Continuing regular exercise during pregnancy: Effect of exercise volume on fetoplacental growth

James F. Clapp III, MD, Hyungjin Kim, BS, Brindusa Burciu, MD, Stephanie Schmidt, MS, Kristin Petry, MS, and Beth Lopez, RN

Cleveland, Ohio

OBJECTIVE: The purpose of this study was to test the null hypothesis that the volume of exercise at different times during pregnancy has no effect on fetoplacental growth.

STUDY DESIGN: Seventy-five women who exercised regularly were evaluated before pregnancy and randomly assigned at 8 weeks' gestation to one of 3 exercise regimens for the remainder of pregnancy. Primary outcome variables included placental growth rate, birth weight, and placental volume at term.

RESULTS: The offspring of the women who were randomly assigned to a high volume of exercise in mid and late pregnancy were significantly lighter (3.39 kg vs 3.81 kg) and thinner (8.3% fat vs 12.1% fat) than those offspring born of women who were randomly assigned to reduce their exercise volume after the 20th week. Maternal weight gain, fresh placental volumes, and histomorphometric indices of placental function were greater in the high-low group.

CONCLUSION: These data indicate that a high volume of moderate-intensity, weight-bearing exercise in mid and late pregnancy symmetrically reduces fetoplacental growth, whereas a reduction in exercise volume enhances fetoplacental growth with a proportionally greater increase in fat mass than in lean body mass.
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Key words: Pregnancy, exercise, growth, fetus, placenta

Earlier studies from our laboratory have demonstrated that either beginning or continuing a regular regimen of weight-bearing exercise throughout pregnancy improves placental growth. Beginning a moderate exercise regimen for the first time in early pregnancy also enhances proportional fetal growth and birth weight; continuing a pre-existing higher volume exercise regimen throughout pregnancy restricts growth of the fetal fat organ, which reduces birth weight.[1-4] Although others have not looked for an effect of exercise on placental growth, they have looked at birth weight and have been unable to demonstrate any exercise effect either in women who continue exercise at reduced levels[5-7] or in women who begin a relatively rigorous program of non–weight-bearing exercise in the mid trimester.[8,9] These differences raised the question: Does the type, timing, duration and/or intensity of the maternal exercise regimen modulate the exercise effect on fetoplacental growth?

Several years ago we began to explore this question. Initially we examined the effects of beginning a regular program of moderate intensity, weight-bearing exercise in early pregnancy and observed that it increased multiple indexes of fetoplacental growth.[3] These differences indicated that both the timing and type of exercise were important variables and that the overall volume of exercise at various times during pregnancy was probably important as well. We therefore designed a second experimental series to test the null hypothesis that exercise volume at different times during pregnancy has no effect on fetoplacental growth.

Material and methods

General. The experimental protocol was approved by the hospital's Internal Review Board for Human Experimentation and used a prospective randomized design in which 80 healthy, regularly exercising (3 or more times each week), non–substance-abusing women were enrolled before pregnancy. At that time, they completed a demographic questionnaire and underwent a physical fitness assessment that included a fixed-rate, progressive incline treadmill evaluation of maximum aerobic capacity (VO_{2max}).[10] No blood or urine tests were performed to

From the Departments of Reproductive Biology and Obstetrics and Gynecology and the Schwartz Center for Metabolism and Nutrition, Case Western Reserve University at MetroHealth Medical Center.
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Reprint requests: James F. Clapp III, MD, Department of Obstetrics and Gynecology, MetroHealth Medical Center, 2500 MetroHealth Dr, Cleveland, OH 44109. E-mail: jfclapp@metrohealth.org.

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further assess general health or to confirm a negative history of smoking or other substance abuse.

After conception (which occurred within 4 months in all cases) and ultrasonic documentation of a viable singleton pregnancy, these women were randomly assigned by envelope draw in week 8 of gestation to 1 of 3 weight-bearing (treadmill, step aerobics, or stair-stepper) exercise regimens, each of which was conducted at a standard intensity (oxygen consumption, 55%-60% of prepregnancy VO_{2max}). The 3 regimens were (1) 20 minutes 5 days a week through week 20, gradually increasing to 60 minutes 5 days a week by week 24 and maintaining that regimen until delivery (Lo-Hi); (2) 40 minutes 5 days a week from week 8 until delivery (Mod-Mod); and (3) 60 minutes 5 days a week through week 20, gradually decreasing to 20 minutes 5 days a week by week 24 and maintaining that regimen until delivery (Hi-Lo). This design provided us with a 3-fold between-group variation in weekly exercise volume in both early and late pregnancy that was quantitated with the use of the duration-intensity index (the product of exercise intensity and exercise time) in both early and late pregnancy.[2,11,12] Thus, women in the Lo-Hi group exercised 1100 units/week in early pregnancy, increasing to 3300 units/week in late pregnancy; the women in the Mod-Mod group exercised 2200 units/week throughout, and the women in the Hi-Lo group exercised 3300 units/week in early pregnancy, decreasing to 1100 units/week in late pregnancy. Given the randomized, prospective study design and the fact that all women worked outside the home and uniformly lead an active lifestyle, we did not think that it would be worthwhile to assess the additional physical activity that is associated with everyday life. Likewise, we did not challenge the veracity of the women in reporting either additional recreational exercise outside of the laboratory or dietary intake.

During pregnancy, all women underwent periodic assessment of weight gain, fat deposition, dietary intake, and placental growth. Exercise sessions were monitored, and exercise intensity was checked every 2 weeks with the use of respiratory calorimetry. A member of the study team was present during labor and delivery and performed morphometric assessment of the placenta and infant at the time of birth. The placentae were then fixed in formalin for later histomorphometric analysis. Neonatal morphometrics were repeated at 5 days of age.

By design, women who did not maintain the specified exercise regimen throughout pregnancy and the women whose antenatal course was abnormal (premature labor, mid-trimester bleeding, pregnancy-induced hypertension, gestational diabetes mellitus, intrauterine growth retardation) were excluded from the data analysis.

Measurement techniques. Oxygen consumption was measured with a mouthpiece, nose clips, and an accurately calibrated indirect calorimetry system.[10] Pregnancy viability was determined by real-time ultrasound scans at 8 weeks of gestation.[1,11] Body weight was determined with the use of an electronic balance beam scale, and maternal fat retention was estimated from the sum of 5-site skinfold thicknesses.[12] Dietary intake was assessed with a weekly random 24-hour dietary recall and analysis using Nutritionist Four software (Hearst Corp, San Bruno, Calif).[13] Morphometric measurements of the newborns were obtained in a standardized fashion with a calibrated scale, tape measure, measurement box, and skinfold calipers.[1,11] Total body electrical conductivity was measured at 5 days of age and used to calculate lean body mass.[14] Antenatal estimates of placental volumes and growth rates were obtained at 16, 20, and 24 weeks of gestation with the use of B-mode ultrasound scanning and a fixed arm transducer, which allowed us to obtain parallel images of the placenta for the calculation of total volume.[2] Gross measurements of the placenta included trimmed blotted weight, volume, and surface area.[1-3,12] After fixation, the volume of the various placental tissues were determined by systematic random sampling and point counting techniques.[3,15] To assure that representative values were obtained, a minimum of 14 blocks were cut per subject, and all sections were read by 2 observers in a blinded fashion. The mean values that were obtained were used in data analysis.

Data management. The sample size calculations used the variance that we had observed in earlier studies for each of our 3 primary outcome variables,[2,3,12,13,15] and indicated that we needed a sample size of 20 per group to detect a 10% difference in the parameters at the 0.05 level, with a power of 0.80. The 3 primary outcome variables included birth weight, mid-trimester placental growth rate, and placental volume at term. Secondary analyses were then used to identify the specific morphometric components that explained the differences that were observed in the primary outcome parameters. These analyses included corrected birth weight (gestational age, sex, parity, and race); the lengths, circumferences, and estimates of fat mass of the offspring; the antenatal placental volumes; and the volumes of the component placental tissues. Other between-group comparisons were simply performed to assure that the groups were comparable in terms of maternal characteristics. Statistix software (Analytical Software, Tallahassee, Fla) was used for data analysis. Between-group comparisons were made with an analysis of variance, followed by the Bonferroni comparison of means. Because measurements of the primary outcome parameters were independent of one another, significance was set at the .05 level. To assess the interaction between placental and fetal growth, correlations between placental parameters and birth weight were sought with the use of least squares regression and the best subset regression technique. Group data are reported as the mean ± SEM.

Table I. Neonatal morphometrics

Characteristic	*Lo-Hi group (± SEM)*	*Mod-Mod group (± SEM)*	*Hi-Lo group (± SEM)*
Birth weight (kg)	3.34 ± 0.07	3.44 ± 0.08	3.90 ± 0.07*
Corrected birth weight† (kg)	3.37 ± 0.07	3.43 ± 0.07	3.82 ± 0.06*
Crown-heel length (cm)	51.1 ± 0.3	51.2 ± 0.3	52.6 ± 0.2‡
Ponderal index	2.49 ± 0.03	2.56 ± 0.04	2.70 ± 0.04*
Head circumference (cm)	34.8 ± 0.2	35.0 ± 0.3	35.5 ± 0.2
Head/abdomen ratio	1.14 ± 0.01	1.13 ± 0.01	1.06 ± 0.01*
Body fat (%)	8.5 ± 0.4	7.9 ± 0.3	12.1 ± 0.7*
Fat mass (kg)	0.29 ± 0.01	0.27 ± 0.01	0.48 ± 0.03*
Lean body mass (kg)	3.06 ± 0.06	3.16 ± 0.07	3.42 ± 0.06‡

*$P < .0001$, significantly different from the other 2 groups.
†Adjustment for gestational age, sex, race, and parity.
‡$P < .001$, significantly different from the other 2 groups.

Results

General. Seventy-five of the 80 women who were enrolled had an uncomplicated pregnancy and completed the protocol. One of the women in each group had a complication (1 woman had recurrent mid-trimester bleeding and intrauterine growth retardation; 2 women had premature labor), and 2 women were noncompliant. Of the 75 remaining women, 26 women had been randomized to the Lo-Hi group; 24 women had been randomized to the Mod-Mod group, and 25 women had been randomized to the Hi-Lo exercise group. Compliance with the exercise regimen was excellent with all subjects in the exercise groups completing more than 18 sessions of appropriate length and intensity each lunar month.

Mean maternal age (31 ± 1 years, 30 ± 1 years, and 32 ± 1 years, respectively), education (16 ± 1 years, 17 ± 1 years, and 17 ± 1 years, respectively), parity (0.5 ± 0.2, 0.4 ± 1, and 0.6 ± 0.2, respectively), prepregnancy weight (59.2 ± 1.2 kg, 60.5 ± 1.1 kg, and 58.9 ± 1.1 kg, respectively), prepregnancy percent of body fat (19% ± 2%, 18% ± 2%, and 19% ± 2%, respectively), VO_{2max} (43.5 ± 2.8, 45.2 ± 3.1 and 42.9 ± 3.5, respectively), average daily caloric intake (47 ± 3 kcal/kg lean body mass, 49 ± 4 kcal/kg lean body mass, and 47 ± 4 kcal/kg lean body mass, respectively), and gestational age at delivery (277 ± 1 days, 278 ± 2 days, and 281 ± 2 days, respectively) were not significantly different between groups. However, pregnancy weight gain and fat retention was significantly less ($P < .02$) in the Lo-Hi group (12.0 ± 0.8 kg vs 14.6 ± 0.9 kg and 15.5 ± 0.9 kg and 2.8% ± 0.2% vs 4.2% ± 0.4% and 5.5% ± 0.4% in the Mod-Mod and Hi-Lo groups, respectively).

Offspring characteristics. Twelve male and 14 female babies were born to women in the Lo-Hi group; 12 male and 12 female babies were born to the women in the Mod-Mod group, and 13 male and 12 female babies were born to women in the Hi-Lo group. All offspring were in good condition at birth (Apgar score, ≥8 at 1 and 5 minutes).

The morphometric characteristics of the offspring are detailed in Table I. Although normally grown, the offspring of the exercising women in the Lo-Hi and Mod-Mod groups were significantly lighter and shorter than the offspring of the women in the Hi-Lo group. These weight differences persisted when they were corrected for the potential confounders of gestational age, sex, race and parity with institutional-specific standards.[16] Lean body mass, the head/abdominal circumference ratio, the Ponderal Index, percentage of body fat, and fat mass were all proportionally less in the Lo-Hi and Mod-Mod groups, which indicated that in utero growth had been symmetric. The infants who were born to the women in the Hi-Lo group, however, were larger, but a greater proportion of their increased weight was due to an increase in fat mass relative to lean body mass. Head circumference was not significantly different among the 3 groups ($P = .11$).

Placental growth and morphometrics. The mid-trimester placental growth rate, gross placental volumes, and volumes of the placental component tissues are detailed in Tables II and III. Mid-trimester growth rates were significantly greater in both the Mod-Mod and Hi-Lo groups, although gross volumes at 20 and 24 weeks and at term were significantly greater only in the Hi-Lo group. Although the gross volume values in the Mod-Mod group were not statistically different from those in the Lo-Hi group, they were consistently in an intermediate position between the Lo-Hi and Hi-Lo groups.

Histologic estimates of the volumes of various component tissues indicate that the placentae of women who decreased exercise in late pregnancy contained a significantly greater volume of functional tissue. This was due, in large part, to an increase in villous tissue, although there was an increase in intervillous space volume as well. The increase in villous volume was due to an increase in the villous volumes at all levels (stem, $P < .05$; intermedi-

Table II. Placental growth rate and gross volumes

Characteristic	*Lo-Hi group (± SEM)*	*Mod-Mod group (± SEM)*	*Hi-Lo group (± SEM)*
Mid-trimester placental growth rate (mL/wk)	23 ± 1*	26 ± 2	27 ± 2
Placental volume at 20 wks (mL)	192 ± 8	210 ± 10	255 ± 17†
Placental volume at 24 wks (mL)	288 ± 8	317 ± 20	365 ± 19*
Placental volume after delivery (mL)	415 ± 10	448 ± 18	513 ± 31†

*$P < .01$, significantly different from the other 2 groups.
†$P < .001$, significantly different from the other 2 groups.

ate, $P < .001$; terminal, $P < .01$), which indicated that a stimulus for growth was present at all levels of the fetal vascular tree and had persisted throughout the pregnancy. Also, the histomorphometric estimates in the Mod-Mod group consistently maintained intermediate values between those values in the Lo-Hi and Hi-Lo groups.

Correlations between corrected birth weight and placental volumes. As anticipated, placental volume, villous volume, and intermediate and terminal villous volumes had strong individual correlations (r^2 between 0.5148 and 0.5691) with birth weight corrected for gestational age, parity, sex, and race of the offspring.[3,15-17] Weaker correlations were also present between mid-trimester placental growth and volumes (r^2 between 0.1884 and 0.2374). Analysis by group consistently improved the correlations only in the Mod-Mod group, in which the highest individual correlation (between corrected birth weight and villous volume) had an r^2 of 0.7093.

Finally, the use of best subset regression controlled for parity with the inclusion of intermediate and terminal villous volumes,[3] maternal weight gain,[11,12] and dietary carbohydrate intake[14] raised the correlation with birth weight further, which indicated that other factors that influence fetoplacental substrate availability also play a role. This approach yielded combined r^2 of 0.7014 for the entire study group and 0.7804 for the Mod-Mod exercise group alone.

Comment

These data warrant several conclusions. First, continuing a regular regimen of weight-bearing exercise throughout pregnancy influences fetoplacental growth in both a time-dependant and exercise volume–dependant fashion. Women who either maintained the moderate volume of exercise throughout the pregnancy or increased their exercise volume in late pregnancy experienced a significantly slower fetoplacental growth rate than those women who maintained a high volume of exercise in early pregnancy and then decreased their exercise volume by two thirds in late pregnancy. It should be pointed out, however, that none of the infants born to women in the first 2 groups were less than the 10th percentile for any morphometric measure other than fat mass, although many of the infants who were born to women in the latter group were >90th percentile for multiple morphometric parameters. Morphometric evidence of overgrowth in the offspring of women whose exercise volume was low in mid and late pregnancy is not a new finding. Indeed, in our earlier work, it was the norm, especially in women who eat primarily processed or "high glycemic" types of carbohydrate.[1,3,12,14] Likewise, morphometric evidence of selective restriction of fetal fat deposition has been the norm in the offspring of women who maintain a high volume of weight-bearing exercise throughout mid and late pregnancy.[4,11] Thus, different patterns of exercise performance at various times during pregnancy have different effects (selective restriction or stimulation) on both size and body composition at birth. This helps to explain the diverse findings in the literature concerning the effects of maternal exercise on birth weight.[1,4-9,18,19] In addition, the data suggest that the type of exercise may also be important, because differences in birth weight are not seen with either low or moderate volumes of non–weight-bearing exercise in mid and late gestation.[4,8,9,19]

Second, two of the observations suggest that the time-specific effect of weight-bearing exercise on birth weight may be primarily determined by its effects on placental development: (1) Birth weights in all the groups correlated with one or more parameters of placental growth and function. (2) The mid-trimester placental growth rate was clearly less in the Lo-Hi group. Most of these women decreased their exercise volume from preconceptional levels in early pregnancy. In contrast, women in the other 2 groups (Mod-Mod and Hi-Lo) maintained or increased their exercise volume in early pregnancy and had larger gross and histomorphometric placental volumes, although these differences were significant only in the Hi-Lo group. Earlier studies indicate that this is the time when growth of the placenta at the level of the intermediate villi is greatest and that growth at this level and time point in pregnancy is stimulated only by a moderate to high volume of exercise, although growth of the terminal villi, which peaks in mid and late pregnancy, is stimulated by a low but not a high volume of exercise.[2,3,15,17] Thus,

Table III. Histomorphometric volumes of the placental tissue components

Characteristic	*Lo-Hi group (± SEM)*	*Mod-Mod group (± SEM)*	*Hi-Lo group (± SEM)*
Functional volume (mL)	385 ± 11	416 ± 20	489 ± 18*
Nonfunctional volume† (mL)	25 ± 3	32 ± 4	26 ± 3
Intervillous space (mL)	154 ± 6	165 ± 10	185 ± 8‡
Villous volume (mL)	231 ± 7	251 ± 11	303 ± 11*
Stem villi (mL)	21 ± 3	21 ± 2	27 ± 3‡
Intermediate villi (mL)	50 ± 2	61 ± 5	73 ± 5*
Terminal villi (mL)	160 ± 6	169 ± 9	204 ± 9§

*$P < .001$, significantly different from the other 2 groups.
†The sum of nonviable tissue (presumably microinfarcts), fibrin deposition, chorionic plate, and decidua.
‡$P < .05$, significantly different from the other 2 groups.
§$P < .01$, significantly different from the other 2 groups.

we speculate that the cutback in exercise volume in early pregnancy may have had a repressive effect on placental growth at the intermediate villous level that was followed by a repression of terminal villous growth when exercise performance was increased later in the pregnancy. We also speculate that maintaining or increasing exercise volume in early pregnancy stimulated placental growth at the level of the intermediate villi, which was followed by a stimulation at the terminal villous level when exercise volume was decreased later in the pregnancy. Taken together, these data are internally consistent and support the concept that either beginning or increasing the volume of weight-bearing exercise during the hyperplastic phase of placental growth may be an important mechanism for improving placental functional capacity, which in turn increases nutrient delivery to and the overall growth rate of the fetus later in gestation.

Third, the between-group differences in placental volume were due to balanced differences in all the component volumes. This is a similar pattern to that seen in the placentae of women who begin a low-volume exercise regimen early in pregnancy but quite different from the pattern seen in the placentae of fit women who continue a preconceptional weight-bearing exercise regimen throughout pregnancy.[3,15] In the latter group, most of the women exercised at much higher intensities throughout pregnancy, and the placental effects were confined to the stem and intermediate villi. Again, this suggests that the different neonatal and placental morphometric effects of exercise probably reflect differences in the timing and overall volume of exercise during the various trimesters of pregnancy.

Fourth, the data support the earlier observational finding that the volume of weight-bearing exercise in late gestation is related to the growth of both the maternal and fetal fat organ.[1,4,11,12] Women who exercised for 300 minutes a week had less weight gain and fat retention and were delivered of lean infants; those women who exercised 200 minutes a week did not have less fat retention but had offspring with significantly less fat in both relative (percentage) and absolute (grams) terms than those women who cut back in late pregnancy to 100 minutes a week of otherwise identical exercise. Perhaps this explains why women who begin and/or maintain a lower volume of regular exercise during pregnancy do not have a reduction in either maternal weight gain or birth weight.[3,5-9,18,19]

Finally, the major finding of the study (that time-specific weight-bearing exercise volumes influence fetoplacental growth) leads us to speculate that different weight-bearing exercise regimens may be of clinical value in both improving normal fetoplacental growth and perhaps preventing and/or treating a variety of disorders of fetoplacental growth. This assumes great importance if the "fetal origins of adult disease" hypothesis is correct. Current findings suggest that this may be the case.[20,21] The data in this area currently indicate that the normally grown fetus who grows to 3700 g at birth has a lower risk of adult disease than a normally grown fetus who weighs 3200 g at birth and has a much lower risk than the infant who weighs 2500 g at birth.

To date healthy women who either begin or maintain a low-volume exercise regimen throughout pregnancy and those who markedly decrease their exercise volume in mid and late pregnancy have been delivered of larger offspring and placentae at term than healthy control subjects.[1,3,4,11,18] This suggests that both these exercise regimens stimulate fetoplacental growth and thus may be useful in improving growth rate in both normal pregnancies and in those pregnancies that are at risk for intrauterine growth retardation. Unfortunately, however, it appears that the amount of exercise that is required to decrease fetal growth rate in mid and late pregnancy may preclude its use for this purpose in gestational diabetes. Regrettably, data in the literature support this conclusion.[22,23] In any case, large prospective randomized clinical trials will be necessary to explore these possibilities in detail.

In summary, a moderate or high volume of moderate intensity, weight-bearing exercise in mid and late pregnancy symmetrically reduces fetoplacental growth and

size at birth, whereas a reduction in exercise volume at that time enhances fetoplacental growth with a proportionally greater increase in neonatal fat mass than in lean body mass. We speculate that this information may prove to be useful in treating normal pregnancy and pregnancies at risk for disorders of fetoplacental growth.

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