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Cardiorespiratory Fitness, Exercise Hemodynamics and Birth Outcomes: The Coronary Artery Risk Development in Young Adults (CARDIA) Study

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Abstract

Objective—Determine associations of cardiorespiratory fitness, exercise systolic blood pressure (SBP), and heart rate recovery (HRR) following a maximal exercise test performed years

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Conceived and designed experiments- ALC, MRC, EPG

Data acquisition-, CEL, BS, PJS, PG, MRC, EPG

Analysis- ALC, SEM

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preceding pregnancy with odds of preterm birth (PTB; <37 weeks gestation) and small for gestational age (SGA; birthweight <10th percentile) delivery.

Design—Prospective, longitudinal

Setting—Multi-site, observational cohort study initially consisting of 2,787 Black and White women aged 18–30 at baseline (1985–86) and followed for 25 years (Y25; 2010–11).

Population—768 women nulliparous women at baseline who reported 1 live birth(s) by the Y25 exam.

Methods—We used Poisson regression to determine associations of exposures with PTB/SGA.

Main Outcome Measures—PTB and/or SGA births

Results—Women with PTB (n=143) and/or SGA (n=88) were younger, completed fewer years of education, and more likely to be black versus women without PTB/SGA (n=546). Women with PTB/SGA had lower fitness; 501±9s vs 535±6s, $p<0.002$, and higher submaximal SBP than women without PTB/SGA; 144±1 versus 142±1mmHg, $p<0.04$. After adjustment, no exercise test variables were associated with PTB/SGA, though the association with HRR and submaximal SBP approached significance in the subset of women who completed the exercise test <5 years before the index birth.

Conclusions—Neither fitness nor hemodynamic responses to exercise, a median of 5 years preceding pregnancy, were associated with PTB/SGA. These findings indicate excess likelihood of PTB/SGA is not detectable by low fitness or exercise hemodynamic responses 5 years preceding pregnancy, but exercise testing, especially HRR and submaximal SBP, may be more useful conducted closer to the onset of pregnancy.

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Keywords

preterm birth; small for gestational age; exercise test

Introduction

Women who experience a preterm birth (PTB; <37+0 weeks gestation) or deliver a small for gestational age (SGA; 10th percentile for weight and gestational age) infant have more subclinical cardiovascular disease (CVD) after the birth (1) and experience higher rates of overt CVD later in life (2, 3). The pathology underlying PTB and SGA may have a vascular origin, and PTB, SGA, and CVD may have similar or shared etiology (3–6). It is possible

that the disease process associated with PTB, SGA, and CVD may begin before pregnancy and may be associated with established CVD risk factors including low cardiorespiratory fitness (7).

Other maternal cardiovascular risk factors (hypertension, inflammation, and dyslipidemia) before and during pregnancy have been linked to PTB and SGA (8–10). We hypothesized the protective effect of fitness on mechanisms in CVD development (e.g., hypertension, inflammation and dyslipidemia) may also extend to birth outcomes. Further, exercise stress testing reveals abnormalities in cardiovascular function that may not be apparent at rest (11). Exaggerated systolic blood pressure (SBP) response and a slower rate of recovery of heart rate upon cessation of exercise (heart rate recovery; HRR) are associated with incident hypertension and CV-related mortality independent of other CVD risk factors (11, 12). SBP at the second stage of an exercise test is associated with other forms of subclinical vascular dysfunction and is not as dependent on individual effort as maximal exercise SBP (13). An exaggerated BP response to submaximal or maximal exercise or slower HRR following maximal exercise may also be associated with PTB/SGA births. Though these indices have been associated with other forms of CVD, their association with PTB and SGA has not been examined.

The study sought to determine whether cardiorespiratory fitness and hemodynamic responses to exercise (SBP and HRR) in the years preceding pregnancy and child birth were associated with risk of PTB and/or SGA. We hypothesized that women who had higher fitness would have lower risk of PTB and/or SGA compared to less fit women, and that women who had higher submaximal and maximal exercise SBP and lower HRR would be more likely to develop PTB/SGA. Furthermore, we hypothesized that the strength of the association between pre-pregnancy fitness and birth outcomes would be reduced after adjusting for other traditional CV risk factors measured at the study examination preceding the first birth because fitness exerts its protective effect against CVD, at least in part, via a reduction in CVD risk factors (14, 15).

Methods

CARDIA Study

The Coronary Artery Risk Development in Young Adults (CARDIA) Study is a multi-center, longitudinal and observational cohort study investigating the determinants of coronary heart disease and associated risk factors in African-American and Caucasian adults and funded by the National Institute of Health. At the baseline exam (1985–1986), 5115 participants (53% women, 52% African-American), aged 18 – 30 yrs were recruited from 4 urban areas: Birmingham, Alabama; Chicago, Illinois; Minneapolis, Minnesota; and Oakland, California. Institutional review boards approved the study at each center and all participants signed written, informed consent. For study details and descriptions of datasets, please see <https://www.cardia.dopm.uab.edu/>. Of the 2,787 women in the study who underwent a fitness test at Y0, we excluded women who reported a birth before Y0 (n=1,008), reported a non-singleton first birth (n=12) did not report any births between the Y0 and Y25 exam (n=875). We excluded women who were missing the gestational age or birthweight information needed to determine PTB/SGA status (n=124). Our final sample

included 768 women whose first birth post-baseline (index birth) was a singleton and classified into one of three groups: term without SGA (referent), PTB, or SGA.

SGA and PTB

Birth outcomes (term without SGA, PTB, SGA) were determined as previously described in CARDIA data (16) for women with singleton pregnancies. PTB was defined as any birth that occurred at between 20 and <37+0 weeks gestation. SGA was defined as birthweight <10th percentile for gestational age (17).

Treadmill Fitness Test

Participants performed a graded, symptom-limited maximal treadmill exercise test using a Balke protocol (18). Briefly, participants completed up to nine, 2-minute stages of gradually increasing speed and incline. Fitness was estimated by test duration in seconds. Categories were created by grouping women into tertiles of low, medium, and high fitness based on the duration of their treadmill test.

Exercise Blood Pressure and Heart Rate Recovery

Blood pressure and heart rate (HR) were measured at each stage of the exercise test. The blood pressure value obtained during the last stage completed by the participant was maximum exercise SBP. SBP at Stage 2 of the test was submaximal SBP (13). Heart rate was obtained at minute 2 of active recovery (slow walking) following cessation of the exercise test. HRR was calculated as: HR at maximal exercise – HR at minute 2 of recovery. Fitness test variables were adjusted for race and maternal age at the exam preceding the index birth, and both unadjusted and adjusted means were used for group comparisons.

Covariates

Self-administered questionnaires and interviews were used to gather reproductive and sociodemographic information, including: age, sex, race, pregnancies, gestational age, infant birth weight, delivery dates, education level, and smoking. Education level was defined as the number of completed years of formal schooling. Self-reported smoking status was classified as either current, former, or never.

Anthropometric and Clinical Characteristics

At each examination, height was measured to the nearest 0.5 cm and weight was measured to the nearest 0.2 kg. Body mass index (BMI) = kg/m². Blood pressure (BP) was measured after a standard, seated rest in triplicate. The final two BP measurements were averaged for analysis. Hypertension was defined as the use of medication for BP control, SBP ≥ 140, or DBP ≥ 90 mmHg. Diabetes was defined as fasting glucose ≥ 126 mg/dl or the use of medication for diabetes. Enzymatic methods were used to measure cholesterol and triglycerides. The Friedewald equation was used to estimate LDL cholesterol, and HDL cholesterol was determined after precipitation of other lipoproteins.

Statistical Analyses

PTB and SGA were combined into one composite outcome because both may be associated with underlying vascular dysfunction, and results were similar when we analyzed PTB and SGA separately. There were nine women who reported both PTB and SGA for the index birth. Normality was assessed with Shapiro-Wilk tests, and non-normally distributed variables were analyzed using non-parametric tests. Differences in descriptive and clinical characteristics and between women by fitness tertiles were evaluated with a chi-square test for categorical variables and one-way ANOVA or Kruskal-Wallis tests for continuous variables. Differences in descriptive and clinical characteristics, treadmill duration, maximal and submaximal SBP and HRR and between women with versus without SGA and/or PTB were evaluated with a chi-square test for categorical variables and t-tests or Wilcoxon rank sum tests for continuous variables. We tested for differences in these variables by PTB/SGA status using Wilcoxon rank-sum tests before and after adjustment for age and race.

When we tested for associations of fitness testing exposures with PTB and SGA as separate outcomes, and our results were similar, so we included the results for the combined condition to maximize statistical power. We tested for interactions by race by including multiplicative interaction terms between race and each exposure along with the lower order terms in our most adjusted model (4). In initial analyses, we found no interaction between race and any of our exposures, so we proceeded with pooled analyses. Because the incidence of PTB/SGA was 29%, we used Poisson regression to generate prevalence ratios and 95% confidence intervals in order to test for the association between treadmill test duration and incident PTB/SGA (combined as one outcome for analysis). We initially performed an unadjusted analysis (Model 1). We then adjusted for demographic and clinical characteristics at the examination immediately preceding the index birth: age, race, education, study center, BMI, current and former smoking, diabetes, and hypertension (Model 2). Although fitness and physical activity are highly correlated(19), we initially included physical activity into a model with fitness in case there was an independent association with birth outcomes. There was no independent association of physical activity with PTB/SGA at the examination immediately preceding the index birth in unadjusted or adjusted analyses ($p>0.51$ for both), so we proceeded without physical activity in our models.

We completed three sensitivity analyses. In the first, we excluded women who developed hypertension or diabetes before the index birth ($n=12$).

In the second sensitivity analysis, we excluded women with self-reported hypertension in pregnancy ($n=131$) and gestational diabetes ($n=39$) because these conditions may contribute to PTB and SGA. We conducted this analysis in the women without self-reported hypertension in pregnancy earlier investigations have shown that women in CARDIA tended to over-report hypertension in pregnancy, but women in CARDIA who did not report hypertension in pregnancy most likely did not have the condition, i.e., the negative predictive value for hypertension in pregnancy is high in CARDIA (4, 20).

Finally, we classified PTB as early or late PTB. Early PTB was birth between 20 and 34 weeks, and late PTB was birth between 34 and 37 weeks. We hypothesized that early PTB

was more likely to have been indicated due to maternal vascular dysfunction, so we tested for associations between fitness test variables and early PTB.

Significance was set at $\alpha=0.05$ and STATA 14.0 (College Station, TX) was used for analysis.

Results

Participants

There was a positive association of fitness tertile with age at the examination immediately preceding the index birth, interval between fitness test and index birth, physical activity, and HDL cholesterol while BMI, SBP, and proportion of women with self-reported gestational diabetes and self-reported gestational hypertension in the index pregnancy decreased as fitness tertile increased (Table 1). At baseline, age, physical activity, and HDL cholesterol were higher while interval between fitness test and index birth, proportion of black women, BMI, and SBP were lower as fitness increased (Table S1).

On average, most women experienced their first birth 5 years following baseline (IQR: 2–7 years). Twenty-nine percent (222/768) of all women in the sample reported PTB ($n=143$; 46 were early PTB and 97 were late PTB) and/or SGA ($n=88$). Nine women reported both PTB and SGA in the index birth. At the examination immediately preceding the index birth, women who reported PTB and/or SGA were more likely to be black, completed fewer years of education, had a shorter interval between the fitness test and index birth, and had higher SBP compared to women who did not have SGA/PTB ($n=546$; Table 2). At baseline, there was no difference in clinical characteristics by PTB/SGA status in women who did not report gestational diabetes or hypertension in the index pregnancy (Table S2).

Treadmill Fitness Test

In unadjusted analysis, women who had PTB/SGA had lower fitness at baseline than women who had PTB/SGA, $p<0.001$, while fitness did not differ by PTB/SGA status after adjustment for age and race, $p=0.64$ (Table 3).

Exercise Blood Pressure and Heart Rate Recovery

There was no difference in adjusted or unadjusted maximum exercise SBP, $p>0.70$ for both (Table 3). Unadjusted submaximal SBP was higher in women with PTB/SGA, $p<0.04$, while adjusted submaximal SBP was similar between groups, $p=0.37$ (Table 3). Unadjusted and adjusted HRR was higher in women who reported PTB/SGA, $p=0.03$ for both (Table 3).

Regression

In unadjusted analysis, treadmill duration, $p<0.03$; and submaximal exercise SBP, $p<0.02$; were associated with incident SGA and/or PTB. After adjustment, the associations were no longer significant, $p=0.49$ (Table 4). No other exercise testing variables were associated with PTB/SGA after adjustment, $p>0.19$ for all (Table 4).

Because there was a between group difference in the time between the fitness test and index birth by PTB/SGA status and an independent association of the time interval between fitness test and first birth, we stratified our cohort at the median interval (5 years) and re-tested for associations. In the group in which the index birth occurred closer (< 5 years, $n=275$) to the fitness test, HRR was associated with PTB/SGA; IRR=1.32, 95% CI=1.12, 1.56, $p=0.001$ in our adjusted model. The association of submaximal SBP with PTB/SGA approached significance, $p=0.07$. No other associations were significant after adjustment, $p>0.05$ for all for associations in the subset of women in which the index birth occurred < 5 years after the fitness test.

Sensitivity Analyses

Omission of the women who developed either hypertension or diabetes before the index birth did not affect our findings, and results were similar in the subset of women without self-reported hypertension or gestational diabetes in the index pregnancy (Table S3). There was no association of early PTB with any of the fitness test variables in adjusted or unadjusted analyses, $p>0.07$ for all.

Discussion

Main Findings

We observed that cardiorespiratory fitness measured prior to pregnancy was lower in women who reported having PTB/SGA, while exercise SBP and HRR were higher. Though women who had PTB/SGA were less fit, fitness was not associated with PTB and/or SGA once other demographic and cardiovascular disease risk factors were taken into account. Hemodynamic responses to exercise, e.g., maximal and submaximal exercise SBP and HRR, were not associated with odds of PTB and/or SGA in the whole cohort. In the subset of women who performed the exercise test < 5 years prior to the index birth, HRR was associated with PTB/SGA. These findings indicate that fitness testing performed in the years immediately preceding pregnancy may be more useful for identifying women at risk for PTB and/or SGA than testing performed 5 years before birth.

Strengths and Limitations

The primary limitation of our study is that we were not able to determine whether the reasons for PTB/SGA in our cohort were related to maternal vascular dysfunction. Given the consistent reduction in CVD risk and improvement in vascular function with increasing fitness, vascular-related PTB/SGA is more likely to be influenced by fitness versus PTB caused by ascending infection or SGA due to constitutional smallness versus SGA attributable to intrauterine growth restriction (21). However, vascular disorders of pregnancy contribute to ~33% of PTB and 30% of SGA in the population, and we believe our findings are a meaningful initial investigation of this question (21, 22). Future investigations may link pre-pregnancy fitness and exercise hemodynamics to birth outcomes and confirm vascular etiology with corresponding placental pathology examinations to determine whether fitness and exercise hemodynamics are associated with vascular-related PTB/SGA. Differences in the quality or timing of prenatal care may have contributed to the exclusion of 124 women who were missing gestational age and birthweight information, which led to their exclusion

from our analysis. We may also not have been powered to detect small or mid-sized effects, especially in the subset of women who performed the exercise test <5 years prior to pregnancy.

The strengths of the study include the longitudinal design that followed women during their reproductive years and the collection of multiple measures of health behaviors and cardiovascular disease risk factors during that time frame. Studies that rely solely on risk factors measured at the time of a fitness assessment, rather than closer to the index birth, may have mistakenly identified a relationship that was completely accounted for in our study by the inclusion of covariates during follow-up. Another strength of our study is the balanced sample of black and white women.

Interpretation

Adverse pregnancy outcomes (including PTB and SGA) are now recognized CVD risk factors for women (3). The importance of primordial prevention (avoidance of risk factors altogether) of CVD has gained attention, and strategies to reduce the development of pregnancy-related CVD risk factors fall into this category (3, 23). Unlike the findings of Carnethon, et al, who reported that higher fitness in early adulthood was associated with lower likelihood of developing traditional CVD risk factors 15 years later (24), we did not find that fitness in the years preceding pregnancy (IQR: 2–7 years) was associated with a lower likelihood of developing the novel CVD risk factors PTB and SGA.

An earlier meta-analysis showed that achieving higher levels of moderate-vigorous physical activity immediately preceding and during pregnancy was associated with less risk of PTB and other adverse pregnancy outcomes (25–27). The authors found no difference in birthweights between women who exercised compared to non-exercising pregnant women. These and our data indicate that high levels of activity or fitness are not associated with greater risk of PTB/SGA, but an upper threshold for benefits associated with moderate-vigorous activity in pregnancy has not been firmly established. In our study, the fitness test was conducted an average of five years prior to the index birth. Given the protective association of physical activity immediately preceding and during pregnancy on some vascular and inflammation-mediated pathways that are believed to contribute to PTB/SGA (9, 28), fitness assessed closer to the onset of pregnancy could be more likely to identify women who will develop PTB/SGA. When we evaluated the association in women with an interval of <5 years between the baseline fitness assessment and birth we found that HRR was associated with PTB/SGA in the women who completed the exercise test <5 years before the index birth, and the association of submaximal and maximal exercise SBP with PTB/SGA approached significance ($p=0.07$).

Exercise BP has been linked to left ventricular hypertrophy, incident hypertension, and CVD (11, 29) independent of traditional risk factors. Submaximal exercise BP (BP at Stage 2 of a graded treadmill exercise test) was associated with endothelial function and arterial stiffness, subclinical forms of CVD, in middle-aged adults (13). Women in our study with PTB/SGA had higher unadjusted submaximal SBP during the exercise test, but maximal and submaximal SBP was not associated with PTB/SGA after adjusting for clinical characteristics and demographics. The women who developed PTB/SGA also had lower

fitness; these findings are consistent with the idea that the women who developed PTB/SGA were exercising a higher relative intensity at Stage 2 of the test compared to women who did not develop PTB/SGA, and this may have contributed to the difference in submaximal SBP between groups.

HRR is believed to represent parasympathetic control of HR, and inadequate HRR has been associated with mortality (12). Greater HRR, e.g., a larger reduction in HR with cessation of exercise, indicates better parasympathetic reactivation and is thought to be cardio-protective (30). HRR improves with fitness, and achieving high fitness is believed to have beneficial effects on the autonomic system (30). HRR was associated with PTB/SGA in women whose fitness test was conducted <5 years from the index birth; this suggests that autonomic balance may influence the likelihood of developing PTB/SGA.

The prevalence of PTB is high in CARDIA, and there is a race disparity in PTB in the CARDIA study and disparities in PTB and SGA nationally (4, 21). Catov, et al., hypothesized that the relatively high percentage of black women in CARDIA might have contributed to the prevalence of PTB in CARDIA being higher than national averages (4). An earlier investigation found that high sensitivity and specificity for PTB in CARDIA, 84% and 89%, respectively, so we believe the characterization of our outcome is accurate (4). The reasons for the race disparities are likely complex, involving biological, social, and genetic factors (21, 31). Strategies to avoid PTB and SGA may also improve the longer-term CVD risk in offspring (3, 32).

Conclusion

We observed that fitness measured on average 5 years before a first birth was not associated with PTB/SGA after adjustment for demographics and cardiovascular risk factors closer in proximity to birth. However, submaximal exercise SBP and HRR may be more useful for identifying women at likely to develop PTB/SGA when measured <5 years prior to pregnancy and birth. Clinicians may recommend cardiorespiratory exercise testing for women planning to become pregnant to assess likelihood of PTB/SGA. Future research could investigate: i) whether exercise testing immediately preceding pregnancy, i.e. during a preconception visit, helps to identify women who develop PTB/SGA, and ii) if exercise testing is associated with PTB/SGA with vascular-specific etiology.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1
Participant characteristics at examination immediately preceding index birth (varied examination year) by fitness tertile

Tertile 1: mean 377 s; range 0–486 s, Tertile 2: mean 520 s; range 487–601 s, Tertile 3: mean 679 s; range: 602–1080 s, EU: exercise units, BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, Gestational Diabetes: gestational diabetes in the index pregnancy, TC: total cholesterol, HTN Pregnancy: reported hypertensive disorder in index pregnancy, HDL: high-density lipoprotein cholesterol, LDL: low-density lipoprotein cholesterol. Data are mean $\pm$ SE. *indicates a difference between tertiles, $p < 0.05$.

	Total Sample n=768	Tertile 1 n=169	Tertile 2 n=296	Tertile 3 n=293	P-value for trend across tertiles
Age (yrs)*	29 $\pm$ 1	29 $\pm$ 1	29 $\pm$ 1	30 $\pm$ 1	<0.001
Time to 1 st Birth (yrs)*	4.8 $\pm$ 0.2	4.5 $\pm$ 0.4	4.7 $\pm$ 0.3	5.5 $\pm$ 0.3	0.01
Black n (%)	314 (41)	129 (76)	130 (44)	51 (17)	<0.001
Current Smoker n (%)	99 (13)	30 (18)	31 (10)	36 (12)	0.08
Physical Activity (EU)*	333 $\pm$ 10	227 $\pm$ 19	323 $\pm$ 15	392 $\pm$ 18	<0.001
Treadmill Duration (s)*	525 $\pm$ 5	342 $\pm$ 8	492 $\pm$ 2	664 $\pm$ 5	<0.001
BMI (kg/m ²)*	24.5 $\pm$ 0.2	28.6 $\pm$ 0.9	24.7 $\pm$ 0.4	23.1 $\pm$ 0.3	<0.001
SBP (mmHg)*	104 $\pm$ 1	104 $\pm$ 1	104 $\pm$ 1	102 $\pm$ 1	0.01
DBP (mmHg)	66 $\pm$ 1	66 $\pm$ 1	67 $\pm$ 1	65 $\pm$ 1	0.06
Diabetes n (%)	3 (<1)	1 (<1)	1 (<1)	1 (<1)	0.90
Hypertension n (%)	9 (1)	4 (2)	4 (1)	1 (1)	0.15
Gestational Diabetes (n, %)*	39 (5)	15 (9)	13 (4)	11 (4)	0.04
HTN Pregnancy (n, %)*	129 (17)	35 (21)	57 (19)	36 (12)	0.03
TC (mg/dL)	179 $\pm$ 2	180 $\pm$ 4	181 $\pm$ 3	179 $\pm$ 3	0.61
HDL (mg/dL)*	59 $\pm$ 1	56 $\pm$ 2	58 $\pm$ 1	61 $\pm$ 1	0.01
LDL (mg/dL)	106 $\pm$ 1	109 $\pm$ 4	108 $\pm$ 3	104 $\pm$ 2	0.07

Table 2
Participant characteristics at examination immediately preceding index birth (varied examination year) by PTB/SGA status

Time to 1st Birth: time interval between treadmill fitness test and index birth, EU: exercise units, BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, Gestational Diabetes: gestational diabetes in the index pregnancy, HTN Pregnancy: reported hypertensive disorder in index pregnancy, TC: total cholesterol, HDL: high-density lipoprotein cholesterol, LDL: low-density lipoprotein cholesterol. Data are mean $\pm$ SE. *indicates a difference between groups, $p < 0.05$.

	Women without SGA/PTB <i>n=546</i>	Women with SGA/PTB <i>n=222</i>	P-value
Age (yrs)*	29 $\pm$ 1	28 $\pm$ 1	0.009
Time to 1 st Birth (yrs)*	5.2 $\pm$ 0.2	4.3 $\pm$ 0.4	0.002
Black n (%)	186 (34)	128 (58)	<0.001
Education (yrs)*	15 $\pm$ 1	14 $\pm$ 1	<0.001
Current Smoker n (%)	63 (12)	36 (16)	0.08
Physical Activity (EU)	342 $\pm$ 12	313 $\pm$ 20	0.16
BMI (kg/m ²)	24.6 $\pm$ 0.3	24.0 $\pm$ 0.4	0.61
SBP (mmHg)*	103 $\pm$ 1	105 $\pm$ 1	0.01
DBP (mmHg)	66 $\pm$ 1	66 $\pm$ 1	0.99
Diabetes n (%)	3 (1)	0 (0)	0.27
Hypertension n (%)	6 (1)	3 (1)	0.77
Gestational Diabetes n (%)	28 (5)	11 (5)	0.91
HTN Pregnancy (n, %)*	82 (15)	47 (21)	0.04
TC (mg/dL)	180 $\pm$ 2	176 $\pm$ 3	0.33
HDL (mg/dL)	59 $\pm$ 1	58 $\pm$ 1	0.70
LDL (mg/dL)	107 $\pm$ 2	105 $\pm$ 3	0.59

Table 3**Exercise test variables by PTB/SGA status**

Means were adjusted for race and age at index birth. Data are means and 95% confidence intervals.

	No PTB/SGA <i>Unadjusted</i>	PTB/SGA <i>Unadjusted</i>	<i>P value</i>	No PTB/SGA <i>Adjusted</i>	PTB/SGA <i>Adjusted</i>	<i>P value</i>
Test Duration (s) n=768	535 (522, 547)	501 (484, 520)	<0.01	547 (542, 553)	511 (501, 521)	0.64
Sub Max SBP (mmHg) n=547	142 (140, 143)	144 (142, 147)	0.04	141 (140, 141)	143 (142, 143)	0.29
Max SBP (mmHg) n=560	161 (159, 162)	161 (159, 164)	0.72	160 (160, 160)	160 (160, 161)	0.37
HRR (bpm) n=748	41 (40.0, 41.9)	43 (41.2, 44.3)	0.03	41 (41.3, 41.4)	41 (41.0, 41.3)	0.02

Table 4
Association between exercise test variables and SGA and/or PTB

Incidence rate ratios (IRRs) for the association between exercise test variables and PTB/SGA in the whole cohort (left columns) and in those women who completed the exercise test < 5 yrs before the index birth (right columns).

	IRR (95% CI) <i>Unadjusted Whole Cohort</i>	IRR (95% CI) <i>Adjusted Whole Cohort</i>	IRR (95% CI) <i>Unadjusted < 5 yr interval</i>	IRR (95% CI) <i>Adjusted < 5 yr interval</i>
Treadmill Test Duration (per 145 seconds)	0.86 (0.77, 0.95)	1.07 (0.88, 1.32)	0.90 (0.74, 1.08)	1.07 (0.84, 1.36)
Max SBP (per 19 mmHg)	1.02 (0.91, 1.15)	1.05 (0.91, 1.23)	1.13 (0.96, 1.31)	1.13 (0.98, 1.30)
Submax SBP (per 18 mmHg)	1.12 (1.00, 1.24)	1.08 (0.98, 1.28)	1.16 (0.98, 1.45)	1.16 (0.98, 1.38)
HRR (per 11 bpm)	1.11 (0.99, 1.24)	1.11 (0.95, 1.30)	1.26 (1.07, 1.48)	1.32 (1.12, 1.56)