Physical Activity in Pregnancy Is Associated with Increased Flow-mediated Dilation

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ABSTRACT

REYES, L. M., S. M. FAROOQ, R. J. SKOW, S. A. BUSCH, K. E. PYKE, R. KHURANA, R. S. CHARI, M. K. STICKLAND, M. DEVOLIN, S. T. DAVIDGE, F. SOBIERAJSKI, A. LUGG, C. D. STEINBACK, and M. H. DAVENPORT. Physical Activity in Pregnancy Is Associated with Increased Flow-mediated Dilation. *Med. Sci. Sports Exerc.*, Vol. 52, No. 4, pp. 801–809, 2020. **Purpose:** To determine the role of moderate-to-vigorous physical activity (MVPA) and sedentary behavior in flow-mediated dilation (FMD) and glucose metabolism during late pregnancy. **Methods:** Seventy normotensive, euglycemic pregnant women (31.6 ± 2.9 yr) in their third trimester (28–39 wk) were recruited. After a fasted blood sample; FMD was measured (brachial artery Doppler ultrasonography, normalized for the shear stimulus [area under the curve]). Anterograde and retrograde shear rate were estimated. Physical activity (MVPA) and sedentary behavior were assessed via accelerometry for seven consecutive days (Actigraph wGT3X-BT). We categorized the women as active (>150 min·wk^{-1}) or inactive (<150 min·wk^{-1}) according to their accelerometry data. Data were corrected for age and gestational age. **Results:** On average, women were sedentary 67.1% ± 8.2% of their waking hours. Active pregnant women (>150 min·wk^{-1} MVPA, n = 32) engaged in 266.7 ± 99.3 min·wk^{-1} MVPA, whereas inactive pregnant women (<150 min·wk^{-1} MVPA, n = 38) engaged in 76.1 ± 42.5 min·wk^{-1} MVPA. The FMD response (normalized to the magnitude of shear stress stimulus) was greater in active compared with inactive pregnant women (6.5 ± 4.4 a.u. vs 3.9 ± 3.5 a.u.; F = 4.619; P = 0.005). The MVPA in active pregnant women was inversely correlated with insulin concentrations (r = −0.556; P = 0.03). In inactive pregnant women, higher amounts of sedentary behavior were associated with lower amounts of retrograde shear rate (r = 0.504; P = 0.02), retrograde blood flow (r = 0.499; P = 0.02), and retrograde velocity (r = 0.508; P = 0.02) during baseline, but not correlated with the FMD response. **Conclusions:** Engaging in MVPA during pregnancy is associated with improved FMD and a lower insulin concentration. Sedentary behavior was not associated with FMD responses. **Key Words:** PHYSICAL ACTIVITY, PREGNANT WOMEN, SEDENTARY BEHAVIOR, FLOW-MEDIATED VASODILATION

Exercise during pregnancy is associated with maternal health benefits including a 40% reduction in the risk of common pregnancy complications including gestational diabetes mellitus, gestational hypertension and preeclampsia, without increasing the risk of adverse fetal outcomes (1–5). This benefit may be conferred via positive cardiovascular adaptations associated with exercise. One of the most prominent hemodynamic changes during pregnancy is the reduction in systemic vascular resistance secondary to a peripheral vasodilation (6). Enhanced vasodilation during pregnancy has been attributed to an increase in flow-mediated dilation pathways (nitric oxide [NO] (7), as well as endothelium-derived hyperpolarization [EDH] (8)).

Flow-mediated dilation (FMD) is an index of endothelium-dependent vasodilation (9) and is widely used to predict cardiovascular morbidity and mortality (10). Pregnancy has been associated with both an improvement (11–13) or no change (14,15) in FMD responses compared with nonpregnant women. In nonpregnant populations, exercise has been associated with an overall enhancement of endothelial function by increasing NO- and EDH-mediated vasodilation (16,17) and improving reactive oxygen species modulation of vasodilation (18,19). However, the impact of moderate-to-vigorous physical activity

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(MVPA) on FMD during pregnancy has been minimally investigated (15,20), especially within the context of the current guidelines for physical activity during pregnancy (3,4). Although a study evaluating self-reported physical activity suggested that exercise is not associated with changes in FMD during pregnancy (15), a clinical trial in pregnant women found that a moderate-to-vigorous intensity aerobic exercise training intervention during pregnancy was associated with an improvement in FMD responses compared with pregnant women who undertook their usual physical activity (20). However, MVPA or "exercise" defines only one aspect of physical activity. At the opposite end of the physical activity spectrum, sedentary behavior is defined as "any waking behavior characterized by an energy expenditure ≤1.5 METs while in a sitting, lying, or reclining posture (21)." In nonpregnant populations, 6 to 8 $h \cdot d^{-1}$ of sedentary behavior has been associated with an increased risk of cardiovascular mortality and incidence of type 2 diabetes independent of physical activity (22). The role of sedentary behavior on FMD responses during pregnancy has not been examined. Understanding the potential influence of sedentary behavior on maternal cardiovascular health is very relevant and important because (a) only 15% of pregnant women adhere to the current guidelines for physical activity during pregnancy (23,24), which recommends women engage in at least 150 $min \cdot wk^{-1}$ of moderate-intensity exercise (3,4); (b) pregnant women are more sedentary and less active than nonpregnant populations, spending approximately 70% of waking hours sedentary (25); and (c) it has been shown that there is an increase in sedentary behavior with increasing gestational age (26).

It is now recognized that shear stress (the frictional force generated by blood flow) and shear pattern (anterograde, retrograde) are important mechanisms influencing endothelial function. Anterograde shear stress is associated with increased NO production (27), whereas retrograde shear stress resulted in an acute decreased endothelial function in males (28). Increased cardiac output and volume expansion can influence shear stress (29). Thus, one could speculate that pregnancy is associated with changes in shear patterns because of the cardiovascular adaptations that women undergo during pregnancy include increased cardiac output and blood expansion. However, the role of MVPA and sedentary behavior on anterograde and retrograde blood flow, velocity, and shear rate in pregnant populations has not been assessed.

Pregnancy is also associated with alterations in glucose metabolism leading to insulin resistance to accommodate the metabolic needs of the growing fetus (30). Women with impaired glucose metabolism and gestational diabetes have an impaired FMD response compared with normoglycemic pregnant women (31) which persists into the postpartum period (32). Physical activity has been suggested to improve vascular function by a combination of mechanisms (glucose metabolism improvement, increase in NO bioavailability (16)); however, this has not been examined during pregnancy.

With this as a background, the purpose of the present study was to determine the role of MVPA and sedentary behavior on FMD and glucose metabolism. We hypothesized that late pregnant women with objectively measured higher levels of MVPA and lower sedentary behavior would have an enhanced FMD response compared with pregnant women with lower MVPA activity levels and higher sedentary behavior. We further hypothesized that pregnant active women would have better glucose metabolism regulation than pregnant inactive women.

METHODS

Seventy normotensive, euglycemic pregnant women in their third trimester were assessed. Participants arrived at the laboratory at 8:00 AM after a 12-h fast. Caffeine and strenuous exercise were also avoided 12 h before testing. All procedures contributing to this work comply with the ethical standards set by the latest revision of the Declaration of Helsinki and had been approved by the Health Research Ethics Board at the University of Alberta (Pro00041144). Written informed consent was obtained from all participants.

Blood Sampling and Hemodynamic Monitoring

Blood samples were drawn from the left antecubital vein and participants were fed a light standardized meal consisting of a whole wheat bagel, jam (no sugar added), and a juice box. Blood samples were centrifuged, separated, and stored at −80°C until analysis. Glucose (hexokinase, Seimens Advia 1800), insulin (chemiluminescence microparticle immunoassay, Abbott Architect i2000), estradiol (electrochemiluminescence, Roche Cobas), progesterone (chemiluminescence competitive immunoassay, Siemens Centaur), and testosterone (two-site sandwich chemiluminescence, Siemens Centaur) were assessed. Homeostatic model assessment of insulin resistance (HOMA-IR) was calculated (fasting serum glucose × fasting serum insulin/22.5 (33).

Heart rate and blood pressure were measured continuously using a standard three-lead electrocardiogram based on lead II, and finger photoplethysmography (Finometer Pro; Finapres Medical Systems, Amsterdam, The Netherlands), respectively. Cardiac output was assessed using the Modelflow algorithm in the Finometer. Participants were seated in a semi-recumbent position in a dentist-style chair in a semi-darkened laboratory.

Flow-mediated Dilation Protocol

Our flow-mediated dilation protocol and analysis adhere with current guidelines for FMD (34). The right arm was positioned on a table at heart level. A blood pressure cuff attached to a manual inflation device was placed on the forearm distal to the elbow. Brachial artery diameter and velocity were recorded using Doppler Ultrasound (General Electric Health Care, USA) with a 60° insonation angle during 3 min of baseline, followed by a manual cuff inflation (5 min, 50 mm Hg above their systolic blood pressure) and release of the cuff (5 min).

FMD Analysis

Brachial artery blood flow velocity. Mean blood velocity was processed using qDAT (General Electric Health

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Care, USA), and recorded in labChart (ADInstruments, USA). Arterial blood velocity during baseline and after cuff release was averaged into 3-s bins. Mean blood velocity was used to calculate blood flow (πr^2 × blood velocity × 60 [mL·min^{-1}]; where r represents brachial artery radius) during baseline and after cuff release. Baseline brachial artery resistance was calculated as (mean arterial blood pressure/cardiac output) and baseline brachial artery conductance was calculated as (cardiac output/mean arterial blood pressure).

Brachial artery diameter. Brachial artery diameter (video saved as. AVI) was measured using an edge-detection software (Brachial Analyzer; Medical Imaging Applications, USA). Baseline, occlusion, and postocclusion diameters were measured frame by frame and then averaged into 3-s bins. Peak diameter and the time required to reach peak diameter were calculated.

Shear rate. As blood viscosity was not measured, we calculated shear rate as follows. Mean shear rate was calculated as 4 × mean blood velocity [cm·s^{-1}]/diameter [mm]. The shear rate stimulus was calculated as the area under the curve (AUC) or the sum of shear rates from cuff release to peak dilation (average shear rate [s^{-1}] × time to peak dilation [s]). In addition, anterograde shear rate (4 × anterograde blood velocity [cm·s^{-1}]/diameter [mm]), retrograde shear rate (4 × retrograde velocity [cm·s^{-1}]/diameter [mm]), and oscillatory shear index (absolute value of retrograde shear rate/absolute value of retrograde shear rate + anterograde shear rate) were calculated during baseline and after cuff release (34).

FMD response. The FMD response was calculated as absolute change (mm) or percentage change.

$$\text{absolute change in FMD} = \text{brachial artery diameter at peak after cuff release} - \text{brachial artery diameter at baseline.}$$

$$\%\ \text{change in FMD} = (\text{brachial artery diameter at peak after cuff release} - \text{brachial artery diameter at baseline}/\text{brachial artery diameter at baseline}) \times 100.$$

This response was normalized by the shear stimulus (AUC), to take into consideration the stimulus magnitude.

$$\text{absolute change in FMD}_{(\text{normalized})} = \text{brachial artery diameter at peak after cuff release} - \text{brachial artery diameter at baseline}/\text{shear stimulus (AUC)}$$

$$\%\ \text{change in FMD}_{(\text{normalized})} = ((\text{brachial artery diameter at peak after cuff release} - \text{brachial artery diameter at baseline}/\text{brachial artery diameter at baseline}) \times 100)/\text{shear stimulus (AUC).}$$

Physical Activity Patterns

Participants were instructed to wear an ActiGraph accelerometer (model wGT3X-BT; ActiGraph LLC, Pensacola, FL) on their right hip during waking hours for seven consecutive days. In addition, participants documented their nonwear times in an activity log. Data were only included in the analysis if the total wear time was over 600 min·d^{-1} on at least 4 d per standard protocols (25). Accelerometers recorded accelerations over 60-s time intervals (epoch). Time spent sedentary, time spent engaging in light activity, and time spent engaging in MVPA was calculated using Freedson accelerometer count ranges (<100 counts per minute, 100–1951 counts per minute, and ≥1952 counts per minute, respectively). In addition, the time accumulated in bouts lasting more than 10 min in duration was also calculated. Data were analyzed using Actilife software (ActiGraph LLC, Pensacola, FL).

Statistical Analysis

The Shapiro–Wilk test was used to assess the normality of the continuous data. According to the distribution of the variables, descriptive data were expressed as mean and SD. A multivariable regression analysis (least squares) between FMD responses, age, gestational age, prepregnancy body mass index (BMI), was run to determine which of the above mentioned variables should be considered as a covariate in our analysis (see Figure, Supplemental Digital Content 1, the analysis showed that age and gestational age should be covariates in our analysis, http://links.lww.com/MSS/B822). We used an allometric scaling technique to control for a potential influence of baseline diameter on the FMD result. (35). Briefly, a log-linked generalized linear model was applied where: the absolute change in FMD was the outcome, and the natural log of the baseline diameter was a covariate. A univariate analysis of variance to determine differences between active (or meeting 150 min MVPA) and inactive (those not meeting 150 min MVPA) women in all the parameters measured was carried out; for these analyses, age and gestational age were considered as covariates. Partial correlations controlling for age and gestational age were carried out between FMD responses and metrics of physical activity, glucose, insulin, HOMA-IR, and sex hormones within the groups. Statistical significance was defined as $P < 0.05$. Data were analyzed using IBM SPSS (IBM Analytics, USA). We have calculated the effect size (G*Power 3.1.9.2; Software, Germany) for the primary outcome as follows: with an effect size ($F = 4.169$), a total sample size of 70; 2 groups, 2 covariates, and numerator $df = 1$. Assuming an α of 0.05. The critical F value was 3.986.

RESULTS

Seventy pregnant women (31.6 ± 2.9 yr) in their third trimester [28–39 wk] were recruited. Following the 2019 Canadian Guideline for Physical Activity throughout Pregnancy (3–5), we categorized the women into active (≥150 min·wk^{-1}) or inactive (<150 min·wk^{-1}) according to their objective accelerometry data.

Active pregnant women (>150 min·wk^{-1} MVPA, $n = 32$) engaged in 266.7 ± 99.3 min·wk^{-1} MVPA, whereas inactive pregnant women (<150 min·wk^{-1} MVPA, $n = 38$) engaged in 76.1 ± 42.5 min·wk^{-1} MVPA ($P < 0.0001$; Table 1). Active pregnant women had higher DBP ($F = 3.039$, $P = 0.03$), higher glucose levels ($F = 3.382$, $P = 0.02$) and lower progesterone levels ($F = 10.443$, $P < 0.0001$) than inactive pregnant women (Table 1).

No differences among the groups were found regarding the brachial artery diameters at baseline, peak or occlusion (Table 1). Time to peak dilation, shear stimulus, absolute, and the percentage

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TABLE 1. Participants' baseline characteristics and univariate analysis of variance between inactive (MVPA <150 min·wk^{-1}; n = 38) and active pregnant women (MVPA >150 min·wk^{-1}; n = 32).

	Inactive Women n = 38	Active Women n = 32	
	Mean ± SD	Mean ± SD	P
Baseline characteristics and hemodynamics			
Gestational age (wk)	33.8 ± 2.8	33.2 ± 2.6	0.3
Age (yr)	31.6 ± 2.6	31.7 ± 3.2	0.9
Weight (kg)	77.5 ± 13.3	77.7 ± 14.7	0.1
Height (m)	1.7 ± 0.1	1.7 ± 0.1	0.5
BMI (kg·m^{-2})	27.9 ± 4.0	27.6 ± 4.0	0.1
Prepregnancy weight (kg)	64.8 ± 11.1	65.9 ± 12.1	0.2
Prepregnancy BMI (kg·m^{-2})	23.4 ± 3.2	23.4 ± 3.5	0.2
Heart rate (BPM)	83 ± 11	81 ± 10	0.2
MAP (mm Hg)	84 ± 8	85 ± 8	0.1
SBP (mm Hg)	112 ± 10	111 ± 10	0.8
DBP (mm Hg)	67 ± 8	68 ± 8	0.03
Cardiac output (L·min^{-1})	7.1 ± 1.2	7.3 ± 1.4	0.5
Systemic vascular resistance (dyn·s^{-1}·cm^{-5})	962.2 ± 172.8	956.1 ± 137.4	0.7
Physical activity			
Sedentary (%)	69.1 ± 8.3	64.7 ± 7.4	0.1
Sedentary time (min·d^{-1}`)	578.4 ± 85.3	549.6 ± 72.7	0.3
Light (%)	29.6 ± 7.9	30.8 ± 7.6	0.9
MVPA (%)	1.4 ± 0.8	4.5 ± 1.6	<0.0001
MVPA (min·wk^{-1})	76.1 ± 42.5	266.7 ± 99.3	<0.0001
MVPA (bout ≥10 min)	17.1 ± 24.3	125.8 ± 96.4	<0.0001
Hormones and metabolic status			
Estradiol (pmol·L^{-1})	63,415 ± 22,765	63,972 ± 24,012	0.5
Progesterone (nmol·L^{-1})	599.5 ± 238.0	538.5 ± 184.5	<0.0001
Testosterone (nmol·L^{-1})	2.2 ± 1.0	2.4 ± 1.4	0.5
Glucose (mmol·L^{-1})	4.2 ± 0.4	4.4 ± 0.4	0.02
Insulin (mmol·L^{-1})	55.3 ± 29.3	55.3 ± 26.1	0.1
HOMA-IR (mmol·L^{-1})	10.5 ± 6.0	10.9 ± 5.4	0.1
Brachial artery characteristics (mm)			
Baseline diameter	3.8 ± 0.5	3.8 ± 0.5	0.4
Peak diameter	4.0 ± 0.5	4.1 ± 0.5	0.1
Occlusion diameter	3.6 ± 0.5	3.8 ± 0.6	0.1
Time to peak dilation (s)	52.6 ± 19.2	44.2 ± 13.8	0.2
Shear stimulus (AUC)	1918.0 ± 747.1	1528.0 ± 799.2	0.1
FMD response			
Absolute change (mm)	0.2 ± 0.2	0.3 ± 0.2	0.1
Absolute change/shear stimulus	14.3 ± 13.0	24.1 ± 16.1	0.002
% Change in FMD	6.1 ± 4.2	8 ± 4.7	0.1
% Change in FMD/shear stimulus	3.9 ± 3.5	6.5 ± 4.4	0.005
Brachial artery velocity (cm·s^{-1})			
Baseline mean velocity	17.2 ± 5.7	13.8 ± 8	0.2
Baseline retrograde velocity	−0.5 ± 0.6	−1.0 ± 1.2	0.01
Baseline anterograde velocity	17.6 ± 5.3	14.8 ± 7.2	0.2
Postocclusion mean velocity	35.0 ± 8.4	32.6 ± 9.6	0.2
Postocclusion retrograde velocity	0 ± 0.1	−0.05 ± 0.1	0.4
Postocclusion anterograde velocity	35.1 ± 8.4	32.7 ± 9.5	0.2
Brachial artery blood flow (mL·min^{-1})			
Baseline mean blood flow	11,754 ± 5052	8796 ± 4839	0.1
Baseline retrograde blood flow	−295.9 ± 381.1	−615.6 ± 683.4	0.02
Baseline anterograde blood flow	12,054 ± 4891	9492 ± 4437	0.1
Postocclusion mean blood flow	23,334 ± 7260	22,530 ± 7938	0.9
Postocclusion retrograde blood flow	−37.1 ± 57.7	−30.6 ± 45.0	0.2
Postocclusion anterograde blood flow	23,376 ± 7248	22,614 ± 7944	0.9
Baseline brachial artery resistance (mm Hg·mL^{-1}·min^{-1})	0.009 ± 0.005	0.03 ± 0.08	0.5
Baseline brachial artery conductance (mL·min^{-1}·mm Hg^{-1})	141.1 ± 60.1	104.7 ± 57.8	0.1
Brachial artery shear rate (s^{-1})			
Baseline mean shear rate	18.4 ± 6.0	14.6 ± 8.4	0.1
Baseline retrograde shear rate	−0.4 ± 0.6	−0.7 ± 0.9	0.1
Baseline anterograde shear rate	18.9 ± 5.6	15.7 ± 7.6	0.2
Postocclusion mean shear rate	38.0 ± 10.0	34.1 ± 10.6	0.02
Postocclusion retrograde shear rate	0 ± 0.1	−0.05 ± 0.1	0.5
Postocclusion anterograde shear rate	38.1 ± 9.9	34.2 ± 10.5	0.02
Baseline Oscillatory Shear Index	0.03 ± 0.1	0.05 ± 0.1	0.1
Postocclusion Oscillatory Shear Index	0.001 ± 0.002	0.001 ± 0.002	0.6

MAP, mean arterial pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure.

change in FMD were not different among the groups. The normalized FMD response, however, was higher in active pregnant women compared with inactive pregnant women (6.5 ± 4.4 vs 3.9 ± 3.5; F = 4.619; P = 0.005). Similarly, a significant difference in FMD between groups was observed when the allometric scaling of the FMD was performed (see Table, Supplemental Digital Content 2, http://links.lww.com/MSS/B823. Briefly, we generated a log-linked generalized linear model where the absolute change in FMD was the outcome, and the natural log of the baseline diameter was a covariate).

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TABLE 2. Correlations between the normalized FMD responses, activity levels, baseline characteristics and hemodynamics, hormones, and metabolic status (controlling for age and gestational age) in active pregnant women (n = 32).

	% Change in FMD Normalized by Shear Stimulus		% of Time Spent in Sedentary Behavior		% of Time Spent Doing Light Activity	
	r	*P*	*r*	*P*	*r*	*P*
Baseline characteristics and hemodynamics						
Weight (kg)	0.057	0.8	0.186	0.5	−0.125	0.7
Height (m)	0.206	0.5	−0.003	1.0	0.024	0.9
BMI (kg·m^{-2})	−0.121	0.7	0.179	0.5	−0.123	0.7
Prepregnancy weight (kg)	−0.004	1.0	0.215	0.4	−0.169	0.5
Prepregnancy BMI (kg·m^{-2})	−0.201	0.5	0.208	0.5	−0.174	0.5
Heart rate (bpm)	−0.401	0.1	−0.476	0.1	0.509	0.1
MAP (mm Hg)	0.061	0.8	−0.141	0.6	0.112	0.7
SBP (mm Hg)	0.348	0.2	−0.234	0.4	0.226	0.4
DBP (mm Hg)	−0.103	0.7	−0.026	0.9	−0.010	1.0
Cardiac output (L·min^{-1})	0.280	0.3	−0.080	0.8	0.152	0.6
Systemic vascular resistance (dyn·s^{-1}·cm^{-5})	−0.282	0.3	−0.048	0.9	−0.058	0.8
Hormones and metabolic status						
Estradiol (pmol·L^{-1})	−0.035	0.9	0.100	0.7	−0.091	0.7
Progesterone (nmol·L^{-1})	−0.059	0.8	0.547	0.0	−0.552	0.033
Testosterone (nmol·L^{-1})	0.149	0.6	−0.282	0.3	0.304	0.270
Glucose (mmol·L^{-1})	0.121	0.7	−0.218	0.4	0.224	0.422
Insulin (mmol·L^{-1})	−0.015	1.0	0.062	0.8	0.040	0.887
HOMA-IR (mmol·L^{-1})	0.002	1.0	0.045	0.9	0.052	0.854

Active pregnant women had greater baseline retrograde velocity (F = 3.867) and baseline retrograde blood flow (F = 3.531), whereas their postocclusion mean shear rate (F = 3.254) and postocclusion anterograde shear rate (F = 3.230) were lower (Table 1).

In active pregnant women, the normalized FMD response, light activity or sedentary behavior were not correlated with any other variables (Table 2). The MVPA (min·wk^{-1}) was positively correlated with systemic vascular resistance (r = 0.607, P = 0.02) and inversely correlated with insulin concentrations and HOMA-IR (Fig. 1). The MVPA bouts ≥10 min were inversely correlated with prepregnancy weight (r = −0.545, P = 0.04), prepregnancy BMI (r = −0.620, P = 0.01), current weight (r = −0.553, P = 0.03), current BMI (r = −0.660, P = 0.007), baseline blood vessel diameter (r = −0.525, P = 0.04), insulin concentrations, and HOMA-IR (Fig. 1).

In inactive pregnant women, the normalized FMD response was not correlated with any other variables (Table 3). Sedentary behavior, light activity, or MVPA were not correlated with glucose levels, insulin or HOMA-IR (Table 3). Interestingly, sedentary behavior was correlated with baseline retrograde flow

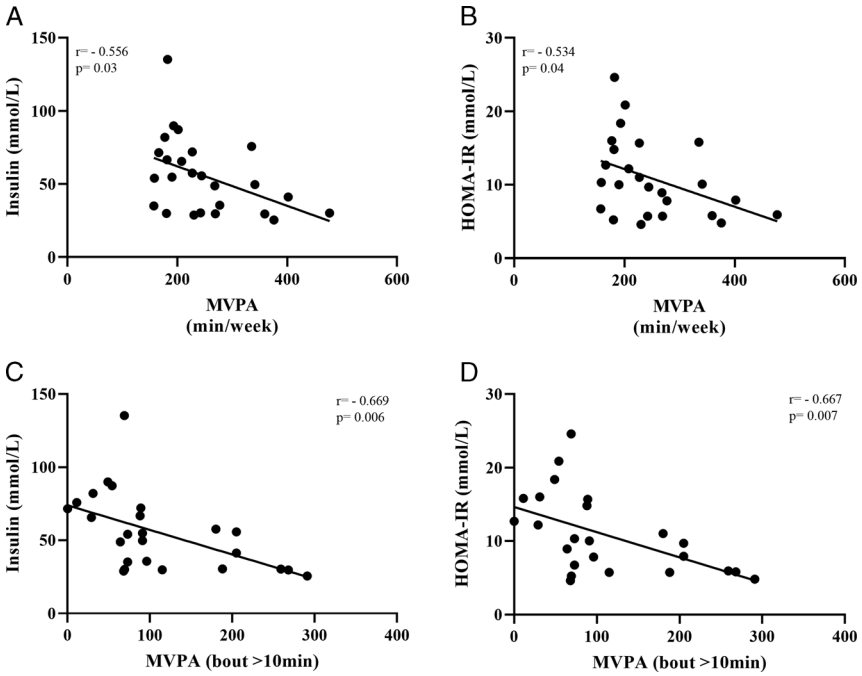

FIGURE 1—Correlations between activity levels and metabolic status (controlling for age and gestational age) in active pregnant women (n = 32). Correlations between moderate-to-vigorous activity presented in minutes per week with (A) insulin; and (B) HOMA-IR. Correlations between moderate-to-vigorous activity presented in bouts ≥10 min with (C) insulin; and (D) HOMA-IR.

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TABLE 3. Correlations between the normalized FMD responses, activity levels, baseline characteristics and hemodynamics, hormones and metabolic status (controlling for age and gestational age) in inactive women (n = 38).

	% Change in FMD Normalized by Shear Stimulus		% of Time Spent in Sedentary Behavior		% of Time Spent Doing Light Activity		MVPA (min·wk^{-1})	
	r	*P*	*r*	*P*	*r*	*P*	*r*	*P*
Baseline characteristics and hemodynamics								
Weight (kg)	0.206	0.4	–0.024	0.9	0.021	0.9	–0.032	0.9
Height (m)	–0.082	0.7	0.152	0.5	–0.166	0.5	0.060	0.8
BMI (kg·m^{-2})	0.275	0.2	–0.049	0.8	0.049	0.8	–0.054	0.8
Prepregnancy weight (kg)	0.196	0.4	0.020	0.9	–0.018	0.9	–0.107	0.6
Prepregnancy BMI (kg·m^{-2})	0.262	0.2	0.011	1.0	–0.005	1.0	–0.160	0.5
Heart rate (B.P.M)	0.049	0.8	0.096	0.7	–0.088	0.7	–0.080	0.7
MAP (mm Hg)	0.018	0.9	0.232	0.3	–0.239	0.3	–0.063	0.8
SBP (mm Hg)	0.155	0.5	–0.150	0.5	0.140	0.5	0.121	0.6
DBP (mm Hg)	–0.011	1.0	0.347	0.1	–0.349	0.1	–0.183	0.4
Cardiac output (L·min^{-1})	0.176	0.4	–0.027	0.9	0.035	0.9	–0.115	0.6
Systemic vascular resistance (dyn·s^{-2}·cm^{-5})	–0.120	0.6	0.149	0.5	–0.162	0.5	0.094	0.7
Hormones and metabolic status								
Estradiol (pmol·L^{-1})	0.032	0.9	0.239	0.3	–0.263	0.2	0.232	0.3
Progesterone (nmol·L^{-1})	–0.064	0.8	0.237	0.3	–0.253	0.3	0.136	0.5
Testosterone (nmol·L^{-1})	0.292	0.2	0.240	0.3	–0.248	0.3	–0.012	1.0
Glucose (mmol·L^{-1})	–0.183	0.4	0.035	0.9	–0.025	0.9	–0.114	0.6
Insulin (mmol·L^{-1})	–0.284	0.2	0.284	0.2	–0.290	0.2	–0.028	0.9
HOMA-IR (mmol·L^{-1})	–0.296	0.2	0.272	0.2	–0.277	0.2	–0.035	0.9

and velocity as well as baseline oscillatory shear index, whereas the opposite was true for light activity (Fig. 2).

DISCUSSION

Our data demonstrate that women who meet or exceed current recommendations of 150 min·wk^{-1} MVPA have better endothelial function compared with women who do not engage in 150 min·wk^{-1} of MVPA. In active pregnant women, MVPA was inversely correlated with insulin concentrations, suggesting that physical activity also enhances glucose metabolism during pregnancy. Interestingly, the correlations between insulin concentrations and HOMA-IR and MVPA were stronger when the bouts of MVPA were ≥10 min, although this is not causative, it may suggest that glucose metabolism is enhanced when longer durations of physical activity are performed. Finally, we found that vascular responsiveness to the FMD test and glucose metabolism was not related to sedentary behavior in either active or inactive women.

Physical activity, FMD, and brachial artery flow. This study sought to address a knowledge gap related to the relationship between physical activity (light activity and MVPA), sedentary behavior, and endothelial function during pregnancy. Endothelial function is influenced by the direction (anterograde, retrograde) and magnitude of shear stress (36). Anterograde shear stress has been associated with an increase in NO production in endothelial cells (27), whereas retrograde shear rate acutely impairs endothelial function (28). Our results demonstrated that active pregnant women had a greater baseline retrograde blood flow and velocity with a higher diastolic blood pressure. Because during the third trimester of pregnancy, blood pressure returns to prepregnancy values, our findings may suggest that active pregnant women have less blood vessel compliance. Nonetheless, these findings need to be interpreted carefully because the magnitude of these differences may not be physiologically relevant.

High levels of sedentary behavior during pregnancy have been associated with excess gestational weight gain, reduced glucose tolerance, elevated cholesterol, and systemic inflammation during pregnancy, all of which would be expected to be detrimental to endothelial function (37,38). Contrary to our hypothesis, sedentary behavior was not found to be associated with detriments in glucose metabolism in our participants. Previous data in women at risk of developing gestational diabetes mellitus have shown that prolonged sedentary time was associated with higher fasting glucose levels (39), whereas in women with gestational diabetes, breaking sedentary behavior was associated with lower fasting and postprandial glucose levels (39). There were no differences between sedentary behavior in our active and inactive pregnant women. Moreover, our participants were otherwise healthy. Thus, given the nature of our cohort of participants (no history of cardiometabolic diseases, cross-sectional assessment during their third trimester), the likelihood of finding relationships between sedentary behavior and FMD and glucose may be lower than anticipated.

Sedentary behavior was not found to be associated with FMD responses in this sample of healthy pregnant women. These findings are aligned with previous findings in older healthy adults, where reducing sedentary time did not improve vascular endothelial function (40). However, in inactive women, greater sedentary time was associated with lower amounts of retrograde shear rate. Putting all the evidence derived from this cohort in context, there were no correlations between anterograde or mean flow and/or shear rate. In addition, no differences between the groups regarding baseline blood vessel diameter, vascular conductance or resistance were found. Hence, given that the order of magnitude of anterograde flow is (5×) higher than the retrograde flow. We believe that this finding is minimally relevant to perfusion.

Finally, physical activity has been associated with enhanced vascular function in nonpregnant populations (16–19); however, this association is less clear in pregnant women. Our data align with results from Ramirez-Velez et al. (20), who showed that MVPA during pregnancy improves endothelial function

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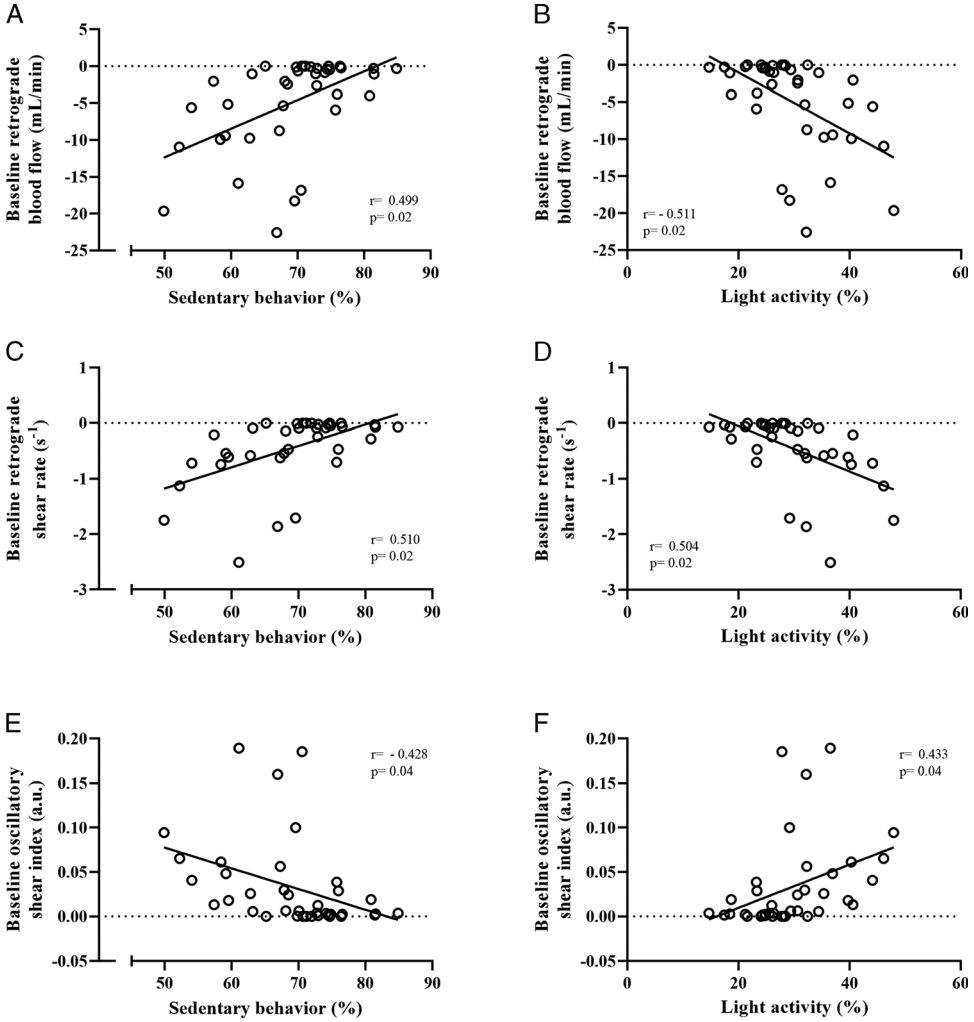

FIGURE 2—Correlations between activity levels and metabolic status (controlling for age and gestational age) in inactive pregnant women (n = 38). Correlations of percentage of time spent in sedentary behavior and baseline (A) retrograde blood flow; (C) retrograde shear rate and (E) oscillatory shear index. Correlations of percentage of time spent in doing light activity and baseline (B) retrograde blood flow; (D) retrograde shear rate; and (F) oscillatory shear index.

(increased FMD) in late pregnancy. This was observed after normalizing the data by the shear stimulus; indicating that this is a critical factor to account for when interpreting FMD results. This is particularly relevant in pregnant populations where increases in blood volume and cardiac output, concurrent with a functional reduction in hematocrit may all influence shear stress.

The discrepancies between our findings and Ramirez-Velez et al., with those from Weissgerber et al. (15), could be explained by a) the authors quantified physical activity using an activity survey. b) Because shear rate responses, FMD response, and diameters were not different among the pregnant groups (active vs inactive). c) Authors acknowledge the sample size as a limiting factor in the study.

The current Canadian Guideline for Physical Activity throughout pregnancy recommends women engage in at least 150 min·wk^{-1} of moderate-intensity exercise (3,4). Women who follow these recommendations have a reduction in the risk of developing hypertensive disorders of pregnancy by approximately 20% (1). One of the potential mechanisms that can explain this would be an improvement of vascular function. Even though we did not follow-up our pregnant women, our cross-sectional data suggest that exercise indeed improves vascular function in this population.

Physical activity, hormones, and cardiometabolic adaptations to pregnancy. Pregnant women undergo several cardiometabolic adaptations to meet the increased metabolic demands of the growing fetus. These adaptations include insulin resistance, and increased glucose utilization, heart rate, stroke volume, and cardiac output while maintaining normal blood pressure (41). Even though we found that fasting glucose level was slightly higher in active women, the difference between the groups was small (0.2 mmol·L^{-1}) and there was no difference in insulin concentrations or HOMA-IR. Nonetheless, MVPA during pregnancy was inversely correlated with fasting insulin concentrations and HOMA-IR only in active pregnant women; suggesting that higher levels of physical activity may influence insulin control in these women. Moreover, the correlations were stronger when MVPA was analyzed as bouts ≥10 min showing that planned physical activity may be better to improve glucose metabolism.

Physical activity patterns appear to have an important influence on sex hormones. Previous data have shown that in healthy,

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sedentary eumenorrheic women, an aerobic exercise program for 16 wk (MVPA, 150 min·wk^{-1}) decreased progesterone levels (42). This is similar to what we observed between our groups of women. However, there were no associations between vascular function and hormone concentrations. Although there is evidence that progesterone may influence vascular tone (43), the magnitude of the observed difference was small, and the physiological relevance remains unclear.

Study limitations. We found that 46% of our sample met the guidelines for exercise during pregnancy, whereas nationally representative cohorts have suggested that only 9% to 15% of women meet these guidelines (23,24). We recruited our participants through posters located in the university areas and through social media posts. Most of the women recruited in our study come from the university area, therefore, a recruitment bias could explain why our population has double the rate of compliance with the guidelines.

Physical activity and sedentary behavior are challenging to quantify, especially during pregnancy (44). Thus, a strength of our study is the use of objectively measured physical activity and sedentary behavior. Although accelerometers do not measure posture (standing vs sitting); a defining feature of sedentary behavior; our accelerometry derived measure of sedentary behavior was similar to data derived from the only two studies using activPAL devices in pregnant women (39,45). Similar to results from Wagnild et al., (39) women in our study spent approximately 9.4 ± 1.4 h·d^{-1} being sedentary, whereas women from the Di Fabio et al., (45) study spent 12.9 ± 2.2 h·d^{-1} in sedentary behavior. However, future studies assessing the relationship between sedentary behavior and FMD should consider the use of an inclinometer.

CONCLUSIONS

In active women, exercise enhances vascular function (FMD responses). Moreover, greater levels of activity may also further benefit glucose metabolism. Combined these data demonstrate the cardiovascular benefits of meeting current guidelines for MVPA during pregnancy (3–5).

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