Structural and functional changes in left ventricle during normotensive and preeclamptic pregnancy

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Simmons, Lisa A., Adrian G. Gillin, and Richmond W. Jeremy. Structural and functional changes in left ventricle during normotensive and preeclamptic pregnancy. Am J Physiol Heart Circ Physiol 283: H1627–H1633, 2002.—In increased cardiac output in pregnancy is associated with cardiac remodeling and possible reduction in contractility, which may worsen in preeclampsia. Left ventricular (LV) geometry and function were compared between nonpregnant controls (n = 12) and normotensive (n = 44) and preeclamptic (n = 15) pregnant women using echocardiography. Load-independent comparisons of LV systolic function compared end-systolic stress (ESS) and rate-corrected velocity of circumferential fiber shortening (VFC). Mean arterial pressures were 101 ± 14 mmHg in preeclampsia, 76 ± 6 mmHg in normotensive pregnancy, and 78 ± 6 mmHg in controls (P < 0.005 vs. preeclampsia). LV mass increased during normotensive pregnancy (66 ± 13 to 76 ± 16 g/m²; P < 0.05; controls, 65 ± 10 g/m²; P < 0.05) and was greater in preeclampsia (90 ± 18 g/m²; P < 0.05). In normotensive pregnancy, ESS decreased (59 ± 9 to 52 ± 11 g/cm²; P < 0.05; controls, 66 ± 14 g/cm²; P < 0.005). ESS was greater in preeclampsia (60 ± 14 g/cm²; P < 0.05). In controls, there was an inverse relationship between ESS and VFC (r = −0.78). The ESS-VFC relationships in normotensive and preeclamptic pregnancy were unchanged from controls. We conclude that LV hypertrophy in normotensive and preeclamptic pregnancy matches changes in cardiac work, and LV contractility is preserved.

More controversial is whether myocardial contractile function also changes in pregnancy. Ejection-phase indices of LV function, including systolic fractional shortening (FS) and mean velocity of circumferential fiber thickening (VFC), have been variously reported to increase (26), remain constant (15), or decrease (24) during pregnancy. The use of these indices is limited by the changes in ventricular loading conditions that occur during pregnancy. The inverse relationship between ventricular end-systolic stress (ESS) and VFC has been described as a load-independent measure of contractility (5). The results of one study (21) that used the ESS-VFC relationship suggest that myocardial contractility is actually reduced during pregnancy. There are even less data about changes in LV diastolic function during pregnancy. Hypertrophy of the left ventricle may result in reduced diastolic compliance (20), whereas hormonal influences such as nitric oxide may have the opposite effect (22).

A change in myocardial contractility during pregnancy has important implications for the care of pregnant women. Vigorous physical exercise programs (isometric exercises in particular), which are increasingly popular but which may also impose further load on the heart, may be inadvisable. In some women, heart failure can occur in pregnancy as a result of new pregnancy-related cardiomyopathy. It is possible that pregnancy-related cardiomyopathy is an abnormal manifestation of changes in myocardial contractility during pregnancy. In other women, preeclampsia, which complicates 5–10% of all pregnancies, imposes an abnormal pressure load on the heart that may result in the worsening of ventricular function.

This study was undertaken with three aims. First, we sought to document the time course of changes in LV geometry and systolic and diastolic functions during normal pregnancy. Second, we sought to ascertain whether myocardial contractility is actually reduced during normal pregnancy. Finally, we examined the hypothesis that an increase in afterload such as that occurring in preeclampsia is associated with detrimental effects on LV function.

PREGNANCY IS ASSOCIATED WITH hemodynamic and hormonal changes that can affect the heart. From the first trimester, there is an increase in cardiac output that places a volume load on the heart. Hormonal changes include increased circulating estrogen and relaxin, which may directly or indirectly affect the heart. During pregnancy, the heart undergoes remodeling similar to that observed in athletes (9, 13) with increases in chamber dimensions, left ventricular (LV) wall thickness, and mass (2, 13, 24) that is consistent with a process of eccentric hypertrophy (15).

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METHODS

Study groups. Fifty-six normotensive women attending the hospital antenatal clinic during their first pregnancy were enrolled. Women with systemic medical conditions including essential hypertension, renal or cardiovascular disease, or diabetes mellitus were ineligible. One woman with twin pregnancy was later excluded, three women had spontaneous abortions, and eight women withdrew from the study. The remaining 44 women each had echocardiographic and hemodynamic studies at 12 ± 2, 22 ± 1, and 32 ± 5 wk gestation and 13 ± 4 wk postpartum. None of these women received vasoactive medication during the study. Fifteen women that were admitted with preeclampsia were studied at 35 ± 4 wk gestation and 15 ± 6 wk postpartum. Preeclampsia was diagnosed when blood pressure was ≥140/90 mmHg after week 20 of pregnancy on more than two occasions at least 6 h apart (1). All women with preeclampsia had significant proteinuria (≥300 mg/24 h or ≥2+ on dipstick test). The preeclamptic women were acutely ill and required antihypertensive therapy (clonidine, n = 12, mean 600 µg daily; hydralazine, n = 6, mean 100 mg daily). No woman received intravenous antihypertensive drugs in the 3 days preceding the study. Hypertension had resolved by the postpartum study in all preeclamptic women, and none received antihypertensive therapy at that time. Twelve age-matched, nonpregnant, nonsmoking, nulliparous women served as controls. Each woman gave her written informed consent before enrolling in the study, which was approved by the hospital Ethics Review Committee.

Hemodynamics. Studies were performed in a quiet, temperature-controlled room, and the women were allowed 15 min of rest before measurements were performed. Blood pressure was measured in the right arm via sphygmomanometer. The peripheral arterial pulse wave was recorded by applanation tonometry of the left radial artery (Millar Instruments) with a dedicated pulse wave analysis system (SphygmoCor, PWV Medical; Sydney, Australia). Pulse wave measurements were acquired in parallel with echocardiography recordings. The central aortic pressure waveform was determined from the radial pressure waveform using a Fourier space transfer function as previously described (3, 14). LV end-systolic pressure (Pes) was recorded as the pressure at the dicrotic notch on the aortic waveform. The intraobserver coefficient of variation in Pes measurements was 1.3%.

Echocardiography. All studies were performed by one investigator (L. Simmons) using a dedicated echocardiography machine (Sonos 1000 2.5- and 3.5-MHz phased-array transducers, Hewlett-Packard) while the women were in a left-lateral decubitus position. M-mode recordings were made from parasternal long- and short-axis views with two-dimensional guidance. All women were in sinus rhythm, and the mean of measurements from three consecutive beats from both the long- and short-axis views was used for data analysis. LV cavity dimensions and septal and posterior wall thicknesses were measured at end diastole (R wave of electrocardiogram) and end systole (maximum posterior motion of septum) and are indicated by d and s, respectively. Intraobserver coefficients of variation for repeated measurements of SWd, PWd, and LVd were 3.4, 2.7, and 0.6%, respectively. Continuous and pulse wave Doppler recordings of diastolic flow across the mitral valve and systolic flow across the aortic valve were made from the apex and suprasternal notch. Stroke volume (SV) was calculated as the product of aortic valve area and the aortic flow-velocity time integral. Stroke work was the product of SV and mean arterial pressure (MAP), and LV minute work was calculated as the product of stroke work and heart rate. Systemic vascular resistance was calculated as the quotient of MAP and cardiac output. The mitral flow E and A wave maximum velocities and durations, mitral deceleration time, and LV isovolumic relaxation time (IVRT) were recorded for three consecutive beats.

LV mass (LVM) was calculated according to the modified cube formula of Devereux and Reichek (7) as follows: LVM = 1.04[(SWd + PWd + LVd)3 − (LVd)3] − 13.6 g. Relative wall thickness was calculated (20) as (PWd + SWd)/LVd). Load-dependent measures of systolic function included LV FS [FS = (LVd − LVE)/(LVd × 100)], systolic wall thickening [(PWd − PWd)/PWd), VCFc [VCFc = (LVd − LVd)/LVd (LVET × 100)], and rate-corrected mean velocity of circumferential fiber thickening (VCFc = VCFc/TRR0.5). The LV ejection time (LVET) was calculated from Doppler recording of flow across the aortic valve and the RR interval time (TRR) from simultaneous electrocardiograms. LV meridional wall thickening (VCFc = (LVd − LVd)/LVd) and the inverse ESS-VCFc relationship serves as an afterload-adjusted and preload-independent measure of myocardial contractility (5).

Statistical analyses. Descriptive data are shown as means and standard deviations. ANOVA for repeated measures was used to compare data between sequential studies in the normotensive pregnancy group. Independent t-tests with Bonferroni correction for continuous data and χ2-tests for categorical data were used for comparisons between normotensive, preeclamptic, and normotensive pregnant, control, and preeclamptic groups (SPSS 8.0; Chicago, IL). A two-tailed P value of <0.05 is described as significant.

RESULTS

Clinical characteristics of the study groups are shown in Table 1. Women were of similar age and nonpregnant body size in each group. MAP values at time of entry into the study were much higher in women with preeclampsia (100 ± 14 mmHg; P < 0.0005 vs. normotensive pregnancy and controls). Women with preeclampsia were delivered of smaller babies at earlier gestation than women with normotensive pregnancy.

Systemic hemodynamics. Systemic hemodynamics are compared between women with normotensive and preeclamptic pregnancies in Table 2. There was a progressive increase in heart rate during normotensive pregnancy, but preeclamptic women had a lower mean heart rate. Relative wall thickness was higher in women with preeclampsia, compared with normotensive pregnancy. LV mass and systolic wall thickening were higher in women with preeclampsia.

Table 1. Clinical characteristics of study groups

<table>
<thead>
<tr>
<th></th>
<th>Controls (n = 12)</th>
<th>Normotensive Pregnancy (n = 44)</th>
<th>Preeclampsia (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>28 ± 4</td>
<td>29 ± 5</td>
<td>32 ± 6</td>
</tr>
<tr>
<td>Height, m</td>
<td>1.66 ± 0.06</td>
<td>1.63 ± 0.06</td>
<td>1.60 ± 0.06</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>59 ± 6</td>
<td>65 ± 10</td>
<td>71 ± 15</td>
</tr>
<tr>
<td>Body surface area, m²</td>
<td>1.63 ± 0.08</td>
<td>1.69 ± 0.14</td>
<td>1.74 ± 0.18</td>
</tr>
<tr>
<td>Time of delivery, wk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>gestation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S1</td>
<td>37 ± 4</td>
<td>37 ± 4</td>
<td></td>
</tr>
</tbody>
</table>

Values are means ± SD; n = no. of women. Body surface area derived from postpartum weight. *P < 0.05; †P < 0.0005, preeclampsia vs. normotensive pregnancy.

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heart rate in the third trimester. MAP was slightly reduced during the second trimester in the normoten-
sive women but returned to control levels by the third
trimester. Preeclamptic women had markedly elevated
blood pressure during the third trimester and still had
higher blood pressure at the postpartum visit. The car-
diatic index increased by a mean of 25% between the
first and third trimesters in the normotensive women
principally as a result of increased heart rate. Cardiac
index did not differ between normotensive and pre-
eclamptic women in the third trimester. The cardiac
work index increased by a mean of 23% during normo-
tensive pregnancy and was further increased in pre-
eclamptic women during the third trimester. Systemic
vascular resistance decreased by a mean of 26% during
normotensive pregnancy but was significantly greater
in preeclamptic women at 35 ± 4 wk.

LV geometry. There was a mean increase of 11% in
LV wall thickness during normotensive pregnancy (Ta-
ble 3). By the postpartum study, wall thickness had
significantly decreased and was similar to nonpreg-
nant controls. The LVd increased slightly during preg-
nancy, but LVd did not change. There was no signif-
ically change in the ratio of wall thickness to cavity
dimensions during normotensive pregnancy. LVM in-
creased by 23% during normotensive pregnancy and
had almost returned to control levels by the postpar-
tum study. The relative increase in LVM exceeded the
change in body size during pregnancy.

Both SWd and PWd values were greater in women
with preeclampsia than normotensive women in the third
trimester, but this difference had partly resolved
postpartum. LV cavity dimensions were similar in nor-
motensive pregnancy and preeclampsia. LVM was sig-
ificantly greater in preeclampsia than normotensive
pregnancy during the third trimester, and this differ-
ence exceeded the small differences in body mass be-
tween the groups. The LV hypertrophy also resolved
postpartum in the preeclampsia group, but LVM was still
greater than in normotensive women. The ratio of
wall thickness to cavity dimension was greater in the
preeclampsia women, which is consistent with a more
concentric pattern of hypertrophy. Comparison of the
control women and the normotensive and preeclamptic
pregnant women shows that LVM was directly related
to cardiac work (Fig. 1). Changes in LVM that occurred
during and after pregnancy were proportional to
changes in cardiac work. The ratio of cardiac work to
LVM was similar in nonpregnant controls and normo-
tensive and preeclamptic pregnancy, which is consis-
tent with normalization of the myocardial oxygen de-
mand by the hypertrophy process (Fig. 1).

Table 3. LV geometry in normotensive and preeclamptic pregnancy

<table>
<thead>
<tr>
<th>Time, wk</th>
<th>Controls</th>
<th>Normotensive Pregnancy</th>
<th>Preeclampsia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1st trimester</td>
<td>2nd trimester</td>
<td>3rd trimester</td>
</tr>
<tr>
<td>BSA, m²</td>
<td>1.63 ± 0.10</td>
<td>1.67 ± 0.13</td>
<td>1.72 ± 0.13</td>
</tr>
<tr>
<td>SWd, mm</td>
<td>6.7 ± 0.9</td>
<td>7.3 ± 1.0</td>
<td>7.4 ± 1.1</td>
</tr>
<tr>
<td>LVd, mm</td>
<td>47.6 ± 3.3</td>
<td>47.8 ± 3.3</td>
<td>48.9 ± 3.1</td>
</tr>
<tr>
<td>LVe, mm</td>
<td>30.6 ± 2.8</td>
<td>30.0 ± 2.7</td>
<td>30.1 ± 2.7</td>
</tr>
<tr>
<td>PWd, mm</td>
<td>6.3 ± 0.8</td>
<td>6.3 ± 0.7</td>
<td>6.6 ± 0.7</td>
</tr>
<tr>
<td>(PWd + SWd)/LVd</td>
<td>0.27 ± 0.04</td>
<td>0.26 ± 0.03</td>
<td>0.27 ± 0.03</td>
</tr>
<tr>
<td>LV mass, g</td>
<td>106 ± 19</td>
<td>111 ± 26</td>
<td>121 ± 24</td>
</tr>
<tr>
<td>LV mass, g/m²</td>
<td>65 ± 10</td>
<td>66 ± 13</td>
<td>70 ± 12</td>
</tr>
</tbody>
</table>

Values are means ± SD. BSA, body surface area; SW, interventricular septum; d, diastolic; s, systolic; LV, left ventricular internal dimension; PW, LV posterior wall. *P < 0.05, †P < 0.005 vs. controls; ‡P < 0.05, §P < 0.005 vs. 32 ± 5 wk normotensive; ¶P < 0.05 vs. 12 ± 2 wk normotensive; †P < 0.05 vs. postpartum normotensive.

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LV systolic function. During the first trimester, indices of LV systolic function in pregnant women were similar to nonpregnant controls. The load-dependent measures of systolic function including LV FS and wall thickening showed a small increase during normotensive pregnancy (Table 4). There was also a small but not significant increase in V\textsubscript{CFC} and a significant decrease in ESS during pregnancy. The inverse relationship between ESS and V\textsubscript{CFC} in control women is shown in Fig. 2. Similar relationships for normotensive women in the first and third trimesters are also shown. Despite the decrease in ESS, there was no significant change in the ESS-V\textsubscript{CFC} relationship during pregnancy. Although LV FS was slightly greater in the preeclampsia group, there were no differences in wall thickening between the normotensive and preeclamptic women. Furthermore, the ESS-V\textsubscript{CFC} relation did not differ between the normotensive and preeclamptic women either in the third trimester or postpartum. The data points for the preeclamptic women fell within 95% confidence limits for normal women despite increased afterload.

LV diastolic function. Data describing LV diastolic function are summarized in Table 5. The IVRT decreased progressively during normotensive pregnancy and remained significantly shorter than in nonpregnant controls at the postpartum visit even though heart rate had returned to nonpregnant levels. The IVRT was significantly shorter in preeclamptic women than in the nonpregnant controls but was similar to normotensive pregnant women and also remained shortened at the postpartum visit. Changes in IVRT in the pregnant women appeared to be not simply related to heart rate. Although peak mitral E wave velocity was unchanged during pregnancy, the E wave duration was increased, which is consistent with increased volumetric flow during early passive filling of the ventricle. Peak A wave velocity was increased compared with controls by the first trimester and increased further by the third trimester, which suggests an increase in the transmitial pressure gradient during atrial systole. Changes in the A wave were only partly reversed by the time of the postpartum study. In preeclamptic women, the peak mitral E wave velocity was greater than in normotensive women during the third trimester, which suggests higher atrial pressures in these women. The A wave velocities were similar in normotensive and preeclamptic women.

DISCUSSION

This study examined the time course of changes in LV geometry and systolic and diastolic functions during normal pregnancy. The results provide reference data about physiological changes in the heart during normal pregnancy and a comparator for diagnosis of disease states such as early cardiomyopathy. Second, we sought to ascertain whether myocardial contractility was actually reduced during normal pregnancy. Our data show that myocardial contractile function is not significantly altered during normal pregnancy. We also examined the hypothesis that an increase in pressure load on the heart is associated with impairment of LV function and found that this was not the case. The heart retains the capacity to meet an increase in afterload even in the third trimester.

LV remodeling. This study has compared the changes in LV geometry in women with normotensive and preeclamptic pregnancy. The ventricular hypertrophy in pregnancy is directly related to increased workload, and hypertrophy is exaggerated in preeclamptic pregnancy. The mean increase in LV wall thickness of

Table 4. LV systolic function in normotensive and preeclamptic pregnancy

<table>
<thead>
<tr>
<th>Time, wk</th>
<th>Controls</th>
<th>Normotensive Pregnancy</th>
<th>Preeclampsia</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st trimester</td>
<td>2nd trimester</td>
<td>3rd trimester</td>
<td>Postpartum</td>
</tr>
<tr>
<td>Time, wk</td>
<td>12 ± 2</td>
<td>22 ± 1</td>
<td>32 ± 5</td>
</tr>
<tr>
<td>FS, %</td>
<td>36 ± 4</td>
<td>37 ± 4</td>
<td>38 ± 4</td>
</tr>
<tr>
<td>SW thickening, %</td>
<td>46 ± 17</td>
<td>47 ± 17</td>
<td>53 ± 16</td>
</tr>
<tr>
<td>PW thickening, %</td>
<td>66 ± 23</td>
<td>66 ± 23</td>
<td>72 ± 16</td>
</tr>
<tr>
<td>V\textsubscript{CFC}, circ/s</td>
<td>1.13 ± 0.11</td>
<td>1.15 ± 0.13</td>
<td>1.18 ± 0.16</td>
</tr>
<tr>
<td>ESS, g/cm²</td>
<td>66 ± 14</td>
<td>59 ± 9</td>
<td>53 ± 11</td>
</tr>
</tbody>
</table>

Values are means ± SE. V\textsubscript{CFC}, rate-adjusted mean velocity of circumferential fiber thickening; ESS, end-systolic wall stress, circ, circumference. *P < 0.05, *P < 0.005 vs. controls; +P < 0.05, +P < 0.005 vs. 32 ± 5 wk normotensive; *P < 0.05 vs. 12 ± 2 wk normotensive.
11% that we observed during normotensive pregnancy is consistent with earlier reports. Robson et al. (24) described an increase in wall thickness of 25% between preconception and late pregnancy and an increase of 12% between 12 and 28 wk gestation. Data from Mabie et al. (19) and Geva et al. (12) also show a 15–20% increase in wall thickness during pregnancy. We observed a mean increase in LVM of 22% between the first and third trimesters, which was due principally to an increase in wall thickness rather than chamber size. This increase in mass was in excess of the increase in body size during pregnancy, which indicates a true hypertrophic response. In contrast, Mone et al. (21) described a lesser increase in LVM, which was similar to the change in body size during pregnancy.

The ratio of wall thickness to ventricular radius did not change during normotensive pregnancy consistent with eccentric hypertrophy in response to increased preload (25). Thus the cardiac remodeling occurring during normal pregnancy is similar to that observed with athletic exercise (11, 17, 18). Elite female athletes exhibit increases in wall thickness of 14% and LV end-diastolic cavity dimension of 6% compared with sedentary women (23). Resolution of the hypertrophy was rapid in the postpartum period. It has been suggested that changes in ventricular geometry may persist for up to a year after delivery (4), but we found that LVM and cavity dimensions were no different from those of control women by 13 wk after delivery. The myocardium can rapidly reverse hypertrophy and remodeling, and there does not appear to be any long-term consequence of pregnancy.

The hypertrophy process appeared to be exaggerated in the preeclamptic women. The LVM and ratio of wall thickness to cavity dimension were greater than in the normotensive pregnancy group. These women exhibited features of concentric hypertrophy in response to the increased afterload of systemic hypertension. This finding is in accord with the early observations of Veille et al. (28). Importantly, there may be more prolonged changes in LV geometry after preeclampsia. The preeclamptic women exhibited resolution of ventricular hypertrophy by 15 wk postpartum, but wall thickness and mass remained greater than in the normotensive women. We do not have longer followup data, and it is possible that further resolution of hypertrophy may

| Time, wk | Controls | 1st trimester | 2nd trimester | 3rd trimester | Postpartum | Normotensive Pregnancy | Preeclampsia | Controls | 1st trimester | 2nd trimester | 3rd trimester | Postpartum | Controls | 1st trimester | 2nd trimester | 3rd trimester | Postpartum |
|----------|----------|---------------|---------------|--------------|------------|-----------------------|--------------|----------|---------------|---------------|--------------|------------|----------|---------------|---------------|--------------|------------|----------|
|          |          |               |               |              |            |                       |               |          |               |               |              |            |          |               |               |              |            |          |
|          |          |               |               |              |            |                       |               |          |               |               |              |            |          |               |               |              |            |          |
| Time, wk |          |               |               |              |            |                       |               |          |               |               |              |            |          |               |               |              |            |          |
|          |          |               |               |              |            |                       |               |          |               |               |              |            |          |               |               |              |            |          |
| Heart rate, beats/min | 65 ± 10 | 76 ± 10† | 78 ± 10† | 85 ± 10‡ | 67 ± 8† | 71 ± 14‡ | 71 ± 10 | 0.79 ± 0.13 | 0.85 ± 0.13 | 0.84 ± 0.16 | 0.77 ± 0.15 | 0.77 ± 0.11 | 0.92 ± 0.20‡ | 0.81 ± 0.13 | 0.38 ± 0.09 | 0.50 ± 0.09† | 0.50 ± 0.10† | 0.55 ± 0.10‡ | 0.46 ± 0.10‡ | 0.55 ± 0.13* | 0.51 ± 0.11* | 0.15 ± 0.77 | 0.11 0.92 | 0.10* 0.55 | 0.13* 0.51 | 0.11* 0.55 |
| Mitrall E wave, m/s | 164 ± 39 | 176 ± 44 | 188 ± 40 | 193 ± 33* | 201 ± 48* | 187 ± 36 | 190 ± 21 | 100 ± 22 | 90 ± 19 | 79 ± 18† | 72 ± 16‡ | 69 ± 10‡ | 72 ± 6† | 73 ± 16‡ | 254 ± 44 | 263 ± 50 | 276 ± 43 | 282 ± 37* | 288 ± 48* | 273 ± 37 | 267 ± 27 | 508 ± 14‡ | 486 ± 104 |
| Deceleration time, ms | 514 ± 114 | 454 ± 121* | 412 ± 79† | 376 ± 63‡ | 523 ± 88§ | 508 ± 14‡ | 486 ± 104 | 100 ± 22 | 90 ± 19 | 79 ± 18† | 72 ± 16‡ | 69 ± 10‡ | 72 ± 6† | 73 ± 16‡ | 254 ± 44 | 263 ± 50 | 276 ± 43 | 282 ± 37* | 288 ± 48* | 273 ± 37 | 267 ± 27 | 508 ± 14‡ | 486 ± 104 |
| IVRT, ms | E wave duration, ms | 514 ± 114 | 454 ± 121* | 412 ± 79† | 376 ± 63‡ | 523 ± 88§ | 508 ± 14‡ | 486 ± 104 | 100 ± 22 | 90 ± 19 | 79 ± 18† | 72 ± 16‡ | 69 ± 10‡ | 72 ± 6† | 73 ± 16‡ | 254 ± 44 | 263 ± 50 | 276 ± 43 | 282 ± 37* | 288 ± 48* | 273 ± 37 | 267 ± 27 | 508 ± 14‡ | 486 ± 104 |
| E and A wave duration, ms | 514 ± 114 | 454 ± 121* | 412 ± 79† | 376 ± 63‡ | 523 ± 88§ | 508 ± 14‡ | 486 ± 104 | 100 ± 22 | 90 ± 19 | 79 ± 18† | 72 ± 16‡ | 69 ± 10‡ | 72 ± 6† | 73 ± 16‡ | 254 ± 44 | 263 ± 50 | 276 ± 43 | 282 ± 37* | 288 ± 48* | 273 ± 37 | 267 ± 27 | 508 ± 14‡ | 486 ± 104 |

Values are means ± SD. IVRT, isovolumic relaxation time. *P < 0.05, †P < 0.005 vs. controls; ‡P < 0.005 vs. 32 ± 5 wk normotensive; §P < 0.05 vs. 12 ± 2 wk normotensive.
occur in these women. Their blood pressure measurements were still slightly elevated at the time of the postpartum visit, and further decreases in blood pressure in subsequent months might be expected to result in further resolution of ventricular hypertrophy.

LV systolic function. The hypothesis that myocardial contractility is reduced during pregnancy is not supported by our data. We found that the ejection-phase indices of FS and \( V_{CFC} \) were actually greater during the third trimester than in nonpregnant controls. These findings contrast with previous reports (12, 15, 20), but are consistent with the cross-sectional data of Rubler et al. (26). Importantly, the load-adjusted index of contractility, the ESS-\( V_{CFC} \) relationship, did not change during normotensive pregnancy. These data show that myocardial contractility is maintained in normotensive pregnant women. These findings are contrary to those of Mone et al. (21), who found a decrease in both FS and the ESS-\( V_{CFC} \) relationship during pregnancy. There may a methodological contribution to this difference, as Mone and colleagues used the second heart sound as a marker of end systole, but this occurs shortly after the maximum posterior motion of the septum. Furthermore, the previous study found no significant change in LV wall thickness during pregnancy and thus no change in the ESS. In contrast, in a larger patient group, we have found that wall thickness increases and ESS decreases during normotensive pregnancy.

Furthermore, we found that myocardial contractility was maintained during the third trimester even when LV afterload was increased in the preeclamptic women. Both LV FS and \( V_{CFC} \) were normal or even slightly increased in the preeclamptic women. Some studies have reported impaired LV systolic function in preeclampsia, although these findings are not uniform (16, 27, 28). Our findings are supported by the data of Escudero et al. (10) and Degani et al. (6). This is the first study to examine the ESS-\( V_{CFC} \) relationship in preeclamptic women during resting conditions in the third trimester. There was no difference between the preeclamptic women and the normotensive women. The only other study of the ESS-\( V_{CFC} \) relationship in preeclamptic women was undertaken during labor (17). That study also found that the ESS-\( V_{CFC} \) relationship was comparable between normotensive and preeclamptic women. Our findings show that the ESS-\( V_{CFC} \) relationship should be used as a measure of myocardial contractility during pregnancy and that any shift in the relationship should be regarded as abnormal and indicative of myocardial dysfunction rather than being an expected feature of pregnancy.

LV diastolic function. Ventricular remodeling and hypertrophy during pregnancy may be expected to result in changes in LV diastolic function. Information about diastolic function during normal pregnancy is limited, and there are no data about diastolic function in preeclampsia. This is at least partly due to the fact that reliable measurements of diastolic function are more difficult to obtain than are measurements of systolic function. This study found a small increase in LV diastolic dimensions during pregnancy in contrast to earlier reports of no change in cavity dimensions (19, 20). The IVRT shortens markedly during pregnancy. Although this may be ascribed simply to the increase in heart rate during pregnancy, it appears that other factors contribute. The shortened IVRT is still evident postpartum when heart rate has returned to nonpregnant levels. Furthermore, preeclamptic women have lower heart rates but still exhibit a shortened IVRT. These findings suggest that active relaxation of the left ventricle at the start of diastole is actually enhanced in pregnancy. The mechanism of the IVRT shortening is as yet unknown, but may well reflect hormonal influences on the myocardium such as effects of increased nitric oxide availability in pregnancy.

We also observed prolongation of mitral E wave duration and deceleration time during normotensive pregnancy, which is consistent with increased passive filling of the left ventricle during early diastole. Mesa et al. (20) have proposed an increased atrial contribution to LV filling during pregnancy. Our data, however, show that the peak mitral A wave velocity increased during pregnancy, which suggests increased transmural pressures and left atrial pressure during atrial systole. The atrial contribution to ventricular filling in late diastole does not, however, appear to increase as much as the early diastolic component during normotensive pregnancy. It is noteworthy that the physiological ventricular hypertrophy that occurs in athletes is associated with changes in mitral flow velocities (8) similar to those found in normotensive pregnancy. In women with preeclampsia, the E wave velocity was greater than in normotensive pregnancy, which suggests that the transmitral pressure gradient during early passive filling was greater and possibly reflects a change in passive myocardial compliance in the more hypertrophied ventricle. Peak A wave velocity and duration were greater in preeclamptic women, which suggests a more important role for atrial systole in filling of the hypertrophied ventricle in these women.

In conclusion, this study provides reference data concerning physiological changes in ventricular structure and function during pregnancy including a load-independent measure of LV contractility. Cardiac hypertrophy during normal human pregnancy is a rapidly occurring adaptive response to increased preload and cardiac work. Systolic contractile function of the left ventricle appears to be maintained compared to the nonpregnant state. In women with preeclampsia, hypertension is associated with exaggerated ventricular hypertrophy, but LV systolic function is unchanged. These changes in cardiac geometry are rapidly reversible within 3 mo postpartum in normotensive women, but resolution remains incomplete in preeclamptic women.

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REFERENCES


