Influence of Supervised Maternal Aerobic Exercise during Pregnancy on 1-Month-Old Neonatal Cardiac Function and Outflow: A Pilot Study

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ABSTRACT

MAY, L. E., S. MCDONALD, C. STEWART, E. NEWTON, C. ISLER, D. STEED, L. A. SARNO, G. A. KELLEY, L. CHASAN-TABER, D. KUEHN, B. R. ALLMAN-TUCKER, C. STROM, A. CLAIBORNE, and X. FANG. Influence of Supervised Maternal Aerobic Exercise during Pregnancy on 1-Month-Old Neonatal Cardiac Function and Outflow: A Pilot Study. *Med. Sci. Sports Exerc.*, Vol. 55, No. 11, pp. 1977–1984, 2023. **Purpose:** The objective of this study is to assess the effects of supervised, recommended levels of prenatal aerobic exercise on 1-month-old infant cardiac function. **Methods:** Eligible pregnant women were randomly assigned to either an aerobic exercise group that participated in 150 min of supervised, moderate-intensity (40% to 59% $\dot{V}O_{2peak}$, 12 to 14 on Borg rating of perceived exertion) aerobic exercise per week for 24 wk or more or a nonexercising group that consisted of 150 min·wk^{-1} of relaxation techniques. One-month-old infant echocardiogram was performed to assess infant *cardiac function*, including heart rate (HR), left-ventricular stroke volume, cardiac output, cardiac index, ejection fraction, fractional shortening, and velocity time integral at the aortic valve. Pearson correlation analyses and linear regression models were performed. **Results:** Prenatal aerobic exercise was negatively correlated with infant resting HR ($r = -0.311$, $P = 0.02$). Similarly, when controlling for infant sex and activity state, exercise level/volume ($\beta = -0.316$; 95% CI, −0.029 to −0.002; $P = 0.02$) predicted resting infant HR ($R^2 = 0.18$, $P = 0.02$). In infants of overweight/obese women, infants of aerobic exercisers had increased fractional shortening ($P = 0.03$). In addition, infant ventricular ejection fraction was correlated with maternal exercise attendance ($r = 0.418$, $P = 0.03$) as well as a trend for exercise level ($r = 0.351$, $P = 0.08$). Similarly, the only significant regression model for infants of overweight/obese women controls infant activity state ($\beta = -0.444$; 95% CI, −0.05 to −0.01; $P = 0.006$) and maternal exercise level ($\beta = 0.492$; 95% CI, 5.46–28.74; $P = 0.01$) predicting infant resting HR ($F = 5.79$, $R^2 = 0.40$, $P = 0.003$). **Conclusions:** The findings of this study demonstrate that women participating in exercise in the second and third trimesters of their pregnancy may have infants with increased cardiac function at 1 month of age. Importantly, the cardiac function effects were further augmented for infants born to overweight/obese women. **Key Words:** CARDIAC FUNCTION, FRACTIONAL SHORTENING, INFANT, PREGNANCY, PRENATAL AEROBIC EXERCISE

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Risk factors for cardiovascular disease (CVD) (e.g., obesity) develop in children as young as 3 yr old (1–8). These observations at a young age suggest *in utero* programming of CVD, possibly consequent to unhealthy maternal lifestyle behaviors throughout pregnancy.

Current research shows women participating in self-reported aerobic exercise throughout the second and third trimesters of pregnancy positively affect the developing cardiovascular system of the fetus and infant (9–12). These studies reported fetuses

and infants of maternal aerobic exercisers elicited lower resting heart rates (HR) and increased HR variability, supporting greater cardiovascular autonomic control (9,10,13). Moreover, these findings highlight the plasticity of the developing fetal cardiovascular system beyond its initial formation in the fourth week of gestation; however, previous studies focused on self-reported exercise and/or levels below current recommendations for pregnant women based on the American College of Obstetricians and Gynecologists (ACOG).

The paucity of studies employing rigorous methods, such as randomized control trial, for prenatal exercise at recommended levels and offspring cardiovascular function, limits the strength of evidence describing the influence of prenatal exercise on offspring cardiovascular development. To address these limitations, the current study analyzed data from a 24-wk randomized controlled supervised exercise intervention trial, which exposed pregnant women to recommended levels of exercise at 150 min of weekly supervised moderate-intensity aerobic exercise or low-intensity stretching/breathing. The primary outcome of the parent study was offspring cardiovascular function, measured via echocardiogram on 1-month-old infants. We hypothesized that 1-month-old infants of aerobic-trained pregnant women would exhibit greater cardiac structure and function characterized by increased stroke volume (SV), cardiac output (CO), cardiac index, and left ventricular ejection fraction compared with 1-month-old infants born to nonexercising pregnant women. Furthermore, we posited that the dose of prenatal aerobic exercise would predict infant cardiac function.

BASIC SCIENCES

METHODS

Study participants. We conducted a prospective, two-arm randomized controlled trial (RCT) exercise intervention, that was partially blinded. Pregnant women were recruited from local obstetric clinics via brochures, flyers, word of mouth, and social media. Inclusion criteria were 1) women with a low-risk, healthy singleton pregnancy, 2) <16 wk of gestation, 2) between 18 and 40 yr old, 3) prepregnancy body mass index (BMI) between 18.5 to 39.0 $kg \cdot m^{-2}$, 4) physician clearance to participate in exercise, 5) able to communicate fluently in English, and 6) able to be contacted via phone and email. Women were excluded from the study if they 1) had preexisting medical conditions (e.g., diabetes, hypertension, and CVD) or comorbidities known to affect fetal development (e.g., systemic lupus erythematosus), 2) were taking medication known to affect fetal development or pregnancy outcomes, or 3) were using tobacco, alcohol, or other recreational drugs. Informed consent was obtained from each participant before participation. This study was approved by the East Carolina University Institutional Review Board and registered on the Clinicaltrials.gov website (Registry #NCT03517293).

Preexercise testing. All participants completed a submaximal exercise treadmill test validated for pregnant women. Briefly, the test continued until volitional fatigue, an HR corresponding to 85% of their age-predicted maximum HR, or rating of perceived exertion >16. Oxygen consumption and carbon dioxide production were assessed via breath-by-breath analysis (TrueOne 2400; Parvo Medics, Sandy, UT) to determine peak oxygen uptake ($\dot{V}O_{2peak}$, mL $O_2 \cdot kg^{-1} \cdot min^{-1}$). Maternal HR was measured continuously with a Polar FS2C HR monitor. This test was performed to determine target HR zones corresponding to maternal HR between 40% and 59% $\dot{V}O_{2peak}$, reflecting moderate exercise intensity (14). The number of participants assessed for eligibility (n = 162), and then enrolled and randomized (n = 140), is provided in Figure 1.

Randomization. Participants were randomized to either an aerobic exercise or nonexercising attention-control group based on computerized sequencing generated using GraphPad software. The participants and exercise trainers were not blinded to group assignment. However, the sonographer and clinic staff were blinded to group assignment.

Exercise intervention. The exercise intervention was performed continuously for 24+ wk. All participants attended three 50-min supervised sessions per week based on their availability. Throughout each session, participants wore Polar FS2C HR monitors for tracking adherence to their prescribed exercise intensity. Sessions began and ended with a 5-min low-intensity walk (treadmill speed ≤3.0 mph).

The *aerobic exercise* group engaged in 50 min of moderate-intensity (40% to 59% $\dot{V}O_{2peak;}$ 12 to 14 on Borg Scale [14]) aerobic exercise (15), meeting the guideline of pregnant women attaining 150 min of weekly moderate-intensity exercise, as recommended by the ACOG and US Department of Health and Human Services (16,17). Participants performed exercise on aerobic equipment of their choice, including treadmills, ellipticals, rowing machine, or stationary bicycles.

The *attention-control* group engaged in 50 min of low-intensity (<40% $\dot{V}O_{2peak}$) stretching and breathing techniques. Stretches were performed on large muscle groups (e.g., legs, chest, and back), and breathing techniques were incorporated during each stretch facilitating focus on relaxation, mindfulness, and body awareness.

Prenatal exercise dose was calculated by multiplying the frequency and duration of weekly sessions by their metabolic equivalent (MET) based on the Compendium of Physical Activities (18,19). MET values varied by the piece of equipment, speed, and resistance at which the exercise was performed. After that, the MET-minutes for each week of the intervention were summed and averaged. The average weekly exercise dose was expressed as MET-minutes per week.

Exercise adherence. Session attendance for all participants was tracked via an electronic record in REDCap (20) and calculated by dividing the number of sessions attended by the total number of possible sessions for the participants' gestation (16 wk until delivery). Participants were considered "adherent" if their attendance was ≥80%.

Infant measurements. At 4 to 5 wk postnatal, an infant echocardiogram was performed at the university-affiliated outpatient clinic by a certified pediatric sonographer, blinded to group assignment, using a Philips ultrasound system (Koninklijke Philips, N.V.). Infant length (meters) was recorded on a length board, and infant weight (kg) was recorded on a calibrated

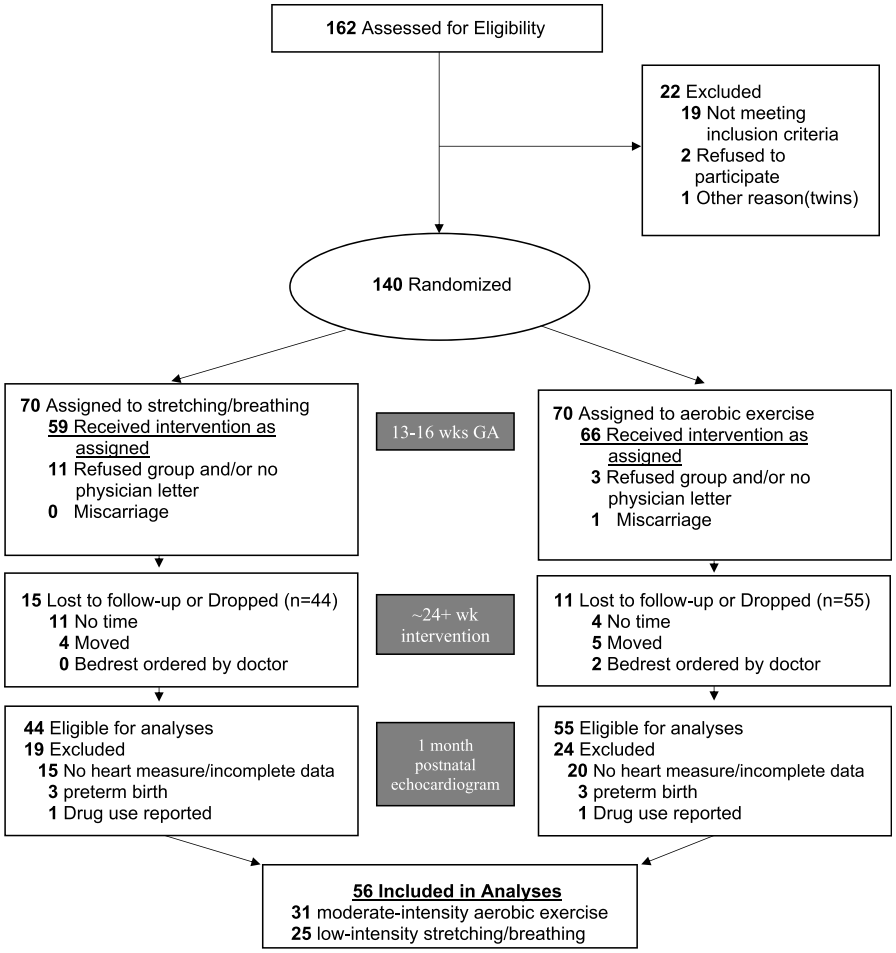

FIGURE 1—CONSORT diagram for participant recruitment and retention.

pediatric scale. One sonographer obtained all images per standard of care protocols in the pediatric cardiology clinic. The infant echocardiogram was used to assess infant anatomical cardiac structures that included aortic valve (AV) diameter. AV diameter was used to calculate outflow tract area ($0.785 \times$ AV diameter^2). The infant echocardiogram also assessed HR (bpm), SV (mL per beat), CO ($L \cdot min^{-1}$), aortic peak velocities ($cm \cdot s^{-1}$), and velocity time integrals (VTI) (cm). SV was also calculated using VTI $\times$ outflow tract area, because this has been shown to have improved prognostic value over ejection fraction (21,22). CO was calculated by multiplying SV and HR. SV and CO were additionally adjusted for body size via body surface area (BSA) (cm^3) to calculate SV index ($mL \cdot m^{-2}$) and cardiac index ($L \cdot m^{-2}$), respectively. Body surface area was calculated based on the Mosteller formula (23): $\sqrt{((\text{infant length} \cdot \text{infant weight})/60)}$. The infant activity state, quiet or active, is critical for interpretation of infant heart measures and was determined by direct observation of infant movement and HR by the sonographer during the echocardiogram.

Maternal and neonatal covariates. Maternal age, parity, gravida, prepregnancy weight and height, gestational diabetes mellitus status (yes or no), gestational weight gain, gestational age, neonatal sex, neonatal weight and length, mode of delivery, and 1- and 5-min APGAR scores were abstracted from prescreening eligibility questionnaires as well as maternal and neonatal electronic health records. Gestational weight gain was calculated by subtracting prepregnancy weight from weight at delivery. Weight at delivery (lb) was extracted from electronic health records; weight before pregnancy (lb) was collected via the prescreening questionnaire. If weight at delivery was unavailable, then the last recorded study weight at 36 wk was used. Prepregnancy BMI (healthy BMI, 18.5 to 24.99; overweight, 25.0 to 29.99; obese, >30) was calculated using height (m), measured by stadiometer, and weight (kg). Birth BMI and prepregnancy BMI were calculated via the following established equation: [weight (kg)]/[height (m)]^2 (24).

Statistical analyses. Sample size was calculated to achieve 80% power ($\beta = 0.20$) at $\alpha \leq 0.05$, based on preliminary infant resting HR data. Two-sided, two-sample t tests were performed and justified a sample size of 76 participants per group to detect a significant difference of 6 bpm, without controlling for activity state. Participants with complete infant echocardiogram data were eligible for analyses. Between-group differences for maternal demographics, pregnancy-related factors, exercise level, and infant cardiovascular function were determined using Student's t tests for normally distributed data (mean, SD) and Wilcoxon rank tests for nonnormally distributed data (median; minimum, maximum). Pearson's chi-square tests were performed

TABLE 1. Maternal descriptive characteristics, cardiac function, and activity level partitioned according to analysis type and group.

ITT			
Characteristics	**Aerobic (n = 31)**	**Control (n = 25)**	***P***
Demographics			
Age (yr)	30.1 ± 3.2	30.5 ± 5.2	0.74
Prepregnancy BMI (kg·m^{-2})	25.7 ± 5.5	25.0 ± 4.7	0.65
Gravida[a]	2 (1, 5)	2 (1, 4)	0.82
Parity[a]	2 (1, 4)	2 (1, 4)	0.89
Cardiac function			
36-wk resting HR (bpm)	83.0 ± 12.1	88.7 ± 15.6	0.15
Activity level			
Exercise (MET-min·wk^{-1})	744.1 ± 279.9	252.5 ± 162.1	<0.0001

Data are reported as mean ± SD.
[a]Values reported as median (minimum, maximum) because of nonnormal distributions.
36 wk, 36 wk of gestation.

for discrete data. To determine the relationship of prenatal aerobic exercise on infant cardiac function, Pearson's correlation analysis was performed. To determine predictors of infant cardiac measures, backward linear regression analysis was performed, which removed nonsignificant covariates. All were performed with the intention-to-treat (ITT) sample (all participants regardless of the adherence) and per protocol (only participants attending ≥80% of sessions). Because obesity is a risk factor of CVD and obesity can be programmed *in utero*, analyses were duplicated on just infants of women with overweight and obesity (OWOB) to assess effects of exercise exposure *in utero*. All statistical analyses were performed using SAS, version 9.4 (SAS, Cary, NC).

RESULTS

Study participant recruitment and retention. Complete data from 56 (31 aerobic, 25 nonexercising) healthy 1-month-olds were eligible for analyses. During the intervention of 24 wk or more, 15 (aerobic exercise (n = 4) and nonexercising (n = 11)) women dropped out of the study, 15 because of a lack of time, 9 because they moved out of the area, and 2 because they were prescribed bed rest by their obstetric provider.

Maternal descriptive characteristics. Maternal demographic characteristics for the ITT sample were similar between groups (Table 1). Significant differences were reported for maternal exercise level/volume (MET-min·wk^{-1}), supporting group allocation (Table 1).

Infant descriptive characteristics. No between-group differences were observed for infant sex distribution, length, weight, or BSA for the ITT sample (Table 2). Although a greater proportion of infants of aerobic exercisers were males, the difference was not significant.

Infant cardiac function and outflow. For the ITT analysis (Table 3), infants from aerobic exercisers had 2% lower HR (3 bpm) and increased SV by 11%, CO by 6%, and cardiac index by approximately 7% relative to infants from controls (Table 3). For the ITT analysis in the *active state*, infants from exercisers had 5% lower HR (7 bpm) and increased SV by 15%, CO by 7%, and cardiac index by approximately 5% relative to infants from controls (Table 4). For the ITT analysis in the *quiet state*, infants from exercisers had 2% lower HR (3 bpm) and increased SV by 10%, CO by 7%, and cardiac index by 8% relative to infants from controls (Table 4).

For the per protocol analysis (Table 3), infants from exercisers had 4% lower HR (6.5 bpm) and increased SV by 7%, CO by 1%, and cardiac index by 4% relative to infants from controls (Table 3). For the stratified per protocol analysis in the *active state* (Table 5), infants from aerobic exercisers had 6% lower HR (10 bpm) and increased SV by 10%, CO by 4%, and cardiac index by ~5% relative to infants from controls (Table 5). For the per protocol analysis in the *quiet state* (Table 5), infants from exercisers had 4% lower HR (7 bpm) and increased SV by 6% and cardiac index by 2% relative to infants from controls (Table 5).

For the correlation analysis, the only significant correlation was pregnancy exercise level with infant resting HR (r = −0.311, P = 0.02). Similarly, when controlling for infant sex and activity state, exercise level (β = −0.316; 95% CI, −0.029 to −0.002; P = 0.02) predicted resting infant HR (R^2 = 0.18, P = 0.02).

Cardiac function and outflow of infants of OWOB women. For the per protocol analysis stratified by activity state, infants from aerobic exercisers who were OWOB had stronger trends with significantly higher left ventricular fractional shortening (P = 0.03) in the active state compared with similar infants of control OWOB women (Table 6). For the per protocol analysis in the *active state*, infants from OWOB aerobic exercisers had 8% lower HR (13 bpm) and increased SV by 5% and cardiac index by 3% relative to infants from OWOB controls, although none of these differences between groups were statistically significant (Table 6). For the per protocol analysis in the *quiet state*, infants from OWOB aerobic exercisers had 10% lower HR (15 bpm) and increased SV by 20% and cardiac index by 9% relative to infants from OWOB controls (Table 6).

For the correlation analysis with infants of women with OWOB, significant associations were observed between pregnancy exercise level and infant resting HR (r = −0.403, P = 0.04), as well as with gestational age (r = 0.417, P = 0.01). Infant left ventricular ejection fraction was also associated with maternal exercise attendance (r = 0.418, P = 0.03) as well as a trend with exercise level (r = 0.351, P = 0.08). Similarly, the only significant regression model for infants of women with OWOB was infant activity state

TABLE 2. Infant descriptive characteristics and morphometrics, by maternal intervention group.

	ITT		
	Aerobic (n = 31)	**Control (n = 25)**	***P***
Sex (% male)	61.3%	44.0%	0.20
Gestational age (wk)	39.3 ± 1.6	39.0 ± 1.5	0.40
Infant length (cm)	53.7 ± 3.7	54.8 ± 3.4	0.27
Infant weight (kg)	4.37 ± 0.56	4.37 ± 0.86	0.98
Body surface area (m^2)	0.25 ± 0.02	0.26 ± 0.03	0.80
BMI (kg·m^{-2})	15.2 ± 2.0	14.8 ± 3.5	0.57

Data reported as mean ± SD, except infant sex represented as percentage of male infants.

TABLE 3. Infant cardiac function and outflow parameters, stratified by maternal intervention group, ITT analysis.

	ITT			Per Protocol		
Cardiac Variables	**Aerobic (n = 31)**	**Control (n = 25)**	***P***	**Aerobic (n = 19)**	**Control (n = 25)**	***P***
HR (bpm)	151.2 ± 17.7	154.3 ± 15.5	0.48	147.8 ± 18.1	154.3 ± 15.5	0.22
Cardiac structure						
Aortic diameter (cm)	0.97 ± 0.12	0.93 ± 0.12	0.22	0.96 ± 0.07	0.93 ± 0.12	0.29
LV outflow tract (cm)	0.83 ± 0.12	0.86 ± 0.13	0.72	0.84 ± 0.12	0.86 ± 0.13	0.91
Left ventricle						
SV (cm^3 per beat)	9.87 ± 3.15	8.88 ± 2.17	0.17	9.54 ± 2.50	8.88 ± 2.17	0.37
CO ($cm^3 \cdot min^{-1}$)	1.46 ± 0.43	1.37 ± 0.30	0.34	1.39 ± 0.31	1.37 ± 0.30	0.84
Cardiac index ($cm^3 \cdot min^{-1} \cdot kg^{-1}$)	5.76 ± 1.53	5.39 ± 1.22	0.32	5.61 ± 1.32	5.39 ± 1.22	0.59
Ejection fraction (%)	68.4 ± 6.3	68.3 ± 6.1	0.94	68.7 ± 5.9	68.3 ± 6.1	0.82
Fractional shortening (%)	37.7 ± 5.3	38.0 ± 5.8	0.84	37.8 ± 5.5	38.0 ± 5.8	0.92
VTI of AV (cm)	14.3 ± 2.7	14.7 ± 3.8	0.65	13.8 ± 2.7	14.7 ± 3.8	0.35

LV, left ventricle.

($\beta = -0.444$; 95% CI, −0.05 to −0.01; $P = 0.006$) and maternal exercise level ($\beta = 0.492$; 95% CI, 5.46–28.74; $P = 0.01$) predicting infant resting HR ($F = 5.79$, $R^2 = 0.40$, $P = 0.003$).

DISCUSSION

Principal findings of the study. The focus of this study was to investigate the effects of a randomized controlled aerobic exercise intervention trial for 24 wk or more in pregnant women on infant cardiac function 1 month after birth. We hypothesized that prenatal aerobic exercisers would enhance 1-month-old infant cardiac function relative to 1-month-old infants of nonexercisers. First, aerobic exercise during pregnancy led to clinically significant increases in infant SV, CO, and cardiac index and decreased infant HR relative to 1-month-old infants of nonexercisers; furthermore, the dose of exercise predicted infant heart measures. Second, we noted stronger patterns in infants of women with OWOB, with statistically significant increases in fractional shortening and a clinically meaningful 20% increase in infant SV. Third, prenatal exercise dose is associated with infant HR; this relationship was stronger in infants of women with OWOB.

Results in the context of what is known. Our initial finding suggests prenatal aerobic exercise decreases infant HR and increases cardiac function measures. A previous study found fetal HR was significantly lower with exposure to maternal aerobic exercise. However, the previous study utilized an 83-channel biomagnetometer, which is more sensitive than echocardiography at detecting fetal cardiac signals (9). Similar to the current findings, previous research reports that aerobic maternal exercise trended toward an association with lower fetal HR and significantly increased right ventricular cardiac function (i.e., SV and CO) relative to fetal heart measures of controls (11). Similar to the current findings, a previous study with a similar sample size noted fetal HR was decreased by 3.6 bpm (2.5%) with increases in left ventricular SV by 11%, CO by 9%, and cardiac index by 8% (11). Furthermore, although one study reported significantly increased HR variability in infants of exercisers, infant HR was only 6 bpm (4%) lower than infants of controls; although not a statistically significant finding, this could be of clinical significance (13). Importantly, a reduction of HR by 5 bpm in adults is associated with clinically meaningful changes in SV ~20% (25) and provides a 14% reduction in all-cause mortality (26). In addition, changes >5 bpm in HR are considered clinically meaningful as they have been associated with a reduced risk of cardiovascular events (27). Studies in men have shown that endurance exercise decreases resting HR by 8 bpm (12%) and increased stroke index (SV relative to BSA) by 18% (28). In addition, resting CO has been shown to increase through 3, 6, and 9 months of aerobic training, coinciding with increased SV and lower peripheral resistance (29). It is possible in the current study that, because of cardiac autonomic development completing postnatally, the exercise exposure was not long enough to elicit changes in resting HR. Interestingly, previous research reports only 4% changes in resting cardiac measures, (i.e., ejection fraction) in athletic compared with sedentary men (30). However, these groups had significantly different

TABLE 4. Infant cardiac function and outflow parameters, stratified by infant activity state and intervention group, ITT analysis.

	Infant Activity State					
	Active			Quiet		
Cardiac Variables	**Aerobic (n = 15)**	**Control (n = 9)**	***P***	**Aerobic (n = 16)**	**Control (n = 16)**	***P***
HR (bpm)	155.8 ± 21.0	163.2 ± 16.9	0.35	146.8 ± 13.0	149.3 ± 15.3	0.59
Cardiac structure						
Aortic diameter (cm)	1.00 ± 0.14	0.92 ± 0.09	0.13	0.95 ± 0.11	0.94 ± 0.13	0.66
LV outflow tract (mm)	0.84 ± 0.15	—	—	0.82	0.86 ± 0.13	—
Left ventricle						
SV (cm^3 per beat)	9.74 ± 3.15	8.49 ± 2.15	0.26	9.99 ± 3.25	9.09 ± 2.214	0.37
CO ($cm^3 \cdot min^{-1}$)	1.47 ± 0.42	1.37 ± 0.30	0.50	1.45 ± 0.46	1.36 ± 0.31	0.55
Cardiac index ($cm^3 \cdot min^{-1} \cdot kg^{-1}$)	5.78 ± 1.4	5.52 ± 1.04	0.62	5.75 ± 1.68	5.32 ± 1.34	0.43
Ejection fraction (%)	68.1 ± 7.2	68.8 ± 5.5	0.81	68.7 ± 5.5	68.0 ± 6.5	0.76
Fractional shortening	38.3 ± 5.8	38.0 ± 5.7	0.93	37.2 ± 4.8	38.0 ± 6.0	0.67
VTI of AV (cm)	13.9 ± 2.1	14.7 ± 5.0	0.62	14.67 ± 3.2	14.65 ± 3.1	0.98

LV, left ventricle.

TABLE 5. Infant cardiac function and outflow parameters, stratified by infant activity state and intervention group, per protocol analysis.

	Infant Activity State					
	Active			Quiet		
Cardiac Variables	Aerobic (*n* = 9)	Control (*n* = 9)	*P*	Aerobic (*n* = 10)	Control (*n* = 16)	*P*
HR (bpm)	153.6 ± 22.3	163.2 ± 16.9	0.32	142.6 ± 12.2	149.3 ± 12.4	0.19
Cardiac structure						
Aortic diameter (cm)	0.97 ± 0.07	0.92 ± 0.09	0.23	0.96 ± 0.08	0.94 ± 0.13	0.67
LV outflow tract (cm)	0.84 ± 0.20	—	—	—	0.86 ± 0.13	—
Left ventricle						
SV (cm^3 per beat)	9.38 ± 2.64	8.49 ± 2.15	0.45	9.68 ± 2.51	9.09 ± 2.21	0.55
CO ($cm^3 \cdot min^{-1}$)	1.42 ± 0.32	1.37 ± 0.30	0.76	1.36 ± 0.32	1.36 ± 0.31	0.97
Cardiac index ($cm^3 \cdot min^{-1} \cdot kg^{-1}$)	5.78 ± 1.2	5.52 ± 1.04	0.62	5.45 ± 1.47	5.32 ± 1.34	0.83
Ejection fraction (%)	68.5 ± 6.7	68.8 ± 5.5	0.93	68.9 ± 5.5	68.0 ± 6.5	0.72
Fractional shortening	37.6 ± 5.9	38.0 ± 5.7	0.87	38.0 ± 5.4	38.0 ± 6.0	0.99
VTI of AV (cm)	13.9 ± 2.2	14.7 ± 5.0	0.64	13.65 ± 3.2	14.65 ± 3.1	0.44

LV, left ventricle.

BASIC SCIENCES

ejection fractions during maximal exercise (30). Furthermore, one study found that exercise duration in the third trimester was a positive predictor of left ventricular ejection fraction of children (31). Although measures were not statistically significant, these changes suggest improved heart function of infants exposed to aerobic exercise *in utero*.

Second, we noted stronger patterns in infants of women with OWOB. Similar to our current findings, another study found that prenatal exercise exposure, and not maternal BMI, influenced improvements in fetal cardiac autonomic development (12). Improvements in left ventricular fractional shortening indicate that infants of women with OWOB have improved cardiac muscle contractility. In a mouse study, aerobic exercise training increased fractional shortening and ejection fraction by 12% (32), which is similar to our finding, that is, significant increases in left ventricular fractional shortening and a 12% increase in left ventricular ejection fraction. Importantly, if a reduction of HR by 5 bpm provides a 14% reduction in mortality (26) and clinically meaningful changes in SV from exercise are ~20% (25), then infants of OWOB aerobic exercisers might have a decreased risk for CVD, with a decreased HR of 15 bpm (10%) and 20% increased SV relative to infants of OWOB nonexercisers. Because OWOB adults and children have higher resting cardiac values (33,34), this partly explains the greater change in resting infant heart measures in response to maternal exercise. Interestingly, newborns of obese women are reported to have reduced cardiac function relative to newborns of normal weight women (35). Therefore, the finding that exercise during pregnancy demonstrates clinically meaningful changes in infants of OWOB women is of high public importance for this population and warrants further investigation.

Third, prenatal exercise dose is associated with infant HR, and this relationship is stronger in infants of women with OWOB. In adults, resting HR is a risk factor for CVD, as clinically significant changes of >5 bpm are associated with a reduced risk of cardiovascular events (27). Although Nyrnes et al. (35) reported no differences in cardiac function of infants of obese pregnant exercisers relative to infants of obese nonexercisers, there was a difference in HR of 5 bpm, despite low exercise adherence. Therefore, we believe exercise dose may play a role in infant cardiac adaptations (35). As further support for this hypothesis, previous research has reported that prenatal exercise dose-dependent effects have been shown to predict maternal lipids and cardiometabolic health, as well as fetal HR, infant birth weight, and adiposity (10,36–39). These findings parallel other studies that demonstrate health benefits, such as decreased incidence of CVD risk factors, CVD, coronary artery disease incidence, and all-cause mortality in nongravid adults, are associated with exercise dose (40–42). As supplement to our data showing an accentuated exercise dose response in OWOB mothers, a study of postmenopausal women demonstrated dose–response effects associated with aerobic exercise and reductions in adiposity, with the effect stronger in obese women (43).

Clinical implications. Supervised prenatal aerobic exercise in OWOB women improves left ventricular fractional

TABLE 6. Infant cardiac function and outflow parameters, stratified by infant activity state and intervention group, per protocol analysis of infants of OWOB women only.

	Infant Activity State					
	Active			Quiet		
Cardiac Variables	Aerobic (*n* = 3)	Control (*n* = 4)	*P*	Aerobic (*n* = 3)	Control (*n* = 8)	*P*
HR (bpm)	155.7 ± 28.7	168.5 ± 12.8	0.13	134.3 ± 5.1	149.4 ± 12.1	0.12
Cardiac structure						
Aortic diameter (cm)	0.97 ± 0.06	0.92 ± 0.06	0.93	0.97 ± 0.02	0.95 ± 0.18	0.23
LV outflow tract (cm)	—	—	—	—	0.97 ± 0.02	—
Left ventricle						
SV (cm^3 per beat)	9.49 ± 1.64	9.01 ± 1.20	0.48	11.72 ± 2.42	9.79 ± 2.52	0.76
CO ($cm^3 \cdot min^{-1}$)	1.47 ± 0.28	1.52 ± 0.22	0.77	1.58 ± 0.34	1.45 ± 0.35	0.78
Cardiac index ($cm^3 \cdot min^{-1} \cdot kg^{-1}$)	5.90 ± 1.19	5.74 ± 0.93	0.60	6.20 ± 2.03	5.70 ± 1.32	0.60
Ejection fraction (%)	74.5 ± 1.4	66.5 ± 5.1	0.23	69.8 ± 3.6	67.6 ± 4.3	0.36
Fractional shortening	39.5 ± 2.9	38.5 ± 8.1	0.03	35.3 ± 2.5	36.7 ± 5.0	0.55
VTI of AV (cm)	14.7 ± 1.21	13.0 ± 2.48	0.45	16.03 ± 1.40	14.52 ± 2.4	0.44

LV, left ventricle.

shortening of infant hearts and suggests improved infant cardiovascular function. From a clinical perspective, obstetric providers should continue to promote 150 min·wk^{-1} of prenatal aerobic exercise, especially for OWOB women.

Research implications. Further research is needed to determine if these changes persist as the child develops. In addition, the effects of supervised exercise in OWOB women during pregnancy on infant health outcomes should be investigated.

Strengths and potential limitations. Strengths of this study include the initial randomized controlled design, including the focus on women achieving recommended levels of exercise during pregnancy. The clinical significance of these findings lends additional support for the ACOG and US Department of Health and Human Services guidelines. To the best of our knowledge, this was the first RCT to examine the effects of supervised exercise at recommended levels during pregnancy to evaluate infant cardiac function. In addition to strengths, we acknowledge potential limitations. First, we had a large dropout rate, which was a limitation; thus, our sample size for per protocol analysis was small. Second, because of clinic schedule and mother availability, we were not able to control for the time of day the recording was completed. Next, we were not powered to test for differences based on maternal BMI influence; thus, future studies should investigate this. Furthermore, there was a lack of longitudinal and more specific measures to determine if changes persist with child development.

CONCLUSIONS

This analysis of an exercise intervention RCT suggests that maternal aerobic exercise at recommended levels during pregnancy may improve infant cardiac function. These findings suggest that exercise dose of maternal aerobic exercise during pregnancy is an important positive influence on infant cardiac measures, especially for infants of OWOB women. Further research is needed to determine if the recommended levels of aerobic exercise during pregnancy provide cardiovascular benefits later in life, including decreasing the risk of CVD.

We are grateful to the women who participated in this study and gave their time and effort. The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation. The results of the present study do not constitute endorsement by the American College of Sports Medicine.

B. R. A. has a podcast about exercise and health-related outcomes ("BENT by Knowledge") and is also the Senior Innovation Scientist for Breakout Lifestyle Fitness, Little Rock, a gym emphasizing resistance training and health-related outcomes. All other authors have no conflicts of interest to disclose.

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Clinical Trials: The IRB ID#: 12-002524. Date of registration with ClinicalTrials.gov was February 13, 2018. The date of initial participation enrollment of the first patient was February 14, 2018. The ClinicalTrials.gov identification number is NCT03517293. The URL registration site is https://register.clinicaltrials.gov/prs/app/template/EditProtocol.vm?listmode=Edit&uid=U0003Z0X&ts=5&sid=S0007SJJ&cx=-uvq9wi. Regarding data sharing of information, de-identified maternal and pediatric data are available at any time upon request and approval of data request from the study team; the data will be shared via an approved HIPAA-protected site.

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