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The Effects of Physical Activity on Arterial Stiffness during Pregnancy: An Observational Study

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Title: The Effects of Physical Activity on Arterial Stiffness during Pregnancy: An Observational Study

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Abstract

The objective of the present study was to investigate the relationship between moderate-to-vigorous physical activity (MVPA) and arterial stiffness in pregnancy. Thirty-nine women participated in this study resulting in 68 measurements in non-pregnant (NP; n=21), first (TM1; n=8), second (TM2; n=20), and third trimesters (TM3; n=19). Compliance, distensibility, elasticity, β -stiffness, and carotid to femoral (central) and carotid to finger (peripheral) pulse wave velocity (PWV) were assessed. MVPA was measured using accelerometry. Multilevel linear regressions adjusted for multiple tests per participant using random effects to generate β coefficients and 95% confidence intervals (CI) were performed. Distensibility, elasticity, β -stiffness, central- and peripheral-PWV did not differ between pregnant and non-pregnant assessments. Carotid artery compliance was higher in TM2 compared to NP. Central PWV (β Coef: -0.14, 95% CI: -0.27, -0.02) decreased from early to mid-pregnancy and increased in late pregnancy. Meeting the MVPA guidelines was significantly associated with central-PWV (Adj. β Coef: -0.34, 95% CI: -0.62, -0.06, $p=0.016$), peripheral-PWV (Adj. β Coef: -0.54, 95% CI: -0.91, -0.16, $p=0.005$), and distensibility (Adj. β Coef: -0.001, 95% CI: -0.002, -0.0001, $p=0.018$), in pregnancy. These results suggest that MVPA may be associated with improved (i.e. reduced) arterial stiffness in pregnancy.

Novelty Bullets

- Central PWV, distensibility, compliance, elasticity, and β -stiffness, but not peripheral PWV, exhibited curvilinear relationships with gestational age
- Central and peripheral PWV were lower in pregnant women who met the physical activity guidelines of 150 minutes of moderate-to-vigorous physical activity per week

Key words: Arterial Stiffness, Pulse Wave Velocity, Physical Activity, Pregnancy

Introduction

Increased arterial stiffness has been linked to an increased risk of developing of cardiovascular disease (Hamilton et al., 2007, Fantin et al., 2012). Pulse wave velocity (PWV) has emerged as the gold standard measure of arterial stiffness due to the large body of evidence indicating its reliability, and reproducibility (Hamilton et al., 2007). Carotid-femoral (central) PWV provides the most clinically relevant measure of arterial stiffness (Laurent et al., 2006). Specifically, increases in central PWV are directly associated with cardiovascular morbidity and mortality (Vlachopoulos et al., 2010). Arterial stiffness can also be measured using ultrasound-derived measurements of arterial pulsatility. Arterial compliance is an index of the elasticity of large arteries based on the relationship between pressure and blood volume. Distensibility is a measure of the artery's ability to respond to cardiac pulsation and relaxation and describes artery wall stiffness. The elastic modulus describes the relationship of stress over strain and is a quantification of the vessel's resistance to being deformed elastically. β -stiffness is an index reflecting arterial stiffness without the influence of blood pressure.

During pregnancy, the cardiovascular system undergoes significant changes to adapt to the needs of the growing fetus and placenta. These changes include increases in heart rate and cardiac output, concurrent with a curvilinear drop in blood pressure over the course of pregnancy (Meah et al., 2016). Systemic (aortic) arterial compliance increases while carotid compliance decreases by 20-30% in healthy pregnancy (Ouzounian and Elkayam, 2012, Mersich et al., 2005). These compliance changes may be due to changes in heart rate, but this has not been confirmed. Numerous studies have shown that in healthy pregnancies central PWV tends to decrease in the second trimester, and then rise in the third trimester (Osman et al., 2017). Increased PWV in the second trimester may be a serious sign of pre-eclampsia risk (Osman et

al., 2018). Central and peripheral PWV do not necessarily reflect ultrasound-derived measures of arterial stiffness (compliance, distensibility, elasticity, and β -stiffness) while these ultrasound-derived measures tend to correlate strongly (Tanaka, 2017). While central and peripheral PWV, and elasticity are moderately BP dependent, there is some evidence that arterial compliance, distensibility, β -stiffness, and elasticity may be less BP dependent (Lim et al., 2015).

There is a large body of evidence that supports physical activity as a means to help prevent the development of CVD (Skow et al., 2017, Curtis et al., 2017, Hughes et al., 2013, Thompson et al., 2003, Viramontes et al., 2016). Physical activity has a beneficial effect on the cardiovascular system through changes in artery function and structural arterial remodelling (Green and Smith, 2018). One pathway from physical activity to cardiovascular health is through a reduction in arterial stiffness (Ashor et al., 2014). While activity has a similar, favorable impact on the cardiovascular system in pregnancy (Cai et al., 2020), whether this is affected through arterial stiffness is not as well understood. In one study, brachial-ankle PWV was found to be lower in the second trimester compared to the postpartum period in women who were inactive during pregnancy, but did not increase in women who took part in physical activity regularly throughout pregnancy (Kawabata et al., 2012). Although this suggests an influence of physical activity, this was inferred based on postpartum measurements which may be independently influenced by persistent cardiovascular remodelling independent. Recently, a pilot study of 18 pregnant women demonstrated a similarly lower carotid-femoral PWV compared to the first and third trimesters (Brislane et al., 2021); however, exercise intervention appeared to result in higher PWV through pregnancy. Therefore, we have identified the relationship between physical activity and arterial stiffness in pregnancy as a gap that still remains in the literature.

The aim of the current study was to examine further the adaptations in arterial stiffness (central and peripheral PWV, carotid artery distensibility, compliance, elasticity, and β -stiffness) across pregnancy and the role of physical activity (e.g., MVPA) in mediating these changes. We hypothesized that meeting the MVPA guidelines (150 minutes/week) would be associated with a decrease in metrics of arterial stiffness in pregnancy.

Methods

Study Participants

Forty-four unique participants completed testing at least once, to be included in one of four groups [nonpregnant (NP), first trimester (TM1), second trimester (TM2), or third trimester (TM3)]. Assessments were conducted on 21 NP women, 13 women in the TM1 (range, 10–12 weeks of gestation), 20 women in the TM2 (range, 20–27 weeks of gestation), and 21 women in the TM3 (range, 30–37 weeks of gestation). Peripheral- or central- PWV measurements were completed in 68 of 75 tests (see Table S1). All participants provided written, informed consent prior to participating. Women were non-smokers and free from cardiovascular, respiratory, or metabolic diseases. All pregnant women had singleton pregnancies and gestational age was calculated using self reported due date. None of the women were taking any regular prescription medications, with the exception of hormonal contraceptives. NP women who were not taking oral/hormonal contraceptives were tested during the early follicular phase of their menstrual cycle, while those who were taking hormonal contraceptives which inhibited menses (Nuva ring, n=1; Min Ovral, n=1; Yasmin, n=1, Yaz, n=1) were tested at their convenience. Ethics approval for this study was obtained from the University of Alberta Health Research Ethics Board

(Pro00040722) and followed institutional guidelines and standards set forth by the Declaration of Helsinki with the exception of registration in a publicly available database.

Study Design

Participants arrived between 7:00-8:00 am following a 12 hour overnight fast. They were instructed to abstain from alcohol, strenuous exercise, and caffeine for at least 12 hrs prior to arrival. Upon arrival, participants were fed a standardized breakfast consisting of a multigrain bagel, jam, and orange juice. Anthropometric measures were collected by a trained research associate using a standard calibrated scale and stadiometer. Pre-pregnancy weight was self-reported. Participants were then seated in a semi-recumbent position (placed at 30° above supine) in a quiet, darkened room maintained at 20-23°C and remained in the semi-recumbent position throughout the remainder of testing. Participants rested quietly for 20 minutes before the cardiovascular assessment was conducted.

Study Measures

Women were instrumented to measure heart rate using a standard lead (II) ECG (ADI bioamp FE132; Colorado Springs, USA). Mean (MAP), systolic (SBP), and diastolic blood pressure (DBP), and cardiac output (CO) were measured using Finometer Pro which uses finger photoplethysmography to measure beat-by-beat blood pressure and the Modelflow algorithm to determine CO (Finometer; Finapres Medical Systems, Amsterdam, The Netherlands). Values were calibrated to the average of three manual resting blood pressure measurements obtained using a sphygmomanometer. Systolic and diastolic diameter of the carotid artery were measured using an ultrasound (8Mhz linear probe, Vivid 7; General Electric, New York, USA). Ultrasound images were taken at the right carotid artery and stored for offline analysis (EchoPAC software V6.2, GE/Vingmed). Carotid artery diameters at diastole and systole were assessed in the

program using manual digital calipers by a trained observer. Corresponding systolic and diastolic blood pressures were retrieved from LabChart. Pressure waveforms for the calculation of PWV were collected via arterial tonometry at the carotid artery (Model SPT.301; Millar, Houston, USA). Blood flow velocity wave-forms from the superficial femoral artery were obtained using pulse-wave Doppler ultrasound (8Mhz linear probe, Vivid 7; General Electric, New York, USA). All data was collected in Lab Chart 7 (ADInstruments, Colorado, USA) at 1000hz.

Data Analysis

Baseline hemodynamics

Following 20 minutes of rest, five minutes of SBP, DBP, HR, and CO at rest were collected. MAP (Laurent et al., 2006) and total peripheral resistance ($TPR = MAP/Q$) (Usselman et al., 2015) were calculated.

Arterial Stiffness

Arterial distensibility, compliance, Peterson's elastic modulus, and β -stiffness were calculated using the following equations:

$$(1) \text{Distensibility} = ((A_S - A_D)/A_D)/(SBP - DBP)$$

$$(2) \text{Compliance} = (A_S - A_D)/(SBP - DBP)$$

$$(3) \text{Elasticity} = (SBP - DBP)/((A_S - A_D)/A_D)$$

$$(4) \beta - \text{Stiffness} = (\ln (SBP/DBP))/((A_S - A_D)/A_D)$$

where A_S is systolic area, A_D is diastolic area, SBP is systolic blood pressure, and DBP is diastolic blood pressure (Laurent et al., 2006, Selzer et al., 2001).

Compliance is most linear under circumstances when vascular cross-sectional diameter is changing to a greater proportion than pulse pressure. Distensibility is similarly sensitive in this scenario, but also takes in account differences in relaxed (diastolic) diameter. Elasticity and beta-stiffness are linear and most sensitive under in scenarios when pulse-pressure is changing to a greater proportion than vessel cross-sectional area. Thus, the use of multiple indices allowed us to perform a more comprehensive and sensitive assessment of vascular function.

Pulse Wave Velocity

The pressure or flow waveforms were collected from the Finometer (proper digital artery), tonometer (common carotid artery), and ultrasound (superficial femoral artery). A foot-to-foot pressure waveform analysis was performed using the following equation:

$$(5) \text{PWV} = \Delta d / \Delta t$$

Where Δd is the distance travelled by the pulse wave, and Δt is the transit time between measurement sites (Hamilton et al., 2007). In the case of central (carotid-femoral) PWV, the foot of the pressure wave at the carotid artery was used in conjunction with the foot of the blood flow velocity waveform obtained from ultrasound recordings. Distance for central-PWV was determined by adding sternal-carotid distance with sternal-femoral distance (Wimmer et al., 2007). The sternal femoral distance was in a mid-axillary line to avoid over estimation of midline measurements in pregnant women. Distance for peripheral-PWV was determined by adding sternal-carotid distance from sternal-finger distance (Townsend et al., 2015).

Accelerometry

Each participant wore an accelerometer (Actigraph; model wGT3X-BT) on their right hip for 7 consecutive days starting on the day after the cardiovascular assessment. Participants

completed a log of sleep, activity, and non-wear times during the accelerometry period. Napping, bathing, and swimming were recorded by participants as non-wear times. Accelerometers were initialized to record accelerations over 60-second epochs (ActiGraph, ActiLife Software V6.). Freedson accelerometer counts for each activity level were set as follows: sedentary (<100 counts per min [cpm]), light activity ($100-1,951$ cpm), and moderate-vigorous physical activity (MVPA, $\geq 1,952$ cpm) (Freedson et al., 1998). A threshold of ≥ 600 minutes per day for a minimum of 4 days was set to be included in analysis.

Statistical Analysis

Due to the unbalanced nature of the study data, we conducted all statistical tests using multilevel linear regression models adjusted for multiple tests per participant during the study period (NP, TM1, TM2, or TM3) using random effects for modelling intra-cluster correlation to generate β coefficients and 95% confidence intervals (CI).

Univariate comparisons between groups (NP, TM1, TM2, TM3) were performed. Multivariable models examining compliance, distensibility, elasticity, β -stiffness, and central and peripheral PWV in the full cohort were conducted where phase of pregnancy (NP (reference) vs pregnant), meeting the MVPA guidelines (≥ 150 min MVPA per week), age, and BMI at the time of measurement were examined as covariates. Multivariable models examining compliance, distensibility, elasticity, β -stiffness, and central and peripheral PWV in pregnancy only were also conducted. Gestational age (weeks) and meeting the MVPA guidelines (≥ 150 min MVPA per week) were included in these models. Statistical significance was set at an alpha level of 0.05. All statistical analyses were performed using STATA 13 (StataCorp, 2013).

Results

Participant characteristics and resting hemodynamics are presented in Table 1 and demonstrate the cardiovascular changes expected with pregnancy. None of the participants developed any pregnancy-related complications during the studied pregnancy. Blood pressure was lower in TM1 compared to NP, but higher in TM3 compared to TM1. HR and CO were increased as pregnancy progressed and TPR was lower in TM1, TM2, and TM3 compared to NP.

While carotid distensibility, elasticity, and β -stiffness were unchanged according to trimester of pregnancy, common carotid artery compliance was higher in TM2 compared to NP (Table 2; $p < 0.05$). MVPA (minutes per week) were highest in NP. MVPA was significantly lower in TM1 and TM3 compared to NP and lower in TM3 compared to TM2.

Central- and peripheral- PWV did not differ between NP, TM1, TM2, and TM3. Being pregnant compared to being non-pregnant was not associated with a change in peripheral- or central- PWV in univariate or adjusted models (Table 3). However, following adjustment for pregnancy, age, and BMI, meeting the MVPA guidelines was associated with a decrease in both peripheral-PWV (Adj. β Coef.: -0.54; 95% CI: -0.91, -0.16, $p = 0.005$) and central-PWV (Adj. β Coef.: -0.30; 95% CI: -0.58, -0.02, $p = 0.04$). Carotid distensibility, elasticity, and β -stiffness did not differ between pregnant and non-pregnant assessments. However, carotid compliance was higher in pregnant assessments. Meeting the MVPA guidelines was not associated with compliance, distensibility, elasticity, or β -stiffness in univariate or multivariable models.

Linear and curvilinear combinations of gestational age were not associated with peripheral-PWV (β Coef: -0.12, 95% CI: -0.28, 0.04, $p = 0.142$, $n = 42$). However, gestational age (squared) was associated with central-PWV (β Coef: -0.14, 95% CI: -0.27, -0.02, $p = 0.024$; $n = 42$; see Figure 1). Meeting the MVPA guidelines was also significantly associated with central PWV and adjustment for meeting the MVPA guidelines decreased the association between gestational

age and central-PWV (Meeting the MVPA guidelines Adj. β Coef: -0.34, 95% CI: -0.62, -0.06, $p=0.016$; Figure 1). Meeting the MVPA guidelines was significantly associated with peripheral-PWV (Adj. β Coef: -0.54, 95% CI: -0.91, -0.16, $p=0.005$). Carotid compliance, distensibility, elasticity, and β -stiffness exhibited curvilinear relationships with gestational age (Figure 2). Following adjustment for gestational age, meeting the MVPA guidelines was associated with 8% lower distensibility in pregnant assessments (Adj. β Coef: -1.1, 95% CI: -1.9, -0.2, $p=0.018$) but was not associated with carotid compliance, elasticity, or β -stiffness.

Discussion

We sought to examine the impact of physical activity patterns on arterial stiffness throughout pregnancy. Data from non-pregnant populations illustrate a connection between increased levels of physical activity and decreased levels of arterial stiffness (Ashor et al., 2014, Kearney et al., 2014, Gando et al., 2010); however, this relationship has not been demonstrated in pregnancy. Although PWV was not different between pregnant and non-pregnant participants, central-PWV exhibited a curvilinear relationship with gestational age. Meeting the MVPA guidelines was strongly associated with lower measures of central- and peripheral-PWV. In pregnant participants, inclusion of meeting the MVPA guidelines as a covariate reduced the significance of the association between gestational age and central-PWV.

Arterial stiffness in pregnancy is positively associated with risk for cardiovascular disorders such as preeclampsia and gestational hypertension (Osman et al., 2018, Robb et al., 2009, Marozio et al., 2019). Our results and others' suggest that physical activity in pregnancy may significantly decrease the risk of these serious cardiovascular disorders through a reduction

in arterial stiffness (Kawabata et al., 2012). Likewise, physical activity has been found to significantly decrease the risk of these disorders in pregnancy (Davenport et al., 2018).

Previous studies have reported changes in aortic compliance over the course of pregnancy (Edouard et al., 1998, Mersich et al., 2005). During pregnancy, there is evidence that systemic arterial compliance increases (Poppas et al., 1997) while the carotid artery stiffens, leading to decreased carotid artery compliance (Mersich et al., 2005). We found carotid compliance to be higher during pregnancy compared to the non-pregnant state, with TM2 values being significantly higher than those in NP. Mersich et al. reported that compliance was lower in TM3 compared to TM1, but was higher in the postpartum compared to TM3 in their study sample (Mersich et al., 2005). A number of studies have found arterial compliance to be lower in TM3 compared to TM2 (Mersich et al., 2005, Visontai et al., 2002), or NP (Yuan et al., 2013). Combined, these findings suggest that compliance changes throughout pregnancy, with increased values in mid-pregnancy, and values in the third trimester that are either similar to or lower than values in pre-pregnancy. It is important to note that we do not yet know if pregnancy may influence postpartum arterial compliance.

Our findings echo those which have found that distensibility increases in mid pregnancy and decreases in the third trimester (Visontai et al., 2002, Mersich et al., 2005, Kärkkäinen et al.). While Yuan et al. found distensibility to be lower in the third trimester compared to the postpartum period, (Yuan et al., 2013) we did not find a meaningful difference between nonpregnant and third trimester measures. Contrary to our hypotheses, higher physical activity was associated with reduced arterial distensibility in pregnant participants. Although aerobic exercise training can increase arterial distensibility, resistance training may decrease

distensibility.(Collier et al., 2010) We did not determine which exercise modalities study participants chose to take part in during their pregnancies.

Artery elasticity and β -stiffness were not different between pregnant and non-pregnant measurements and were not associated with physical activity level. Contrariwise to compliance and distensibility, arterial elasticity and β -stiffness decreased in the second trimester and rebounded in the third trimester. These results emulate previous findings.(Mersich et al., 2005, Kärkkäinen et al.) However, Yuan and colleagues found β -stiffness to be higher in pregnant compared to non-pregnant participants. (Yuan et al., 2013)

We did not find measures of PWV to be statistically different between pregnant and non-pregnant participants. However, central, but not peripheral-PWV changed significantly over the course of pregnancy with a decreasing trend from the first to second trimester and increasing trend from the second to third trimester. These results align with the findings of multiple studies which have also observed a decrease in PWV from the first to second trimester and an increase (sometimes non-significant) in PWV from the second to third trimester (Osman et al., 2017, Robb et al., 2009, Gomez et al., Pandey et al., 2014, Khalil et al.). However, other authors have reported that PWV (carotid-radial and carotid-femoral) did not change significantly with gestation (Macedo et al.) or continued to decrease into the third trimester (Mersich et al., 2005). Turi et al. reported that peripheral (brachial) PWV decreased over the course of pregnancy in a study of 471 pregnant individuals (Turi et al., 2020). Central-PWV reflects the stiffness of the common carotid artery, aorta and the common femoral artery (Townsend et al., 2015). Comparatively, these arteries are larger and have higher elastic properties compared to peripheral arteries, such as the proper digital artery, the site of measurement for peripheral-PWV in this study (London and Pannier, 2010). Peripheral arteries have higher muscular and lower elastic

properties and have smaller diameters compared to central arteries (Hoeks et al., 1999). Since the peripheral arteries are less elastic, they may be less compliant and accommodating to the blood volume changes that occur over the course of pregnancy. Changes in nitric oxide (Delacrétaz et al., 1995, Wilkinson et al., 2002), blood volume, progesterone, and relaxin have been proposed as mechanisms to explain the drop in central-PWV from the first to second trimester of pregnancy (Khalil et al., 2009). Inhibition of nitric oxide (McEniery et al., 2006, Holden et al., 1998), increased cardiac output, and circulatory volume (Wykrętowicz et al., 2011) may explain the increase in central-PWV from mid-pregnancy to term.

In general, physical activity decreases steeply over the course of pregnancy, with a slight rise in TM2 above TM1 and TM3 levels (Gaston and Cramp, 2011, Liu et al., 2010). In the present study, physical activity was highest in the non-pregnant group, but was also higher in TM2 compared to TM1 and TM3. We observed relatively high physical activity levels in our sample, with 83% of non-pregnant and 60% of pregnant participants obtaining 150 minutes of MVPA per week. In the full cohort and pregnant participants alone, meeting the MVPA guidelines was significantly associated with central- and peripheral-PWV. This is in line with results from the general population (Edwards et al., 2012). However, adjustment for meeting the MVPA guidelines nullified the association between arterial stiffness and gestational age. We posit that there is a possibility that the increased physical activity observed in TM2 in our sample may have contributed to the decrease in arterial stiffness observed in this trimester. This is speculative as interventional data to establish causality are lacking.

Strengths and limitations

There are some considerations when examining the results of this study. First, the literature recommends performing arterial stiffness measurements in a supine position (Townsend et al., 2015). To accommodate our participants' comfort and safety, measurements were taken in a semi-recumbent position to avoid compression from the growing uterus on the great vessels as pregnancy progressed. Second, distance measurements for PWV calculations were taken across the body. While this has been validated in the non-pregnant population, this has not been validated in the pregnant population and may differ due to the difficulty of measuring across a pregnant individual's body. Performing longitudinal assessment on individuals over the course of each individual pregnancy, from pre-pregnancy to the third trimester, provides a more in-depth view of specific changes that occur during pregnancy. Logistically, recruiting individuals prior to conception and following them over the nine months of their pregnancy is difficult. To account for the unbalanced nature of our data (with data collection from participants across multiple phases) we opted to include multilevel modelling with adjustment for intra-class correlation within participant measures. The methodology employed in the present study followed previously validated measures when possible.

Future directions

Moving forward there are still many gaps in the literature that need to be examined. There is a lack of longitudinal measures of arterial stiffness from pre-conception, through pregnancy and the postpartum period. Additionally, physical activity and behaviour patterns should also be measured across these time points to better understand their impact on arterial stiffness during pregnancy. These findings, along with others, show promising results for physical activity as an intervention for reduced arterial stiffness. Moving forward an RCT

examining a physical activity intervention would be beneficial to help explore this relationship further.

Conclusions

The results from this study suggest that there is a significant relationship between aortic and peripheral PWV and physical activity in pregnancy. Based on these results we support the notion that higher MVPA levels during pregnancy may help to improve the arterial stiffness profile of individuals over the course of pregnancy. These are positive findings and may have beneficial implications in the future, especially for individuals who are at risk for developing pregnancy related cardiovascular diseases such as preeclampsia.

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Competing interests statement

Competing interests: the authors declare there are no competing interests.

Contributors' Statement

MHD and CDS planned the study. RS, FS, KF, and CM conducted the study and collected measurements. KF and FS analyzed the study data. BAM completed the statistical analysis. KF, BAM, and MHD drafted the manuscript. CDS, RS, CM, and FS contributed significantly to the writing of the manuscript.

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Data AVAILABILITY

The data from this study is not available.

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Tables

Table 1. Participant characteristics and baseline hemodynamics

	Non-pregnant	TM1	TM2	TM3
N	21	8	20	19
Gestational age, weeks* <i>n</i> =47	n/a	11 ± 1 [§]	24 ± 1 [‡]	33 ± 2 ^{‡§}
Age, years* <i>n</i> =68	28 ± 6 [§]	30 ± 5	31 ± 4 [†]	31 ± 4 [†]
Non-pregnant/pre-pregnancy BMI, kg/m ² * <i>n</i> =66	23.6 ± 3.4	23.0 ± 1.7	23.1 ± 2.7	23.1 ± 2.7
Current BMI, kg/m ² <i>n</i> =66	23.6 ± 3.4 [§]	23.5 ± 2.3 [§]	25.9 ± 4.3 ^{†‡}	26.6 ± 2.3 ^{†‡§}
Mean arterial pressure, mmHg* <i>n</i> =68	93 ± 10 [‡] §	80 ± 3 [†]	82 ± 7 [†]	87 ± 7 [†] §
Systolic blood pressure, mmHg* <i>n</i> =68	115 ± 17 [‡]	99 ± 23 [†]	107 ± 10	112 ± 8 [‡]
Diastolic blood pressure, mmHg* <i>n</i> =68	74 ± 7 [‡] §	59 ± 12 [†] §	65 ± 7 [†] ‡	70 ± 8 [‡]
Heart rate, bpm* <i>n</i> =68	69 ± 9 [‡] §	75 ± 9 [†] §	80 ± 8 [†] ‡	83 ± 9 [†] ‡ §
Cardiac output, L/min* <i>n</i> =68	5.8 ± 1.1	6.2 ± 1.3	7.0 ± 1.5 [†]	7.3 ± 1.5 [†] ‡
Total peripheral resistance, mmHg/L/min* <i>n</i> =68	16.4 ± 3.3 [‡] §	13.4 ± 2.8 [†]	12.1 ± 2.3 [†]	12.3 ± 2.8 [†]

Values are means ± SD. BMI, body mass index; TM1, trimester 1; TM2, trimester 2; TM3, trimester 3.

* Main effect across all groups, $P < 0.05$; † Different from NP; ‡ Different from TM1; § Different from TM2; || Different from TM3.

Table 2. Arterial stiffness and physical activity variables

	Non-pregnant	TM1	TM2	TM3
Peripheral-PWV, m/s <i>n</i> =66	6.7 ± 0.7	6.8 ± 0.4	6.4 ± 0.6	6.9 ± 0.9
Central-PWV, m/s <i>n</i> =67	4.5 ± 0.7	4.5 ± 0.4	4.1 ± 0.5	4.3 ± 0.7
Compliance, mm ² /mmHg* <i>n</i> =64	0.11 ± 0.02 [§]	0.12 ± 0.03	0.15 ± 0.04 [†]	0.13 ± 0.05
Distensibility, 10 ⁻³ /mmHg <i>n</i> =64	4.1 ± 1.0	3.8 ± 0.8	4.8 ± 1.7	4.1 ± 1.7
Elasticity, E (mmHg)) <i>n</i> =64	542.3 ± 132.9	559.5 ± 109.5	472.6 ± 130.3	581.0 ± 203.0
β-Stiffness, β <i>n</i> =64	5.8 ± 1.6	6.8 ± 1.5	5.7 ± 1.5	6.7 ± 2.4
Sedentary % <i>n</i> =63	66.9 ± 8.0	69.3 ± 5.2	68.5 ± 7.5	69.5 ± 9.1
Light % <i>n</i> =63	28.7 ± 8.1	27.3 ± 6.1	27.7 ± 7.3	27.6 ± 8.8
MVPA %* <i>n</i> =63	4.4 ± 2.6	3.4 ± 1.4	3.8 ± 2.2	2.9 ± 2.0 [†] [§]
MVPA/week, min* <i>n</i> =63	287 ± 178 [‡]	211 ± 82 [†]	238 ± 137	168 ± 125 [†] [§]
Meeting MVPA Guidelines per week, count (%) <i>n</i> =63	15/18 (83.3%)	6/8 (75.0%)	13/18 (72.2%)	8/19 (42.1%)

Values are means ± SD

* Main effect across all groups, *P* < 0.05; [†] Different from NP; [‡] Different from TM1; [§] Different from TM2; ^{||} Different from TM3.

1 **Table 3. Linear regression of Central- and Peripheral- PWV (m/s).**

	Central-PWV				Peripheral-PWV			
	Univariate Model		Multivariable Model *		Univariate Model		Multivariable Model *	
	B coef (95% CI)	p-value	Adj B coef (95% CI)	p-value	B coef (95% CI)	p-value	Adj B coef (95% CI)	p-value
Non-Pregnant	Ref	0.14	Ref	0.29	Ref	0.86	Ref	0.43
Pregnant	-0.24 (-0.55, 0.08)		-0.19 (-0.53, 0.16)		-0.03 (-0.42, 0.35)		-0.17 (-0.60, 0.26)	
Not Meeting MVPA Guidelines	Ref	0.06	Ref	0.04	Ref	0.01	Ref	0.005
Meeting MVPA Guidelines	-0.26 (-0.52, 0.01)		-0.30 (-0.58, -0.02)		-0.49 (-0.86, -0.13)		-0.54 (-0.91, -0.16)	
	Compliance				Distensibility			
	Univariate Model		Multivariable Model *		Univariate Model		Multivariable Model *	
	β Coef. (95% CI)	p-value	Adj β Coef. (95% CI)	p-value	β Coef. (95% CI)	p-value	Adj β Coef. (95% CI)	p-value
Non-Pregnant	Ref	0.02	Ref	0.04	Ref	0.50	Ref	0.48
Pregnant	0.02 (0.004, 0.046)		0.03 (0.001, 0.05)		0.3 (-0.5, 1.0)		0.3 (-0.6, 1.2)	
Not Meeting MVPA Guidelines	Ref	0.87	Ref	0.61	Ref	0.56	Ref	0.67
Meeting MVPA Guidelines	0.002 (-0.020, 0.023)		0.006 (-0.02, 0.03)		-0.2 (-1.0, 0.5)		-0.2 (-1.0, 0.6)	
	Elasticity				β-Stiffness			
	Univariate Model		Multivariable Model *		Univariate Model		Multivariable Model *	
	β Coef. (95% CI)	p-value	Adj β Coef. (95% CI)	p-value	β Coef. (95% CI)	p-value	Adj β Coef. (95% CI)	p-value
Non-Pregnant	Ref	0.84	Ref	0.85	Ref	0.31	Ref	0.51
Pregnant	-8.45 (-91.86, 74.95)		-9.19 (-106.17, 87.80)		0.51 (-0.47, 1.49)		0.38 (-0.74, 1.50)	
Not Meeting MVPA Guidelines	Ref	0.99	Ref	0.93	Ref	0.45	Ref	0.46
Meeting MVPA Guidelines	0.63 (-83.25, 84.52)		-3.83 (-91.16, 83.51)		-0.37 (-1.35, 0.60)		-0.38 (-1.38, 0.63)	

2 * Multivariable models adjusted for age and current BMI

Figure captions

Figure 1. Prediction of central-PWV (m/s) based on gestational age and meeting the moderate-to-vigorous physical activity (MVPA) guidelines (≥ 150 minutes per week). Black triangles = not meeting the MVPA guidelines; grey circles = meeting the MVPA guidelines. Significant difference between those meeting and those not meeting the MVPA guidelines ($p > 0.05$).

Figure 2. Prediction of A) compliance, B) distensibility, C) elasticity, and D) stiffness based on gestational age and meeting the moderate-to-vigorous physical activity (MVPA) guidelines (≥ 150 minutes per week). Black triangles = not meeting the MVPA guidelines; grey circles = meeting the MVPA guidelines. *denotes significant difference between those meeting and those not meeting the MVPA guidelines ($p > 0.05$).

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338x190mm (300 x 300 DPI)

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