Pregnancy significantly increases maternal heart rate, plasma volume, stroke volume, and cardiac output. The left ventricle increases its size without significantly increasing its wall thickness. This increases the radius-to-wall thickness ratio, which in turn increases wall stress. This increase in wall stress could in turn decrease left ventricle performance. Paralleling this eccentric enlargement, peripheral resistance decreases during pregnancy, which in turn decreases wall stress and improves ventricular performance. We have previously shown that, during stationary upright bicycle exercise, systolic function and cardiac output are well maintained during the first and the second half of pregnancy even at maximal intensity. Early in pregnancy, the increase in cardiac output is mostly due to an increase in heart rate and contractility reserve. During the second half of pregnancy, however, the increase in cardiac output is mostly due to an increase in stroke volume. We concluded that left ventricular systolic function is well maintained during maximal exercise in spite of the physiologic increase in the left ventricle radius-to-wall thickness ratio. Transmitral ventricular diastolic function has recently been recognized as an important component to the overall cardiac performance in normal adults and in patients with congestive heart failure. Determination of left ventricular chamber stiffness can be assessed by measuring the time for the deceleration of early left (mitral) ventricular filling. Exercise-induced tachycardia shortens the duration of diastole and thus the diastolic filling time. Diastolic filling must increase its filling rate in spite of the shortened diastole without increasing left atrial pressure because this may compromise pulmonary function to accommodate for increased demands in stroke volume and in cardiac output. The purposes of this study were (1) to compare resting diastolic function of pregnant and nonpregnant women, (2) to describe the effects of advancing pregnancy on diastolic filling patterns, (3) to describe the left ventricular diastolic filling response to stationary bicycle exercise during pregnancy and the postpartum period

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OBJECTIVE: The purpose of this study was to determine the effects of pregnancy and of maximal exercise on left ventricular diastolic filling response.

STUDY DESIGN: Transmitral pulsed Doppler echocardiography was obtained in 10 healthy women during each trimester of pregnancy and at 12 weeks after delivery. Doppler studies were performed at rest and at each exercise workload. The P-R interval, the early and atrial peak flow velocities, the mitral early deceleration time, and the isovolumetric relaxation time were analyzed. Data are expressed as the mean and standard deviation of the mean. Values obtained during the last trimester of pregnancy were used as the pregnant value; values at the 12 weeks after delivery were used as the nonpregnant value. Paired t-test, analysis of variance, and mixed models were used to determine significance with a probability value of <.05.

RESULTS: Pregnancy significantly increased the early and atrial peak flow velocities. Pregnancy decreased the P-R interval, the early deceleration time, and the isovolumetric relaxation time. Exercise significantly decreased these diastolic functions; but pregnancy, in any of the 3 trimesters, did not significantly affect this response.

CONCLUSION: Pregnancy increased left ventricular diastolic chamber stiffness at rest and shifted left ventricular diastolic filling during exercise from predominantly early to atrial filling. This finding suggests that there is an increase in left ventricular chamber stiffness during maximal upright bicycle exercise in pregnancy. (Am J Obstet Gynecol 2001;185:822-7.)

Key words: Pregnancy, Doppler echocardiography, exercise, diastolic function

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ventricular diastolic function during maximal exercise during pregnancy, and (4) to determine diastolic function during increasing bicycle workload.

**Material and methods**

**Study population.** To achieve our 4 aims, a total of 10 healthy women were studied 3 times during pregnancy and once at 12 weeks after delivery. Subjects were recruited during the first trimester from our private offices. A first trimester ultrasound scan was performed to assess gestational age and to confirm singleton gestation. All subjects exercised 2 to 3 times per week before and during pregnancy. All subjects gave written informed consent, which was previously approved by the institutional review board on human research of the hospital. No maternal or fetal abnormalities were noted on physical or ultrasound examination. None of the subjects was taking medications, except prenatal vitamin supplementation.

The first exercise study was performed during the first trimester (16 weeks) and repeated during the second (29 weeks) and third (36 weeks) trimesters. All subjects were again studied during the postpartum period at 12 weeks. Values obtained during the last trimester of pregnancy were used as the pregnant value, and values obtained during the postpartum study were used as the “nonpregnant” value.

**Exercise testing protocol.** Exercise tests were performed in early morning or early afternoon 2 hours after a light breakfast or lunch. Participants were asked not to ingest caffeine for >4 hours. Exercise was performed on an electronically braked bicycle (CPX 2000; MedGraphics, Minneapolis, Minn) with expired gas analysis and venous lactate measurement. The initial workload was at no resistance for a 3-minute period and was advanced thereafter by 25-W increments in 3-minute stages. Heart rate was measured by continuous electrocardiographic monitoring; blood pressure was measured by a mercurial sphygmomanometer during the last minute of each workload and at peak. An experienced exercise physiologist who was blinded to the subject group conducted testing. Participants were encouraged to exercise to the limit of their symptoms. All participants discontinued exercise if they achieved their targeted heart rate (85% of age-predicted maximal heart rate) or until symptoms developed that precluded safe continuation of the test (dyspnea, leg cramps, and fatigue).

**Echocardiography.** Echo-Doppler examinations were performed as previously described with the use of an ultrasound imaging system (Sonos 5500; Hewlett-Packard, Palo Alto, Calif) fitted with a multiple frequency sector transducer, an S-VHS video recorder, and an optical digital disk recorder. Standard 2-dimensional images were obtained by American Society of Echocardiography guidelines in the parasternal long and short axes and in the apical 4-and 2-chamber views. Particular care was taken to ensure that comparable anatomic views are obtained between stages and that artefactual foreshortening of the left ventricle apex was avoided. The best images at end expiration from each stage were also acquired as continuous digital cine-loops and recorded onto the optical disk. Gain, filter, and depth settings were adjusted to optimize delineation of endocardial borders. Image-directed pulsed-wave spectral Doppler tracings of mitral valve inflow were recorded from the left ventricular apical view. A small sample volume was placed at the mitral valve leaflet tips, and the transducer position was adjusted to align the cursor as close to perpendicular to the mitral valve anulus as possible and to maximize blood flow velocity and to minimize spectral dispersion. Tracings were made at a 100-mm/sec sweep speed, and several multiple-beat digital cine-loops were recorded on the optical disk for later analysis.

**Echo processing and analysis.** After a review of the tape and optical disk, the best cine-loop was selected and acquired onto a digital disk with the use of a Nova Microsonics (Palo Alto, Calif) digital echocardiography workstation, as previously described in our laboratory. Files were then renamed in code to obscure the identity of the subject. Triplicate analyses were performed by tracing on a digital pad the endocardial borders of selected stop-frame images during end diastole and end systole in the apical 2- and 4-chamber views. Analyses of the Doppler tracings were performed off-line by a single observer who was blinded to patient group and who used a Nova Microsonics digital echocardiography workstation, as previously described in our laboratory. The 3 best tracings were analyzed, and the results were averaged. Early diastolic blood flow deceleration time was measured as the time from the peak early filling velocity to the termination of early filling. In tracings in which low-velocity filtration of Doppler signals or the onset of late (atrial) filling obscured the termination of early diastolic flow, the flow velocity slope was extrapolated to the baseline. Early and atrial peak filling velocity, isovolumetric relaxation time (IVSR), and the P-R interval were assessed at rest and at the second minute of each of the 3-minute exercise periods (Fig 1).

**Statistical analysis.** Means and SD were calculated for each hemodynamic parameter studied. We used paired t-tests to compare pregnant and nonpregnant values that were obtained during the third trimester and values obtained during the postpartum period. Values obtained at maximum exercise were then compared with values obtained at rest. The effects of increasing the level of exercise at each of the trimesters of pregnancy were analyzed by analysis of variance for each hemodynamic parameter at each gestational age. Mixed model with the SAS Institute, Inc (Cary, NC) statistical package was employed for all modeling. These analyses incorporated the longitudinal aspect of the design by estimating slopes for individ-
ual study participants (random effects) and estimating overall average slopes for all study participants (fixed effects). Significance was achieved if the probability value was <.05.

**Results**

**Obstetric outcome.** The average gestational age at delivery was 39.8 ± 0.9 weeks. Eight women had a spontaneous vaginal delivery, and 2 women had a cesarean delivery for failure to progress. The average birth weight was 3375 ± 307 g, and all infants had Apgar scores ≥7 at 1 minute and ≥8 at 5 minutes. No significant medical or obstetric complications (such as preterm labor or hypertensive disorders) developed.

**Maternal P-R interval.** The P-R interval is measured from the beginning of the P wave to the beginning of the R wave, which represents the time taken from the start of the excitation at the pacemaker to the beginning of ventricular depolarization. At rest, pregnancy (third trimester values) significantly decreases the P-R interval when compared with the resting nonpregnant state (124 ± 11 msec vs 141 ± 19 msec, respectively; \( P < .01 \)). Maximal upright bicycle exercise significantly decreased this interval for both pregnant (124 ± 11 vs 111.7 ± 19 msec; \( P < .01 \)) and nonpregnant subjects (141 ± 19 vs 107.2 ± 21 msec; \( P < .01 \)), but there was no significant difference in the P-R interval between the pregnant and the nonpregnant state (111.7 ± 19 msec vs 107.2 ± 21 msec, respectively; \( P = \) not significant). There was no significant difference in the mean P-R interval with increasing bicycle exercise between any of the first, second, or third trimesters of pregnancy (\( P = \) not significant) (Fig 2).

**Resting diastolic function: pregnant versus nonpregnant**

**Mitral early and atrial peak blood flow velocities.** The maximal early peak velocity is measured from the beginning of the ascending part of the Doppler waveform to the peak of the mitral early wave. It represents the phase of early and rapid diastolic filling. The maximal atrial peak velocity is, in turn, measured from baseline to the peak of the atrial waveform (Fig 1). It represents the phase of atrial or late ventricular filling. Although the early/atrial ratio at rest during pregnancy (third trimester values) was lower than the early/atrial ratio obtained in the nonpregnant state (1.29 ± 0.25 cm/sec versus 1.42 ± 0.25 cm/sec, respectively), this did not achieve significance (\( P < .06 \)).

**Mitral early deceleration time.** The mitral early deceleration time is measured from the early peak velocity to its extrapolation to baseline (Fig 1). This is related to the intrinsic stiffness of the left ventricular chamber. Pregnancy significantly decreased the early mitral deceleration time when compared with that of the nonpregnant status (181.3 ± 32 msec vs 215.0 ± 29 msec, respectively; \( P < .03 \)) (Fig 2). A decrease in early deceleration time denotes an increase in left ventricular chamber stiffness.

**Isovolumetric relaxation time.** The ISVR is measured from the time the atrioventricular and the semilunar valves are closed to the opening of the atrioventricular valves. During that time, blood flow is at a standstill. The ventricle relaxes because of its inherent elastic recoil, which represents the phase of isovolumetric relaxation of diastolic filling. Pregnancy significantly decreased the ISVR when compared with nonpregnant status (92.0 ± 10 msec vs 107.9 ± 12 msec, respectively; \( P < .0009 \)) (Fig 2).
pregnancy (Prest = 92.0 ± 10 msec vs Pexer = 46.7 ± 4 msec; \( P < .01 \)) but also during the nonpregnant state (NP rest = 107.9 ± 12 msec vs NPexer = 45.6 ± 10 msec; \( P < .01 \)). There was no difference, however, in ISVR between the pregnant and the nonpregnant state during exercise (Pexer = 46.7 ± 4 msec vs NPexer = 45.6 ± 10 msec; \( P = \) not significant).

Resting diastolic function with advancing pregnancy

Mitral early and atrial peak flow velocities. Values for the early and the atrial peak blood flow velocities were compared at rest between the first, second, and third trimesters of pregnancy. The values for the early peak during the first, second, and third trimesters were 85.2 ± 15.6 cm/sec, 75.7 ± 8.5 cm/sec, and 71.0 ± 8.8 cm/sec, respectively, and were not statistically significant from one another. The values for the atrial peak during the first, second, and third trimesters were 58.5 ± 7.3 cm/sec, 52.9 ± 10.7 cm/sec, and 56.7 ± 8.6 cm/sec, respectively, and were not statistically significant from one another. Thus, advancing gestational age did not significantly affect the early and the atrial velocities.

Mitral early deceleration time. Maximal upright bicycle exercise significantly decreased this value not only during pregnancy (\( P_{\text{rest}} = 181.3 ± 32 \) msec vs \( P_{\text{exer}} = 124.0 ± 32 \) msec; \( P < .01 \)) but also during the nonpregnant state (\( P_{\text{rest}} = 215.0 ± 29 \) msec vs \( P_{\text{exer}} = 110.1 ± 27 \) msec; \( P < .01 \)). There was no difference, however, in early deceleration time between the pregnant and the nonpregnant state during exercise (\( P_{\text{exer}} = 124.0 ± 32 \) msec vs \( P_{\text{exer}} = 110.1 ± 27 \) msec; \( P = \) not significant) (Fig 4).

Isovolumetric relaxation time. Maximal upright bicycle exercise significantly decreased this value not only during pregnancy (\( P_{\text{rest}} = 92.0 ± 10 \) msec vs \( P_{\text{exer}} = 46.7 ± 4 \) msec; \( P < .01 \)) but also during the nonpregnant state (\( P_{\text{rest}} = 107.9 ± 12 \) msec vs \( P_{\text{exer}} = 45.6 ± 10 \) msec; \( P < .01 \)). There was no difference, however, in ISVR between the pregnant and the nonpregnant state during exercise (\( P_{\text{exer}} = 46.7 ± 4 \) msec vs \( P_{\text{exer}} = 45.6 ± 10 \) msec; \( P = \) not significant).

Fig 3. Representation of the early and atrial peak flow velocity during pregnancy (P, defined as third trimester) and during the nonpregnant (NP) state. Pregnancy significantly increased both the early (E) and the atrial (A) peak flow velocities when compared with those of the nonpregnant state. The early/atrial ratio was not significantly different between pregnant and nonpregnant states.

Fig 4. Representation of the early deceleration time during each of the 3 trimesters of pregnancy and the postpartum period. As illustrated in Fig 2, there was a significant difference between the third trimester of pregnancy and the postpartum period; however, there was no difference in these values among each of the trimesters of pregnancy. Exercise did significantly decrease the early deceleration time in all trimesters of pregnancy, but pregnancy did not influence these values.

Maximal upright bicycle exercise significantly decreased this value not only during pregnancy (\( P_{\text{rest}} = 92.0 ± 10 \) msec vs \( P_{\text{exer}} = 46.7 ± 4 \) msec; \( P < .01 \)) but also during the nonpregnant state (\( P_{\text{rest}} = 107.9 ± 12 \) msec vs \( P_{\text{exer}} = 45.6 ± 10 \) msec; \( P < .01 \)). There was no difference, however, in ISVR between the pregnant and the nonpregnant state during exercise (\( P_{\text{exer}} = 46.7 ± 4 \) msec vs \( P_{\text{exer}} = 45.6 ± 10 \) msec; \( P = \) not significant).

Resting diastolic function with advancing pregnancy

Mitral early and atrial peak flow velocities. Values for the early and the atrial peak blood flow velocities were compared at rest between the first, second, and third trimesters of pregnancy. The values for the early peak during the first, second, and third trimesters were 85.2 ± 15.6 cm/sec, 75.7 ± 8.5 cm/sec, and 71.0 ± 8.8 cm/sec, respectively, and were not statistically significant from one another. The values for the atrial peak during the first, second, and third trimesters were 58.5 ± 7.3 cm/sec, 52.9 ± 10.7 cm/sec, and 56.7 ± 8.6 cm/sec, respectively, and were not statistically significant from one another. Thus, advancing gestational age did not significantly affect the early and the atrial velocities.

Mitral early deceleration time. Maximal upright bicycle exercise significantly decreased this value not only during pregnancy (\( P_{\text{rest}} = 181.3 ± 32 \) msec vs \( P_{\text{exer}} = 124.0 ± 32 \) msec; \( P < .01 \)) but also during the nonpregnant state (\( P_{\text{rest}} = 215.0 ± 29 \) msec vs \( P_{\text{exer}} = 110.1 ± 27 \) msec; \( P < .01 \)). There was no difference, however, in early deceleration time between the pregnant and the nonpregnant state during exercise (\( P_{\text{exer}} = 124.0 ± 32 \) msec vs \( P_{\text{exer}} = 110.1 ± 27 \) msec; \( P = \) not significant) (Fig 4).
trimesters of pregnancy. ISVR during the first, second, and third trimesters were 83.5 ± 14.1 msec, 95.5 ± 13.7 msec, and 92.0 ± 10.0 msec, respectively, and were not statistically different from one another. Thus, advancing gestational age did not significantly affect the isovolumetric relaxation.

Diastolic function with progressive exercise stages

**Mitral early and atrial ratio.** To determine whether increasing levels of bicycle exercise affected the early/atrial ratio and to determine whether this was influenced by the trimester of pregnancy, we performed 2 sets of statistical analyses. We first calculated the difference from baseline to maximum exercise for each patient at each trimester for the early/atrial ratio. Increasing exercise workload resulted in a significant decrease in the early/atrial ratio only during the first (P < .01) and second trimesters (P < .04). No such decrease was observed during the third trimester (P = .83). To determine whether, within the pregnant state, early/atrial values obtained for the first, second, or third trimester were different from one another, we performed a mathematic fit of all the values with the use of a repeated measures mixed model. The curves for the early/atrial ratio obtained across the entire exercise workload were not significantly different from each other. Thus, advancing gestational age did not significantly affect the early/atrial ratio during pregnancy.

**Mitral early deceleration time.** We performed similar analyses to determine the effects of an increasing level of bicycle exercise and advancing gestational age on mitral early deceleration time. Increasing exercise workload resulted in a significant decrease in the early deceleration time in all the trimesters of pregnancy (all P values were <.002). There were no significant differences in the values obtained across the entire exercise workload range in any of the 3 trimesters. Thus, there is no difference in the early deceleration time during exercise in any of the trimesters of gestation (Fig 5).

**Isovolumetric relaxation time.** We performed similar analyses to determine the effects of increasing level of bicycle exercise and advancing gestational age on ISVR. Increasing exercise workload significantly decreased the ISVR in all the trimesters of pregnancy (all P values <.002). ISVR did not significantly change during the 3 study periods.

**Comment**

Pregnancy significantly affected the diastolic filling response at rest when compared with the nonpregnant status. Most of the measurements of diastolic filling were decreased during pregnancy. This was mostly due to an increase in maternal heart rate at rest. As maternal heart rate increases, diastolic filling is decreased. Notably, early deceleration time was decreased mildly by pregnancy, which denoted an increase in diastolic left ventricular stiffness. Yet, in spite of significantly shortened diastolic filling time, the early/atrial ratio was not significantly changed during pregnancy. Although the early/atrial ratio at rest did not achieve statistical significance, it tended to be lower in the third trimester than during the nonpregnant period. This may indeed be due to the small patient population that was studied. Our results would suggest that the normal functioning heart during pregnancy has adequate diastolic function reserve in the cardiac cycle because it does not have to resort to the atrial "kick" for proper filling during diastole. Diastolic function was significantly affected by upright bicycle exercise in both pregnant and nonpregnant subjects. The present study indicates, however, that diastolic ventricular filling patterns were not significantly altered by the pregnancy at maximal exercise, in spite of the physiologic baseline heart rate previously described during pregnancy. With the exercise-induced tachycardia during maximal exercise, ventricular filling time is markedly shortened. Yet, we found that pregnant women maximized the early and the atrial diastolic filling rate. Although we did not measure transmural pressure, improved diastolic emptying was most likely accomplished by improving the relative left ventricular "suction" across the mitral valve. Mechanisms for this increase in the suction effect across the transmural valve have previously been investigated in the normal heart of nonpregnant women, but not during pregnancy, at rest. In spite of a significant decrease in the mitral early deceleration time and in the ISVR during maximal exercise and the suggestion that there is an increase in diastolic left ventricular stiffness, cardiac output is well maintained.

Gestational age did not appear to influence diastolic filling function, because we found no significant differences in these parameters during a progressive increase in...
the stages of pregnancy. Of note, exercise did affect diastolic filling patterns, but pregnancy did not significantly affect this response. There was, however, a significant difference in the response of the early/atrial ratio with increasing workload between pregnant and nonpregnant women. Although the early peak blood flow velocities increased in both sets of women, the atrial peak blood flow velocities were significantly different between the 2 groups. Taken together, the data lead us to speculate that the diastolic function is impaired at maximal exercise during pregnancy and that this may be a limiting factor in exercise performance during pregnancy. Kitzman et al have shown that, in patients with heart failure who have preserved left ventricle systolic function, the limiting factor during exercise is related to a failure to increase left ventricle end-diastolic volume despite marked elevation in left ventricle filling pressure. At maximal exercise, left ventricular relaxation can be impaired during pregnancy, which results in an increase in left ventricular pressure that may limit pregnant women during maximum exercise. The degree of ventricular relaxation and elastic ventricular recoil, pressures from the atria, and pressures-volume characteristics of these structures are many of the factors that influence this early filling.

Our results would indicate that although both pregnancy and exercise significantly influence the diastolic filling response, pregnancy in itself (at any trimester of pregnancy) does not seem to adversely affect left ventricular diastolic filling properties. At maximum exercise during pregnancy, however, there may be a decrease in left ventricular compliance, which in turn may affect ventricular relaxation and ventricular filling and thus may affect stroke volume and cardiac output. The exact mechanism for this apparent decrease in ventricular compliance is not readily apparent, but it is known that, to accommodate for the physiologic increase in plasma volume that occurs during normal pregnancy, the left ventricular chamber increases its radius-to-wall thickness ratio. As a result, the volume pressure curve will be shifted upward and to the left, higher on the diastolic curve. This will result intrinsically in a decrease in ventricular compliance. Hormonal changes that occur during pregnancy may, in part, be responsible for these changes; however, this is purely conjectural.

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