittsburgh, PA 15213

E-mail: catovjm@upmc.edu