Morphological and Functional Adaptation of the Maternal Heart During Pregnancy

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Background—Pregnancy provides a unique model to study the adaptation of the heart in a physiological situation of transient load changes. The aim of this study was to assess the performance of the left ventricle (LV) in normal, uncomplicated pregnancies while considering the actual LV load and shape.

Methods and Results—Serial echocardiographic examinations were performed in 51 women in each pregnancy trimester and 3 to 6 months after delivery. Data from 10 nulliparous, age-matched women were used as the control. Conventional parameters of LV function (ejection fraction) as well as myocardial deformation (strain) were interpreted, taking into consideration maternal hemodynamics and LV shape. Cardiac output increased during pregnancy because of a higher stroke volume in early pregnancy and a late increase in heart rate, whereas total vascular resistance decreased. Progressive development of eccentric hypertrophy was observed, which subsequently recovered postpartum. Sphericity index decreased from the first to the third trimester (1.92±0.17 versus 1.71±0.17) and returned postpartum to values comparable to the control. Although higher LV stroke work was noted toward the third trimester (5.9±1.1 versus 5.3±1.0 Newton meter, P<0.001), ejection fraction showed no significant changes. LV strain decreased significantly in late pregnancy (−19.5±2% to −17.6±1.6%, P<0.001) and returned to baseline values after delivery (−19.5±2%).

Conclusions—Pregnancy is a physiological process associated with increased cardiac performance and progressive LV remodeling. These changes are not directly reflected by parameters traditionally considered to describe systolic function, such as ejection fraction and longitudinal deformation. While ejection fraction was insensitive to the functional changes, the transient decrease in longitudinal deformation becomes only plausible when considering the changes in LV geometry. (Circ Cardiovasc Imaging. 2012;5:289-297.)

Key Words: pregnancy  ■  ventricular function  ■  remodeling  ■  echocardiology

Pregnancy provides a unique model to study morphological, hemodynamic, and functional adaptation of the heart in a physiological situation of transient preload and afterload changes. Moreover, the characterization and understanding of maternal cardiac function during normal pregnancy is of clinical importance for the recognition of cardiac pathology because heart disease is the leading cause of nonobstetric mortality during pregnancy.¹

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evolution of myocardial contractility during pregnancy to the associated physiological changes in cardiac load and geometry remains a question to be answered.

Novel echocardiographic parameters of myocardial deformation, such as strain and strain rate (SR) have been shown to be closely related to the functional state of the myocardium and to be more sensitive in the early detection of its subtle changes. They have been successfully applied to LV function assessment in normal individuals and in different pathologies.

In a variety of pathophysiological conditions, changes in LV load often are accompanied by changes in LV shape through a process of remodeling. In volume overload states, LV dilatation and eccentric hypertrophy are compensatory mechanisms frequently associated with changes in the LV from an ellipsoid to a more-spherical shape. Such geometry and loading changes can alter functional evaluation of the LV by classical parameters, such as EF or shortening fraction, as well as novel deformation parameters. In this study, we performed a comprehensive assessment of the effects of normal pregnancy on LV mechanics using standard and novel morphological and functional echocardiographic parameters while considering LV load and shape.

Methods

Study Population and Protocol

After confirmation of a viable single pregnancy during a routine obstetric visit, 64 consecutive, healthy pregnant women were prospectively enrolled in the 2 participating institutions. All subjects were free of known cardiovascular disorders, none was taking medication with known cardiovascular effects, and all had normal physical and 2D echocardiographic findings on a screening examination.

Four visits were planned during the study: 1 during each pregnancy trimester (trimester 1, 12–14 weeks; trimester 2, 22–24 weeks; trimester 3, 32 weeks) and 1 at 3 to 6 months postpartum. At each visit, the normal course of pregnancy was confirmed by an obstetric examination.

Echocardiographic Examination

Patients were scanned in a left decubitus position from the parasternal and apical window with Vivid 7 and Vivid E9 ultrasound scanners (GE Vingmed Ultrasound) with a 2.5-MHz transducer. Standard echocardiograms were recorded to obtain morphological and traditional functional parameters.

Color-coded tissue Doppler imaging (TDI) from apical 4-chamber, 2-chamber, and apical long-axis views and the right ventricular (RV) free wall were acquired to extract regional longitudinal strain, SR, and velocity parameters. Three consecutive cycles were obtained wall by wall using a narrow image sector angle to achieve high frame rates between 180 and 220 frames/s and an optimal alignment of the cardiac walls with the ultrasound beam direction. All images were stored digitally for later offline analysis using dedicated software (EchoPac BT08; GE Vingmed Ultrasound).

Echocardiographic Data Analysis

Grayscale Data Analysis

Data from all 4 examinations of all patients were analyzed in random order. LV dimensions were measured according to the joint recommendations of the American Society of Echocardiography and European Association of Echocardiography. To overcome the frequent problem of diameter overestimation when using 2D-targeted M-mode in oblique parasternal images, measurements were performed directly on 2D images. Parasternal long-axis measurements included LV internal diameter at end diastole (LVEDD) and at end systole, septal wall thickness at end diastole (SWTd), posterior wall thickness at end diastole (PWTd), and the LV outflow tract diameter.

LV mass was estimated based on the formula validated by Lang et al as follows: $0.8 \times [1.04 \times (\text{LVEDD} + \text{SWTd} + \text{PWTd}) - \text{LVEDD}] + 0.6 \text{ g}$. Relative wall thickness was calculated as $2 \times \text{PWTd}/\text{LVEDD}$.

In the apical 4-chamber view, left atrium end-systolic area as well as mitral septal and mitral lateral annulus plane displacement were measured. LV sphericity index was calculated as the ratio of major LVEDD/minor LVEDD in apical 4-chamber view.

Hemodynamic Data Analysis

Classical pulse-wave interrogation of transmural and LV outflow tract flow. LV stroke volume was calculated as the product between the LV outflow tract velocity-time integral and the cross-sectional area. Cardiac output was obtained by multiplying stroke volume with the heart rate. The LVEF and LV end-diastolic and end-systolic volumes were measured using the biplane Simpson method. Pulse-wave TDI at the level of the septal and lateral mitral annulus was used for the measurement of systolic, early, and late diastolic velocities. All parameters were averaged over 3 cardiac cycles.

Total vascular resistance ( dyn·s·cm$^{-5}$) was calculated as $80 \times \text{mean arterial pressure}/\text{cardiac output}$, where mean arterial pressure is calculated as [systolic blood pressure+$2 \times \text{diastolic blood pressure}]/3$. LV stroke work was estimated as the product of mean arterial pressure and stroke volume.

Myocardial Doppler Analysis

Regional longitudinal strain and SR curves were extracted from 3 regions of interest of 12 mm length positioned in the basal, mid, and apical segment of each LV wall and from 2 regions of interest in the RV free wall. The regions of interest were manually tracked over the cardiac cycle to remain within the same part of the myocardium. All strain and SR curves were averaged over 3 consecutive beats. Linear drift compensation was applied to strain estimates. Mitral and aortic valve opening and closure were defined based on pulsed-wave blood pool Doppler tracings. Peak ejection values were calculated as peak negative SR and strain between valve opening and closure. Segmental strain and SR values were averaged per patient and per visit to determine LV average systolic strain and SR. LV circumferential and radial strain were measured by speckle tracking echocardiography from short-axis views at the level of the papillary muscles.

Statistical Analysis

Descriptive data are presented as mean±SD. The changes of hemodynamic and echocardiographic parameters over time were assessed using mixed models with an unstructured covariance matrix and time as the fixed effect and Bonferroni post hoc correction for multiple comparisons. The following comparisons were made: T1 versus T2, T1 versus T3, T1 versus P, T2 versus T3, T2 versus P, T3 versus P, so a Bonferroni correction factor of 6 was used. The analysis provides estimates of the parameter for each time point versus baseline and the significance of the estimate. This type of statistical analysis was chosen over ANOVA for repeated measurements to account for missing data in data sets. Pregnancy data were compared with controls using independent sample t tests. We used SPSS version 16.0 (SPSS, Inc) statistical software. $P<0.05$ was considered statistically significant.
Interobserver and Intraobserver Agreement

All imaging data were analyzed by one observer (O.S.) in random order. The intraobserver agreement for 2D measurements and myocardial deformation parameters was assessed by a repeated analysis of 10 data sets for 2D and 5 data sets for TDI at least 1 month after the initial analysis and blinded to the initial results. The interobserver agreement was assessed on the same data sets by a second observer (S.G.). The agreement between the 2 measurements was expressed using the 95% CI determined as the mean of the differences ± 1.96 SD.31

Study Population

From the initially enrolled 64 participants, those with poor-quality images (4 participants) and pregnancy-related pathology (1 late miscarriage, 1 mild preeclampsia, 2 times arterial hypertension during pregnancy, 1 preterm labor necessitating tocolytic therapy) and those lacking at least 2 visits during pregnancy (4 participants) were excluded from the analysis. Fifty-one pregnant women were finally included in the analysis. Their mean age was 30 ± 3 years (range, 19–37 years). The mean age of the 10 participants of the control group was 29 ± 1.5 years (P not significant).

Evolution of Clinical and Hemodynamic Characteristics

Evolution of clinical characteristics and hemodynamic parameters of the study population during normal pregnancy and postpartum are reported in Table 1. Systolic, diastolic, and mean arterial blood pressures showed a decreasing tendency in the second trimester followed by a slight increase toward the third. Total vascular resistance decreased during pregnancy, reaching a nadir in the second trimester, and did not change significantly during the third (Figure 1). Cardiac output, stroke volume, and heart rate evolved toward the third trimester (Figure 2).

Table 1. Clinical and Hemodynamic Data

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control (13 wk [12–16 wk])</th>
<th>Trimester 1 (23 wk [22–24 wk])</th>
<th>Trimester 2 (32 wk [32–33 wk])</th>
<th>Trimester 3 (4 mo [3–6 mo])</th>
<th>Postpartum</th>
<th>P Value*</th>
<th>P Value Control vs Postpartum</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. participants</td>
<td>10</td>
<td>46</td>
<td>49</td>
<td>50</td>
<td>31</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>56 ± 6</td>
<td>64 ± 9</td>
<td>68 ± 9</td>
<td>75 ± 10†</td>
<td>66 ± 8§</td>
<td>&lt;0.001</td>
<td>0.006</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>110 ± 10</td>
<td>109 ± 10</td>
<td>106 ± 13</td>
<td>112 ± 11</td>
<td></td>
<td></td>
<td>115 ± 10‡</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>64 ± 6</td>
<td>64 ± 7</td>
<td>61 ± 7</td>
<td>67 ± 8‡</td>
<td>68 ± 8‡</td>
<td>0.001</td>
<td>0.18</td>
</tr>
<tr>
<td>MAP, mm Hg</td>
<td>79 ± 6</td>
<td>79 ± 7</td>
<td>76 ± 8</td>
<td>82 ± 8‡</td>
<td>84 ± 6‡</td>
<td>0.001</td>
<td>0.09</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>70 ± 13</td>
<td>75 ± 11</td>
<td>76 ± 8</td>
<td>80 ± 10†</td>
<td>69 ± 11§</td>
<td>0.001</td>
<td>0.77</td>
</tr>
<tr>
<td>TVR, dyn · s · cm⁻⁵</td>
<td>1634 ± 489</td>
<td>1310 ± 242</td>
<td>1176 ± 214†</td>
<td>1199 ± 258†</td>
<td>1602 ± 238‡§§</td>
<td>&lt;0.001</td>
<td>0.78</td>
</tr>
<tr>
<td>Stroke volume, mL</td>
<td>59 ± 12</td>
<td>66 ± 10</td>
<td>71 ± 10†</td>
<td>71 ± 11†</td>
<td>62 ± 11§</td>
<td>&lt;0.001</td>
<td>0.37</td>
</tr>
<tr>
<td>Cardiac output, L/min</td>
<td>4.1 ± 0.9</td>
<td>4.9 ± 0.9</td>
<td>5.3 ± 0.9</td>
<td>5.6 ± 1†</td>
<td>4.3 ± 0.4‡§</td>
<td>&lt;0.001</td>
<td>0.34</td>
</tr>
<tr>
<td>Stroke work, Nm</td>
<td>4.7 ± 1</td>
<td>5.3 ± 1.0</td>
<td>5.4 ± 1.2</td>
<td>5.9 ± 1.1†</td>
<td>5.2 ± 1.0§</td>
<td>&lt;0.001</td>
<td>0.16</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD, unless otherwise indicated. SBP indicates systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; TVR, total vascular resistance; Nm, Newton meter.

*P values derived from linear mixed-effects model.
†P < 0.05 vs trimester 1 using Bonferroni post hoc correction for repeated measurements.
‡P < 0.05 vs trimester 2 using Bonferroni post hoc correction for repeated measurements.
§P < 0.05 vs trimester 3 using Bonferroni post hoc correction for repeated measurements.
|Significantly different versus Trimester 2.

Figure 1. Course of mean arterial pressure and total vascular resistance during pregnancy and postpartum. Data are presented as mean ± SD. Control indicates age-matched group of nonpregnant, healthy volunteers, and postpartum indicates data collection 3 to 6 months after delivery. Trim 1...3 indicates data collection during trimesters 1...3. *P < 0.05 versus Trim 1. †P < 0.05 versus Trim 2. &P < 0.05 versus Trim 3.

Figure 2. Cardiac output, stroke volume, and heart rate evolution during pregnancy. Data are presented as mean and 95% CI. Note the differential contribution of stroke volume and heart rate to the continuing increase in cardiac output. bpm indicates beats per minute; Trim, trimester. *P < 0.05 versus Trim 1. †P < 0.05 versus Trim 2. &P < 0.05 versus Trim 3.
Table 3. Longitudinal Strain and Strain Rate Evolution During Pregnancy

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control (13 wk [12–16 wk])</th>
<th>Trimester 1 (23 wk [22–24 wk])</th>
<th>Trimester 2 (32 wk [32–33 wk])</th>
<th>Trimester 3 (4 mo [3–6 mo])</th>
<th>Postpartum (4 mo [3–6 mo])</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average systolic strain, %</td>
<td>−19.1±1.8</td>
<td>−19.5±2</td>
<td>−19.1±1.5</td>
<td>−17.6±1.6†</td>
<td>−19.5±2‡</td>
</tr>
<tr>
<td>Average systolic strain rate, s⁻¹</td>
<td>−1.14±0.1</td>
<td>−1.27±0.12</td>
<td>−1.21±0.13</td>
<td>−1.12±0.12†</td>
<td>−1.18±0.1§</td>
</tr>
<tr>
<td>Systolic strain apical segments, %</td>
<td>−19.6±2</td>
<td>−20.3</td>
<td>−19.4±2.5</td>
<td>−18.3±2.6†</td>
<td>−20.5±2.7§</td>
</tr>
<tr>
<td>Systolic strain mid segments, %</td>
<td>−19.4±2.4</td>
<td>−19.7±2.4</td>
<td>−19.3±2.6</td>
<td>−17.7±2.5†</td>
<td>−19.9±2.2§</td>
</tr>
<tr>
<td>Systolic strain basal segments, %</td>
<td>−18.2±1.8</td>
<td>−18.8±2.5</td>
<td>−18.7±2.2</td>
<td>−17.2±4.4‡</td>
<td>−18.3±2.5†</td>
</tr>
</tbody>
</table>

Data are presented as mean±SD. P values derived from linear mixed-effects model.
†P<0.05 vs trimester 1 using Bonferroni post hoc correction for repeated measurements.
‡P<0.05 vs trimester 2 using Bonferroni post hoc correction for repeated measurements.
§P<0.05 vs trimester 3 using Bonferroni post hoc correction for repeated measurements.
Measurement Variability
The interobserver agreement for echocardiographic measurements (mean ± 1.96 SD) was −0.3 ± 3.1 mm for LV diameters, −0.0 ± 1.8 mm for wall thickness, and 0.9 ± 14 mL for stroke volume, whereas the intraobserver variability for the same parameters showed values of 0.4 ± 2.6 mm, 0.0 ± 1.7 mm, and −1.3 ± 14 mL, respectively. For deformation parameters, interobserver agreement was 0.0 ± 0.5 s−1 for SR and −0.4 ± 7% for strain at the segmental level and 0.1 ± 0.2 s−1 for SR and −0.5 ± 3% for strain for global measurements. Intraobserver variability ranged from 0.0 ± 0.3 s−1 and 0.4 ± 5% for segmental and 0.0 ± 0.1 s−1 and 0.6 ± 1% for average LV SR and strain parameters, respectively.

Feasibility
Color-coded TDI data were available in 3138 of 3348 segments (feasibility, 94%). Doppler-derived strain and SR curves were analyzable in 2778 LV segments (feasibility, 88.5%) and in 72% of the RV segments. Speckle tracking echocardiography-derived circumferential and radial strain data of the LV were measurable in 87%.

Discussion
The main determinants of LV myocardial performance are the loading conditions (preload, afterload), contractility, and heart rate.32 A complete assessment of contractile LV func-
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The global performance of the heart as a pump is described as physiological hypertrophy.35 Hypertrophy is commonly triggered, leading to increased LV wall thickness, LV mass, and longitudinal and transverse chamber diameters. Sphericity index decreases during pregnancy, indicating a more-spherical shape of the left chamber toward the third trimester. All changes were reversed in the postpartum period. Similar to previous studies,8 we found a normalized LV mass already at 3 to 6 months after delivery, although some other data suggest persistence of modified mass for even 1 year.34

Pregnancy promotes a reversible hypertrophy, with no long-term effects on cardiac function, and often is described as physiological hypertrophy.35 Hypertrophy is commonly seen as a primary mechanism of the heart to reduce stress on the ventricular walls.36

### Hemodynamic Changes

Pregnancy is considered mainly a state of increased volume load of the maternal heart driven by the necessity of the developing fetus to get an adequate blood supply. Cardiac output and indicators of preload, such as ventricular volumes and left atrial size, increase progressively.3–9 In the present study, cardiac output was already increased at the end of the first trimester, which is in concordance with previous studies that reported an increase in cardiac output as early as the 5th week of gestation. LV afterload, the pressure against which the ventricle ejects the blood, was maximally decreased during midpregnancy and tended to increase in the third trimester, despite the reduced total vascular resistance in both the second and third trimesters.

### Morphological Changes

As a response to the demand, morphological changes are triggered, leading to increased LV wall thickness, LV mass, and longitudinal and transverse chamber diameters. Sphericity index decreases during pregnancy, indicating a more-spherical shape of the left chamber toward the third trimester. All changes were reversed in the postpartum period. Similar to previous studies,8 we found a normalized LV mass already at 3 to 6 months after delivery, although some other data suggest persistence of modified mass for even 1 year.34

Pregnancy promotes a reversible hypertrophy, with no long-term effects on cardiac function, and often is described as physiological hypertrophy.35 Hypertrophy is commonly seen as a primary mechanism of the heart to reduce stress on the ventricular walls.36

### Table 4. Longitudinal Systolic Strain: Wall-by-Wall Analysis

<table>
<thead>
<tr>
<th>Strain, %</th>
<th>Control</th>
<th>Trimester 1 (13 wk [12–16 wk])</th>
<th>Trimester 2 (23 wk [22–24 wk])</th>
<th>Trimester 3 (32 wk [32–33 wk])</th>
<th>Postpartum (4 mo [3–6 mo])</th>
<th>P Value*</th>
<th>P Value Control vs Postpartum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inferoseptum</td>
<td>−20.7±2.6</td>
<td>−21.1±3.3</td>
<td>−19.9±3.3</td>
<td>−18.4±2.7†</td>
<td>−20.9±3§</td>
<td>0.001</td>
<td>0.68</td>
</tr>
<tr>
<td>Anterolateral</td>
<td>−18.3</td>
<td>−17.6±2.8</td>
<td>−18.1±3.3</td>
<td>−16.5±3</td>
<td>−17.5±3</td>
<td>0.08</td>
<td>0.67</td>
</tr>
<tr>
<td>Anterior</td>
<td>−19±2.6</td>
<td>−19.6±3</td>
<td>−20±3</td>
<td>−18.6±3</td>
<td>−21.3±3</td>
<td>0.03</td>
<td>0.90</td>
</tr>
<tr>
<td>Inferior</td>
<td>−19.6±2.2</td>
<td>−20.2±3</td>
<td>−20±3</td>
<td>−18.6±3</td>
<td>−21.3±3</td>
<td>0.02</td>
<td>0.09</td>
</tr>
<tr>
<td>Inferolateral</td>
<td>−16.8±2.2</td>
<td>−18.4±3</td>
<td>−17.8±3.3</td>
<td>−16.5±3</td>
<td>−17.6±3.7</td>
<td>0.07</td>
<td>0.65</td>
</tr>
<tr>
<td>Anteroseptum</td>
<td>−19.9±2.2</td>
<td>−20.5±3</td>
<td>−18.9±3.3</td>
<td>−17.2±2.6† ‡</td>
<td>−19.8±3§</td>
<td>0.001</td>
<td>0.71</td>
</tr>
</tbody>
</table>

Data are presented as mean±SD.

*P values derived from linear mixed-effects model.
†P<0.05 vs trimester 1 using Bonferroni post hoc correction for repeated measurements.
‡P<0.05 vs trimester 2 using Bonferroni post hoc correction for repeated measurements.
§P<0.05 vs trimester 3 using Bonferroni post hoc correction for repeated measurements.

### Table 5. RV Free Wall Deformation Parameters

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control</th>
<th>Trimester 1 (13 wk [12–16 wk])</th>
<th>Trimester 2 (23 wk [22–24 wk])</th>
<th>Trimester 3 (32 wk [32–33 wk])</th>
<th>Postpartum (4 mo [3–6 mo])</th>
<th>P Value*</th>
<th>P Value Control vs Postpartum</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV S, basal segment, %</td>
<td>−28.7±2.9</td>
<td>−30.2±7.1</td>
<td>−31.2±7.1</td>
<td>−28.1±7.5</td>
<td>−29.7±8.9</td>
<td>0.11</td>
<td>0.79</td>
</tr>
<tr>
<td>RV S, apical segment, %</td>
<td>−33.7±4.8</td>
<td>−35.4±7.5</td>
<td>−31.4±7.0</td>
<td>−28.2±6.7†</td>
<td>−32.9±7.4</td>
<td>0.001</td>
<td>0.68</td>
</tr>
<tr>
<td>RV SR, basal segment, s−1</td>
<td>−1.38±0.32</td>
<td>−2.09±0.76</td>
<td>−1.97±0.6</td>
<td>−1.64±0.47†</td>
<td>−1.64±0.44†</td>
<td>0.008</td>
<td>0.19</td>
</tr>
<tr>
<td>RV SR, apical segment, s−1</td>
<td>−1.91±0.37</td>
<td>−2.35±0.69</td>
<td>−2.13±0.6*</td>
<td>−1.79±0.45†</td>
<td>−2.17±0.5†</td>
<td>0.001</td>
<td>0.29</td>
</tr>
<tr>
<td>Average RV S, %</td>
<td>−31.2±2.4</td>
<td>−32.8±5.1</td>
<td>−31.3±5.1</td>
<td>−28.2±5.54† ‡</td>
<td>−31.3±6.7</td>
<td>0.002</td>
<td>0.9</td>
</tr>
<tr>
<td>Average RV SR, s−1</td>
<td>−1.64±0.24</td>
<td>−2.22±0.63</td>
<td>−2.05±0.44</td>
<td>−1.71±0.4† ‡</td>
<td>−1.9±0.39</td>
<td>0.001</td>
<td>0.15</td>
</tr>
</tbody>
</table>

Data are presented as mean±SD. RV indicates right ventricular; S, strain; SR, strain rate.

*P values derived from linear mixed-effects model.
†P<0.05 vs trimester 1 using Bonferroni post hoc correction for repeated measurements.
‡P<0.05 vs trimester 2 using Bonferroni post hoc correction for repeated measurements.
How To Determine Cardiac Function?

In the past, cardiac function during pregnancy has been estimated using different echocardiographic M-mode and 2D parameters as well as TDI, and a plethora of conflicting results have been published. In the present study, global cardiac performance as expressed by LV stroke work was increased during pregnancy. Deformation parameters, however, did not parallel this increase. Although conventional EF showed no significant changes, longitudinal deformation even decreased significantly in all levels of the LV during late pregnancy. We conclude from these findings that strain measurements detect subtle changes more sensitively than EF. This is in concordance with other studies comparing the 2 parameters in circumstances of subtle myocardial dysfunction.19,23

We also conclude that the observed longitudinal deformation changes are no indicator of an adverse effect of pregnancy on global cardiac function or clinical status. Rather, regional myocardial deformation, measured as longitudinal strain, reflects myocardial function modulated by regional loading conditions. The latter depends not only on preload and afterload of the ventricle, but also on chamber size and wall thickness (law of Laplace).32 Therefore, both strain and EF cannot be used as a surrogate of myocardial function changes when load and chamber geometry change at the same time.

In this context, we interpret the unchanged longitudinal deformation between the first and second trimester as a result of decreased global afterload (decreased mean arterial pressure), which is balanced by the increasing ventricular size and allows an increase in stroke volume and cardiac output (Figure 2). Our findings confirm previous mathematical modeling showing that even at a constant contractile state, a larger ventricle needs less regional fiber shortening to produce the same stroke volume.21 This inverse relation between strain and heart size has also been confirmed by animal experiments.37 However, during the first trimester, a higher deformation rate suggests a status of increased contractility as response to the hemodynamic changes of early pregnancy. Between the second and the third trimester, strain decreased significantly despite an increasing stroke work. We interpret this finding as a result of the further increase in LV dimensions combined with higher afterload and heart rate (Figure 5), which are not completely balanced by the mild increment in wall thickness. At that time, the increase in cardiac output can be mainly explained by a higher heart rate.

Changes reverse after delivery and approximate the findings in nonpregnant volunteers (Figure 5). Although during pregnancy longitudinal strain, velocity, and displacement decrease in parallel, only postpartum strain values return to normal. Based on such velocity and displacement measurements, a contractile dysfunction in late pregnancy and postpartum has been discussed in previous studies.15,38 Based on our data, however, we suggest that the remodeling of the LV needs to be considered. Figure 6 shows that mitral annulus systolic excursion parallels the course of strain if adjusted for LV length.

Limited data regarding RV longitudinal function during pregnancy are available. Increase in cardiac output during early pregnancy is associated with higher RV strain rate values, suggesting an adaptive increase in contractile function. Thereafter, values return to baseline. Strain only shows a transient apical decrease in late pregnancy. RV end-diastolic pressure increases between 25 and 35 weeks have been invasively described.2 However, because RV pressure was not analyzed in the present data, RV myocardial work cannot be reliably assessed in this context.
Limitations
Preconception measurements were not available in the present study subjects. Although not absolutely necessary for our conclusions, we added a group of nonpregnant volunteers to have a comparison to normal cardiac function of women of the same age.

The size of the studied population, although comparable with most longitudinal pregnancy studies, is relatively small and challenged by dropouts, a frequent problem encountered in pregnancy longitudinal studies. Despite this limitation, the present data allow for the identification of both significant geometric and significant hemodynamic changes during pregnancy.

Because postdelivery hemodynamic and morphological parameters return slowly to baseline, which can take as long as 6 months, some of the parameters might underestimate the actual changes during pregnancy, although the time range for postpartum visits was large and comparable to other studies. This problem is partly solved by the addition of the nonpregnant group.

The trends for cardiac output values in the present group are similar to early pregnancy studies but with somehow smaller absolute values. Heart rate and the values for LV outflow tract diameter, which are lower than those in the classical Robson et al study, might explain these differences. Most studies report a heart rate increase of 10 beats/min during pregnancy, whereas the change was smaller in the present group with no maternal or fetal pathology.

Systolic pressure as measured by sphygmomanometry at the level of the brachial artery, as used in the present study, is different from the central systolic aortic pressure due to the level of the brachial artery, as used in the present study, present group with no maternal or fetal pathology.

Deformation calculations were based on TDI, which is susceptible to misalignment between the Doppler beam and the wall motion direction. To minimize angle problems, we chose to overestimate the actual stroke work of the ventricle. We are confident, however, that the parameter still reliably reflects the relative changes during pregnancy.

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Clinical Implications
The data show that local deformation parameters are more sensitive to subtle myocardial changes than classical parameters and, therefore, may be used as possible screening tools for the early detection of pregnancy-associated disorders like peripartum cardiomyopathy or preeclampsia. Because even those parameters reflect myocardial function only modulated by ventricular geometry, shape changes of the ventricle during pregnancy must be considered, or normal values need to be adjusted to the gestational age. In the present study population, only a limited number of women developed pregnancy-associated complications, making statistical analysis inappropriate. Further studies are needed to assess the value of the technique in different pathologies.

Conclusions
This study describes morphological and hemodynamic changes of the LV during uncomplicated pregnancy and provides reference data about longitudinal LV deformation. Pregnancy is a physiological condition with increased global cardiac performance. We could show that parameters traditionally considered to describe systolic function fail to demonstrate that. While EF appears to be insensitive under clinical conditions, longitudinal deformation can only be interpreted when considering the changes in preload, afterload, and LV geometry, which occur at the same time. A future clinical use of these parameters for the detection of functional abnormalities during pregnancy would require either reference values for each time point of a normal pregnancy or correction for LV geometry and load.

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Disclosures
None.

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