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Research Article

Maternal Exercise Type and Fetal Echocardiographic Measures

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Abstract

Background/Aims: While aerobic exercise during pregnancy has been specifically shown to benefit fetal heart dimensions and outflow, the exercise type-specific effects of resistance and combination (resistance and aerobic) exercise have not been explored. The study was performed to independently assess the effects of resistance, aerobic and combination exercise on fetal heart measures in late pregnancy.

Materials and Methods: This study utilized 3 exercise intervention groups (aerobic AE n=61, combination AERE n=40, or resistance RE n=33) in comparison to a non-exercise control group (n = 50). At 35-36 weeks of gestation, fetal echocardiographs were obtained via ultrasonography and analyzed for heart rate, cardiac chamber size, and cardiac outflow diameters. Between-group mean differences in fetal measures were assessed by one-way ANOVA for continuous (fetal heart rate, ventricle diameter, stroke volume, cardiac output, vascular diameter) variables.

Results: Prenatal exercise altered left ventricular stroke volume and aortic diameter in AE and RE groups, respectively. Maternal exercise dose was significantly ($p < .05$) and negatively correlated with most measures, including fetal heart rate. Further, fetal heart rate was predicted by maternal fitness level, while fetal right and left ventricular measures were dependent on maternal exercise attendance.

Conclusion: These data suggest that different prenatal exercise types are safe for fetal heart development, and that compliance with the recommended prenatal exercise dose contributes to beneficial outcomes.

Keywords: fetus, pregnancy; echocardiography; exercise; cardiac output; ventricle; stroke volume

Introduction

Evidence for the programming of fetal cardiovascular health during the prenatal period has emerged through the past two decades [1–6]. Prenatal exercise can reduce risk factors for cardiovascular disease in both mother [5, 7–10] and infant [2, 3, 5, 6, 9, 11–14]. Cardiovascular disease risk factors are present in early childhood (15), and it is therefore of interest to assess cardiac adaptations in the developing fetus in response to prenatal exercise. Fetal echocardiography (echo) is the most direct mode of assessing size and function in the developing heart [16–22]. The current study will focus on whether prenatal exercise type influences fetal cardiac chamber and vascular size as well as functional measures, such as cardiac output [23, 24]. Studies consistently show that aerobic exercise training in adults for >6 weeks leads to increased [25, 26] resting stroke volume and cardiac output [27, 28], with specific increases of end-diastolic diameter and left ventricular stroke volume [29]. These adaptations provide a greater capacity for oxygen delivery to exercising skeletal muscle and myocardium [26, 28, 30]. It has been shown that maternal physical activity [1] and aerobic exercise [2, 3] alter fetal heart outcomes and could influence healthy cardiovascular function throughout the lifespan. Resistance exercise training has been shown to induce similar volumetric responses during acute exercise [44] and is recommended alongside aerobic exercise for cardiovascular health (45. In contrast, resistance exercise has not been thought to induce plasma volume expansion to the same extent, as evidenced by lack of stroke volume changes with prolonged training [45, 46]. Thus, there is no reason to expect changes in this outcome within the fetus. However, while there is evidence to the suggest that combination exercise benefits left ventricular diastolic volume and mass [47], relatively few studies prescribe combination exercise [48].

In hypothesizing how prenatal exercise might influence fetal heart characteristics, we entertained the idea that some exercise type-specific changes to chamber structure occur *in utero*. This is supported by evidence of altered fetal HR and heart rate variability (HRV) [1, 2, 6], and positive associations [13] and causation [6] relationships seen between prenatal exercise and heart function in the fetus and child. As a complement to these observations, it is the aim of this study to determine if any exercise type influences fetal cardiac adaptations.

This investigation was completed as a study on the effects of prenatal exercise types on mother and infant health outcomes [5]. Our hypothesis was that exercise would alter fetal echocardiographic characteristics in a type-specific manner. We expected that 1) prenatal aerobic exercise would increase cardiac dimensions and outflow, 2) that concurrent aerobic and resistance exercise would have a less pronounced effect than aerobic exercise on cardiac dimensions and outflow, and 3) there would be little effect of resistance training on cardiac dimensions and outflow.

Materials and Methods

Study Participants

The current report is a secondary analysis of the data from a single blinded, prospective, randomized control trial (RCT) investigating the influence of different exercise types throughout pregnancy on fetal and infant outcomes. The primary focus for this analysis was to determine the influence of distinct types of prenatal exercise on fetal heart outcomes (i.e., cardiac output, stroke volume, etc.). All protocols were approved by the East Carolina University Institutional Review Board. Women enrolled in the study met the following criteria: clearance from a health care provider to participate in physical activity; between 18 and 40 years of age; pre-pregnancy body mass index (BMI; $kg \cdot m^{-2}$) between 18.5-39.9 $kg \cdot m^{-2}$; singleton pregnancy; ≤16 weeks gestation; no current alcohol, tobacco, or medication use. Criteria for exclusion included smoking, pre-existing diabetes mellitus, hypertension, cardiovascular disease, and comorbidities and/or medications known to affect fetal growth and well-being such as systemic lupus erythematosus.

Ethics Statement

This study used ultrasound echocardiographs collected from participants enrolled in the ENHANCED (Enhanced Neonatal Health and Neonatal Cardiac Effect Developmentally) Study (IRB#: 12-002524, ClinicalTrials.gov Identifier: NCT03517293). Approval for this study was obtained from the East Carolina University Institutional Review Board and written informed consent was obtained from each participant upon enrollment. All experimental procedures were conducted at East Carolina University.

Pre-Intervention Exercise Testing & Randomization

Following study enrollment, participants completed a submaximal exercise treadmill test to determine individual aerobic capacity and calculate specific target HR (THR) ranges for moderate-intensity exercise training. Peak oxygen consumption (VO_2peak) was estimated via the modified Balke protocol previously validated for pregnant women [49]. To minimize exposure and potential risk associated with exercise testing after the start of the COVID-19 pandemic, women recruited following March 2020 did not complete the treadmill protocol, and THR zones for aerobic exercise were determined based on their pre-pregnancy physical activity level and age, using published guidelines [49]. THR zones for the aerobic exercise components corresponded to maternal HR at 60 to 80% of maximal oxygen consumption, reflecting moderate intensity. After completing this test, participants were randomized via computerized sequencing (GraphPad software) to aerobic, resistance, combination (aerobic and resistance), or a stretching/breathing comparison group.

Exercise Intervention

All participants were supervised by trained exercise instructors in the university facilities and followed a standard protocol. All sessions started at 16 weeks' gestation and were performed three times weekly until delivery [7]. All participants' sessions began with a 5-minute warm-up, 50 minutes of their randomized group activity, and ended with a 5-minute cool-down. Women were supervised to maintain THR corresponding to moderate intensity (60%-80% maximal oxygen consumption, 40–59% VO_2peak, and 12-15 rated perceived exertion) throughout the exercise session regardless of training mode. HR monitoring (Polar FS2C) ensured appropriate target HR ranges were maintained; target HR zones validated for pregnant women were utilized [49].

The aerobic exercise (AE) group completed moderate intensity training on treadmills, ellipticals, recumbent bicycles, rowing and/or stair-stepping equipment. To maintain the appropriate HR zone, speed and grade were adjusted on the treadmill, and resistance and speed levels were adjusted on the elliptical and recumbent bike. The resistance exercise (RE) group completed sessions of two to three sets of 15 repetitions of each exercise at ~ 60% of 1 repetition maximum (1-RM) [5]. Lifts were performed in circuit with minimal rest using seated machines (Cybex) (leg extension, leg curl, shoulder press, chest press, triceps extension, latissimus dorsi pull down), dumbbells (biceps curls, lateral shoulder raises, front shoulder raises), resistance bands/dumbbells, exercise balls, benches, and/or mats. The combination exercise (AE+RE) group performed half of the aerobic protocol and half of the resistance protocol exercises in five circuits, with minimal rest lasting 4.5-5 minutes each. Resistance exercises were performed at 15 repetitions (same exercises and equipment as RE group), while the aerobic exercises were performed on the same equipment as the AE group. Moderate intensity was monitored the same way as the aerobic group.

The control group performed stretching, breathing, and flexibility exercises for the duration of the session. Stretches targeted major muscle groups; breathing exercises combined stretches and breathing; flexibility exercises consisted of stretches with controlled breathing. Low intensity was confirmed during sessions using HR (<40% VO_2peak). To ensure that the proper intensity was achieved during sessions, the Borg scale rating of perceived exertion (RPE 6-20), and the "talk test" were used. HR monitoring (Polar FS2C) ensured appropriate target HR ranges were maintained; target HR zones validated for pregnant women were utilized [49]. Supervised exercise and stretching/breathing sessions took place at one of two university-affiliated gyms. Participants were included in the data analyses if their exercise attendance (number of exercise sessions completed/number of exercise sessions possible) was ≥80%.

Fetal Measurements

At 34-36 weeks gestation, an obstetric ultrasound scan and fetal echocardiogram were performed with a Logiq P5 ultrasound system (General Electric [GE] Healthcare, New York City, NY) between 12:00 and 1:00 PM at the University-affiliated outpatient clinic by a certified sonographer who was blinded to group assignment. One sonographer obtained all images for study participants. These procedures were validated previously and found reliable in healthy, normal pregnancies producing accurate measurements of the fetal cardiac chamber dimensions and physiologic measures of cardiac function.[50–53] Fetal echocardiograms were used to assess fetal morphometric and anatomic cardiac structures that included estimated fetal weight (grams), body length (centimeters), pulmonary valve diameter and aortic valve diameter, respectively. Body length was calculated based on a standard formula of $6.18 + 0.59 \cdot$ femur length (millimeters) [54]. The pulmonary and aortic outflow tract diameters were used to calculate outflow tract area ($0.785 \cdot \text{diameter}^2$). The fetal echocardiogram was used to assess HR ($\text{beats} \cdot \text{min}^{-1}$), stroke volume ($\text{mL} \cdot \text{beat}^{-1}$), cardiac output ($\text{L} \cdot \text{min}^{-1}$), and pulmonary and aortic peak velocities ($\text{cm} \cdot \text{sec}^{-1}$). Cardiac output was calculated as the product of stroke volume and HR. Stroke volume and cardiac output were additionally adjusted for body size via body surface area

(BSA) using the Mosteller formula: $\sqrt{((fetal\ length \cdot fetal\ weight)/60)}$ (55). The BSA was then used to calculate stroke volume index (mL · $(m^2)^{-1}$) and cardiac index (L · $(m^2)^{-1}$), respectively. Fetal activity state was determined by visual inspection of the HR pattern as described previously [56].

Statistical Analysis

Based on our preliminary fetal HR data, with at least 80% power, analysis justified a sample size of 34 participants per group to detect a statistically significant difference of 6 beats/minute at a two-tailed alpha level of .05. Participants with complete fetal echocardiogram data were eligible for analyses. Analysis of covariance (ANCOVA) models were performed for both *intention-to-treat* (exercise dose as received) and *per-protocol* (participants attending ≥80% of exercise sessions) analysis. To determine the effects of prenatal exercise on fetal cardiac function, ANCOVA regression models were performed while controlling for fetal activity state during the echocardiogram (active vs quiet), maternal peak aerobic capacity (VO_2 peak), and additional covariates via stepwise regression analysis. To assess the relationship between prior aerobic fitness and fetal heart outcomes, bivariate Pearson correlation coefficients were used to examine the association between VO_2peak (relative ml▪kg^{-1}▪min^{-1}; absolute L▪min^{-1}) and all fetal echocardiograph outcomes. All statistical analyses were performed using SAS (version 9.4, SAS Institute Inc., Cary, NC) & SPSS software (version 28.0.1.1, SPSS Inc. IBM Corp., Chicago, IL) software.

Maternal Covariates

Maternal age, parity, gravida, pre-pregnancy weight and height, were collected from pre-screening eligibility questionnaires. Pre-pregnancy BMI (healthy BMI 18.0-19,49; Overweight 19.5-29.99, Obese ≥30) was calculated using height (m), measured by stadiometer, and weight (kg) collected from the pre-screening eligibility questionnaire. Maternal pre-pregnancy BMI was calculated via the following established equation: [weight (kg)] / [height (m)]^2.

Results

Maternal Descriptive Statistics

Responses were obtained for 373 pregnant women interested in the study. Eighty-seven participants were excluded due to not meeting inclusion criteria, 44 for not accepting the proposed exercise regimen, 12 for not obtaining a physician clearance letter, and two who were confirmed to have a multifetal pregnancy. Our final analysis included 184 participants (control *n=50*, aerobic *n=61*, combination *n=40*, or resistance *n=33*). For the *intention-to-treat* analysis, participants were similar in age, gravida, race/ethnicity, and pre-pregnancy BMI between groups (Table 1). We had a diverse population with 21% participants self-reporting as a black or indigenous people of color (Table 1). For the *per-protocol* analysis, of the exercising women, a total of 87 women met ≥80% adherence for exercise training throughout the ~24 weeks (aerobic *n=41*, combination *n=27*, resistance *n=19*).

Table 1: Maternal descriptive characteristics per analysis and exercise group.

	Intention-to-treat					Per-protocol				
Variable	**CON**	**AE**	**RE**	**AERE**	**p**	**CON**	**AE**	**RE**	**AERE**	**p**
Age y	29 ± 4	31 ± 4	32 ± 4	30 ± 4	.07	29 ± 4	32 ± 4	32 ± 3	30 ± 4	.02
pP BMI	26 ± 5	24 ± 5	26 ± 5	25 ± 3	.15	26 ± 5	24 ± 3	25 ± 5	25 ± 3	.07
Gravida	2 (1,4)	2 (1,5)	2 (1,5)	1 (1,7)	.28	2 (1,4)	2 (1,5)	2 (1,5)	1 (1,3)	.58
Parity	1 (0,3)	0 (0,2)	1 (0,3)	0 (0,3)	.08	1 (0,3)	1 (0,2)	1 (0,3)	0 (0,2)	.34
Activity										
Absolute VO_2 peak[1]	1.58 ± 0.3	1.63 ± 0.4	1.67 ± 0.3	1.79 ± 0.4	.08	1.58 ± 0.3	1.71 ± 0.4	1.70 ± 0.3	1.81 ± 0.4*	.05
Relative VO_2 peak[2]	21.7 ± 4	23.8 ± 5	22.9 ± 4	24.3 ± 5	.08	21.7 ± 4	24.7 ± 5*	23.7 ± 4	25.0 ± 5*	.01
METmin/wk	355 ± 133	676 ± 273**	577 ± 183**	658 ± 232**	<.0001	355 ± 133	771 ± 231*	598 ± 176*	703 ± 218*	<.0001

Data are reported as mean ± SD. [a]Gravida & parity data reported as median (minimum, maximum). *Significantly higher than control, p<.05, **p<.001; pP Pre-pregnancy body mass index expressed in kg*m^{-2}; VO_2peak[1] measured absolute (L/min); VO_2peak[2] measured relative to body weight (ml▪kg^{-1}▪min^{-1}); METmin/wk exercise dose expressed as metabolic equivalents * minutes per week; y years; kg kilograms; m meters; VO_2 volume of oxygen consumed; L liters; min minutes; mL milliliters; wk week; CON control; AE aerobic exercise; RE resistance exercise; AE+RE combination aerobic and resistance exercise.

Fetal Echocardiographic Results

All echocardiographic measures were in the normal acceptable range for all fetuses. For the *intention-to-treat* analysis, there were no between-group differences observed for any fetal cardiac measures (Table 2). For the *per-protocol* analysis, there were no between group differences noted for fetal echocardiographic outcomes (Table 2). Of all measurements included in the *per-protocol* analysis, 105 (80%) fetal echocardiographs were obtained in the active fetal state (control *n=29*, aerobic *n=33*, combination *n=26*, resistance *n=17*). For *per-protocol* in the active fetal activity state, there were differences in LV stroke volume in RE, aortic diameter in AE, and trends (p=.06) of increased pulmonic diameter outflow in RE relative to controls (Table 3). In our small sample size for *per-protocol* in the quiet activity state, we noted trends (p=.08) for differences in pulmonic to aortic diameter ratio in the RE group compared to controls (Table 3).

Table 2: Fetal cardiac function and outflow parameters per analysis type and group.

	Intention-to-treat					Per-protocol				
Variable	**CON**	**AE**	**RE**	**AERE**	***p***	**CON**	**AE**	**RE**	**AERE**	***p***
HR *bpm*	138 ± 13	137 ± 10	139 ± 9	138 ± 8	.85	138 ± 13	136 ± 8	137 ± 10	138 ± 8	.84
Right ventricle	**CON**	**AE**	**RE**	**AERE**	***p***	**CON**	**AE**	**RE**	**AERE**	***p***
SV cm^3 ▪ $beat^{-1}$	6.2 ± 2.5	5.7 ± 1.6	5.5 ± 1.7	6.3 ± 1.2	.18	6.2 ± 2.5	6.0 ± 1.6	5.4 ± 1.5	6.3 ± 1.2	.31
SVI cm^3 ▪ $beat^{-1}$ ▪ kg^{-1}	2.3 ± 1.0	2.1 ± 0.6	2.1 ± 0.7	2.3 ± 0.5	.41	2.3 ± 1.0	2.2 ± 0.6	2.1 ± 0.6	2.3 ± 0.5	.57
CO cm^3 ▪ min^{-1}	880 ± 367	798 ± 234	774 ± 258	870 ± 174	.24	880 ± 367	821 ± 242	751 ± 221	878 ± 164	.30
CI cm^3 ▪ min^{-1} ▪ kg^{-1}	324 ± 145	290 ± 88	298 ± 100	318 ± 66	.39	324 ± 145	294 ± 86	288 ± 987	318 ± 70	.46
EF *%*	58 ± 20	56 ± 16	52 ± 21	58 ± 15	.50	58 ± 20	58 ± 17	51 ± 20	59 ± 15	.48
PVV_{peak} cm ▪ sec^{-1}	82 ± 11	81 ± 10	82 ± 10	84 ± 13	.57	82 ± 11	82 ± 10	81 ± 9	85 ± 14	.56
PVV_{flow} cm ▪ sec^{-1}	106 ± 16	104 ± 12	105 ± 14	109 ± 17	.52	106 ± 16	105 ± 12	106 ± 14	111 ± 18	.45
PD *mm*	10.6 ± 1.2	10.3 ± 0.9	10.6 ± 1.0	10.3 ± 1.2	.32	10.6 ± 1.2	10.3 ± 0.7	10.9 ± 1.0	10.3 ± 1.2	.10
Left ventricle	**CON**	**AE**	**RE**	**AERE**	***p***	**CON**	**AE**	**RE**	**AERE**	***p***
SV cm^3 ▪ $beat^{-1}$	6.5 ± 1.9	6.1 ± 1.5	5.9 ± 1.7	6.3 ± 1.3	.47	6.5 ± 1.9	6.2 ± 1.6	5.5 ± 1.8	6.6 ± 1.3	.11
SVI cm^3 ▪ $beat^{-1}$ ▪ kg^{-1}	2.4 ± 0.7	2.3 ± 0.6	2.3 ± 0.7	2.3 ± 0.6	.81	2.4 ± 0.7	2.2 ± 0.6	2.1 ± 0.8	2.4 ± 0.6	.43
CO cm^3 ▪ min^{-1}	900 ± 268	848 ± 205	827 ± 255	875 ± 190	.57	900 ± 268	848 ± 210	750 ± 258	909 ± 187	.10
CI cm^3 ▪ min^{-1} ▪ kg^{-1}	325 ± 102	309 ± 82	322 ± 102	325 ± 87	.81	325 ± 102	304 ± 79	291 ± 105	333 ± 87	.35
EF *%*	72 ± 25	67 ± 21	69 ± 23	72 ± 20	.66	72 ± 25	67 ± 21	62 ± 23	75 ± 21	.20
AVV_{peak} cm ▪ sec^{-1}	103 ± 14	107 ± 16	105 ± 11	103 ± 14	.57	103 ± 14	107 ± 17	106 ± 11	104 ± 15	.71
AVV_{flow} cm ▪ sec^{-1}	117 ± 20	119 ± 24	115 ± 16	113 ± 21	.67	117 ± 20	118 ± 25	115 ± 15	114 ± 21	.88
AD *mm*	8.4 ± 0.9	8.1 ± 0.9	8.4 ± 0.9	8.0 ± 0.9	.14	8.4 ± 0.9	8.0 ± 0.9	8.3 ± 1.0	8.1 ± 0.9	.25
A:P ratio	0.79 ± 0.1	0.78 ± 0.1	0.80 ± 0.1	0.78 ± 0.1	.87	0.79 ± 0.1	0.78 ± 0.1	0.77 ± 0.1	0.80 ± 0.1	.84

Data are reported as mean ± SD. *Significant values, $P<.05$. HR heart rate; bpm beats per minute; SV stroke volume; SVI stroke volume index; CO cardiac output; CI cardiac index; EF ejection fraction; PVV pulmonary valve velocity; PD pulmonary diameter; AVV aortic valve velocity; AD aortic diameter; A:P aorta: pulmonary valve diameter; min minutes; cm centimeters; kg kilograms; sec seconds; mm millimeters; CON control; AE aerobic exercise; RE resistance exercise; AE+RE combination aerobic and resistance exercise.

Table 3: *Per-protocol* fetal cardiac function and outflow per fetal activity state and intervention group.

	Active					Quiet				
Variable	**CON**	**AE**	**RE**	**AERE**	***p***	**CON** *n=12*	**AE** *n=6*	**RE** *n=2*	**AERE** *n=2*	***p***
HR *bpm*	141 ± 13	137 ± 8	139 ± 9	138 ± 8	.36	130 ± 10	130 ± 7	125 ± 9	128 ± 4	.87
Right ventricle	**CON**	**AE**	**RE**	**AERE**	***p***	**CON**	**AE**	**RE**	**AERE**	***p***
SV cm^3 ▪ $beat^{-1}$	6.0 ± 2.0	6.0 ± 1.7	5.3 ± 1.6	6.4 ± 1.2	.23	6.8 ± 3.6	5.6 ± 1.4	6.0 ± 1.4	5.8 ± 0.1	.85
SVI cm^3 ▪ $beat^{-1}$ ▪ kg^{-1}	2.3 ± 0.7	2.1 ± 0.6	2.1 ± 0.7	2.3 ± 0.5	.53	2.5 ± 1.5	2.3 ± 0.7	2.2 ± 0.0	2.3 ± 0.1	.99
CO cm^3 ▪ min^{-1}	856 ± 291	843 ± 245	751 ± 232	883 ± 166	.34	945 ± 530	640 ± 95	744 ± 116	759 ± 9	.66
CI cm^3 ▪ min^{-1} ▪ kg^{-1}	318 ± 106	298 ± 88	288 ± 92	318 ± 72	.58	340 ± 223	255 ± 61	281 ± 27	305 ± 1	.87
EF *%*	60 ± 21	58 ± 16	51 ± 21	59 ± 15	.33	53 ± 16	58 ± 21	58 ± 13	56 ± 5	.91
PVV_{peak} cm ▪ sec^{-1}	82 ± 11	81 ± 10	82 ± 9	86 ± 14	.58	83 ± 10	82 ± 10	71 ± 7	85 ± 15	.47
PVV_{flow} cm ▪ sec^{-1}	107 ± 15	105 ± 13	108 ± 15	112 ± 18	.33	103 ± 18	107 ± 9	96 ± 2	96 ± 21	.77
PD *mm*	10.7 ± 1.3	10.3 ± 0.7	11.0 ± 0.9	10.3 ± 1.3	.06	10.6 ± 1.0	10.2 ± 0.6	9.3 ± 0.3	9.3 ± 0.2	.11
Left ventricle	**CON**	**AE**	**RE**	**AERE**	***p***	**CON**	**AE**	**RE**	**AERE**	***p***
SV cm^3 ▪ $beat^{-1}$	6.6 ± 1.9	6.2 ± 1.6	5.2 ± 1.7*	6.5 ± 1.3	.04	6.2 ± 2.1	6.0 ± 1.3	7.4 ± 1.5	7.5 ± 0.3	.65
SVI cm^3 ▪ $beat^{-1}$ ▪ kg^{-1}	2.5 ± 0.7	2.2 ± 0.6	2.0 ± 0.7	2.4 ± 0.6	.12	2.1 ± 0.7	2.4 ± 0.6	2.9 ± 1.3	3.0 ± 0.2	.27
CO cm^3 ▪ min^{-1}	920 ± 276	850 ± 225	730 ± 258	907 ± 191	.05	840 ± 248	833 ± 111	922 ± 252	956 ± 10	.87
CI cm^3 ▪ min^{-1} ▪ kg^{-1}	340 ± 102	300 ± 80	282 ± 97	332 ± 88	.12	284 ± 92	333 ± 81	367 ± 186	384 ± 9	.45
EF *%*	75 ± 25	67 ± 22	61 ± 24	74 ± 21	.11	62 ± 26	66 ± 21	73 ± 22	94 ± 1	.38
AVV_{peak} cm ▪ sec^{-1}	103 ± 14	107 ± 17	105 ± 11	105 ± 15	.72	103 ± 15	104 ± 17	108 ± 6	96 ± 1	.85
AVV_{flow} cm ▪ sec^{-1}	120 ± 19	119 ± 25	116 ± 15	115 ± 21	.77	110 ± 22	108 ± 23	109 ± 13	95 ± 11	.82
AD *mm*	8.5 ± 0.9	7.9 ± 0.8	8.3 ± 1.0	8.1 ± 0.9	.04	8.0 ± 0.9	8.7 ± 1.0	8.8 ± 0.3	7.8 ± 0.1	.36
A:P ratio	0.81 ± 0.1	0.77 ± 0.1	0.75 ± 0.1	0.79 ± 0.1	.15	0.76 ± 0.1	0.85 ± 0.1	0.95 ± 0.1	0.85 ± 0.1	.08

Data are reported as mean ± SD. *Significantly lower than control, P<.05. HR heart rate; bpm beats per minute; SV stroke volume; SVI stroke volume index; CO cardiac output; CI cardiac index; EF ejection fraction; PVV pulmonary valve velocity; PD pulmonary diameter; AVV aortic valve velocity; AD aortic diameter; A:P aorta: pulmonary valve diameter; min minutes; cm centimeters; kg kilograms; sec seconds; mm millimeters; CON control; AE aerobic exercise; RE resistance exercise; AE+RE combination aerobic and resistance exercise.

Measures of maternal exercise dose were significantly, but weakly correlated with many fetal echocardiographic outcomes, as was maternal fitness level (Table 4). After controlling for covariates, pre-pregnancy fitness and type-specific prenatal dose were found as significant predictors of fetal heart outcome (Tables 5-8). Of note, fetal heart rate was predicted by fetal activity state and maternal fitness level (Table 5). Maternal exercise attendance predicted fetal RV and LV measures (Tables 6 & 7), while attendance and exercise type both predicted the diameter of aortic and pulmonary outflow tract (Table 8).

Measure	***p* value**	**Pearson Correlation**
Avg Weekly Frequency		
RV SV	.03	.173
Avg Weekly Duration (min)		
fHR	.02	-.184
Aortic Valve Diameter	.02	-.175
Pregnancy METmin/wk		
LV CO	.03	-.175
Aortic Valve Diameter	.02	-.185
16 wk rHR		
fHR	.04	.205
Relative VO_2peak (ml*kg*min^{-1})		
fHR	.01	-.209
LV CO	.01	-.201
LV CI	.02	-.196
Aortic Valve Diameter	.04	-.161
Absolute VO_2peak (L/min)		
fHR	<.001	-.327
LV CO	.01	-.360
Aortic Valve Diameter	.01	-.196
Aortic Valve: Pulmonary Valve	.03	-.166
Maternal Age (yrs)		
RV SV	.04	-.161
RV CO	.01	-.226
RV CI	.01	-.198
Pulmonary Valve Diameter	.04	.158
LV CO	.04	-.169
Aortic Valve: Pulmonary Valve	.03	-.170

fHR fetal heart rate in bpm (beats per minute); rHR maternal resting heart rate bpm; RV right ventricle; LV left ventricle; SV stroke volume; SVI stroke volume index; CO cardiac output; CI cardiac index.

Table 4: Correlation between maternal exercise dose and fetal heart outcomes.

	p value	95% CI Lower Bound	95% CI Upper Bound	Beta Value	Std Error
Fetal HR	***p* value <.0001* Adjusted R^2 = 0.350, F=7.164**				
Absolute VO_2peak (L/min)	<.0001	-16.624	-7.088	-11.856	2.389
FAS	.04	0.171	7.064	3.62	1.727
36 wk rHR	.08	-0.014	0.281	0.133	0.074
Exercise Attendance	.08	-20.460	3.489	-8.486	6.000
Exercise Volume (METmin/wk)	.56	-0.005	0.001	0.002	0.003
Fetal HR	***p* value <.0001* Adjusted R^2 = 0.373, F=8.001**				
Absolute VO_2peak (L/min)	<.0001	-17.520	-7.765	-12.642	2.444
FAS	.02	0.655	7.358	4.001	1.679
36 wk rHR	.17	-1.120	6.319	2.599	1.863
Exercise Attendance	.54	-8.168	4.350	-1.909	3.136
Average Exercise Duration (min)	.08	-9.689	0.614	-4.537	2.581
FAS fetal activity state; rHR maternal resting heart rate.					

Table 5: Regression models to predict fetal HR.

	p-value	95% CI Lower Bound	95% CI Upper Bound	Beta Value	Std Error
Right Ventricle (RV)					
RV Stroke volume (mL)[1]	***p* value = 0.002* Adjusted R^2 = 0.290**				
Exercise Attendance	<.0001	0.962	3.374	2.168	0.602
16 wk rHR	.04	-1.889	-0.048	-0.969	0.459
FAS	.057	-1.100	0.016	-0.542	0.278
Pre-Pregnancy BMI	.02	-1.804	-0.136	-0.970	0.416
RV Stroke Index (mL/kg) [2]	***p* value = 0.007* Adjusted R^2 = 0.260**				
Exercise Attendance	.048	0.006	1.140	0.573	0.282
FAS	.007	-0.600	-0.100	-0.350	0.124
Absolute VO_2peak (L/min)	.09	-0.842	0.061	-0.390	0.225
RV Cardiac Output (mL) [3]	***p* value = 0.007* Adjusted R^2 = 0.260**				
Exercise Attendance	.007	78.515	471.688	275.101	97.825
Pre-Pregnancy BMI	.03	-266.406	-10.318	-138.362	63.717
16 wk rHR	.07	-276.205	12.811	-131.697	71.910
RV Cardiac Index (mL/kg) [4]	***p* value = 0.04* Adjusted R^2 = 0.169, F = 2.181**				
Exercise Attendance	.03	7.135	160.019	83.577	38.0188
FAS	.09	-73.044	5.106	-33.969	19.434
RV Ejection Fraction [5]	***p* value = 0.003* Adjusted R^2 = 0.248, F = 3.508**				
Exercise Attendance	.01	3.550	27.483	15.517	5.966
Absolute VO_2peak (L/min)	.03	-20.944	-0.821	-10.883	5.016
Pre-Pregnancy BMI	.11	-15.870	1.652	-7.109	4.368
Exercise Volume (METmin/wk)	.11	-1.743	15.631	6.944	4.331

FAS fetal activity state; rHR maternal resting heart rate; BMI body mass index.

Models also included: 1) 36 wk rHR, infant sex, maternal relative VO2; 2) 36 wk rHR, 16 wk rHR, Exercise type, Maternal Age, Prepregnancy BMI, infant sex, weekly exercise duration, pregnancy METs; 3) 36 wk rHR, maternal age, gestational age at birth, FAS, average weekly exercise duration, relative VO_2peak; 4) pregnancy Metmin/wk, 16 & 36 wk rHR, absolute VO_2peak, exercise type, pre-pregnancy BMI, 5) 16 & 36 wk rHR, maternal age, FAS.

Table 6: Regression models to predict fetal RV outcomes.

	p-value	95% CI Lower Bound	95% CI Upper Bound	Beta Value	Std Error
Left Ventricle (LV)					
LV Stroke Volume (mL)[6]	***p* value = 0.049* Adjusted R^2 = 0.152, F = 1.997**				
Exercise Attendance	.001	0.989	3.701	2.345	0.675
Exercise Intensity (METs)	.01	-1.700	-0.256	-0.979	0.360
FAS	.11	-1.068	0.111	-0.479	0.293
Parity	.09	-0.095	1.328	0.617	.354
LV Stroke Index (mL/kg)[7]	***p* value = 0.02* Adjusted R^2 = 0.153, F = 2.466**				
Exercise Attendance	.01	0.148	1.124	0.636	0.244
Exercise Intensity (METs)	.02	-0.581	-0.047	-0.314	0.134
FAS	.0497	-0.451	-0.000	-0.223	0.113
Parity	.05	-0.003	0.500	0.249	0.126
LV Cardiac Output (mL/min)[8]	***p* value = 0.01* Adjusted R^2 = 0.215, F = 2.761**				
Exercise Attendance	.001	122.022	467.478	294.750	85.952

Absolute VO_2peak (L/min)	.03	-268.574	-12.537	-140.556	63.704
FAS	.06	-163.347	3.848	-79.750	41.600
Parity	.05	-1.070	182.595	90.762	45.697
Gestational Age (wks)	.04	3.594	194.976	99.285	47.617
Exercise Intensity (METs)	.04	-191.235	-3.483	-97.359	46.714
LV Cardiac Index (mL/min/kg)[9]	***p* value = 0.01* Adjusted R^2 = 0.150, F = 3.024**				
Exercise Attendance	.006	26.427	147.076	86.751	30.187
Absolute VO_2peak (L/min)	.06	-102.021	1.281	-50.370	25.847
FAS	.03	-71.996	-2.955	-37.476	17.275
Parity	.03	4.124	71.956	38.040	16.972
LV Ejection Fraction[10]	***p* value = 0.03* Adjusted R^2 = 0.094, F = 2.890**				
Exercise Attendance	.004	7.707	39.956	23.832	8.083
Parity	.07	-0.530	16.713	8.092	4.322

FAS fetal activity state; rHR maternal resting heart rate; BMI body mass index.

Models also included: 6) 16 & 36 wk rHR, pre-pregnancy BMI, infant sex, weekly exercise duration, absolute VO_2peak; 7) 36 wk rHR, pre-pregnancy BMI, infant sex, gestational age at birth, weekly exercise duration; 8) 16 & 36 rHR, weekly exercise duration; 9) 36 wk rHR, gestational age at birth; 10) 36 wk HR, Pregnancy METmin/wk.

Table 7: Regression models to predict fetal LV outcomes.

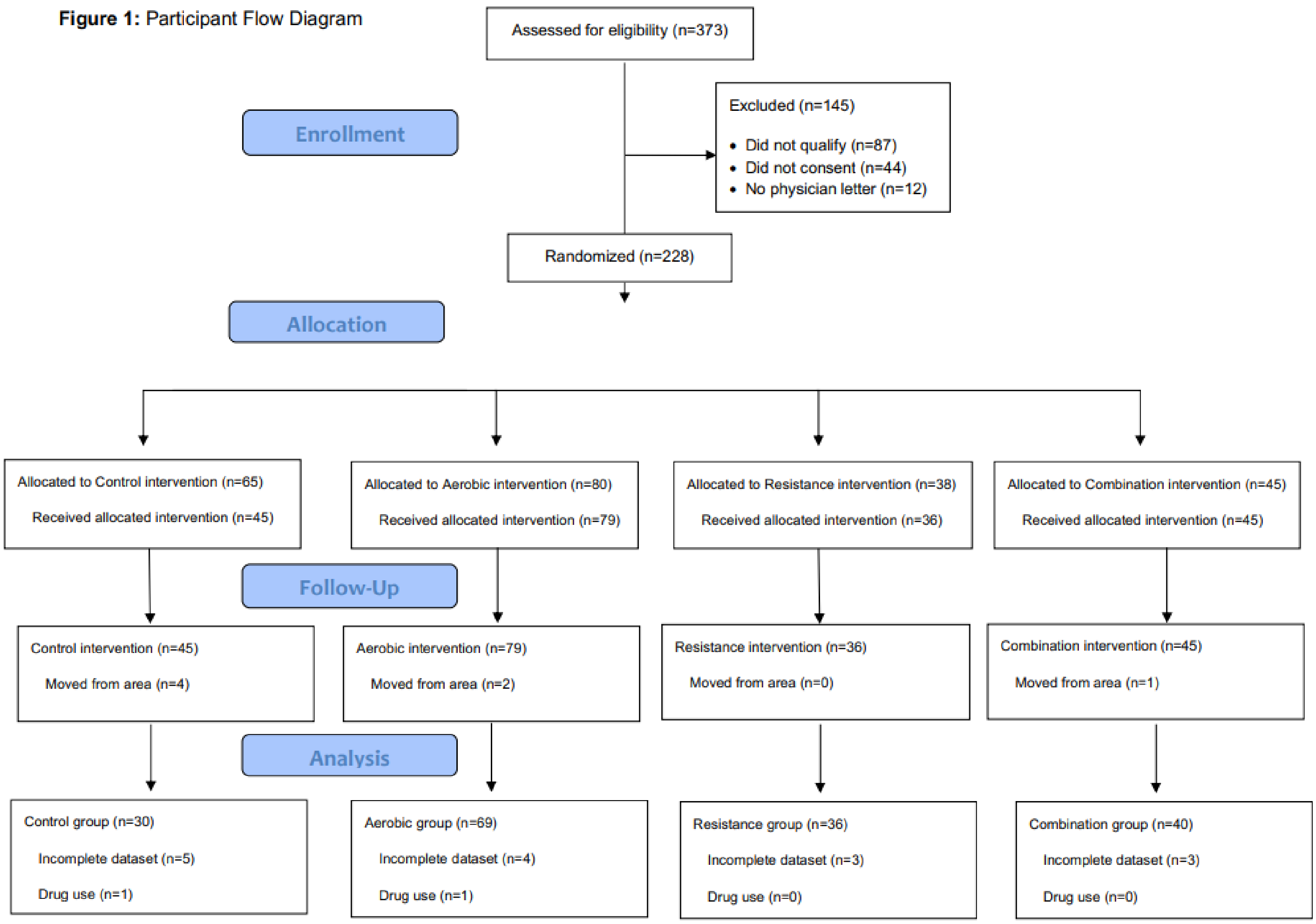
	p-value	95% CI Lower Bound	95% CI Upper Bound	Beta Value	Std Error
Outflow Diameters					
Pulmonary Diameter [11]	***p* value = 0.001* Adjusted R^2 = 0.224, F = 3.664**				
Exercise Attendance	.003	-1.719	-0.375	-1.047	0.337
Exercise Type: Aerobic	.04	-.648	-0.012	-0.330	0.159
Exercise Type: Resistance	.001	0.142	1.003	0.573	0.216
Exercise Type: Combination	.15	-0.591	0.090	-0.251	0.170
Exercise Type: Control	.97	-0.375	0.391	0.008	0.192
Gestational Age (wks)	.07	-0.756	0.033	-0.361	0.198
Aortic Diameter[12]	***p* value = 0.0492* Adjusted R^2 = 0.156, F = 1.958**				
FAS	.03	-0.816	-0.045	-0.431	0.192
Exercise Type: Aerobic	.26	-.833	0.233	-0.300	0.266
Exercise Type: Resistance	.02	0.137	1.596	0.866	0.363
Exercise Type: Combination	.22	-0.990	0.233	-0.378	0.305
Exercise Type: Control	.78	-1.508	1.132	-0.188	0.657
Absolute VO_2peak (L/min)	.05	-1.353	0.006	-0.673	0.338
Aortic: Pulmonary Valve Diameter[13]	***p* value = 0.0492* Adjusted R^2 = 0.156, F = 1.958**				
Exercise Attendance	.01	0.023	0.137	0.080	0.029
FAS	.003	-0.074	-0.017	-0.046	0.015
Infant Sex: Male	.10	-0.032	0.003	-0.015	0.009
Infant Sex: Female	.10	-0.003	0.032	0.015	0.009

FAS fetal activity state; rHR maternal resting heart rate; BMI body mass index.

Models also included: 11) 36 wk rHR, pre-pregnancy BMI, infant sex; 12) attendance, 16 & 36 wk rHR, maternal age, parity, pregnancy METs; 13) 36 wk HR, parity.

Table 8. Regression models to predict fetal outflow.

Figure 1: Participant Flow Diagram



Discussion

The aim of this study was to determine the influence of prenatal exercise type on fetal cardiac measures [5]. Our hypothesis was that prenatal aerobic exercise would increase cardiac dimensions and outflow, with a less pronounced increase in combination, and little difference in resistance from control. The fetal heart showed little differences between groups in *per-protocol* analysis; however, there are significant associations with measures of maternal exercise, as well as maternal fitness and fetal heart measures. While maternal exercise attendance, regardless of type, predicts all fetal heart measures, maternal fitness predicted fetal heart rate and resistance exercise and attendance predicted outflow size. Importantly, it was encouraging that prenatal resistance and aerobic exercise, either alone or in combination, are safe to the developing fetal cardiovascular system. Thus, current exercise recommendations during pregnancy appear to be appropriate [7, 57, 58].

Contrary to previous reports from our group [3, 6, 13, 14, 59], prenatal aerobic exercise did not yield any significant changes in fetal heart outcomes, whether specific to the right or left ventricle. We did not observe an increase in fetal RV measures as we have in previous prenatal aerobic exercise groups [6], In the *per-protocol* analysis, no between-group differences in fetal RV cardiac variables were observed. This could reflect methodological discrepancies between studies. Fetal pulmonary valve velocities and diameter were similar between groups, though May et al. showed significant increases of velocity-time integral and diameter in prenatal aerobic exercisers [6], Potentially this is due to a limitation in estimating hemodynamics from echocardiography in feti, due to the fetus in the control group also receiving cardiovascular benefits [60], and/or due to the normal weight participants diluting the effect which is typically stronger in overweight and obese women and their feti [61]. When further controlling for fetal activity status, no significant between-group differences were found in fetal echo outcomes, possibly due to smaller sample sizes. Previous findings of increased active fetal state in prenatal exercisers [6] was also present in the current study. While the total number of participants was similar across control and exercise groups, fetal echocardiograms obtained on prenatal exercisers were more frequently obtained in an active fetal state than the control group. Although there were no detectable differences for fetal heart measures based on type of prenatal exercise, this further supports that all exercise types during pregnancy are safe for the fetus and do not alter normal cardiac development.

Interestingly, maternal exercise attendance, regardless of type, was found to predict all fetal heart measures, while pre-pregnancy fitness predicted fetal heart rate, and resistance exercise and attendance predicted outflow size. Differences in fetal HRV, an indicator of cardiac autonomic nervous development, in resistance exercisers has been seen in other studies with self-reported exercise [3].

To the best of our knowledge, this is the first randomized controlled trial of this size, with a supervised exercise program, at recommended levels, performed in a cohort of pregnant women across a range of BMIs. In addition, the three exercise groups studied are more externally valid, as women often perform combination and resistance training during pregnancy. In addition to strengths, there are potential limitations. For example, a limitation of our study design is the estimation of fetal cardiac measures with ultrasound echocardiography. While the current study employed certified and experienced sonographer, fetal echocardiographs are difficult to standardize the orientation for accurate fetal measures. It has been previously reported that the smallness of the heart, and relatively accelerated HR contribute to difficulties in obtaining accurate, standardized measurements [66]. In addition, while the velocity time integral has been suggested to assess the fetal heart more accurately [67]. it was not performed in the current study. Importantly, previous research finds stronger associations in offspring of overweight/obese women; however, we were not able to stratify based on BMI due to sample size.

Conclusions

The responses of the fetal heart to prenatal resistance and aerobic exercise are within normal ranges, as exercise of any type had similar fetal echocardiogram outcomes. Similar measures were found in fetal cardiac responses to prenatal resistance, aerobic, or combination exercise. Importantly, maternal exercise attendance, regardless of type, predicts fetal heart measures. Further, an interesting relationship of fetal HR to maternal fitness warrants continuing research. A larger sample is needed to evaluate the influence of exercise types on cardiac function in offspring of overweight-obese women. Importantly, all exercise types during pregnancy are safe for fetal cardiac function.

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