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Physical activity and maternal-fetal circulation measured by Doppler ultrasound

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Abstract

Objective—To examine the association of physical activity on maternal-fetal circulation measured by uterine and umbilical artery Doppler flow velocimetry waveforms.

Study Design—Participants included 781 pregnant women with Doppler ultrasounds of the uterine and umbilical artery and who self-reported past week physical activity. Linear and generalized estimating equation regression models were used to examine these associations.

Results—Moderate-to-vigorous total and recreational activity were associated with higher uterine artery pulsatility index (PI) and an increased risk of uterine artery notching as compared to reporting no total or recreational physical activity, respectively. Moderate-to-vigorous work activity was associated with lower uterine artery PI and a reduced risk of uterine artery notching as compared to no work activity. No associations were identified with the umbilical circulation measured by the resistance index.

Conclusion—In this epidemiologic study, recreational and work activity were associated with opposite effects on uterine artery PI and uterine artery notching, though associations were modest in magnitude.

Keywords

work; recreational activity; maternal-fetal blood flow; pregnancy; Doppler flow velocimetry waveforms; preeclampsia

Introduction

The American College of Obstetricians and Gynecologists (ACOG) encourages pregnant women, in the absence of either medical or obstetric complications, to engage in regular,

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Conflict of Interest
The authors declare no conflict of interest.

moderate intensity exercise.[1] This recommendation is based on scientific evidence that moderate intensity exercise during pregnancy is not generally associated with adverse fetal and maternal outcomes.[2, 3, 4] Regular physical activity and exercise during pregnancy may alter the maternal haemodynamic system and placental function by increasing placental volumes and growth rates.[5, 6] Enhanced placental growth and vascularity may be an adaptive response to intermittent reductions in feto-placental blood flow during exercise.[7] It has been hypothesized that these effects may increase the rate of placental perfusion and transfer function and reduce the fraction of nonfunctional tissue in the placenta,[8, 9] which might be beneficial for both the mother and the fetus.[7]

Doppler ultrasound provides a non-invasive way to examine placental blood flow and placental vascular resistance on the maternal and fetal sides of the placenta, enabling information about the maternal-fetal circulation.[10, 11] For example, when placental impedance increases, the uterine and umbilical arterial diastolic flow decreases, which is associated with persistence of a diastolic notch in uterine arteries or with either low, absent, or even reversed end-diastolic blood flow in the umbilical artery that can be detected by Doppler ultrasound.[10, 12, 13] Numerous studies have established an association between abnormal Doppler velocimetry waveforms in the uterine and umbilical arteries and adverse pregnancy outcomes such as pre-eclampsia, intrauterine growth retardation, and prediction of fetal distress, perinatal mortality, or admission to the neonatal intensive care unit, but the association is weaker in low risk pregnant women.[10, 13, 14, 15,16, 17, 18]

Several randomized clinical trials have evaluated the immediate effect of maternal exercise on maternal-fetal circulation with Doppler velocimetry, although the sample sizes have been small. Most measurements were taken before and soon after exercise. Findings for the uterine artery Doppler indices have not been consistent, including studies finding no meaningful changes,[19, 20, 21] an increase in the indices,[22, 23, 24] and an increase followed by a decrease in the indices following bouts of exercise.[25, 26] More consistently, studies have found no change in umbilical artery Doppler indices with exercise.[19, 22, 23, 24] These studies were conducted on small samples; thus, no general conclusion has been made regarding the acute effect of physical exercise on resistance of maternal-fetal blood flow.

We are not aware of any observational studies that report on associations between physical activity during pregnancy and changes of Doppler flow measurements of the uteroplacental unit. The present study provides a comprehensive analysis of overall physical activity and several components of physical activity on maternal-fetal circulation during mid-pregnancy.

Methods

Study Population

This analysis includes participants in the third phase of the PIN (Pregnancy, Infection, and Nutrition) Study, a prospective study examining etiologic factors (physical activity, stress, and placental vascular compromise) for preterm delivery. The study protocol was approved by the Institutional Review Board at the University of North Carolina – Chapel Hill. Women seeking services before 20 weeks' gestation from prenatal clinics at the University of North Carolina Hospitals between January 2001 and June 2005 were asked to participate with written informed consent. Exclusion criteria included being less than age 16, non-English speaking, not planning to continue care or deliver at the study site, carrying multiple gestations, or not having a telephone for the phone interviews. During the course of pregnancy, the women were asked to complete two research clinic visits and two telephone interviews. After excluding women who enrolled in the study a second or third time, women who did not complete Doppler ultrasounds of either or both of uterine and umbilical artery at two clinic visits, or who did not complete the first telephone interview with information from a one-week physical activity recall, leaving 781 women in the analysis.

Physical Activity Measurement

A one-week recall of physical activity was obtained from the phone interview at 17–22 weeks' gestation. The questionnaire included six separate sections for work, recreational, outdoor household, indoor household, child/adult care, and transportation, with evidence for validity and reliability reported elsewhere.[27] The questionnaire assessed frequency and duration of all moderate and vigorous physical activities the women participated in during the past week. For example, a question regarding participation in particular modes of recreational activity stated: "In the past-week, did you participate in any non-work, recreational activity or exercise, such as walking for exercise, swimming, dancing, that caused at least some increase in breathing and heart rate?" If the woman answered "Yes", the interviewer asked her to list all types of recreational activities. For each type of activity, the woman reported the number of sessions in the past week, duration of each session, and her perception of the intensity classified as: "fairly light", "somewhat hard", and "hard or very hard", from the Borg scale.[28] For scoring based on absolute intensity, we assigned an intensity code for each activity using metabolic equivalent (MET) from published tables.[29]

In this analysis, we focused on total activity and two typical types of physical activity (work, recreational activity) since national guidelines or recommendations focus on these specific types of activities.[1, 30] To address perceived or relative intensity, for each type of activity we calculated the total number of hours/week overall and in "fairly light", "somewhat hard" and "hard or very hard" intensity (the latter two defines moderate to vigorous intensity). To examine absolute intensity, we multiplied the hours/week in each activity by its corresponding MET value and summed them up to calculate total MET-hours/week and MET-hours/week for moderate to vigorous activity, defined as activities with a MET value >=4.8, which corresponds to the lower range of moderate intensity for women 20–39 years of age.[31] Total activity was calculated by summing up all the values for all activity types. Each physical activity variable in the analysis was categorized into four levels: 1) no activity, 2) fairly light activity, 3) moderate to vigorous activity less than or equal to the median value among participants that reported that activity, and 4) moderate to vigorous activity greater than the median value. The only exception was for moderate to vigorous work activity, which had a low prevalence, so we collapsed the variable into three categories.

Outcome Measurement

During the first clinic visit, at 15–20 weeks' gestation, the sonographer performed Doppler ultrasonography to obtain flow velocity waveforms in the uterine arteries (left and right). During the second clinic visit, at 24–29 weeks' gestation, Doppler ultrasonography was similarly performed in the uterine arteries, as well as the umbilical artery. The woman lay in a semi-recumbent position, and both uterine arteries were examined at their crossing with the external iliac artery using a 3.5 MHz transabdominal probe. For the umbilical artery, Doppler velocity waveforms were obtained from the free-floating loop of the umbilical cord during fetal quiescence. Doppler waveform indices were calculated from computerized planimetry as systolic/diastolic (S/D) ratio, pulsatility index (PI) in the uterine artery measures, and as resistance index (RI) in the umbilical artery measures. Also, presence of an early diastolic notch in the uterine arteries or umbilical artery, presence and direction of diastolic flow in umbilical artery, and location of the placenta, categorized as anterior, posterior, left lateral, right lateral, previa and fundal in the uterine cavity were recorded.

For the uterine artery analysis, PI was chosen as a continuous outcome measure, because of its nearly normal distribution and having very few outliers. The mean of the left and right artery PI measurements was used for the final analysis. We also used a dichotomous variable that indicated the presence of an early diastolic notch in either or both the left and right uterine arteries.

For the umbilical artery analysis, RI was chosen as a continuous outcome measure because of its nearly normal distribution in the study population. With very few participants with adverse umbilical artery outcomes, such as notch present or reversed diastolic flow in the umbilical artery Doppler, we did not analyze these measures. A summary of Doppler waveform indices used in this study are presented in Table 1.

Covariate Measurement

Other information on participants was obtained from the first phone interview at 17–22 weeks' gestation and medical records. Sociodemographic variables included age at enrollment, race (white, black, other), marital status, completed years of education, and household percentage of poverty for 2001.[32] Pre-pregnancy body mass index (BMI) was calculated from self-reported weight and measured height (kg/m^2) and categorized based on the Institute of Medicine guidelines.[33] Adequacy of total weight gain was calculated as a ratio of observed weight to expected weight based on the Institute of Medicine guidelines in effect during the time of data collection.[33] Pregnancy and medical history variables included reproductive history (parity, history of stillbirth, miscarriage, and abortions), chronic hypertension, pre-existing diabetes, and bleeding during pregnancy. Lifestyle behaviors included prepregnancy BMI, smoking, alcohol consumption, and drug use. All of these covariates were explored as potential confounders in each of the models. Gestational age at the ultrasound measurements was included in all models.

Statistical Analyses

Multiple linear regression modeling was performed for the umbilical RI and started with full models, including physical activity, all covariates as previously described, gestational age at the time of ultrasound, and placental location. We used a backward elimination approach to remove variables from the model.[34] Two criteria were used for elimination of a variable: 1) p-value for the t-test for the presence of this variable in the model exceeding 0.10, indicating the variable did not contribute meaningfully to the prediction of umbilical RI, and 2) removal of the variable from the model not changing the estimate of coefficients for physical activity exposure measure by more than 10%, indicating the variable was not a confounder. We retained any confounder identified in any of the three physical activity models in all final models, together with gestational age at the second ultrasound measure. Lastly, to account for other types of physical activity when examining the association with work and recreational activity, we included a continuous variable ("other physical activity") defined by subtracting of the specific exposure activity value of interest from the total activity value in the final models. We reported corresponding regression coefficients and p-values for physical activity variables in each model.

We fit generalized estimating equation (GEE) models to the uterine artery Doppler data using PROC GENMOD with REPEATED statement in SAS (SAS Institute Inc., Cary, NC) for the continuous outcome as mean uterine PI, measured twice.[35] We reported beta regression coefficients with 95% confidence intervals and p-values for physical activity variables in each model. The betas had an interpretation as the association of a 1-level change in each exposure on mean uterine PI as a continuous outcome, controlling for all other covariates and adjusting for the longitudinal clustering. Also using GEE models for the presence of a notch in either or both uterine arteries, as a dichotomous outcome, measured twice, we reported crude and adjusted relative risk (RR) with their confidence intervals. All final models were adjusted for appropriate confounders (i.e., removal of the variable did not change the physical activity exposure estimate by more than 10%), gestational age at the first and second clinic visit, placental location at the second visit, and "other physical activity". Reproductive history (parity, history of stillbirths, miscarriages, and abortions), bleeding during pregnancy, prepregnancy BMI, adequacy of maternal weight gain, alcohol use, and drug use were not confounders in any model, and thus are not adjusted for in the multivariable analyses. Pregnancy outcomes (e.g. preeclamsia, preterm birth) which were evaluated at the termination of pregnancy were not included in the analysis as confounders or effect modifiers.

Results

Descriptive Characteristics

Distribution of sociodemographic, lifestyle, and pregnancy characteristics of study participants are presented in Table 2. Women were mostly white, married, and well-educated. Almost 40% of women were overweight or obese. At 17 to 22 weeks' gestation, 30% of women reported at least some work-related physical activity in the past week and 63% reported at least some recreational physical activity.

We compared characteristics of women who were included in the analysis (n=781) and those who were eligible, but were not included (n=1094) because of lack of information on Doppler ultrasound or one-week recall physical activity (data not shown). Chi-square statistics were used for comparison. We found no differences between the included and excluded groups ($p>0.05$) on most characteristics (e.g., age, race, education, marital status, general health, pre-pregnancy BMI, parity, maternal weight gain, adequacy of prenatal care, and smoking). Also, no differences between the included and excluded groups were found regarding regular exercise before pregnancy, and during the first and second trimester of pregnancy. However, women who were included in the analysis were more likely to have a lower percent below poverty than women not included in the analysis.

Physical Activity and Uterine Artery PI and Early Diastolic Notching

At the first clinic visit the mean uterine PI was 1.15 (SD=0.46), and 29% had an early diastolic notch present in either or both uterine arteries. At the second clinic visit the mean uterine PI was 0.88 (SD=0.28), 11% had a notch present in either or both uterine arteries, and the mean umbilical RI was 0.66 (SD=0.06).

Table 3 displays the GEE models for the relationship between perceived intensity of physical activity and the two outcomes, mean uterine PI and any uterine artery notching at either or both first and second clinic visit. Moderate to vigorous total and recreational activity above the median were both associated with higher uterine PI as compared to no total or recreational physical activity, respectively (beta coefficient = 0.092 (95% CI 0.006, 0.178) and 0.073 (95% CI 0.003, 0.144)). Moderate to vigorous work activity was associated with lower uterine PI (beta coefficient = −0.107 (95% CI −0.164, −0.049) as compared to reporting no work activity. The risk of any uterine artery notching was higher among women reporting moderate to vigorous recreational activity above the median compared to those reporting no recreational physical activity (RR adjusted = 1.75 (95% CI 1.11–2.75)).

Physical Activity and Umbilical RI

The multiple linear regression models between physical activity and the umbilical RI are described in Table 4. Total, recreational, and work physical activity at any level of intensity were not associated with the umbilical artery RI.

Sensitivity Analysis

All results presented in Tables 3 and 4 were recalculated using absolute intensity (in MET-hours per week) for physical activity, rather than perceived intensity (in hours per week). The findings were quite similar (data not shown). We also explored all recreational and work models without further adjustment for "other physical activity" and our interpretations did not meaningfully change (data not shown).

Discussion

To our knowledge, this is the first epidemiologic study to investigate the association between physical activity and vascular resistance in the uterine and umbilical artery blood flow. We found that moderate to vigorous total and recreational physical activity above the median was associated with a higher uterine artery PI and notching, which was in agreement with previous randomized trials assessing acute exercise response.[22, 23, 24] In contrast, we observed a lower uterine artery PI among women reporting moderate to vigorous work activity, suggesting a reduction of impedance in uterine circulation. We can only speculate as to the reason for the differences in associations between recreational and work activities; it may be that recreational activities by nature are shorter-term and episodic in contrast to work activities which may occur throughout the day.

We found an increased risk of the presence of any uterine artery notching among women reporting moderate to vigorous recreational activity above the median, and somewhat higher for total physical activity, suggesting somewhat higher chronic impedance of uterine artery circulation. However, we also found a reduced risk of uterine artery notching among women reporting moderate to vigorous work activity.

A link between physical activity and increased resistance in the uteroplacenta is plausible biologically. In normal pregnancy, maternal haemodynamic adaptations, including changes in vascular tone, increase of placental bed blood flow through hormonally mediated vascular growth and remodeling, and decreased adrenergic response, lead to low vascular impedance in the uteroplacenta and decreased placental vascular resistance.[9, 11, 36] Among women engaging in exercise during pregnancy, many other biological effects are observed including increased resting maternal plasma volume, intervillous space blood volume, enhanced fetoplacental growth, placental function and vascularity.[5, 6, 7] Observations in the placental biopsy after delivery reveal a significantly greater total vascular volume and total capillary volume in the placental villi among women engaging in exercise.[8] Other important findings in the placental biopsy included increased total villous surface area, increased cell proliferation, and reduced fraction of nonfunctional tissue.[8, 37] The chronic effects on these physiological and functional changes increase overall placental perfusion, placental bed blood flow at rest, and both oxygen and substrate delivery.[7, 8] All of these changes imply a reduction of resistance in the placental blood flow among women engaging in exercise during pregnancy, consistent with the apparent reduction in resistance associated with work activity but not to our total and recreational activity findings.

Our study found no associations between types of physical activity, including work and recreational activity, at any level of intensity with the umbilical Doppler RI. Umbilical resistance reflects fetal circulation and our findings support the null observations of other randomized trials assessing acute response of exercise.[19, 22, 23, 24]

Strengths and Limitations

In this study, physical activity was collected through a one-week recall questionnaire to capture comprehensive information on the type, frequency, duration, and intensity of all types of physical activity during pregnancy. We assessed the intensity of each activity using

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both perceived (self-reported) and absolute intensity (from the compendium of physical activities).[29] Outcome data were measured at one or two different time points during pregnancy, taking into account the variability of these measures along with gestational age. Information on key confounders was collected in detail, allowing us to evaluate the effects of specific types of physical activity and we were able to control for other activities simultaneously.

However, several limitations of this study should be noted. Although there is evidence to support the validity and reliability of the physical activity questionnaire among pregnant women,[27] measurement error is inevitable based on of self-reports. Physical activity can be variable over a short period of time, so that physical activity measured in a one-week period may not be representative over a longer interval, especially during pregnancy. Such misclassification of exposure is likely to be random with respect to the outcomes and therefore, is most likely to bias relationships toward the null. Doppler velocimetry indices were also subject to some variances between and within ultrasonographers. The findings could also be biased by inadequate adjustment for unmeasured confounding such as nutrition status or stress during pregnancy. Timing between measures of physical activity and the Doppler ultrasound exams may introduce some biases due to variable patterns of physical activity during pregnancy.

Conclusion

In this epidemiologic study, recreational and work activity were associated with opposite effects on uterine artery PI and uterine artery notching, though associations were modest in magnitude. No association was found between physical activity and umbilical circulation measured by the RI. Future studies could consider a time series design with multiple prospective measurements of both physical activity and Doppler indices during pregnancy. Other parameters, such as middle cerebral artery Doppler indices, could be included in future studies.

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Table 1

Doppler waveform indices used in this study

Arteries examined	Outcome Indices	Time of measurement	Calculation
Uterine arteries	Mean of Pulsatility Index (PI)	Measured twice at 15–20 and 24–29 weeks' gestation	PI = (S−D)/A
	Any early diastolic notch in either or both uterine arteries	Measured twice at 15–20 and 24–29 weeks' gestation	Yes or No
Umbilical artery	Resistance Index (RI)	Measured once at 24–29 weeks' gestation	RI = (S−D)/S

PI: Pulsatility index, RI: Resistance index, S: Peak systolic velocity, D: End-diastolic velocity, A: Time-averaged maximum velocity

Table 2

Selected sociodemographic, lifestyle, and pregnancy characteristics of the study participants (N = 781).

	Number	Percent
Age in years		
<=20	76	9.7
21–34	596	76.3
>=35	109	14.0
Race		
White	548	70.2
Black	161	20.6
Other	72	9.2
Marital status		
Not married	226	28.9
Education in years		
High school or less (<=12)	181	23.2
Some college (13–15)	162	20.7
College graduation	438	56.1
Percent of the poverty line based on household income		
<100	120	16.1
100–200	100	13.4
>200	526	70.5
Body mass index before pregnancy		
Underweight < 19.8 kg/m^2	104	13.5
Normal: 19.8–<26.0 kg/m^2	369	48.0
Overweight: 26–<29.0 kg/m^2	88	11.4
Obese: >=29.0 kg/m^2	208	27.1
Chronic hypertension	67	9.0
Preexisting diabetes	36	4.8
Smoking		
Non-smoker	492	69.2
Past smoker	104	14.6
Current smoker	115	16.2

Table 3

The associations between self-reported physical activity (using perceived intensity at 17–22 weeks' gestation) and mean uterine artery pulsatility index (PI) and the risk of any uterine artery notching at both Doppler measurements (N = 781).

			Mean uterine artery PI*			Risk of any uterine artery notching	
	N	**%**	**Beta**	**95% CI of Beta**	**p-value**	**RR unadjusted (95% CI)**	**RR adjusted (95% CI)†**
Total physical activity (median = 2.75 hrs/wk)							
No activity‡	52	6.6	Reference			1.00	1.00
Fairly light total activity	224	28.7	0.063	(−0.023, 0.149)	0.15	0.87 (0.48, 1.57)	1.09 (0.54, 2.22)
MV total activity <= the median	256	32.8	0.059	(−0.026, 0.143)	0.18	0.84 (0.46, 1.50)	1.23 (0.61, 2.49)
MV total activity > the median	249	31.9	0.092	(0.006, 0.178)	0.04	1.01 (0.56, 1.81)	1.48 (0.73, 2.99)
Recreational activity (median = 2.0 hrs/wks)							
No recreational activity‡	293	37.5	Reference			1.00	1.00
Fairly light recreational activity	185	23.7	0.038	(−0.026, 0.102)	0.25	1.11 (0.76, 1.62)	1.25 (0.82, 1.92)
MV recreational activity <= the median	175	22.4	0.045	(−0.019, 0.109)	0.17	1.21 (0.82, 1.78)	1.43 (0.93, 2.18)
MV recreational activity > the median	128	16.4	0.073	(0.003, 0.144)	0.04	1.59 (1.04, 2.39)	1.75 (1.11, 2.75)
Work activity							
No work activity‡	546	69.9	Reference			1.00	1.00
Fairly light work activity	146	18.7	−0.014	(−0.075, 0.046)	0.64	1.00 (0.69, 1.44)	1.19 (0.80, 1.77)
Some MV work activity	89	11.4	−0.107	(−0.164, −0.049)	≤0.001	0.61 (0.39, 0.98)	0.64 (0.38, 1.08)

RR: relative risk, CI: confidence interval, MV: moderate to vigorous

Median among participants who reported at least some moderate to vigorous physical activities.

*Adjusted for household percentage of poverty (<100, 100–200, >200), pre-existing diabetes (yes, no), smoking (no, past, current), gestational age at first and second visit (weeks), and other physical activity.

†Adjusted for household percentage of poverty (<100, 100–200, >200), pre-existing diabetes (yes, no), smoking (no, past, current), gestational age at first and second visit (weeks), placental location at second visit (anterior, posterior, other) and other physical activity.

‡referent group, women with no specific activity.

In all models, variables with more than two levels were coded as indicator variables.

Table 4

The association between past week physical activity (using perceived intensity at 17–22 weeks of pregnancy) and umbilical artery resistance index at 24–29 weeks of pregnancy (N = 781).

Modeling with physical activity in perceived intensity*		
	Beta (95% CI)	**p-value**
Total physical activity (median = 2.75 hrs/wk)		
No activity†	Reference	
Fairly light total activity	0.005 (−0.013, 0.021)	0.62
MV total activity <= the median	0.009 (−0.011, 0.027)	0.39
MV total activity > the median	0.007 (−0.014, 0.019)	0.50
Recreational activity (median = 2.0 hrs/wk)		
No recreational activity†	Reference	
Fairly light recreational activity	−0.002 (−0.021, 0.009)	0.79
MV recreational activity <= the median	0.002 (−0.016, 0.017)	0.71
MV recreational activity > the median	−0.004 (−0.017, 0.011)	0.58
Work activity		
No work activity†	Reference	
Fairly light work activity	−0.005 (−0.013, 0.006)	0.43
Some MV work activity	0.001 (−0.010, 0.014)	0.86

CI: confidence interval, MV: moderate to vigorous.

Median among participants who reported at least some moderate to vigorous activities.

*Adjusted for household percentage of poverty (<100, 100–200, >200), weight gain ratio of observed weight/expected weight based on IOM guidelines (<1, 1–<2, >=2), gestational age at second visit (weeks), placental location at second visit (anterior, posterior, other), and other physical activity.

†referent group, women with no specific activity.

In all models, variables with more than two levels were coded as indicator variables.