Relationship Between Pregnancy Complications and Subsequent Coronary Artery Disease Assessed by Coronary Computed Tomographic Angiography in Black Women

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ORIGINAL ARTICLE

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BACKGROUND: Maternal pregnancy complications, particularly preeclampsia and gestational diabetes mellitus, are described to increase the risk for subsequent coronary artery disease (CAD). In addition, black women are at higher risk for CAD. The objective of this study was to compare the prevalence and extent of CAD as detected by coronary computed tomographic angiography (CCTA) in black women with and without a history of prior pregnancy complications.

METHODS: We retrospectively evaluated patient characteristics and CCTA findings in groups of black women with a prior history of preterm delivery (n=154), preeclampsia (n=137), or gestational diabetes mellitus (n=148), and a matched control group of black women who gave birth without such complications (n=445). Univariate and multivariate analyses were performed to assess risk factors of CAD.

RESULTS: All groups with prior pregnancy complications showed higher rates of any (≥20% luminal narrowing) and obstructive (≥50% luminal narrowing) CAD (preterm delivery: 29.2% and 9.1%; preeclampsia: 29.2% and 7.3%; and gestational diabetes mellitus: 47.3% and 15.5%) compared with control women (23.8% and 5.4%). After accounting for confounding factors at multivariate analysis, gestational diabetes mellitus remained a strong risk factor of any (odds ratio, 3.26; 95% CI, 2.03–5.22; *P*<0.001) and obstructive CAD (odds ratio, 3.00; 95% CI, 1.55–5.80; *P*<0.001) on CCTA.

CONCLUSIONS: Black women with a history of pregnancy complications, particularly gestational diabetes mellitus, have a higher prevalence of CAD on CCTA while only a history of gestational diabetes mellitus was independently associated with any and obstructive CAD on CCTA.

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Key Words: coronary artery disease ■ diabetes mellitus ■ heart diseases ■ preeclampsia ■ pregnancy

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CLINICAL PERSPECTIVE

In this current study, we evaluated the prevalence of coronary atherosclerosis as detected by coronary computed tomographic angiography in black women with prior pregnancy complications. Women were grouped into those with a history of preterm delivery, preeclampsia, gestational diabetes mellitus, and a control group. All groups with prior pregnancy complications had higher rates of obstructive (≥50% luminal narrowing) coronary atherosclerosis on coronary computed tomographic angiography compared with the control group. After accounting for confounding variables, gestational diabetes mellitus remained a strong predictor of obstructive coronary atherosclerosis. Our findings indicate that black women with prior pregnancy complications, especially gestational diabetes mellitus, should be considered at increased risk for subsequent coronary heart disease and healthcare providers should monitor affected women more aggressively for obstructive coronary artery disease and associated risk factors.

Pregnancy complications, particularly preeclampsia and gestational diabetes mellitus, have been associated with an increased incidence of subsequent maternal cardiovascular disease.[1–8] Less is known about the cardiovascular effects of other pregnancy complications.[9,10] To date, one study evaluating white females observed coronary artery disease (CAD) on computed tomography (CT) in 30% of women with a history of preeclampsia in comparison to 18% of women in the control group.[11] Racial variations have been documented in development of CAD.[12–14] Black women have a higher prevalence of cardiovascular risk factors and poorer outcome after developing CAD than women of other races.[15–18] In this study, we sought to evaluate the effect of 3 pregnancy complications in black women: preterm delivery, preeclampsia, and gestational diabetes mellitus, on the subsequent prevalence, extent, and severity of CAD detected by coronary CT angiography (CCTA) compared with a matched control group of black women without reported prior pregnancy complications.

METHODS

Patient Selection

In this retrospective multicenter study, data of hospitals within the Medical University of South Carolina health network were incorporated and approved by the respective institutional review boards with a waiver of written informed consent. We performed searches in our electronic medical chart and perinatal databases and cross-referenced results with the CCTA database to identify black women who had undergone CCTA between June 2005 and May 2014 within our hospital network and had encountered pregnancy complications earlier in life. No age cutoffs were applied.

These patients were divided into 3 groups according to their pregnancy complication as defined in the medical charts: preterm delivery (group 1), preeclampsia (group 2), and gestational diabetes mellitus (group 3). Women with a known history of multiple or repeated pregnancy complications were not included. We also identified a control group of black women (group 4) who had undergone CCTA during the same timeframe and had previously given birth without known pregnancy complications. The medical records did not enable identification of pregnancy-related hypertension or fetal growth restriction. Exclusion criteria were (1) missing data about pregnancy complications and baseline characteristics analyzed in this study; (2) abortion or miscarriage; (3) nonspontaneous preterm delivery including induced preterm delivery to treat preeclampsia; (4) history of any myocardial or coronary disease before pregnancy; (5) occurrence of a major adverse cardiovascular event before CCTA; (6) any cardiac intervention including coronary catheter angiography before CCTA; and (7) CCTA examinations which were deemed nondiagnostic because of either severe motion or beam-hardening artifacts, or poor contrast opacification of the coronary arteries.

Baseline characteristics, including age at CCTA, age at delivery, gravidity, and body mass index were collected from patients' medical records. In multiparous women, we noted the maternal age at first delivery. The presence of risk factors for CAD including smoking history (including pack years), as well as history of hypertension, type 2 diabetes mellitus, and hyperlipidemia as reported in the electronic medical chart system were recorded at the time of CCTA by medical staff. The medical records did not provide coronary risk factor data before pregnancy. The diagnosis of hypertension, diabetes mellitus, and hyperlipidemia, rather than specific criteria for each, were gathered. Patients with type 1 diabetes mellitus were excluded. To allow for comparison of the 4 groups while limiting the influence of patient characteristics that may affect the personal risk for developing CAD, we used propensity score matching in a 1:1 fashion for the groups with pregnancy-associated complications to derive a control group matched on age at CCTA, age at first delivery, number of pregnancies, body mass index, and smoking history.

Evaluation of CCTA Examinations

We analyzed the CCTA reports available from clinical routine as access to image data sets were no longer available in the majority of cases. Thus, no dedicated read-out for the purpose of this study was performed. At the time of the CCTA, examinations had been evaluated by experienced, board-certified cardiovascular imaging physicians for the presence of any visible calcified, noncalcified, or mixed coronary plaque (luminal narrowing of ≥20%) as well as any obstructive CAD (luminal narrowing of ≥50%) in the left main, left anterior descending, left circumflex, or right coronary artery. Indications for CCTA were evaluation for suspected CAD or assessment of acute chest pain. In patients with multiple CCTA examinations, the

most recent was included. No reports on coronary segments with stents or bypass grafts were evaluated because prior cardiovascular intervention was an exclusion criterion.

Statistical Analysis

Normality of distribution for continuous variables was assessed by distributional diagnostic plots. The Kruskal-Wallis rank test and Dunn test were used to assess equality of populations for non-normally distributed variables. Pearson χ^2 test and logistic regression were used to compare proportions of categorical variables across groups. Ordinal variables were treated as categorical. The control group (group 4) served as the reference group. Univariate logistic regression was used to identify explanatory variables of CAD. Multivariate logistic regression was then performed to test the null hypotheses of no association between having any CAD and pregnancy complications and of no association between presence of obstructive atherosclerosis and pregnancy complications. In these models, the adjustment was performed for covariates that were significant at the 20% level in univariate analysis and for known risk factors for CAD. Nonadjusted and adjusted odds ratios (OR) were estimated for the outcome of having any CAD and the outcome of having obstructive atherosclerosis for black women with and without pregnancy complications. All analyses were performed with commercially available software (StataCorp. 2013. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP, TX).

RESULTS

Demographics

A total of 439 black women who had previously experienced pregnancy complications and who had undergone clinically indicated CCTA between June 2005 and May 2014 within our hospital network were included (Figure 1). Preterm delivery had occurred in 154 women (35.1%), while 137 women (31.2%) had experienced preeclampsia, and 148 women (33.7%) had gestational diabetes mellitus. The matched control group of black women who had undergone CCTA and had previously given birth without reported pregnancy complications consisted of 445 women. Baseline characteristics of the black women in our study with and without prior pregnancy complications are summarized in Figure 2 and Table 1. Women with a history of gestational diabetes mellitus (group 3) had a higher prevalence of type 2 diabetes mellitus compared with all other groups (P<0.001), while women with a history of preterm delivery showed a lower prevalence compared with the control group (P<0.001).

Findings at Coronary CT Angiography

An overview of findings on CCTA within all patient groups is shown in Figure 3 and Table 2. The highest rates for presence of any CAD (≥20% luminal narrowing) detected on CCTA were found among black women with a history of gestational diabetes mellitus (47.3%, group 3), significantly higher (P<0.003) compared with women with either a history of preterm delivery (29.2%, group 1) or of preeclampsia (29.9%, group 2), as well as the control group (23.8%, group 4). Differences between the latter 3 groups were not significant (P≥0.15). Similarly, the highest rates for the presence of obstructive CAD (≥50% luminal narrowing) were observed in black women with a history of gestational diabetes mellitus (15.5%; P<0.001 compared to all other groups), while differences between the other 3 groups were nonsignificant (P≥0.11).

Results from univariate analysis about the relationship between presence of any CAD (≥20% luminal narrowing) as well as obstructive CAD (≥50% luminal narrowing) and patient characteristics are summarized in Table 3. Gestational diabetes mellitus was the only pregnancy complication that showed a strong correlation with the presence of any CAD (odds ratio [OR], 2.87; 95% CI, 1.94–4.24; P<0.001) or obstructive CAD (OR, 3.22; 95% CI, 1.76–5.92; P<0.001). Age at first delivery was associated with the presence of any CAD (OR, 1.06; 95% CI, 1.03–1.09; P<0.001) in women with and without pregnancy complications but not obstructive CAD (OR, 1.00; 95% CI, 0.95–1.05; P=0.96). A history of smoking, type 2 diabetes mellitus, hyperlipidemia, as well as age when undergoing CT were all associated with both any as well as obstructive CAD.

After accounting for covariates that were significant at the 20% to 25% level at univariate analysis as well as those of clinical relevance, multivariate analysis demonstrated that the presence of any CAD was associated with prior pregnancy complications for black women with a history of gestational diabetes mellitus (group 3; OR, 3.26; 95% CI, 2.03–5.22; P<0.001), while there was no evidence of such an association for women with a history of preterm delivery (group 1; OR, 1.49; 95% CI, 0.94–2.37; P=0.09) or women with a history of preeclampsia (group 2; OR, 1.47; 0.90–2.38; P=0.12). Similarly, there was a strong association between a history of gestational diabetes mellitus and the presence of obstructive coronary artery atherosclerosis on CCTA (OR, 3.00; 95% CI, 1.55–5.80; P=0.001) but not preterm delivery (OR, 1.97; 95% CI, 0.96–4.03; P=0.06) or preeclampsia (OR, 1.34; 95% CI, 0.61–2.99; P=0.46). Results from multivariate analysis are summarized in Table 4.

DISCUSSION

The results of our study indicate that among 884 black women with similar baseline characteristics and traditional risk factors for atherosclerotic cardiovascular disease, a history of pregnancy complications is associated with a higher prevalence of CAD on CCTA imaging. After accounting for relevant baseline characteristics and cardiovascular risk factors on multivariate analysis, a history of gestational diabetes mellitus remained a

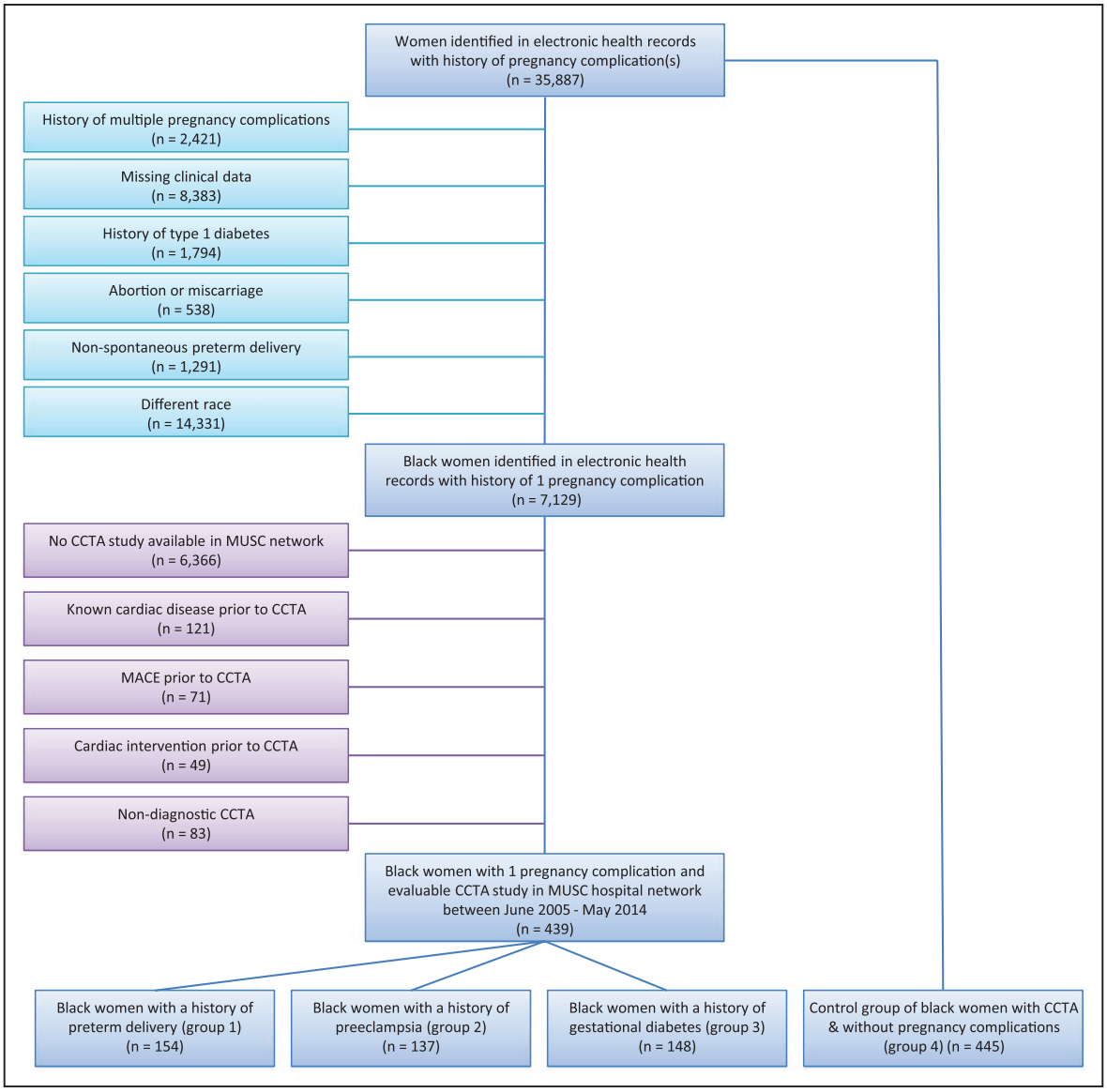

Figure 1. Flowchart of study population.
Flowchart displaying the selection process of the study population. CCTA indicates coronary computed tomography angiography; MACE, major adverse cardiovascular event; and MUSC, Medical University of South Carolina.

strong risk factor for the presence of any (≥20% luminal narrowing) as well as obstructive (≥50% luminal narrowing) CAD. Our results support the concept that women who experience pregnancy complications, particularly gestational diabetes mellitus, have a higher risk for CAD and should subsequently be monitored more closely for coronary risk factors than women without such pregnancy complications.

Preterm Delivery

Catov et al[19] reported an OR of 2.85 for the development of cardiovascular disease in women who had delivered a preterm infant after adjusting for race, as 47% of the population in their study were black. In our study, preterm delivery was associated with an increase in the presence of obstructive coronary disease compared with the control group (9.1% versus 5.4%) while baseline characteristics and rates for cardiovascular risk factors were similar. However, this association did not reach statistical significance after accounting for influencing factors during multivariate analysis. The pathophysiological mechanism underlying the relationship between preterm delivery and the development of maternal CAD remains unclear, but excess endocrine stimulation has been proposed as a potential causative factor.[20] Pharmacological therapy to treat hypertension, which is commonly used in treatment of preeclampsia, has also shown favorable results in the treatment of preterm delivery.[21] However, patients with coexisting preeclampsia and preterm delivery were excluded from our study because of the exclusion criteria of multiple

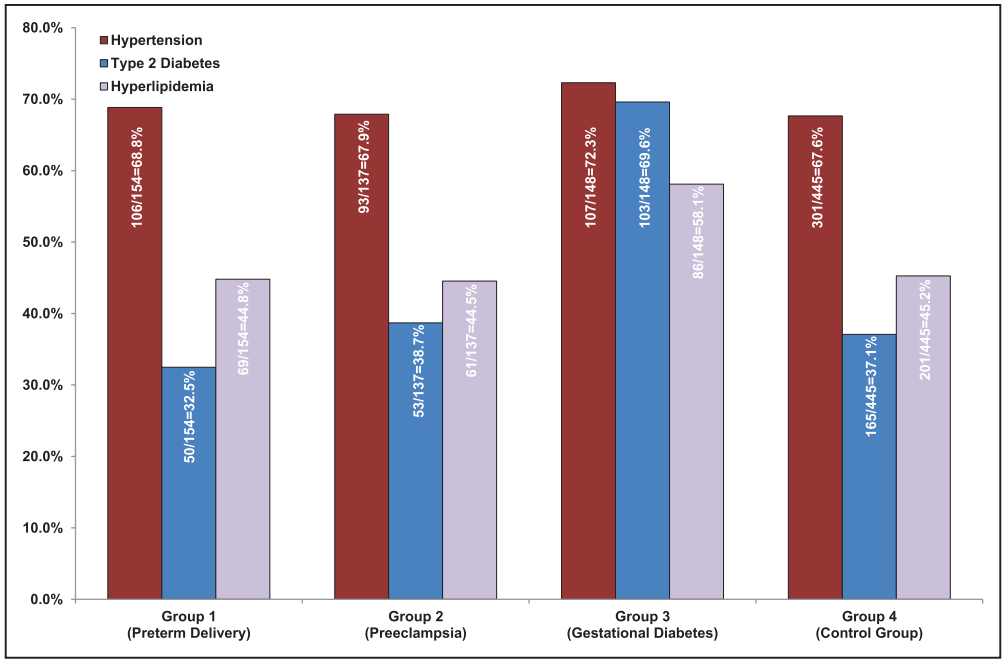

Figure 2. Prevalence of cardiovascular risk factors.
Graph shows the prevalence of cardiovascular risk factors within the study groups. Red bars represent hypertension, blue bars represent type 2 diabetes mellitus, and purple bars represent hyperlipidemia. Black women with a history of gestational diabetes mellitus (group 3) had a higher prevalence of type 2 diabetes mellitus compared to all other groups ($P<0.001$), while women with a history of preterm delivery showed a lower prevalence compared to the control group ($P<0.001$). Other comparisons between groups for prevalence of type 2 diabetes mellitus ($P\geq0.3$) as well as for all other characteristics ($P\geq0.2$) did not reach statistical significance.

pregnancy complications. Regardless, the prevalence of hypertension was similar among patients with a history of preterm delivery and the control group in our study.

Preeclampsia

Preeclampsia during pregnancy has been identified in multiple studies as a risk factor for subsequent cardiovas-

Table 1. Baseline Characteristics of Black Women With and Without Pregnancy Complications

Parameter	With Pregnancy Complications			Control Group	*P* Value
	Preterm Delivery (n=154)	Preeclampsia (n=137)	Gestational Diabetes Mellitus (n=148)	No Pregnancy Complications (n=445)	
BMI, kg/m²	32.0 (11.0); 17.7–65.3	32.6 (8.6); 22.4–78.5	30.9 (9.1); 17.7–65.3	31.8 (10.7); 15.7–80.5	0.63
Age at delivery	22 (7); 14–35	22 (8); 14–35	23 (7); 14–34	21 (8); 14–42	0.20
Pregnancies	1 pregnancy: 84 (54.6%)	1 pregnancy: 67 (48.9%)	1 pregnancy: 81 (54.7%)	1 pregnancy: 244 (54.8%)	0.84
	2 pregnancies: 51 (33.1%)	2 pregnancies: 53 (38.7%)	2 pregnancies: 48 (32.4%)	2 pregnancies: 121 (27.2%)	0.84
	3 or more pregnancies: 19 (12.3%)	3 or more pregnancies: 17 (12.4%)	3 or more pregnancies: 19 (12.4%)	3 or more pregnancies: 80 (18.0%)	0.84
Age at CCTA	<40 y: 42 (27.3%)	<40 y: 37 (27.0%)	<40 y: 41 (27.7%)	<40 y: 78 (17.5%)	0.44
	40–<50 y: 75 (48.7%)	40–<50 y: 68 (49.6%)	40–<50 y: 61 (41.2%)	40–<50 y: 267 (60.0%)	0.44
	50–<60 y: 33 (21.4%)	50–<60 y: 28 (20.4%)	50–<60 y: 34 (23.0%)	50–<60 y: 94 (21.1%)	0.44
	≥60 y: 4 (2.6%)	≥60 y: 4 (2.9%)	≥60 y: 12 (8.1%)	≥60 y: 6 (1.4%)	0.44
Time between delivery and CCTA	22.4 y	21.9 y	21.0 y	23.0 y	0.25
Prevalence of hypertension	106 (68.8%)	93 (67.9%)	107 (72.3%)	301 (67.7%)	0.76
Prevalence of type 2 diabetes mellitus	50 (32.5%)	53 (38.7%)	103 (69.6%)	165 (37.1%)	Group 3 vs 4 <0.001, Other ≥0.27
Prevalence of hyperlipidemia	106 (68.8%)	93 (67.9%)	107 (72.3%)	301 (67.6%)	0.76
Active smoking history	57 (37.0%)	55 (40.2%)	54 (36.5%)	164 (36.9%)	0.91
Pack years	8 (8); 1–50	8 (4); 1–58	6 (6); 1–36	10 (7); 2–32	0.87

Continuous variables are shown as median and range (interquartile range), binary and ordinal variables are shown as count (%). BMI indicates body mass index; and CCTA, coronary computed tomography angiography.

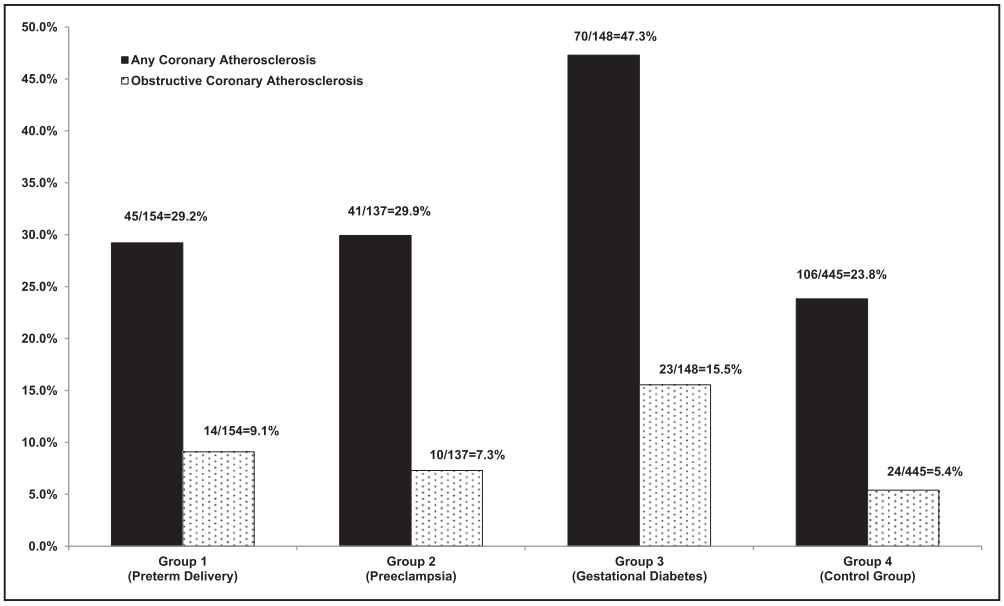

Figure 3. Findings at coronary computed tomography (CT) angiography.
Graph shows findings of coronary artery disease (CAD) at coronary CT angiography in the study groups. Solid bars represent any CAD (≥20% luminal narrowing). Dotted bars represent obstructive CAD (≥50% luminal narrowing). All 3 pregnancy complications were associated with higher rates of obstructive CAD compared with the control group. This association remained significant for gestational diabetes mellitus (odds ratio, 3.26; 95% CI, 2.03–5.22; *P*<0.001), after accounting for confounding variables during multivariate analysis, including body mass index, smoking status, type 2 diabetes mellitus, hypertension, hyperlipidemia, and age at the time of the CT examination.

cular disease.[22–25] Preeclampsia has been characterized as a systemic disease that manifests itself during pregnancy, but with effects that persist after delivery and result in impaired endothelial and angiogenetic function.[26–28] In a recent study in 164 mainly white women with a history of preeclampsia significant CAD was observed in 4.3%.[11] We found a higher incidence of significant CAD in our patient population of black women, which might be due to the fact that our imaging was clinically indicated. In addition, we observed a small relative increase in obstructive CAD in those with prior preeclampsia compared with the control group (7.3% versus 5.4%). A meta-analysis reported a doubling in risk for cardiovascular disease following preeclampsia in women <56 years of age.[22] The observed differences between the meta-analysis and our study may be partly explained by our younger average patient age of 44.3 years. Similar to preterm delivery, this association did not persist after accounting for influencing factors during multivariate analysis. Preeclampsia was the pregnancy complication with the lowest relative increase in obstructive CAD in our study, although rates for the presence of any CAD were similar to preterm delivery; this may be partially attributed to the relatively small size of our patient groups. Endothelial dysfunction has been identified as one of the underlying mechanisms contributing to hypertension during pregnancy, which could ultimately result in preeclampsia.[29] Pregnancy induces significant hemodynamic stress with increased total blood volume and cardiac output. Preeclampsia may merely represent an indicator of personal predisposition to hypertensive disease.[30] The metabolic and hemodynamic stress of

Table 2. Findings at Coronary CT Angiography

Parameter	With Pregnancy Complications			Control Group	*P* Value
	Preterm Delivery (n=154)	Preeclampsia (n=137)	Gestational Diabetes Mellitus (n=148)	No Pregnancy Complications (n=445)	
Any CAD (≥20% luminal narrowing)	45 (29.2%)	41 (29.9%)	70 (47.3%)	106 (23.8%)	Group 3 vs 4 <0.001; other ≥0.15
Obstructive CAD (≥50% luminal narrowing)	14 (9.1%)	10 (7.3%)	23 (15.5%)	24 (5.4%)	Group 3 vs 4 <0.001; other ≥0.11
In LM vessel territory	3.9%	8.0%	10.1%	4.9%	
In LAD vessel territory	24.7%	27.0%	37.2%	25.6%	
In LCX vessel territory	10.4%	13.1%	18.2%	9.2%	
In RCA vessel territory	14.3%	17.5%	19.6%	13.0%	

Variables are shown as count (%). CAD indicates coronary artery disease; CT, computed tomography; LAD, left anterior descending; LCX, left circumflex; LM, left main; and RCA, right coronary artery.

Table 3. Univariate Analysis of the Relationship Between Presence of Any and Obstructive CAD and Other Variables

	Any CAD (≥20% Luminal Narrowing)			Obstructive CAD (≥50% Luminal Narrowing)		
Parameter	**Odds Ratio**	**95% CI**	***P* Value**	**Odds Ratio**	**95% CI**	***P* Value**
Pregnancy complications combined						
Group 4	Reference			Reference		
Combined groups 1, 2, 3	1.76	1.32–2.36	<0.001	2.10	1.26–3.50	0.004
Pregnancy complications by group						
Group 4	Reference			Reference		
Group 1	1.32	0.88–1.99	0.18	1.75	0.88–3.48	0.11
Group 2	1.37	0.89–2.09	0.15	1.38	0.64–2.97	0.41
Group 3	2.87	1.94–4.24	<0.001	3.22	1.76–5.92	<0.001
Pregnancy-related characteristics						
Number of pregnancies:						
1	Reference			Reference		
2	0.78	0.57–1.08	0.14	0.80	0.46–1.38	0.42
3 or more	0.48	0.30–0.76	0.002	0.63	0.29–1.38	0.25
Age at delivery (per each additional year)	1.06	1.03–1.09	<0.001	1.00	0.95–1.05	0.96
Patient characteristics						
BMI	0.99	0.98–1.01	0.55	1.05	1.02–1.07	0.001
Smoking status	2.38	1.77–3.20	<0.001	2.48	1.51–4.05	<0.001
Diabetes mellitus	1.86	1.34–2.49	<0.001	2.76	1.66–4.59	<0.001
Hypertension	1.30	0.94–1.78	0.11	1.49	0.85–2.63	0.16
Hyperlipidemia	1.63	1.22–2.18	0.001	2.69	1.60–4.54	<0.001
Age category when undergoing CT:						
<40 y	Reference			Reference		
40–<50 y	2.46	1.47–4.10	0.001		0.78–3.83	0.18
50–<60 y	14.79	8.55–25.59	<0.001	3.79	1.67–8.60	0.001
60 y and over	48.95	15.33–15635	<0.001	5.65	1.69–18.87	0.005
Age when undergoing CT (per each additional year)	1.15	1.13–1.18	<0.001	1.07	1.04–1.11	<0.001

Group 1, preterm delivery; Group 2, preeclampsia; Group 3, gestational diabetes; and Group 4, no pregnancy complications. BMI indicates body mass index; CAD, coronary artery disease; and CT, computed tomography.

pregnancy may uncover preexisting abnormalities.[31] It has also been suggested that preeclampsia may cause irreparable damage to the vascular endothelium or the kidneys leading to subsequent vascular disease.[22] In our study, however, similar high rates of hypertension were observed in patients with prior preeclampsia and within the control group, although data on the prevalence of hypertension before pregnancy were not available. Nevertheless, Samadi et al[32] reported excess rates of maternal hypertension and chronic hypertension preceding pregnancy in black women compared with women of other races. This may potentially have an effect on hypertension rates later in life.

Gestational Diabetes Mellitus

Diabetes mellitus is a well-known risk factor for the development of atherosclerotic and cardiovascular disease, especially in women.[33] However, black women appear to be at an increased risk for diabetes mellitus and subsequent vascular disease.[34] The amount of weight gained during pregnancy is a direct predictor for the development of gestational diabetes mellitus, which increases the risk of developing type 2 diabetes mellitus. This increased risk is most remarkable within 10 years after delivery.[35,36] Black women appear to be at a substantially higher risk for sustained weight gain and gestational diabetes mellitus during pregnancy, as well as the development of type 2 diabetes mellitus following pregnancy than women of other races.[37–39] Our imaging results are in agreement with these reports as our black women with a history of gestational diabetes mellitus had significantly higher rates of metabolic disease including type 2 diabetes mellitus, hyperlipidemia, and hypertension than black women who experienced different pregnancy complications and those in the

Table 4. Multivariate Logistic Regression Analysis for Outcome of Any and Obstructive CAD Adjusted for Covariates

	Any CAD (≥20% Luminal Narrowing)			Obstructive CAD (≥50% Luminal Narrowing)		
Parameter	**Odds Ratio**	**95% CI**	***P* Value**	**Odds Ratio**	**95% CI**	***P* Value**
Pregnancy complications combined						
Group 4	Reference			Reference		
Combined groups 1, 2, 3	1.92	1.37–2.68	<0.001	2.09	1.23–3.57	0.007
Pregnancy complications by group						
Group 4	Reference			Reference		
Group 1	1.49	0.94–2.37	0.09	1.97	0.96–4.03	0.06
Group 2	1.47	0.90–2.38	0.12	1.34	0.61–2.99	0.46
Group 3	3.26	2.03–5.22	<0.001	3.00	1.55–5.80	0.001
Pregnancy-related characteristics						
Number of pregnancies						
1	Reference			Reference		
2	0.83	0.57–1.21	0.34	NA	NA	NA
3 or more	0.57	0.33–0.97	0.04	NA	NA	NA
Age at delivery	1.00	0.97–1.04	0.83	NA	NA	NA
Patient characteristics						
BMI	1.00	0.97–1.02	0.79	1.05	1.02–1.08	0.001
Smoking status	2.22	1.58–3.11	<0.001	2.55	1.51–4.30	<0.001
Diabetes mellitus	1.39	0.96–2.02	0.09	1.79	1.00–3.20	0.05
Hypertension	0.94	0.63–1.40	0.76	0.78	0.41–1.48	0.45
Hyperlipidemia	1.26	0.88–1.80	0.22	2.10	1.19–3.72	0.01
Age when undergoing CT (per each additional year of age)	1.15	1.12–1.18	<0.001	1.06	1.02–1.09	0.001

Multivariate analysis was adjusted for covariates that were found significant at the 20%–25% level on univariate analysis as well as those of clinical relevance. Variables included for both groups were BMI, smoking status, type 2 diabetes mellitus, hypertension, hyperlipidemia, age at first birth, and age when undergoing the CCTA examination. According to these criteria for inclusion in the multivariate analysis, the number of pregnancies as well as the age at first birth were included in the analysis of the presence of any CAD (≥20% luminal narrowing), but excluded in the analysis of presence of obstructive CAD (≥50% luminal narrowing) due to lack of significance on univariate analysis. Group 1, preterm delivery; Group 2, preeclampsia; Group 3, gestational diabetes mellitus; and Group 4, no pregnancy complications. BMI indicates body mass index; CAD, coronary artery disease; CCTA, coronary computed tomography angiography; and CT, computed tomography.

control group. Consequently, we also found the highest rates of obstructive CAD among black women with a history of gestational diabetes mellitus compared with our other evaluated patient cohorts. Compared with women in the control group, women with a history of gestational diabetes mellitus were 3 times more likely to have obstructive CAD even after accounting for confounding factors, including type 2 diabetes mellitus during multivariate analysis. Higher rates of vascular dysfunction have been reported, even in nondiabetic women with prior gestational diabetes mellitus.[40] Obesity remains a key clinical predictor for the development of type 2 diabetes mellitus in addition to parental diabetes mellitus, metabolic syndrome, elevated fasting glucose levels, low-high–density lipoprotein cholesterol, and elevated triglyceride levels.[41] Of the 3 major pregnancy complications we analyzed, black women with gestational diabetes mellitus may benefit the most from early and continuous treatment during pregnancy as well as early and prolonged postpartum follow-up to ultimately mitigate the risk for developing type 2 diabetes mellitus and subsequent CAD.[17,34,42]

Study Limitations

This study is retrospective and bias might have occurred because of this design. We did not include control groups of women from other races to directly investigate the effect of black race in women with and without pregnancy complications. Because of the study design, the potentially summative effect of multiple pregnancy complications was not analyzed. Data about the prevalence of cardiovascular risk factors before pregnancy as well as the time interval of onset following pregnancy was not available. In addition, data on prior imaging studies of the heart, current medication, personal as well as family history of cardiovascular disease, and clinical outcome was not available. Also, hemoglobin A1c was not measured systematically at the time of the CCTA examination; hence, we could not control our analysis

for patients with poorly controlled diabetes mellitus. Furthermore, in multiparous women, our data did not reveal the key pregnancy during which complications were observed nor information whether a complication had occurred at a single or all pregnancies. Finally, our results for the presence of CAD were solely based on results from clinically indicated CCTA imaging. Data of subsequent imaging studies to confirm the presence of obstructive CAD or information on plaque morphology was not available. While CCTA has very high sensitivity for the detection of coronary artery stenosis, confirmation by invasive coronary catheter angiography was not systematically obtained. In addition, CCTA tends to overestimate the degree of coronary artery stenosis and, therefore, has only moderate specificity. Thus, the prevalence of obstructive CAD in our study may be overestimated. Conversely, silent CAD in black women with a history of pregnancy complications who did not undergo CCTA was not examined by our study design and may have been missed. Finally, our findings might have limited generalizability given that our cohort was retrospectively included and underwent clinically indicated CCTA.

Conclusions

Preterm delivery, preeclampsia, and gestational diabetes mellitus were all associated with CCTA imaging findings of any CAD and obstructive CAD in black women with an average age younger than 50 years, compared with a matched control group without a history of these pregnancy complications. This association remained significant for gestational diabetes mellitus after accounting for confounding variables during multivariate analysis. Black women with a history of gestational diabetes mellitus were 3 times more likely to have a CCTA showing obstructive CAD compared with the control group. Consequently, healthcare providers should consider pregnancy complications a risk factor for future CAD, especially in black women with gestational diabetes mellitus and monitor affected women more aggressively for coronary risk factors for premature atherosclerosis.

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Disclosures

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