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Early Biomarkers of Subclinical Atherosclerosis in Obese Adolescent Girls with Polycystic Ovary Syndrome

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Abstract

Objectives—Because in obese youth, pulse wave velocity (PWV), an early CVD marker, is elevated, we tested if obese girls with PCOS have higher PWV and carotid intima-media thickness (cIMT) compared with obese and normal-weight control girls without PCOS and whether PWV and cIMT correlate with inflammatory and circulating endothelial function biomarkers.

Study design—Cross-sectional study of PWV and cIMT in 91 obese girls with PCOS (OB-PCOS), 30 obese controls (OB-non-PCOS), and 19 normal-weight controls (NW-non-PCOS). Body composition, blood pressure, fasting glucose, insulin, lipid concentrations and endothelial function biomarkers were measured. OB-NonPCOS and OB-PCOS girls underwent 2-hour oral glucose tolerance testing.

Results—PWV was higher in OB-PCOS (664±24 cm/s) and OB-NonPCOS (624±37 cm/s) compared with NW-NonPCOS (468±13 cm/s, $p<0.001$), with no differences in cIMT. Systolic BP (SBP), LDL and non-HDL cholesterol were higher, and HDL cholesterol and indices of insulin sensitivity were lower in OB-PCOS and OB-NonPCOS compared with NW-NonPCOS. Vascular

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cell adhesion molecule-1 (VCAM-1) and hsCRP were higher in OB-PCOS compared with NW-NonPCOS. PWV correlated with adiposity (r_s=.46), insulin sensitivity index (HOMA-IR r_s=.31), SBP (r_s=.24; p ≤0.003 for all) and free testosterone (r_s=.24; p=0.03). In multiple regression analysis with PWV as the dependent variable and age, race, BMI, PCOS and dysglycemia as independent variables, only BMI was an independent contributor to the model (r^2=0.068, p=0.003).

Conclusions—In adolescent girls, obesity and not PCOS appears to be associated with heightened CVD risk. Increased PWV, VCAM-1 and hsCRP may be the earliest subclinical atherosclerosis biomarkers in obese girls with PCOS.

Keywords

pulse wave velocity; intima media thickness; adhesion molecules

Polycystic ovary syndrome (PCOS) is believed to be the most common endocrine disorder with a prevalence of approximately 5 – 10% among U.S. women (1). PCOS is frequently associated with obesity, insulin resistance (IR), diabetes, hypertension and dyslipidemia, conditions conducive to increased cardiovascular disease (CVD) risk (1). Indeed the prevalence of the metabolic syndrome is increased in both adult women and adolescents with PCOS (2). Girls with PCOS are not only more overweight but are 4.5 times more likely to have metabolic syndrome than age matched NHANES III girls after adjusting for body mass index (BMI) (2, 3). Moreover, impaired glucose tolerance and type 2 diabetes mellitus are more prevalent in both adult women and adolescents with PCOS (4, 5).

In women with PCOS, evidence of subclinical CVD was shown by increased PWV and cIMT (10). However, controversy continues whether CVD is increased in PCOS. Epidemiological data demonstrate greater CV events and lower survival (11) whereas other studies show no increased prevalence of CVD in women with PCOS compared with non-PCOS women (12, 13).

Data are limited with respect to subclinical CVD using imaging or circulating endothelial function biomarkers in adolescent girls with PCOS. Based on our previous observations of increased PWV in obese adolescent boys and girls compared with their normal weight peers (14), we hypothesized that obese adolescent girls with PCOS will have evidence of subclinical CVD and increased inflammatory and circulating endothelial function biomarkers. Therefore, this study was undertaken to examine PWV and cIMT in obese adolescent girls with PCOS (OB-PCOS), in comparison with obese control peers (OB-NonPCOS) and normal weight controls (NW-NonPCOS), and to assess the relationships between PWV, cIMT, insulin sensitivity, and traditional and non-traditional CVD markers.

Methods

Overweight/obese adolescent girls (n=91) with a diagnosis of PCOS (6, 15) were recruited from the PCOS Center at Children's Hospital of Pittsburgh, 30 otherwise healthy OB-NonPCOS were recruited from the Weight Management and Wellness Center at Children's Hospital of Pittsburgh, and 19 healthy NW-NonPCOS (BMI <85th percentile) were recruited

through newspaper and hospital advertisements. OB-NonPCOS and NW-NonPCOS had regular menses and no clinical evidence of hyperandrogenism. The diagnosis of PCOS was made based on the presence of clinical signs and symptoms of hyperandrogenism and/or biochemical hyperandrogenemia, consistent with the Endocrine Society Clinical Practice Guidelines and our publications (6, 15–17). Many girls with PCOS were recruited shortly after their diagnosis in our PCOS Center and before pharmacologic therapy was initiated. Inclusion criteria were age 10–20 years, postmenarche, and Tanner stage III-V. Exclusion criteria were: (1) pregnancy; (2) preexisting diabetes; (3) use of medications that impact carbohydrate or lipid metabolism (oral contraceptive pills [OCP], metformin, anti-epileptics, anti-psychotics, statins, fish oil); and (4) smoking history. The investigation was approved by the Institutional Review Board and performed in the Pediatric Clinical and Translational Research Center of Children's Hospital of Pittsburgh and The Department of Epidemiology Ultrasound Research Laboratory at the University of Pittsburgh. Parental informed consent and child assent were obtained from all participants before participation in accordance with the ethical guidelines of Children's Hospital of Pittsburgh.

Each participant underwent a physical examination, height, weight, waist and hip circumference measurements. Fasting blood was obtained for lipid profile, glucose, insulin and HbA1c, adipokines (leptin, adiponectin), inflammatory marker (high-sensitivity C-reactive protein or hsCRP) and circulating soluble cell adhesion molecule biomarkers (intercellular adhesion molecule-1 (ICAM-1), vascular adhesion molecule-1 (VCAM-1) and E-selectin). DXA was performed in all participants to assess body composition. Obese participants with and without PCOS had a 2-hour oral glucose tolerance test to assess glucose tolerance, and a free testosterone panel to assess for hyperandrogenemia. Dysglycemia was defined as a fasting plasma glucose ≥ 100 mg/dL, 2-hour glucose ≥ 140 mg/dL, or both. Age-specific BMI z-scores were calculated utilizing Epi Info™ (Version 3.3.2, Centers for Disease).

Carotid IMT and aortic PWV were measured at the Ultrasound Research Laboratory of the Department of Epidemiology at the University of Pittsburgh, a key laboratory in multiple adult and pediatric trials (7, 14, 18, 19). Using a Toshiba (Toshiba American Medical Systems, Tustin, CA) SSA-270A scanner equipped with a linear 5 MHz transducer, the right and left carotid artery was interrogated. Although this transducer is a lower frequency than recommended in published standards (20), lower frequency probes are used in obese populations where the vessel may be deeper. Detailed B-mode images of the near and far walls of the distal common carotid artery (one cm proximal to the carotid bulb), far wall of the bulb, and first centimeter of the far wall of the internal carotid artery were obtained in end-diastole from each side for a total of 8 images. These images were digitized for later reading using a semi-automated edge detection software (21). The scanning and reading protocols that were used are well established (14, 19). Intima-media thickness measures were obtained by electronically tracing the lumen-intima interface and the media-adventitia interface across a 1-cm segment; one measurement was generated for each pixel over the area, for a total of approximately 140 measures for each segment. For analyses, the mean and maximum values of the average readings at all 8 locations were used. The URL requires certification of sonographers and readers, and monitors quality control with several ongoing quality control systems. Monthly repeat scans were performed by two separate sonographers

on the same day and several of the scans were reviewed to monitor the inter-sonographer (scanning) reproducibility. Quality control was also performed between readers on a regular basis. Quarterly, scans were read by two separate readers to monitor inter-reader reproducibility. Reproducibility of cIMT measures was excellent with an intra-class correlation coefficient between sonographers of 0.82–0.97 and within reader of 0.87–0.99 across the study period.

To measure aortic pulse-wave velocity, two unidirectional transcutaneous Doppler flow probes (model 810-a, 10 MHz; Parks Medical Electronics, Aloha, OR) were used; one to detect the pulse wave as it reaches the right carotid artery and one to detect the pulse wave as it reaches the right femoral artery. The time required for the pulse wave to travel from one probe to the other, combined with the distance between the two probes, allowed for the calculation of central pulse wave velocity and was performed several times until waveforms were clear. Heart rate monitoring was used to score the waveforms. Three runs were performed for each participant, and the mean of waveforms from all usable runs was used in analyses, reducing the measurement variability.

Plasma glucose was measured with a glucose analyzer (YSI, Yellow Springs, OH). Insulin, adiponectin, and leptin were measured using a commercially available radioimmunoassay kit (Linco Research, St. Louis, MO). Fasting lipids were analyzed using the standards of the Centers for Disease Control and Prevention. hsCRP was analyzed by nephelometry, total testosterone was measured by HPLC tandem mass spectrometry and free testosterone was measured by equilibrium dialysis at Esoterix Inc (Calabasas Hills, CA). ICAM-1, VCAM-1 and E-selectin were quantified using a commercially available double-sandwich enzyme-linked immunoassay kit (R&D Systems, Minneapolis, MN).

Statistical analyses

HOMA-IR was calculated (www.ihoma.co.uk) using the formula: (fasting glucose (mg/dL) × fasting insulin (μU/mL) × 0.0555)/22.5. Statistical procedures were performed using SPSS version 22 (SPSS Inc., Chicago, IL). Differences in continuous variables among the three groups were tested with either a one-way ANOVA or the nonparametric Kruskall-Wallis test or Mann-Whitney U test for two group comparison, based on the nonviolation of statistical assumptions. Where differences existed among groups, post-hoc multiple comparisons were performed using Bonferroni correction. For categorical variables, three-group comparison was made by Pearson Chi-square. Pearson correlation (r) for parametric and Spearman correlation (r_s) for non-parametric measures were performed for PWV and cIMT. Multiple regression analysis was used to quantify the independent contributions to PWV. Statistical significance was set at $p \leq 0.05$.

Results

Table I summarizes the characteristics of the participants. The OB-PCOS group was slightly older, but all adiposity measures were comparable between OB-PCOS and OB-NonPCOS and significantly higher than NW-NonPCOS. Total, free and % free testosterone concentrations were higher in OB-PCOS compared with OB-NonPCOS.

PWV was significantly higher in OB-PCOS and OB-NonPCOS girls compared with NW-NonPCOS before and after adjusting for age, race and blood pressure (Figure 1, A) (adjusted mean: 676 ± 30 cm/s OB-PCOS, 623 ± 64 cm/s OB-NonPCOS, and 457 ± 55 cm/s NW-NonPCOS, p ANOVA=0.002). Mean and maximum cIMT were not different between the three groups (mean: 0.516 ± 0.004 mm OB-PCOS, 0.531 ± 0.01 mm OB-NonPCOS, 0.531 ± 0.01 mm NW-NonPCOS [Figure 1, B]; maximum: 0.634 ± 0.007 mm OB-PCOS, 0.650 ± 0.01 mm OB-NonPCOS, 0.645 ± 0.03 mm NW-NonPCOS, p ANOVA=0.56).

Fasting glucose and HbA1c were similar among the three groups and glucose tolerance did not differ between OB-NonPCOS and OB-PCOS girls (Table I). Surrogate estimates of insulin sensitivity including fasting insulin concentration, HOMA-IR, and leptin/adiponectin were impaired in OB-PCOS and OB-NonPCOS compared with NW-NonPCOS. Although total cholesterol did not differ among the three groups, LDL and non-HDL cholesterols were higher and HDL cholesterol lower in OB-PCOS and OB-NonPCOS vs. NW-NonPCOS girls. TG and TG/HDL ratio were significantly higher in OB-PCOS girls compared with their obese and lean counterparts. SBP was significantly higher in OB-PCOS and OB-NonPCOS compared with NW-NonPCOS, but did not differ between OB-NonPCOS and OB-PCOS even after controlling for age, race and waist circumference. VCAM-1 was significantly different among the three groups, and higher in OB-PCOS compared with NW-NonPCOS (post-hoc p=0.015), and ICAM-1 and E-selectin did not differ among the groups (Figure 2). hsCRP was significantly higher in OB-PCOS and OB-NonPCOS compared with NW-NonPCOS, but did not differ between OB-NonPCOS and OB-PCOS (Figure 2).

PWV showed the highest correlation with BMI, followed by HOMA-IR, SBP, free testosterone (Figure 3), TG (r=.23, p=0.012), HDL (r=−.25, p=0.005), and hsCRP (r_s=.24, p=0.009) but not with total testosterone, LDL, non-HDL cholesterol, VCAM-1, ICAM-1 or E-selectin. cIMT did not correlate with any of the above variables. There were five OB-PCOS girls and one OB-NonPCOS who had PWV >1200 cm/s and three OB-PCOS girls with free testosterone >25 pg/mL (Figure 3). There were no unique physical or metabolic characteristics common among the six with high PWV or the three with high free testosterone that would differentiate them from the others. Excluding these six subjects from the PWV correlations did not change the findings (BMI r_s=.52, HOMA-IR r_s=.34, SBP r_s=.27, free testosterone r_s=.27, p <0.05). To examine if among obese girls, hyperandrogenemia or other factors explain an additional component of the variance in PWV besides BMI, stepwise multiple regression analyses were performed with PWV as the dependent variable and age, race, BMI and PCOS status without or with the variables that showed significant univariate correlations to PWV (dysglycemia, SBP, hsCRP, TG, HDL, and HOMA-IR) as independent variables (Table II; available at www.jpeds.com). Seven percent of the variance in PWV was explained by the model which contained age, race, BMI, PCOS and dysglycemia (model p ANOVA=0.003), and BMI was the only significant contributor to the model (Table II).

Discussion

Kelly et al (22) first demonstrated increased PWV in obese women with PCOS compared with BMI-matched non-PCOS controls, and further studies confirmed these findings

showing that age (23), SBP (23, 24) and presence of PCOS phenotype (23) are significant determinants of PWV (23, 24). In contrast, Moran et al and Cussons et al found no differences in PWV between obese and non-obese PCOS women and their overweight or BMI-matched controls, respectively with age, glucose tolerance, mean arterial pressure and hsCRP, but not adiposity, predicting PWV (25, 26). Our present PWV findings are in agreement with Cussons et al and Ketel et al who demonstrated that obesity and not PCOS was associated with greater arterial stiffness in young adult women with PCOS and obese controls compared with their lean PCOS and normal weight control counterparts (27). On the other hand, early endothelial dysfunction in PCOS is reported by demonstrating lower flow-mediated dilation and nitrate-mediated dilation in the brachial artery compared with matched controls, largely independent of obesity (28). Additionally, numerous adult studies have shown adverse structural changes in cIMT in premenopausal women with PCOS compared with age and/or BMI-matched non-PCOS controls (29). Furthermore, coronary artery and aortic calcification are increased in women with PCOS compared with controls, with the presence of PCOS, age and BMI as significant determinants of coronary artery calcification (30). These contrasting results between our PWV and cIMT findings in adolescent girls with PCOS and adult women are important and could merely be a reflection of chronology, where the initial obesity-driven alteration may over time and with aging evolve into a PCOS-associated abnormality against the backdrop of persistent hyperandrogenism.

Despite the growing evidence of subclinical CVD in adult women with PCOS, the increased risk for CVD in them remains controversial (31). Two large prospective studies each with greater than 20 years of follow-up found that there was no increased prevalence of nonfatal/fatal CVD events in women with PCOS (12, 13). On the other hand, a sub analysis of the NHLBI sponsored Women's Ischemia Syndrome Evaluation (WISE) study found that women with PCOS had a greater number of CV events (OR 1.71) and lower event free survival compared with non-PCOS women (11).

Insulin resistance is a well-known risk factor for CVD (5, 32). In adult women with PCOS, improvement in insulin sensitivity with troglitazone was associated with reduced carotid IMT progression rates, and worsening of insulin sensitivity with high dose OCP was associated with increased arterial stiffness (33, 34). Elevated TG/HDL, a marker of IR and/or the metabolic syndrome both in adults and in children, has been proposed to be an atherogenic index (35). Based on these, IR and elevated LDL, triglycerides and TG/HDL in the present study suggest a pro-atherogenic state in PCOS and obesity. However, in addition to IR, long-standing hyperandrogenemia may play a role in vascular changes observed in adulthood (10). Even though free testosterone correlated with PWV in our obese adolescents, lack of a significant contribution of the PCOS condition to the variance in PWV in the regression model suggests that PCOS per se in obese adolescents may not play a role over and above obesity in the altered PWV. Queries related to the role of obesity vs. PCOS per se in modulating PWV would best be addressed in a study which includes normal-weight PCOS vs. obese PCOS girls. Until then, we postulate that obesity initially pulls the trigger for changes in PWV in obese PCOS adolescents. However, the persistence of hyperandrogenemia together with dyslipidemia and IR may lead over time and with aging to the reported differences in PWV in adult women with PCOS compared with their BMI-

matched controls. Contrary to adult studies cited above, a randomized trial comparing drosperinone/ethinyl estradiol to rosiglitazone in adolescents with PCOS did not show any changes in PWV with either treatment, despite improvement in free testosterone with both treatments and insulin sensitivity with the latter (17). Perhaps the lack of improvement in adiposity in part contributed to the lack of PWV change.

Numerous adult studies from a meta-analysis have also shown adverse structural changes in cIMT in premenopausal and postmenopausal women with PCOS compared with age and/or BMI-matched non-PCOS controls (29). The literature regarding cIMT in pediatric obesity is inconsistent with some studies showing increased cIMT, mediated in part by IR (36), SBP (36, 37), BMI, glucose and hsCRP (37). In contrast, others have shown no differences in cIMT (38), including our current and prior study (14). An additional study showed a correlation between total and calculated free testosterone and cIMT in 160 obese adolescent girls independent of BMI and IR (39), whereas our study found no such associations among our 121 PCOS and OBCN girls combined. These observations in youth and adults suggest that increases in cIMT may evolve over time and with aging against the backdrop of persistence of obesity, other CV risk factors (including but not limited to hsCRP) and hyperandrogenism.

Pediatric literature regarding PWV in obesity is limited and conflicting too, with several studies reporting increased PWV with increasing adiposity in youth (14, 40) with HbA1c and insulin sensitivity being independent predictors of PWV in one study (14) and decreased cardiorespiratory fitness and measures of adiposity as independent predictors in the other (40). Another study showed lower PWV in obese, primarily female subjects compared with lean controls, which the authors suggested may reflect general vasodilatation (41). A study by Urbina et al examined obese and obese insulin resistant adolescents and young adults compared with lean controls and revealed that HOMA, a surrogate index of insulin sensitivity, was not an independent determinant of PWV, but BMI and blood pressure were (42). The latter data are consistent with our findings with respect to BMI and HOMA. These contrasting findings are also likely explained by differences in study populations, including varying sample sizes (40, 42), younger (40) vs. older participants (42), and males (14, 40–42) or prepubertal subjects (40).

Although there are a few cross-sectional adolescent PCOS studies that evaluated CVD risk factors and IR, and incorporated control comparison groups (43, 44), none included ultrasonographic arterial structural or functional imaging modalities. Two interventional studies in adolescent PCOS investigated PWV (17) and cIMT (45), but both were limited in that they did not include control groups. The second study was a 12-month lifestyle intervention that showed that cIMT only improved in those that demonstrated a reduction in BMI SDS (45), further attesting to the important role of obesity in this age group. Our prior work in adolescent girls with PCOS demonstrated that 6 months of insulin sensitization (rosiglitazone) or OCP did not change body weight, cIMT or PWV (17).

Circulating biomarkers of CVD include the soluble cell adhesion molecules ICAM-1, VCAM-1 and E-selectin, elevations in which are believed to reflect early abnormal endothelial status contributing to increased CVD risk. VCAM-1 concentrations in our

adolescent girls with OB-PCOS were similar to OB-NonPCOS but greater than NW-NonPCOS, similar to a number of studies in the pediatric obesity literature (46–48) but with no prior data in adolescent PCOS. Several adult studies have shown that VCAM-1 concentrations were higher in PCOS women compared with BMI-matched overweight controls (49, 50). Even though no correlation was demonstrated in our pediatric study, one adult study showed a positive correlation between VCAM-1 and total testosterone concentrations (49). Taken together, it could be hypothesized that in youth the initial alteration in VCAM-1 may be driven by obesity, but over time and with persistence of hyperandrogenemia together with obesity VCAM expression is induced further and becomes pronounced in adulthood in PCOS women. Lastly, with regards to CRP, and a metaanalysis revealed that women with PCOS have elevated circulating CRP independent of obesity compared with controls (51), a study by Talbott et al (52) in adult women with PCOS found that CRP was not a significant independent predictor of cIMT when BMI was taken into account. However, another adult PCOS study found CRP but not adiposity, predicted PWV (25). In our study, hsCRP was greater in OB-PCOS and OB-NonPCOS compared with NW-NonPCOS groups. Although hsCRP correlated with PWV but not cIMT, it was not an independent predictor of PWV. In the pediatric literature, a paucity of data exists on the association of hsCRP and subclinical markers of atherosclerosis (53), and to our knowledge there are no published data in youth with PCOS.

A limitation of our study is the absence of normal-weight adolescent girls with PCOS, the numbers of whom diagnosed are few in any PCOS, Endocrinology or Adolescent Medicine clinic, and the relatively small sample size of the healthy normal-weight and obese control groups. However, our NW-NonPCOS and OB-NonPCOS group sample sizes are comparable with other pediatric (43) and adult (9, 10, 27, 50, 54) cross-sectional studies. Although selection bias of NW-NonPCOS and OB-NonPCOS could be contributory, there was no known family history of PCOS in our NW-NonPCOS subjects, and similar to the general US population, most of our OB-NonPCOS subjects had some family history of obesity, diabetes or CVD. Lastly, it remains to be determined whether or not the observed statistically significant increase in PWV in obese girls with PCOS is clinically meaningful. Long-term longitudinal studies are needed to examine the progression of these statistical outcomes and their clinical translation.

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List of Abbreviations

PCOS	Polycystic Ovary Syndrome
PWV	pulse wave velocity
cIMT	carotid intima-media thickness
OB-PCOS	obese PCOS
OB-NonPCOS	obese controls
NW-NonPCOS	normal-weight controls
VCAM-1	vascular cell adhesion molecule-1
IR	insulin resistance
CVD	cardiovascular disease
OCP	oral contraceptive pills
hsCRP	high-sensitivity C-reactive protein
ICAM-1	intercellular adhesion molecule-1

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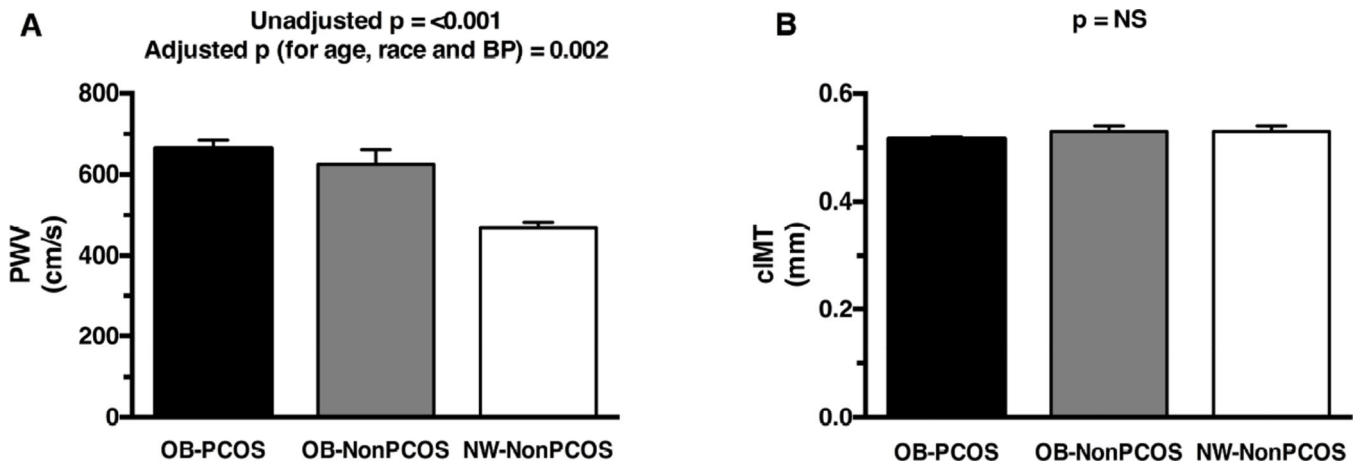

Figure 1.

A, Pulse wave velocity in OB-PCOS girls vs. OB OB-NonPCOS vs. (NW OB-NonPCOS).

B, Carotid intima-media thickness in OB-PCOS girls vs. OB-NonPCOS vs. NW-NonPCOS.

* Post-hoc OB-PCOS vs. NW-NonPCOS p<0.001; † post-hoc OB-NonPCOS vs. NW-NonPCOS p<0.001; NS, not significant.

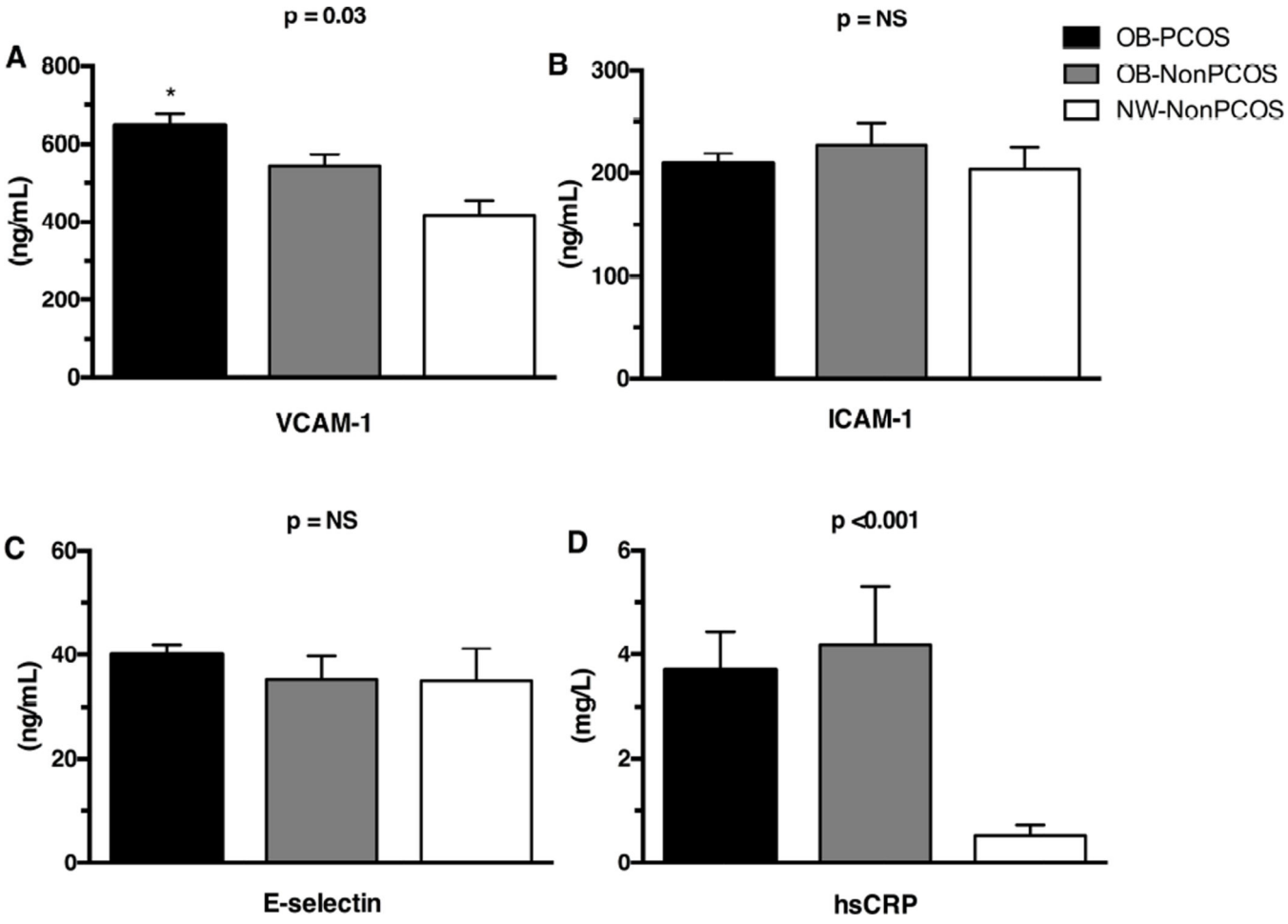

Figure 2.

A, Vascular adhesion molecule-1 (VCAM-1), B, intercellular adhesion molecule-1 (ICAM-1), C, E-selectin, and D, high sensitivity C-reactive protein (hsCRP) in OB-PCOS girls vs. OB-NonPCOS vs. NW-NonPCOS. * Post-hoc OB-PCOS vs. NW-NonPCOS $p \leq 0.015$; † post-hoc OB-NonPCOS vs. NW-NonPCOS $p < 0.001$; NS, not significant.

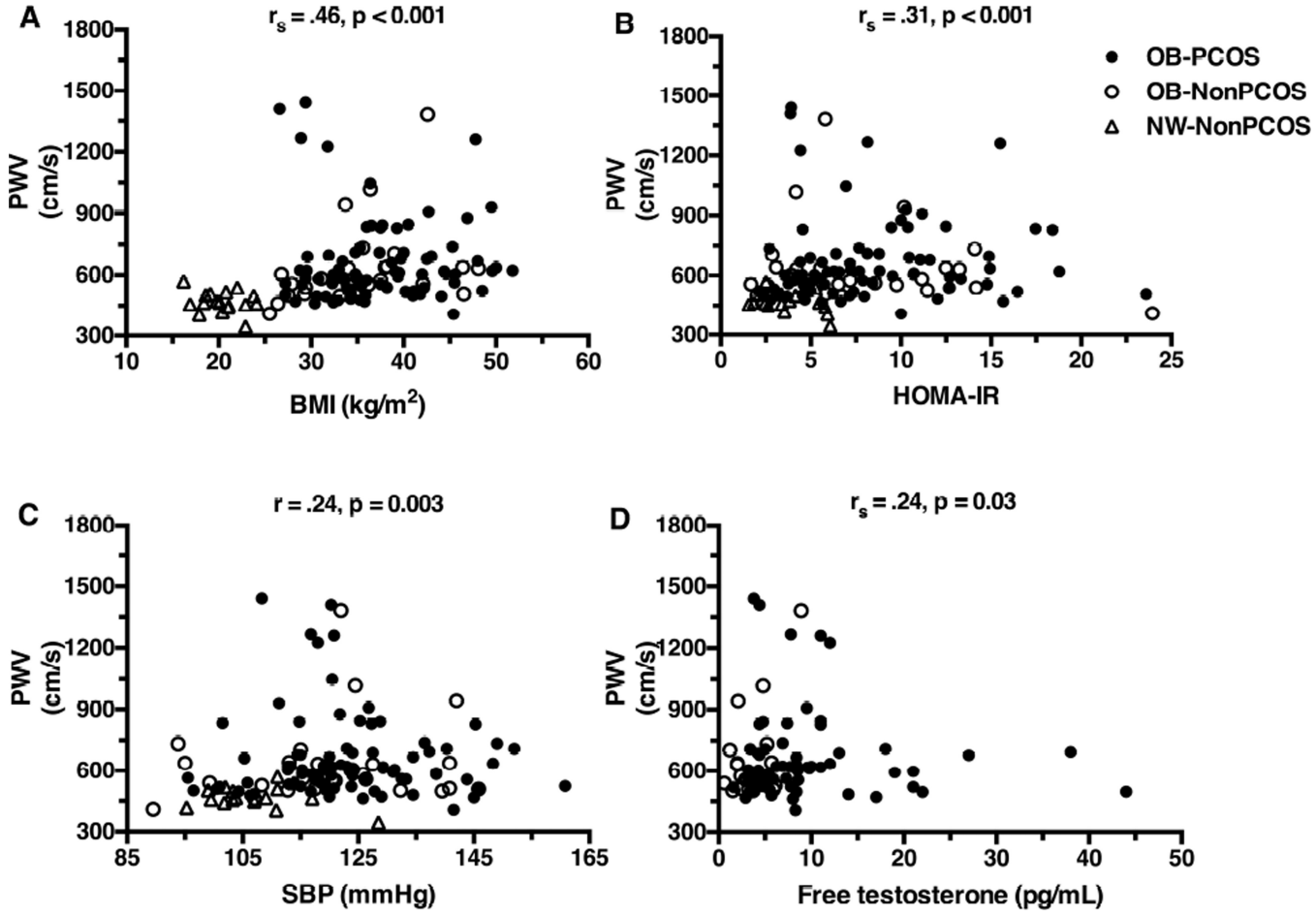

Figure 3.

Correlation between PWV and A, BMI, B, HOMA-IR, C, systolic blood pressure, and D, free testosterone.

Table 1

Participants' physical and metabolic characteristics

	OB-PCOS (n = 91)	OB-NonPCOS (n = 30)	NW-NonPCOS (n = 19)	P ANOVA
Age (years)	15.8 ± 0.2**	14.6 ± 0.3	14.9 ± 0.5	0.006
Race (% of each group)				0.001
AW	68	27	58	
AA	23	63	42	
Other	9	10	0	
Total testosterone (ng/dL)	41.9 ± 2.7	22.5 ± 2.3		<0.001
Free testosterone (pg/mL)	9.2 ± 0.9	3.6 ± 0.5		<0.001
% free testosterone (%)	2.4 ± 0.2	1.6 ± 0.1		0.002
BMI (kg/m^2)	37.9 ± 0.7	35.3 ± 1.1†	20.7 ± 0.6*	<0.001
BMI z-score	2.2 ± 0.03	2.2 ± 0.1†	0.2 ± 0.1*	<0.001
Waist circumference (cm)	107.6 ± 2.0	101.4 ± 3.6†	72.6 ± 1.5*	<0.001
Hip circumference (cm)	121.3 ± 1.7	116.9 ± 3.0†	86.8 ± 2.0*	<0.001
Waist-to-hip ratio (WHR)	0.88 ± 0.01	0.87 ± 0.01	0.84 ± 0.02	ns
% body fat	46.8 ± 1.0	47.6 ± 1.1†	27.0 ± 2.2*	<0.001
HbA1c (%)	5.4 ± 0.05	5.4 ± 0.1	5.3 ± 0.1	ns
Fasting glucose (mg/dL)	87.2 ± 1.0	88.9 ± 1.2	87.9 ± 1.6	ns
Glucose tolerance (% of each group)				
NGT	76	87		
Dysglycemia	24	13		
Fasting insulin (μU/mL)	34.0 ± 1.8	32.9 ± 4.2†	18.3 ± 1.6*	<0.001
HOMA-IR	8.3 ± 0.5	7.2 ± 0.9	4.0 ± 0.4*	<0.001
Cholesterol (mg/dL)	161.4 ± 3.6	158.6 ± 5.1	144.3 ± 6.6	ns
LDL (mg/dL)	94.5 ± 3.1	99.5 ± 4.9†	77.0 ± 5.5*	0.02
TG (mg/dL)	119.7 ± 6.3**	83.8 ± 6.7	75.3 ± 13.3*	<0.001
HDL (mg/dL)	42.9 ± 1.2	42.9 ± 1.4†	52.2 ± 2.7*	0.003
Non-HDL cholesterol (mg/dL)	118.5 ± 3.4	115.7 ± 5.4†	92.1 ± 5.2*	0.004
TG/HDL	3.1 ± 0.2**	2.1 ± 0.2†	1.6 ± 0.4*	<0.001
SBP (mmHg)	123.3 ± 1.4	120.0 ± 2.6†	108.1 ± 2.0*	<0.001
DBP (mmHg)	64.9 ± 0.8	62.3 ± 1.3	60.5 ± 1.3	ns
Leptin (ng/mL)	46.6 ± 2.0	44.4 ± 4.2†	13.8 ± 1.6*	<0.001
Adiponectin (μg/mL)	6.9 ± 0.3	8.1 ± 0.7†	13.7 ± 1.3*	<0.001
Leptin/Adiponectin	8.1 ± 0.5	7.2 ± 0.9†	1.2 ± 0.2*	<0.001

OB-NonPCOS: obese control, NW-NonPCOS: normal weight control, OB-PCOS: obese PCOS, AW-American White, AA- African American, ns: not significant, NGT: normal glucose tolerance

Post hoc

† p<0.05 NW-NonPCOS vs. OB-NonPCOS,

* p<0.05 NW-NonPCOS vs. OB-PCOS,

** p<0.005 OB-NonPCOS vs. OB-PCOS.

Table 2

Multivariable Regression Analysis with PWV as the Dependent Variable and Age, Race, BMI, PCOS condition and Cardiometabolic Parameters as Independent Variables

Model	Independent variables	Standardized $\beta_{(BMI)}$	Model R^2	P ANOVA
1	Age, race, BMI, PCOS condition	.262	0.069	0.003
2	Model 1 + dysglycemia	.262	0.068	0.003
3	Model 2 + SBP, hsCRP	.227	0.052	0.016
4	Model 3 + HOMA-IR, TG, HDL	.227	0.052	0.016

BMI was the only significant contributor within each model. Therefore, standardized β values shown are only for BMI. Standardized β values indicate the number of standard deviations that PWV will change as a result of one standard deviation change in BMI.