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Intraabdominal fat, insulin sensitivity, and cardiovascular risk factors in postpartum women with a history of preeclampsia

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Abstract

Objective—Women who develop preeclampsia have a higher risk of future cardiovascular disease and diabetes compared to women who have uncomplicated pregnancies. We hypothesized that women with prior preeclampsia would have increased visceral adiposity that would be a major determinant of their metabolic and cardiovascular risk factors.

Study Design—We compared intraabdominal fat (IAF) area, insulin sensitivity index (S_I), fasting lipids, low-density lipoprotein relative flotation rate, and brachial artery flow-mediated dilatation in 49 women with prior preeclampsia and 22 controls who were at least 8 months postpartum and matched for age, parity, body mass index, and months postpartum. Women were eligible if they did not smoke tobacco, use hormonal contraception, have chronic hypertension, or have a history of gestational diabetes.

Results—The groups were similar for age (mean ± SD: prior preeclampsia 33.4 ± 6.6 vs control 34.6 ± 4.3 years), parity (median: 1 for both), body mass index (26.7 ± 5.9 vs 24.0 ± 7.3 kg/m^2), and months postpartum (median [25th-75th percentile]: 16 [13-38] vs 16.5 [13-25]). There were no significant differences in IAF area and SI. Despite this, women with preeclampsia had lower high-density lipoprotein (46.0 ± 10.7 vs 51.3 ± 9.3 mg/dL; $P < .05$), smaller/denser low-density lipoprotein relative flotation rate (0.276 ± 0.022 vs 0.289 ± 0.016; $P = .02$), higher systolic (114.6 ± 10.9 vs 102.3 ± 7.5mmHg) and diastolic (67.6 ± 7.5 vs 60.9 ± 3.6 mm Hg; $P < .001$) blood pressures, and impaired flow-mediated dilatation (4.5 [2-6.7] vs 8.8 [4.5-9.1] percent change, $P < .05$) compared to controls. In a subgroup analysis, women with nonsevere preeclampsia (n = 17) had increased IAF (98.3 [60.1-122.2]) vs 63.1 [40.1-70.7] cm^2; $P = .02$) and decreased SI (4.18 [2.43-5.25] vs 5.5 [3.9-8.3] × 10^{-5} min^{-1}/pmol/L; $P = .035$) compared to the controls, whereas

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women with severe preeclampsia (n = 32) were not different for IAF and S_I. IAF was negatively associated with S_I and positively associated with cardiovascular risk factors even after adjusting for the matching variables and total body fat.

Conclusion—Women with prior preeclampsia have an atherogenic lipid profile and endothelial dysfunction compared to matched control subjects despite having similar adiposity and insulin sensitivity, suggesting that there are mechanisms separate from obesity and insulin resistance that lead to their cardiovascular risk factors. Visceral adiposity may have a role in contributing to these risk factors in the subgroup of women who have preeclampsia without severe features.

Keywords

body fat distribution; cardiovascular risk factors; endothelial dysfunction; insulin resistance; preeclampsia

Women who develop preeclampsia are more likely to be obese,[1-5] be insulin resistant,[6-10] have an atherogenic lipoprotein phenotype,[5,11,12] and have markers of endothelial dysfunction.[13,14] Although the clinical manifestations of preeclampsia resolve postpartum, women have abnormalities remote from delivery including lower insulin sensitivity,[7] higher blood pressures,[15-19] an atherogenic lipoprotein phenotype,[15] and endothelial dysfunction.[20] The persistence of these abnormalities suggests that they have an underlying condition, presumably the metabolic syndrome.[21] Indeed, recent studies have shown that the metabolic syndrome is more common in women with a history of preeclampsia[22-24] and that they have an increased risk of developing complications associated with the metabolic syndrome such as cardiovascular disease[25-31] and diabetes mellitus.[32-34]

We and other investigators have demonstrated in other populations that visceral adiposity is a significant determinant of the metabolic syndrome[35] and its features including decreased insulin sensitivity[36-39] and β-cell function,[39,40] impaired glucose tolerance,[41] elevated blood pressure,[35,42] and dyslipidemia.[35,38,43] Visceral fat is metabolically active as a source of free fatty acids[44,45] and adipokines, such as adiponectin,[46,47] tumor necrosis factor (TNF)-α,[45,48,49] and plasminogen activator inhibitor (PAI)-1[50,51]; many of these factors have been shown to be elevated in women with preeclampsia,[11,52-54] but the studies that measured these factors in women with preeclampsia did not quantify visceral adiposity. Our group was specifically interested in evaluating the role that visceral adiposity and insulin resistance play in contributing to cardiovascular risk factors in women with a history of preeclampsia. We hypothesized that visceral adiposity would be a major determinant of their metabolic and cardiovascular risk factors.

Materials and Methods

Study design

This was a cross-sectional study comparing body fat distribution, insulin sensitivity, β-cell function, fasting lipids, hepatic lipase activity, and endothelial function between postpartum women who had either an uncomplicated pregnancy (control group) or a history of preeclampsia (prior preeclampsia group). The study was approved by the University of

Washington Institutional Review Board prior to initiation. All subjects provided written informed consent to participate.

Subjects

Subjects were recruited by advertisement in the greater Seattle area and underwent a screening visit that included a history and physical examination with a fasting blood draw. Women were eligible if they were at least 8 months postpartum and premenopausal. They were excluded if they smoked tobacco, used hormonal contraception or medications that would impact glucose metabolism or lipids/lipoproteins, were pregnant, or had a fasting plasma glucose ≥110 mg/dL, an abnormal complete blood cell count, liver transaminases ≥1.5 × normal, a serum creatinine ≥1.4 mg/dL, a history of chronic hypertension, diabetes, renal disease, autoimmune disease, fetal anomalies or aneuploidy, or multi-fetal gestation. All women underwent screening for gestational diabetes as a part of standard practice in our region and had normal results on either the 1-hour oral glucose challenge test or 3-hour oral glucose tolerance test. Women diagnosed with gestational diabetes in any pregnancy were excluded.

Women in the prior preeclampsia group had medical record documentation of the following criteria for preeclampsia: systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg on 2 occasions 6 hours apart and persistent 1+ proteinuria (between 30-100 mg/dL) on random urine samples or total protein ≥300 mg/24-hour urine collection. Women in the prior preeclampsia group were further characterized by whether they had features of severe preeclampsia: elevated transaminases, thrombocytopenia, severe blood pressure elevation (systolic ≥160 mm Hg or diastolic blood pressure > 110 mm Hg), renal insufficiency, and neurological symptoms.[55] Women in the control group delivered their babies at ≥39 weeks' gestation and had normal blood pressures documented throughout their prenatal course, labor and delivery, and postpartum. The 2 groups were matched for age (within 5 years), body mass index (BMI) (within 2.5 kg/m^2), time since delivery (within 4 weeks), and parity (within 1 delivery).

Measurements

Study procedures were performed on 2 consecutive days during the subjects' follicular phase of the menstrual cycle at the University of Washington General Clinical Research Center. Study participants were instructed to avoid exercise or strenuous activity 24 hours prior to the visit. Dietary assessments were not performed.

Anthropometrics and body fat distribution and composition

BMI (kg/m^2) was calculated from the average of 3 weight and height measurements. Waist circumference was measured in the standing position at the level midway between the lateral lower rib margin and the iliac crest. To determine total and regional body fat and lean content, dual-energy x-ray absorptiometry (DEXA) was performed on the general clinical research center.[56] A computed tomography (CT) scan was performed in the department of radiology to quantify intraabdominal fat (IAF) and subcutaneous fat (SCF) areas.[57,58] A single observer who was blinded to group assignment made the DEXA and CT measurements. The coefficient of variation (CV) for the DEXA scan measurement of total

fat mass is 1.67% (personal communication with Danielle Yancey, Bachelor of Science in Exercise Science, Research Scientist and Exercise Physiologist in the Nutrition Research and Body Composition Core at the University of Washington Medical Center, March 4, 2014). The CV for the SCF and visceral fat areas for the same scan on 10 separate days is 1.5%.[48]

Frequently sampled intravenous glucose tolerance test

Following a 12-hour overnight fast, an insulin-modified frequently sampled intravenous glucose tolerance test (FSIGT) was performed to quantify the insulin sensitivity index (S_I) using minimal model of glucose kinetics[59] of Bergman et al.[60] The acute insulin response to glucose was quantified as the incremental insulin response above baseline from 2-10 minutes following glucose administration. β-cell function (the disposition index) was calculated by adjusting the acute insulin response to glucose for the prevailing S_I.[61]

Assays

All chemical analyses were performed on blood samples obtained after a 12-hour overnight fast and stored at −70°C. Plasma glucose levels were determined in duplicate using a glucose oxidase method (Beckman, Palo Alto, CA). Plasma immunoreactive insulin levels were measured in duplicate using a modification of the double antibody radioimmunoassay technique.[62] Total, low-density lipoprotein (LDL), and high-density lipoprotein (HDL) cholesterol and triglyceride levels were determined by standardized methodologies at the Northwest Lipid Research Laboratories.[63] LDL relative flotation rate (Rf), which characterizes LDL peak buoyancy, was determined by density gradient ultracentrifugation.[64] Hepatic lipase activity, which leads to more atherogenic, smaller, denser LDL,[65,66] was measured in plasma after heparin bolus.[63]

Endothelial- and endothelial-independent vasodilation

Longitudinal images of the brachial artery were digitized from the video output of a standard clinical ultrasound scanner (HDI 3000 or HDI 5000; Philips Medical Systems, Bothell, WA) using a frame grabber on a personal computer under control of custom image capture software.[67] A linear 5- to 12-MHz scanhead or a compact linear 5- to 10-MHz scanhead was used for the ultrasound imaging. Image acquisition was gated with an ECG signal so that all images were captured at end diastole and collected for every cardiac cycle. The baseline brachial artery diameter was measured over 1 minute after the subject had been at rest for 10 minutes. Reactive hyperemia was produced using a pneumatic tourniquet placed around the upper arm and inflated to 40 mm Hg greater than the subject's systolic pressure for 4 minutes. The maximum diameter was obtained during a 2-minute interval following cuff release. Endothelial-dependent vasodilation (flow-mediated dilatation [FMD]) was calculated as the maximum diameter expressed as a percentage of the baseline measurement. Sublingual nitroglycerin 0.4 mg was given 15 minutes after cuff deflation. Images were collected between 2-10 minutes to obtain the maximum diameter. Endothelial-independent vasodilation (nitroglycerine-mediated dilatation) was calculated as the maximum diameter expressed as a percentage of the baseline diameter.

Sample size calculation

Sample sizes were calculated for S_I based on published data for postpartum women who had preeclampsia ($8.5 \pm 2.3 \times 10^{-5}$ min^{-1} $pmol/L^{-1}$) compared to controls ($11.4 \pm 4.3 \times 10^{-5}$ min^{-1} $pmol/L^{-1}$)[7]. To detect a difference in S_I, 38 women in the preeclampsia group and 19 in the control group were needed for 90% power at a .05 significance level.

Statistical analyses

Continuous variables are presented as mean ± SD or median with the 25th and 75th percentiles if not normally distributed. Categorical variables are presented as absolute number and percentages and compared using χ^2 or Fisher exact test. Linear regression analyses were used to assess the relationships between the independent variables and the continuous, dependent variables of interest. Group assignment was included as an indicator variable. In these models, we assessed whether the differences between the groups were independent of BMI and measures of adiposity. We also adjusted for potential confounding variables and the matching variables. Logarithmic transformation was performed as necessary to satisfy the statistical assumptions of linear regression. We performed a subgroup analysis after categorizing women with preeclampsia into 2 groups based on the presence or absence of severe features. In these models, group was entered as a factor variable to allow comparisons between the control and each preeclampsia group. All statistical analyses were 2-sided. Statistical significance was considered for $P < .05$. Statistical analyses were performed using STATA 13.0 for Windows (STATA Corp, College Station, TX).

Results

There were no differences between the groups in the matching variables, frequencies of exercise, or first-degree relatives with type 2 diabetes mellitus, obesity, hypertension, and cardiovascular disease (Table 1). The majority (65.3%) of the women in the prior preeclampsia group had severe features; 46.9% delivered <36 weeks' gestation.

In contrast to our hypothesis, women with prior preeclampsia did not have greater adiposity as compared to the controls (Table 2). In linear regression models containing the matching variables, only BMI was significantly associated with waist circumference (coefficient 0.0084 ± 0.0009; $P < .001$), percent body fat (coefficient 0.9508 ± 0.1343; $P < .001$), IAF area (coefficient 0.0245 ± 0.0032; $P < .001$), and SCF area (coefficient 0.0296 ± 0.0037; $P < .001$). Consistent with the women having similar body fat distributions, we found no significant differences in S_I (Table 2). When total body fat, IAF area, and SCF area were added to the model, IAF area was an independent predictor of S_I (coefficient −0.000042 ± 0.000013; $P = .002$), whereas SCF area, total body fat, and BMI were not.

Women with prior preeclampsia had higher blood pressures than controls (Table 3) even after adjusting for exercise and family history ($P < .001$ and $P = .001$, respectively). In models containing the matching variables, prior preeclampsia (coefficient 10.5 ± 2.5; $P < .001$) and BMI (coefficient 0.534 ± 0.180; $P = .004$) were the significant predictors of systolic blood pressure. When total body fat, IAF area, and SCF area were added to the

model, only prior preeclampsia (coefficient 10.5 ± 2.5; $P < .001$) independently predicted systolic blood pressure. Prior preeclampsia was the only predictor of diastolic blood pressure (coefficient 6.02 ± 1.71; $P = .001$). Women with prior preeclampsia also had less FMD compared to controls (Table 3). The association remained significant (coefficient −0.212 ± 0.102; $P = .04$) after adjusting for the matching variables. There were no significant associations between these variables, total body fat, IAF and SCF area, and FMD.

Women with prior preeclampsia had a more atherogenic lipoprotein phenotype as compared to controls (Table 3). In the multivariate regression model, IAF area (coefficient −0.0013 ± 0.0005; $P = .016$) independently predicted HDL levels, but BMI, total body fat, SCF area, and prior preeclampsia did not. Women with prior preeclampsia had increased hepatic lipase activity and lower LDL Rf compared to controls. In the multivariate regression models, IAF area (coefficient −0.0000419 ± 0.0000106; $P < .001$) significantly predicted smaller, denser LDL; whereas prior preeclampsia (coefficient −0.0098 ± 0.005; $P = .055$) and the matching variables, total body fat, and SCF area did not.

In our subgroup analysis, women with nonsevere preeclampsia were more obese and had a central fat distribution; elevated triglycerides; smaller, denser LDL; and lower HDL levels compared to women with severe preeclampsia and controls (Table 4). Women with non-severe preeclampsia also had significantly lower S_I, higher blood pressures, and elevated hepatic lipase activity compared to controls. In contrast, women with severe preeclampsia were not significantly different from controls with the exception of having higher blood pressures. After adjusting for BMI, the differences between the groups were no longer statistically significant for S_I, IAF and SCF areas, triglycerides, and hepatic lipase. However, systolic (coefficient 12.4 ± 3.3; $P < .001$) and diastolic (coefficient 6.0 ± 2.2; $P = .008$) blood pressures, HDL levels (coefficient −0.0730 ± 0.0298; $P = .02$), and LDL Rf (coefficient −0.0191 ± 0.0067; $P = .005$) remained significantly different between the groups. In multivariate regression models, IAF area significantly predicted S_I (coefficient −0.000042 ± 0.000014; $P = .003$), HDL levels (coefficient −0.0012 ± 0.0005; $P = .036$), and LDL Rf (coefficient −0.0000346 ± 0.0000109; $P = .001$), whereas BMI, total body fat, and SCF area did not.

Comment

In our study of healthy postpartum women who were matched for BMI, women with prior preeclampsia had higher blood pressures, an atherogenic lipoprotein phenotype, and endothelial dysfunction compared to women who had uncomplicated pregnancies. We anticipated that women with prior preeclampsia would also have greater visceral adiposity and be insulin resistant. Only women with nonsevere preeclampsia had increased visceral adiposity and decreased insulin sensitivity. Moreover, it was their increased visceral adiposity and not their higher BMI or total body fat that significantly determined their metabolic and cardiovascular risk factors. Collectively, our data support that there are mechanisms separate from obesity and insulin resistance that lead to the cardiovascular risk factors in women with prior preeclampsia; yet, visceral adiposity may have a role in contributing to these risk factors in the subgroup of women who have preeclampsia without severe features.

In our population of healthy postpartum women, visceral adiposity was independently associated with insulin sensitivity, blood pressure, and an atherogenic lipoprotein phenotype, whereas BMI, total body fat, and SCF were not associated with these variables. We have previously shown that visceral adiposity is more important than abdominal SCF in determining the metabolic syndrome[35] and insulin resistance.[37] IAF likely has a pathophysiologic role as it is a source of free fatty acids,[44,45] TNF-α,[45,48,49] and PAI-1.[50,51] Women who develop preeclampsia have elevated levels of free fatty acids,[11,68] TNF-α,[52,69,70] and PAI-1[53,54] that contributes to their cardiovascular disease risk through proinflammatory effects, oxidative stress, impaired fibrinolysis, and enhanced angiotensin II production.[50,71-73] In our study only women with nonsevere preeclampsia had increased visceral adiposity that was associated with their insulin resistance and cardiovascular risk factors.

Preeclampsia is a heterogeneous disorder for which numerous pathophysiological mechanisms have been suggested to lead to the endothelial dysfunction and clinical manifestations. There are conflicting results about the role of insulin resistance in the development of preeclampsia. Several studies have suggested that insulin resistance[74-76] and increased adiposity[77] is a characteristic of women with mild but not severe forms of preeclampsia. In contrast, other studies have identified insulin resistance and the metabolic syndrome in severe[16,24,78] but not with mild hypertensive complications.[79,80] Inconsistent results have likely occurred due to differences in the methods used for assessing insulin sensitivity, time since delivery, genetic differences in the study populations, sample size, and whether matching was performed for BMI. Furthermore, some investigators included women who subsequently developed chronic hypertension or had gestational diabetes.[16,24,76,81,82] Our study excluded women with chronic hypertension or a history of gestational diabetes. Our study also differed from others due to the majority of our participants having a history of severe pre-eclampsia. This allowed us to evaluate differences between severe and non-severe preeclampsia. Only women with nonsevere preeclampsia had increased visceral adiposity that was associated with their insulin resistance and cardiovascular risk factors, suggesting that they have different pathophysiological mechanisms involved in the development of preeclampsia compared to women with severe features.

Our study's major strengths include measuring abdominal fat areas by CT and quantifying insulin sensitivity using minimal model of glucose kinetics of Bergman et al[60] from the FSIGT. Other studies performed in women with a history of preeclampsia used a surrogate measure of insulin sensitivity such as fasting insulin, Homeostatic Model Assessment of Insulin Resistance, or Quantitative Insulin Sensitivity Check Index or estimated insulin sensitivity from oral glucose or meal tolerance tests.[16,17,22,23,76] Fasting insulin primarily reflects hepatic insulin sensitivity and is best reserved for studies where a more accurate measurement of insulin sensitivity is not feasible.[83] Oral glucose tolerance tests are useful for estimating glucose tolerance but not insulin sensitivity and have poor reproducibility.[83] In contrast, the FSIGT has a CV comparable to the hyperinsulinemic-euglycemic clamp and correlates with estimates of insulin sensitivity in healthy populations such as ours.[83] Although the FSIGT is less reliable in individuals with impaired insulin secretion or significant insulin resistance, our study population only included women who had normal

glucose tolerance testing during pregnancy and a postpartum fasting glucose level <110 mg/dL and thus would be considered a healthy population. Additional strengths of our study include performing a dynamic measurement of endothelial function instead of using biochemical markers. We rigorously screened and characterized our study subjects to reduce the risk of misclassification. Furthermore, the study procedures were performed during the follicular phase of the menstrual cycle since variations in insulin sensitivity occur during the menstrual cycle.[84]

One of our study limitations is that matching for BMI likely attenuated the differences we found between the groups as well as recruiting women who passed a screening evaluation that included blood pressure and fasting glucose levels. Our rationale for matching BMI and excluding women with hypertension was to extend what was already known about the association between obesity and certain risk factors for diabetes and cardiovascular disease. We wanted to show that even in a healthy population, women with preeclampsia would have increased visceral adiposity, lower insulin sensitivity, and more cardiovascular risk factors. We did not anticipate that matching for BMI would eliminate the association between insulin resistance and preeclampsia since other studies have shown differences in insulin sensitivity[7,16] in postpartum women who were matched for BMI. In addition, we have previously shown that insulin resistance and the metabolic syndrome are critically dependent on visceral adiposity regardless of BMI.[35,37,41,85] We did not match for race or ethnicity in our study but prospectively tracked our enrollment to ensure that our study groups reflected the greater Seattle area and were balanced. Other investigators have demonstrated that race is associated with differences in insulin sensitivity, visceral adiposity, and cardiovascular risk factors.[86-88] Therefore, we would include it as a matching variable in future studies. An additional limitation to our study is that the control subjects volunteered in response to advertisement. It is possible that women who volunteer are more likely to have an interest in their glucose metabolism and cardiovascular risk due to a family history. Indeed, the control subjects had similar frequencies to the prior preeclampsia subject of first-degree relatives with type 2 diabetes and cardiovascular diseases; this was a surprising finding since women with preeclampsia are more likely to have a family history.[89-91] Another limitation of our study is that its cross-sectional design cannot address whether the women's baseline risk factors increase their likelihood of developing preeclampsia or whether preeclampsia itself leads to changes that result in them developing future cardiovascular and metabolic risk factors. Furthermore, there may be residual confounding from unmeasured variables. Lastly, our sample size did not allow us to detect smaller differences in insulin sensitivity between the groups than what was assumed for the sample size calculation. We also performed multiple comparisons that could have increased the likelihood of incorrectly rejecting the null hypothesis for some of our analyses. However, the statistically significant findings in our study were consistent across univariate and multivariate analyses as well as in the subgroup analyses, supporting that they were valid findings.

Women with a history of preeclampsia would benefit from early surveillance and counseling about their risk of future complications, and be encouraged to pursue lifestyle modifications that reduce the risk of developing diabetes and cardiovascular disease. Cusimano et al[92] suggest using a screening tool that accounts for a history of pregnancy-related complications as an early clinically identifiable marker of future cardiovascular risk. Earlier identification

of women for lifestyle modifications has obvious benefits such as reducing the weight gained after the index pregnancy and during future pregnancies. Aerobic training in women with a history of preeclampsia improves the components of the metabolic syndrome, brachial artery FMD, vascular structure, and autonomic function.[93] In addition to long-term benefits of lifestyle modifications, women who exercise prior to a subsequent pregnancy may lower the risk of a recurrent hypertensive complication.[94,95] Furthermore, women who adopt lifestyle modifications to reduce their weight and risk of cardiovascular and metabolic complications may beneficially impact the health of their own children who have been shown to have a higher risk of cardiovascular complications as they age.[96-98]

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Table 1
Characteristics of women with prior preeclampsia and control subjects

Characteristic	Prior preeclampsia (n = 49)	Controls (n = 22)	*P* value
Age, y	33.4 ± 6.6	34.6 ± 4.3	.4
Primiparous, n (%)	29 (59.2)	11 (50.0)	.7
BMI, kg/m^2	26.7 ± 5.9	24.0 ± 7.3	.1
Months postpartum	16 [13−38]	16.5 [13−25]	.8
Race, n (%)			
Caucasian	35 (71.4)	15 (68.2)	.9
Other	8 (16.3)	3 (13.6)	
Unknown	6 (12.2)	4 (18.2)	
Exercise, n (%)	28 (57.1)	16 (72.7)	.5
Family history, n (%)			
Type 2 diabetes mellitus	13 (26.5)	6 (27.3)	.9
Obesity	19 (38.8)	7 (31.8)	.4
Hypertension	25 (51.0)	10 (45.5)	.5
Preeclampsia	7 (14.3)	1 (4.5)	.2
Coronary artery disease	2 (4.1)	1 (4.5)	1.0
Cerebrovascular disease	9 (18.4)	2 (9.1)	.3

Data are mean ± SD or median [25th—75th percentile].
BMI, body mass index.

Table 2

Body composition, fat distribution, insulin sensitivity, and glucose metabolism in women with prior preeclampsia compared to control subjects

Demographic	Prior preeclampsia (n = 49)	Controls (n = 22)	*P* value
Total body fat, g	26,411.1 ± 11,874.8	28,315.9 ± 12,715.7	.6
Percent total fat	38.0 ± 9.5	37.3 ± 9.3	.8
Trunk/total body fat	50 ± 6.4	50 ± 4.5	.8
Percent total lean	60.1 [56.7−68.8]	63.6 [53.8−69.2]	1.0
Waist circumference, cm	84.7 ± 15	81.0 ± 11.2	.3
IAF area, cm^2	60.1 [39.6−90.9]	63.1 [40.1−70.7]	.7
SCF area, cm^2	282.9 [172.7−426.1]	226.9 [177.3−425.6]	.5
IAF/SCF	0.228 [0.211−0.274]	0.247 [0.166−0.302]	.9
Fasting glucose, mg/dL	87.3 [84.7−92.6]	88.6 [84.8−92.2]	.7
S_I, $\times 10^{-5}$ min^{-1}/pmol/L	4.4 [3.2−6.8]	5.5 [3.9−8.3]	.1
AIRg, pmol/L	358.6 [242.2−474.8]	340.5 [219.4−528.2]	1.0
DI, min^{-1}	0.0159 [0.0094−0.0211]	0.0195 [0.0121−0.0292]	.2

Data are mean ± SD or median [25th—75th percentile].

AIRg, acute insulin response to glucose; *DI*, disposition index; *IAF*, intraabdominal fat; *SCF*, subcutaneous fat; S_I, insulin sensitivity index.

Table 3

Cardiovascular disease risk factors in women with prior preeclampsia compared to control subjects

Characteristic	Prior preeclampsia (n = 49)	Controls (n = 22)	*P* value
Systolic BP, mm Hg	114.6 ± 10.9	102.3 ± 7.5	< .001
Diastolic BP, mm Hg	67.6 ± 7.5	60.9 ± 3.6	< .001
FMD (% change)	4.5 [2−6.7]	8.8 [4.5−9.1]	< .05
NMD (% change)	19.4 [16.4−23]	22.5 [16.8−26.3]	.2
Total cholesterol, mg/dL	166.0 ± 30.0	169.6 ± 41.4	.7
HDL cholesterol, mg/dL	46.0 ± 10.7	51.3 ± 9.3	< .05
Triglycerides, mg/dL	69 [52−100]	55 [45−80]	.2
LDL cholesterol, mg/dL	104 [84−123]	103 [83−114]	.6
LDL peak buoyancy (Rf)	0.276 ± 0.022	0.289 ± 0.016	.02
Hepatic lipase activity, nmol/mL/min	308 [224−393]	243 [217−286]	.04

Data are mean ± SD or median [25th—75th percentile].

BP, blood pressure; *FMD*, flow-mediated dilatation; *HDL*, high-density lipoprotein; *LDL*, low-density lipoprotein; *NMD*, nitroglycerine-mediated dilatation; *RF*, relative flotation rate.

Table 4
Comparison of women with history of preeclampsia based on severity of preeclampsia

Characteristic	Nonsevere preeclampsia (n = 17)	Severe preeclampsia (n = 32)	Controls (n = 22)	*P* value Nonsevere vs severe Control vs nonsevere Control vs severe
Age, y	35.0 ± 7.5	32.5 ± 5.9	34.6 ± 4.3	.2
				.7
				.3
BMI, kg/m^2	29.6 [24.4–32.4]	24.7 [20.9–27.5]	24.0 ± 7.3	.01
				.007
				.4
Primiparous, n (%)	11 (64.7)	18 (56.3)	11 (50.0)	.5
				.2
				.8
Months postpartum	15 [11–35]	17.5 [13–39]	16.5 [13–25]	.8
				.4
				1.0
Waist circumference, cm	91.5 ± 16.2	81.1 ± 2.3	81.0 ± 11.2	.02
				.02
				.9
Total body fat, g	33,632.8 ± 11,990.4	25,491.3 ± 12,345.6	26,140.7 ± 12,098.5	.02
				.07
				.8
Percent total fat	40.7 ± 8.9	36.6 ± 9.7	37.3 ± 9.3	.1
				.2
				.9
IAF, cm^2	98.3 [60.1–122.2]	56.4 [38.6–75.1]	63.1 [40.1–70.7]	.004
				.02
				.7
SCF, cm^2	389.2 [263.0–572.5]	243.8 [148.2–367.9]	226.9 [177.3–425.6]	.02
				.07
				.8
S_I, $\times 10^{-5}$ min^{-1}/pmol/L	4.18 [2.43–5.25]	4.71 [3.59–7.28]	5.5 [3.9–8.3]	.1
				.04
				.5
DI, min^{-1}	0.0153 [0.0072–0.0183]	0.0169 [0.0099–0.0223]	0.0195 [0.0121–0.0292]	.2
				.1
				.5
Systolic BP, mm Hg	117.7 ± 11.7	112.9 ± 10.3	102.3 ± 7.5	.2
				< .001

Characteristic	Nonsevere preeclampsia (n = 17)	Severe preeclampsia (n = 32)	Controls (n = 22)	*P* value Nonsevere vs severe Control vs nonsevere Control vs severe
				< .001
Diastolic BP, mm Hg	68.5 ± 7.5	67.0 ± 7.5	60.9 ± 3.6	.5
				.001
				.002
FMD (% change)	4.5 [2.9−6.3]	5.0 [1.6−7.2]	8.8 [4.5−9.1]	.7
				.08
				.1
Total cholesterol, mg/dL	167.3 ± 33.5	165.3 ± 28.6	169.6 ± 41.4	.7
				.8
				.6
HDL cholesterol, mg/dL	40.8 ± 7.5	48.7 ± 11.2	51.3 ± 9.3	.01
				.001
				.3
Triglycerides, mg/dL	101 [69−134]	63.5 [50.5−82.5]	55 [45−80]	.02
				.02
				.8
LDL cholesterol, mg/dL	106 [91−123]	98 [81−121.5]	103 [83−114]	.5
				.5
				.8
LDL peak buoyancy (Rf)	0.266 ± 0.022	0.281 ± 0.021	0.289 ± 0.016	.01
				.001
				.2
Hepatic lipase activity, nmol/mL/min	319 [237−444]	286 [215.5−387.5]	243 [217−286]	.3
				.045
				.3

Data are mean ± SD or median [25th—75th percentile].

BMI, body mass index; *BP*, blood pressure; DI, disposition index; *FMD*, flow-mediated dilatation; *HDL*, high-density lipoprotein; *IAF*, intraabdominal fat; *LDL*, low-density lipoprotein; *RF*, relative flotation rate; *SCF*, subcutaneous fat; S_I, insulin sensitivity index.