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ORIGINAL RESEARCH

Cardiovascular Adaptation in Normal Pregnancy With 2D and 3D Echocardiography, Speckle Tracking, and Radial Artery Tonometry

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ABSTRACT

BACKGROUND Comprehensive cardiovascular assessment in normal pregnancy using advanced techniques has limited data.

OBJECTIVES The aim of the study was to evaluate cardiovascular changes in normal pregnancy using two-dimensional/three-dimensional (3D) echo and applanation tonometry in healthy pregnant women.

METHODS Two-dimensional/Doppler, speckle tracking strain, 3D echocardiography, and vascular compliance by applanation tonometry were performed during the first, second, and third trimesters and postpartum.

RESULTS There were 45 healthy women (96% Hispanic) included. The heart rate increased in all trimesters vs postpartum (70.538 ± 9.208 beats/min, 74.878 ± 8.094 beats/min, 74.107 ± 9.231 beats/min vs 61.613 ± 9.790 beats/min, $P < 0.001$). A 3D left ventricular (LV) end systolic volume (34.583 ± 6.946 mL, 39.405 ± 7.345 mL, 45.994 ± 15.180 mL, 36.077 ± 7.116 mL), LV end diastolic volume (83.672 ± 14.022 mL, 91.512 ± 14.602 mL, 97.581 ± 19.864 mL, 85.163 ± 13.960 mL), right ventricular (RV) end systolic volume (30.690 ± 6.194 mL, 35.390 ± 7.345 mL, 40.929 ± 15.178 mL, 30.740 ± 6.911 mL), RV end diastolic volume (77.074 ± 14.875 mL, 86.871 ± 16.783 mL, 92.926 ± 18.083 mL, 78.267 ± 15.07 mL), and cardiac output increased ($P < 0.01$ for all) in the 2nd and 3rd trimester. LV longitudinal strain rate (SR) (−1.242 ± 0.350, −1.194 ± 0.181, −1.231 ± 0.263 vs −1.068 ± 0.218, $P < 0.05$) increased in all trimesters, RV longitudinal SR (−1.612 ± 0.314, −1.540 ± 0.284, −1.281 ± 0.748 vs −1.361 ± 0.306) in the 1st and 2nd trimester, $P < 0.01$), left atrial SR (1.735 ± 0.461, 1.687 ± 0.540, 1.588 ± 0.0.526 vs 1.414 ± 0.325), and right atrial SR (2.389 ± 0.582, 2.264 ± 0.741, 2.241 ± 0.793 vs 1.861 ± 0.600) in all trimesters, ($P < 0.05$). Left atrial volume increased in 2nd and 3rd trimesters, left atrial contraction velocity in 3rd trimester ($P < 0.05$), and pulmonary vein systolic filling velocity throughout pregnancy ($P < 0.001$). E/e' ratio did not change and LV ejection duration increased. Systolic augmentation of central aortic pressure decreased throughout.

CONCLUSIONS Increased contractility of all four cardiac chambers, LV ejection-duration, and reduced LV afterload provide efficient cardiovascular adaptation despite increased chamber volumes and heart rate during normal pregnancy. (JACC Adv. 2024;3:101360) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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ABBREVIATIONS AND ACRONYMS

BP = blood pressure

LA = left atrial/left atrium

LV = left ventricular

LVEDV = left ventricular end-diastolic volume

LVEF = left ventricular ejection fraction

LVESV = eft ventricular end-systolic volume

RA = right atrial/right atrium

RV = right ventricular

3D = 3-dimensional

The cardiovascular system undergoes multiple hemodynamic changes during pregnancy. It is well described that there are increases in plasma volume, heart rate, and cardiac output with a decrease in systemic vascular resistance[1-9] during pregnancy. Studies have been prospective[1,3-5,8] as well as cross-sectional.[2,6] These studies have, however, shown conflicting data on left ventricular (LV) fractional shortening and contractility measured by velocity of circumferential fiber shortening (Vcfc). Some studies showed an increase in LV ejection fraction (EF),[2] others showed a decrease in Vcfc[3-5] or LVEF,[10] and some showed no change in LVEF or Vcfc during pregnancy.[8,9] LV relaxation function measured by tissue Doppler velocities has been reported as decreased without change in LV filling pressure,[7] while other studies have shown an increased LV relaxation velocity in the second trimester, decreased E'/e' ratio [11] and increased pulmonary vein systolic wave as well as atrial reversal wave,[12] which has been suggested to reflect decrease in LV diastolic function. Shortening of LV isovolumic relaxation time and lengthening of E-wave deceleration time were shown in another study.[13] The main technique used in the prior studies was two-dimensional (2D) echocardiography (echo) in the evaluation of LVEF and spectral Doppler including tissue Doppler imaging for diastolic function. Tissue Doppler is affected by geometric assumptions and loading changes such as increased LV volumes and LV foreshortening due to an upward shift in the cardiac apex from a distended uterus in later stages of pregnancy. Three-dimensional (3D) echo is superior to 2D echo in quantifying LV and right ventricular (RV) function and chamber size.[14-17] Speckle tracking echocardiography technique assesses chamber shortening or thickening by tracking the motion of myocardial speckles and can analyze cardiac chamber deformation in various cardiac segments to provide a "non-Doppler" assessment of both global and regional motion of the myocardium.[18,19] Unlike tissue Doppler, it is independent from the relationship between cardiac displacement movement and the ultrasound angle and is less load dependent.

Changes in vascular tone during pregnancy may precede or parallel changes in cardiac systolic or diastolic function, and a close association between LV diastolic function and arterial stiffness has been shown in the nonpregnant state.[20] Arterial stiffness has been measured using PW Doppler flow velocities in the ascending aorta and noninvasive subclavian artery pulse wave pressure tracings during pregnancy.[5] Applanation tonometry is an easy and validated technique that provides assessment of the intrinsic vascular properties and provides an assessment of central aortic pressure using transfer function from the radial artery pulse tracing and has been shown superior to measuring brachial artery blood pressure (BP).[21] There is a paucity of data on using 3D and speckle tracking echo in pregnant women along with vascular compliance to evaluate changes in cardiac chamber volume, deformation, and relationship with vascular compliance. The aim of this study was to assess cardiac performance during pregnancy using 2D/Doppler, 3D and speckle tracking echo and correlate the measurements to the changes in arterial compliance determined by applanation tonometry.

MATERIALS AND METHODS

STUDY POPULATION AND PROTOCOL. Forty-five consecutive healthy pregnant women were prospectively enrolled in a single center. Subjects had no known cardiovascular disease nor were taking medications with cardiovascular effects. Exclusion criteria were pre-eclampsia or eclampsia during previous pregnancy, previous fetal growth restriction, hypertension, or diabetes. All patients gave written informed consent, and the protocol was approved by the institutional review board.

ECHOCARDIOGRAPHIC EXAMINATION. Study visits occurred once during each trimester and once at postpartum. At each visit, in addition to routine antenatal examinations, a complete 2D and a

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full-volume 3D transthoracic echocardiogram were performed, as well as radial artery tonometry.

2D, pulsed wave, continuous wave and tissue Doppler echocardiography was performed by registered cardiac sonographers in accordance with the American Society of Echocardiography chamber quantitation and Doppler measurement guidelines,[22-24] with the Philips iE33 ultrasound system (Philips Healthcare) equipped with a variable frequency S5-1 pure wave 2D transducer and an X3-1 3D transducer.

Continuous wave Doppler across tricuspid valve was used to assess RV-right atrial gradient, and peak pulmonary artery pressure was obtained.[24] At least three consecutive cine loops were recorded and stored digitally for later off-line analysis using dedicated software (ProSolv, Fuji).

After the standard echo examination, imaging was performed for 2D strain imaging. Zoomed views of the right atrium (RA), left atrium (LA), LV, and RV in the apical 4-chamber and short axis views at mid-papillary muscle level were acquired, with a frame rate of 60 to 100 frames/s. This frame rate is recommended by the vendor to combine temporal resolution with an acceptable lateral definition to enhance the feasibility of the tracking technique. The high frame rate acoustic capture gray-scale images were analyzed offline using the velocity vector imaging (VVI) software (Syngo VVI, Siemens Medical Solutions USA Inc) by a single observer blinded to the stage of pregnancy (R.R.). Longitudinal and circumferential LV strain (S) and strain rate (SR) were measured in the apical 4 chamber view. LV radial S and SR were measured in the short-axis view at the mid-papillary muscle level. RV, LA, and RA longitudinal S and SR were measured in apical 4-chamber view. The endocardial border was initially manually defined by the user. Subsequently, VVI automatically tracked the endocardial border throughout the cardiac cycles, and the resulting velocity vectors in the 2-dimensional plane were displayed throughout the cardiac cycle. When processing of the trace was complete, the user reviewed the tracking and modified the traces if necessary. From the same tracked contour of the endocardium, the software measured S and SR. Mean global S and SR data were derived for each of the 18 LV segments, for septal and lateral RV-free walls, and for LA and RA in the 4-chamber view.

Three-dimensional data were acquired in a full-volume data set from the apical view using the X3-1 transducer. Separate full volume sweeps covering the entire LV and RV were obtained during mid-expiratory breath-hold so as to minimize stitch artifacts. The data sets were digitally stored and processed offline by a single observer (M.L.) using the Tom Tec software with 3D LV and RV analysis package (Tom Tec Imaging Systems) loaded on a dedicated workstation.

ECHOCARDIOGRAPHIC MEASUREMENTS. Measurements made from the images obtained from the apical windows included LA volume and LV stroke volume calculated as the product of LV outflow tract time velocity integral and cross-sectional area. Cardiac output was obtained by multiplying stroke volume with the heart rate. Echocardiographic measurements were performed by 2 trained readers. Appendix I describes echo measurements and equations used and off line 3D processing for LV and RV volumes.

SPHYMOCOR-RADIAL ARTERY TONOMETRY. After 2D and 3D echo were completed, radial artery pressure waveforms were acquired using a high-fidelity pressure transducer (Millar Instruments) on the patient's wrist by an elastic band and connected to a SphygmoCor device.[25] Measurements were taken from the same arm as the BP. Ten sequential pulse waveforms of high fidelity were recorded. Data quality information comprising of beat-to-beat variability and quality of radial artery tracing was displayed for radial artery contour. Measurements were only accepted if a green signal was displayed on the monitor indicating measurements with an average pulse height of 80 or above, pulse height variation of 5 or below, diastolic variation of 5 or below, and shape deviation of 3 or below. The following hemodynamic data was derived and displayed on the computer from the radial and the reconstructed central pressure waveforms[26]: augmentation index corrected to a heart rate of 75 (AIx_{75} – magnitude of peripheral wave reflections at the aorta in early systole thereby causing increased LV afterload), ejection duration, and oxygen consumption and supply measured as subendocardial viability ratio (SEVR, also known as Buckburg index) (Supplemental Appendix).

STATISTICAL ANALYSIS. Categorical data were summarized as numbers and percentages. Continuous data were presented as mean ± SD. Differences in echocardiographic variables between the different time points were analyzed using paired t-tests. Bonferroni correction (using a correction factor of 6) was performed to account for multiple comparisons. To account for the variable sample size at each trimester and postpartum and for variable gestational week of pregnancy within each trimester, a random mixed effect model for repeated measures was used to assess hemodynamic and echo characteristics. Likelihood ratio test was used to evaluate the

correlation structure. Pearson's correlation coefficient was used to evaluate the relationship between 2D and 3D echo measurements. To determine interobserver and intraobserver variability of echocardiographic measurements, variables for 10 randomly selected patients were analyzed by 2 independent readers and by one reader on 2 separate occasions. The agreement between the two measurements was analyzed using the intraclass correlation coefficient and Bland-Altman statistics. The limits of agreement are expressed by the mean difference ±2 SDs. For important variables, we estimated differences and their CIs between average values during the 3 trimesters and compared these against postpartum values. Statistical analysis was performed using StataIC 12 (StataCorp LP) and R version 4.2.2 using package *arsenal* and *lme4*. All statistical tests were two-sided, and a value of $P < 0.05$ was considered statistically significant.

RESULTS

STUDY POPULATION. We enrolled 45 subjects with a mean age of 29 ± 6 years (range, 18-43 years), 96% Hispanic. All subjects completed at least two echo exams at the predetermined time points. Forty-five, 36, 31, and 28 women had serial evaluations at 1st, 2nd, and 3rd trimesters and postpartum, respectively. Thirty-one subjects completed at least three, and 27 subjects had echocardiographic measurements from all four time points. The prenatal echo exam during the 1st trimester was completed at 9.6 ± 2.1 weeks of pregnancy, at 22.2 ± 3.2 weeks during the 2nd, and at 33.8 ± 2.9 weeks during the 3rd trimester. The postpartum echo exam was performed at 9.9 ± 11.9 weeks after delivery. Among the women studied, 22% were nulliparous, and the rest had at least one prior pregnancy. An additional 32 women, 26.7 ± 6.6 years (range 18-42 years), 97% Hispanic, who consented to the study and underwent the first study visit but did not return for the remainder of pregnancy were excluded from the study. Apart from younger age (26.7 ± 6.6 years, $P < 0.05$) and higher tissue Doppler lateral mitral annular E' velocity (17.55 ± 3.94 cm/s vs 15.89 ± 2.81 cm/s, $P < 0.05$), likely higher due to a younger age, there was no other demographic, hemodynamic, or echocardiographic difference between the two groups.

Four women developed gestational diabetes. All women had full-term, uncomplicated deliveries except one who delivered prematurely at 30 weeks. Average gestational age at delivery was 37.4 ± 3.4 weeks. All subjects remained in normal sinus rhythm throughout pregnancy and postpartum follow-up.

HEMODYNAMIC DATA: RADIAL ARTERY TONOMETRY. Clinical and hemodynamic data measured during each trimester and postpartum are presented in Table 1. Compared to the postpartum, the heart rate during pregnancy was significantly higher, peaking at 2nd and 3rd trimesters ($P < 0.001$). There was a decrease in peripheral systolic BP in the second trimester but no changes in diastolic BP. Central aortic systolic pressure declined during pregnancy with a significant decrease in pulse pressure throughout. AIx_{75} and SEVR significantly declined throughout pregnancy (Table 1). Ejection duration as a percent of cardiac cycle increased throughout pregnancy compared to postpartum. Stroke work—a noninvasive measure of cardiac function that integrates relevant systolic, diastolic, and systemic parameters—increased favorably during late pregnancy. Correlation coefficients for AIx_{75} and central systolic BP, diastolic BP, and pulse pressure were 0.53, 0.33, and 0.53, respectively ($P < 0.001$).

ECHOCARDIOGRAPHIC DATA. Left ventricular structure and function by 2D echo. Serial 2D echo parameters are shown in Table 2. There was a trend for an increase in LV end-diastolic, end-systolic diameter, and LV mass. Septal wall thickness increased during pregnancy without significant changes in the posterior wall thickness. LV meridional end systolic wall stress using average inter ventricular septum (IVS) and posterior wall thickness did not change significantly. LV fractional shortening and Vcfc remained unchanged throughout.

Right ventricular structure and systolic function by 2D echo. There was no significant increase in RV size, except in the mid RV region, in the 4-chamber view. RV function increased in systole by lateral tricuspid annular S' (showing increased longitudinal RV function) as well as during diastole by lateral E'. (Table 2). Right atrial area also increased (Table 2).

Left ventricular diastolic function. Diastolic function parameters are displayed in Table 3. There was a no significant change in mitral E velocity or in mitral inflow deceleration time during pregnancy. Mitral E/A ratio progressively decreased throughout pregnancy, reflecting largely the increase in mitral A velocity. Medial and lateral e' velocities decreased as the pregnancy progressed; however, there was no significant increase in E/e'_{av} ratio. Correlation coefficient between AIx_{75} and E/A ratio was −0.31 ($P = 0.0002$), and averaged e' was −0.25 ($P = 0.003$), showing some effect of afterload on LV relaxation. Pulmonary vein systolic flow velocity into the LA

TABLE 1 Demographic and Hemodynamic Characteristics of the Study Population

	1st Trimester (n = 45)	2nd Trimester (n = 36)	3rd Trimester (n = 31)	Postpartum (n = 28)	*P* Values[μ]
Weight (lbs)	148.8 ± 29.2	153.6 ± 28.4*	163.4 ± 30.6	146.5 ± 31.0	<0.001
Weight (kg)	66.795 ± 14.210	70.014 ± 13.201	74.446 ± 12.586	66.978 ± 13.958	0.101
Body surface area (m^2)	1.726 ± 0.195	1.747 ± 0.184	1.813 ± 0.194	1.704 ± 0.198	0.004
SBP (mm Hg)	109.231 ± 12.877	104.488 ± 11.009	107.643 ± 13.940	105.419 ± 8.842	0.155
DBP (mm Hg)	64.359 ± 8.949	61.561 ± 7.652	64.964 ± 11.400	64.613 ± 9.113	0.357
Mean BP (mm Hg)	79.250 ± 9.260	76.395 ± 8.628	79.571 ± 9.194	79.473 ± 9.483	0.413
Heart rate (bpm)	70.538 ± 9.208	74.878 ± 8.094	74.107 ± 9.231	61.613 ± 9.790	<0.001
Aortic SP (mm Hg)	93.421 ± 10.663	89.073 ± 10.051	94.148 ± 15.486	96.233 ± 8.897	0.094
Aortic DP (mm Hg)	65.026 ± 9.027	62.683 ± 7.815	65.852 ± 11.465	65.400 ± 9.343	0.472
Aortic PP (mm Hg)	28.605 ± 5.539	26.439 ± 4.806	28.259 ± 6.791	30.767 ± 5.847	0.020
Mean aortic pressure	62.904 ± 28.595	65.126 ± 22.052	58.076 ± 33.893	73.237 ± 16.095	0.129
Aortic Aug Press (mm Hg)	3.051 ± 3.456	1.857 ± 3.482	2.733 ± 5.298	7.533 ± 3.391	<0.001
Aortic Aug Press 75 (%)	7.051 ± 9.744	5.786 ± 13.452	7.067 ± 13.946	17.500 ± 8.669	<0.001
Ejection duration (%)	37.200 ± 4.033	39.419 ± 4.387	37.867 ± 4.108	34.500 ± 4.024	<0.001
SEVR (%)	143.875 ± 23.789	132.442 ± 27.111	138.100 ± 21.334	162.133 ± 26.243	<0.001
TVR-peripheral ($dyn \cdot s/cm^5$)	1,688 ± 426	1,304 ± 249	1,261 ± 310	1,734 ± 366	0.001
TVR-central ($dyn \cdot s/cm^5$)	1,627 ± 431	1,250 ± 239	1,179 ± 329	1,656 ± 346	0.001
Stroke work-peripheral (Nm)	6.251 ± 1.681	6.203 ± 1.290	7.171 ± 1.276	6.364 ± 1.312	0.019
Stroke work-central (Nm)	5.642 ± 1.301	5.914 ± 1.091	6.990 ± 1.283	6.183 ± 1.274	0.01

Data as mean ± SD. *P* value comparing pregnancy stages using mixed model regression analysis adjusting for gestational age in weeks and sample size in each trimester.
BSA = body surface area; BP = blood pressure; DBP = diastolic blood pressure; Nm = Newton-meter; PP = pulse pressure; SBP = systolic blood pressure; TVR = total vascular resistance.

remained elevated during pregnancy, as did pulmonary vein atrial reversal.

Left and right ventricular function by 3D echo. Table 4 shows 2D and 3D assessments of LV volumes; stroke volume and LVEF during pregnancy. No significant change in volumes was detected on 2D echo. 2D LV end systolic volume (ESV) and LV end diastolic volume (EDV) during the third trimester were significantly lower than by 3D volumes; whereas 2D and 3D volumes were similar in the first trimester and postpartum. By 3D echo, LVEDV increased progressively during each trimester and returned to baseline postpartum (Table 4). LV stroke volume increased by 12% toward the third trimester and decreased postpartum; however, the 3D LVEF, although showing a slight decline in the third trimester at 56% ± 2%, remained within physiological range during pregnancy. Similar to the LV, the RV EDV, ESV, and stroke volume also increased during pregnancy without change in RVEF. The correlation coefficient for 2D and 3D LVEDV measurements were 0.52 ($P = 0.0004$) during the first trimester and 0.69 ($P = 0.0001$) postpartum and were lower for the second trimester (0.42, $P = 0.005$) and the third trimester (0.45, $P = 0.007$).

SPECKLE TRACKING (DEFORMATION) IMAGING. Table 5 shows 2D strain data of all 4 cardiac chambers. There was no significant change in LV, RV, LA, or RA strain. However LV, LA, and RA strain rates increased throughout pregnancy, and RV longitudinal strain rates were increased in the first and second trimesters.

Correlation was observed between LV longitudinal strain and strain rate with LV end systolic and end diastolic volumes on 3D (Figure 1). No correlation was found between strain and strain rate with 2D measurements except between LV longitudinal strain and 2D LVEF (r = 0.261, $P = 0.001$).

Differences among important study variables during pregnancy vs postpartum state are shown in Table 6 with robust confidence intervals for radial artery tonometry and strain rate data.

REPRODUCIBILITY OF MEASUREMENTS. The intraobserver and interobserver agreement for 2D echo Doppler among 2 readers were: 0.51% ± 4.6%; 0.51% ± 4.6% for LV velocity time integral; 1.04% ± 3.2%; 1.57 ± 7.6%; and 3.67% ± 3.6%; 6.42% ± 4.8% for E wave deceleration time, respectively. The intraobserver agreement for LV 3D volume measurements was 2.1 ± 3.2 (r = 0.99) and for strain measurements was 1.5% ± 7% for LV longitudinal strain and 3% ± 5% for LV longitudinal strain rate.

DISCUSSION

PRINCIPAL FINDINGS. Our study shows that efficient cardiac and vascular adaptations during pregnancy

TABLE 2 Two-Dimensional Echocardiographic Characteristics of the Study Population

	1st Trimester (n = 45)	2nd Trimester (n = 36)	3rd Trimester (n = 31)	Postpartum (n = 28)	*P* Values
LV diastolic diameter (cm)	4.673 ± 0.408	4.796 ± 0.370	4.841 ± 0.380	4.813 ± 0.371	0.209
LV systolic diameter (cm)	3.162 ± 0.398	3.242 ± 0.403	3.304 ± 0.419	3.354 ± 0.350	0.179
LV PW thickness-diastole (cm)	0.697 ± 0.125	0.695 ± 0.127	0.695 ± 0.128	0.700 ± 0.097	0.998
IVS thickness-diastole (cm)	0.758 ± 0.137	0.809 ± 0.147	0.835 ± 0.163	0.820 ± 0.153	0.102
LV PW thickness-diastole (cm)	0.697 ± 0.125	0.695 ± 0.127	0.695 ± 0.128	0.700 ± 0.097	0.998
LV PW thickness-systole (cm)	1.114 ± 0.173	1.117 ± 0.161	1.087 ± 0.203	1.110 ± 0.243	0.918
IVS thickness-systole (cm)	1.086 ± 0.180	1.158 ± 0.130	1.193 ± 0.164	1.191 ± 0.176	0.021
Average wall thickness-systole (cm)	1.101 ± 0.153	1.137 ± 0.126	1.140 ± 0.155	1.151 ± 0.182	0.472
LV mass (gms)	109.081 ± 27.556	116.630 ± 26.008	121.700 ± 32.719	121.172 ± 30.777	0.191
LV meridional ESWS (gms/cm^2)	50.271 ± 10.938	49.064 ± 12.040	53.569 ± 15.837	54.499 ± 13.533	0.021
LV fractional shortening (%)	0.323 ± 0.057	0.323 ± 0.064	0.315 ± 0.064	0.303 ± 0.055	0.568
LVOT VTI	21.509 ± 4.514	22.743 ± 4.515	20.612 ± 2.777	21.417 ± 2.765	0.143
LVOT diameter	1.899 ± 0.153	1.921 ± 0.146	1.911 ± 0.142	1.913 ± 0.123	0.932
Stroke volume	59.074 ± 11.819	65.506 ± 14.499	61.788 ± 10.520	61.820 ± 11.711	0.219
LV cardiac output (Doppler) (<0.001)	4.017 ± 1.007	4.913 ± 0.978	4.665 ± 0.916	4.034 ± 0.985	<0.001
LV circumferential fiber shortening (circ/s)	0.960 ± 0.131	0.902 ± 0.149	0.945 ± 0.202	0.903 ± 0.162	0.411
LA diameter (cm)	3.531 ± 0.515	3.727 ± 0.509	3.858 ± 0.543	3.507 ± 0.391	0.009
LA volume (ml)	42.105 ± 11.890	49.949 ± 13.582	51.548 ± 12.592	54.849 ± 17.269	<0.001
LA indexed volume (ml/m^2) (cm)	25.484 ± 5.369	28.985 ± 7.097	28.778 ± 5.757	31.778 ± 7.933	0.002
RV D1 (diameter at annulus) (cm)	3.349 ± 0.573	3.354 ± 0.614	3.474 ± 0.577	3.384 ± 0.447	0.775
RV D2 (diameter at mid RV) (cm)	2.754 ± 0.374	2.643 ± 0.465	2.562 ± 0.431	2.449 ± 0.303	0.017
RV D3 (length from base to apex) (cm)	7.271 ± 0.546	7.113 ± 0.690	6.878 ± 0.711	6.853 ± 0.812	0.091
RA area (cm^2)	13.95 ± 3.211	15.277 ± 2.597	15.517 ± 2.150	14.875 ± 2.302	0.005
Tricuspid annular E′ (cm/s)	13.302 ± 2.520	13.477 ± 3.772	11.826 ± 4.299	11.353 ± 2.813	0.030
Tricuspid annular S′ (cm/s)	12.878 ± 1.721	13.495 ± 2.502	13.021 ± 2.526	11.737 ± 1.428	0.009
Tricuspid annular plane systolic excursion (cm)	1.952 ± 0.304	1.993 ± 0.329	1.993 ± 0.365	1.918 ± 0.297	0.794
Pulmonary artery systolic pressure (mm Hg)	20.516 ± 5.763	22.636 ± 6.977	24.659 ± 7.910	23.513 ± 7.961	0.112

Data as mean ± SD. *P* value comparing pregnancy stages using mixed model regression analysis.

BSA = body surface area; ESWS = end systolic wall stress; IVS = interventricular septum; LA = left atrial; LV = left ventricular; LVOT = left ventricular outflow tract; PW = posterior wall; RA = right atrial; RV = right ventricular; Vcfc = velocity of circumferential fiber contraction = ([LVIDD−LVIDS]/LVIDD)/LVETxRR interval; VTI = velocity time integral. Wall stress: (0.334 P×LVIDS)/(PWS [1+ (PWS/LVIDS)]).

allow for continued increases in cardiac output throughout pregnancy. Progressive increase in LV and RV volumes as well as LA volume and RA size occurs as pregnancy advances, paralleling the known increases in plasma volume during pregnancy. Load-dependent parameters including LVEF, tissue Doppler LV, and RV early diastolic velocities decreased in late pregnancy, along with a trend for decrease in mitral inflow early diastolic velocity, and LV, RV, LA, and RA longitudinal strain in late pregnancy. There was no change in LV strain or strain rate in the circumferential plane in a volume overloaded "globular" LV during pregnancy. However, the longitudinal strain rate—a more volume-independent measure of cardiac deformation—remained elevated for all cardiac chambers throughout pregnancy. LV radial strain rate also showed a trend for an increase throughout pregnancy. These changes reversed in the postpartum period. These adaptations, along with increased atrial contribution to cardiac output and persistent decline in central and peripheral vascular resistance, led to reduction in systolic augmentation of BP and in LV afterload throughout pregnancy and allowed a continual increase in LV stroke volume until the end of pregnancy. Increase in heart rate, increased cardiac volumes, cardiac deformation rate, and cardiac ejection duration (after adjusting for heart rate) provided increasing demand for cardiac output in pregnancy (**Central Illustration**).

FINDINGS IN THE LIGHT OF EARLIER STUDIES. Earlier studies have shown increased cardiac dimensions, heart rate, cardiac output, and stroke work along with a decrease in BP and peripheral vascular resistance during pregnancy.[1-9] Systolic function variously measured by fractional shortening, LVEF, or Vcfc during normal pregnancy has been variably reported to improve,[2] remain unchanged,[8,9] or even decline [3-5,10] during pregnancy. Fractional shortening and Vcfc, which measure LV circumferential function, are limited due to measurements of LV dimension in a single plane. Some studies were limited due to

TABLE 3 LV Diastolic Function: Echo Doppler Characteristics of the Study Population

	1st Trimester (n = 45)	2nd Trimester (n = 36)	3rd Trimester (n = 31)	Postpartum (n = 28)	*P* Value
Mitral E (cm/s)	93.629 ± 15.946	92.356 ± 15.228	87.864 ± 17.314	86.009 ± 16.257	0.145
Mitral A (cm/s)	56.509 ± 12.275	57.471 ± 10.851	64.289 ± 13.672	57.497 ± 13.808	0.038
E wave deceleration time (ms)	172.776 ± 28.457	176.458 ± 30.636	176.403 ± 28.829	178.273 ± 24.096	0.855
E/A ratio	1.722 ± 0.431	1.665 ± 0.466	1.407 ± 0.328	1.523 ± 0.355	0.005
E velocity with Valsalva (cm/s)	81.294 ± 18.457	82.627 ± 17.603	78.616 ± 16.016	73.541 ± 13.873	0.143
A velocity with Valsalva (cm/s)	52.215 ± 15.808	56.524 ± 13.015	62.312 ± 13.623	54.650 ± 14.219	0.034
E/A ratio with Valsalva	1.924 ± 2.032	1.528 ± 0.469	1.293 ± 0.273	1.385 ± 0.295	0.092
e' septal annulus (cm/s)	10.917 ± 2.229	10.258 ± 2.008	9.470 ± 2.168	9.940 ± 1.482	0.017
E/e'septal	8.941 ± 2.312	9.267 ± 2.092	9.646 ± 2.483	8.758 ± 2.072	0.390
e' lateral annulus (cm/s)	15.975 ± 2.772	14.830 ± 2.645	13.942 ± 2.549	14.654 ± 2.560	0.058
Average e'	13.424 ± 2.195	12.461 ± 1.978	11.728 ± 1.883	12.297 ± 1.600	0.002
E/e'_{av}	5.898 ± 1.890	6.245 ± 1.919	6.746 ± 1.303	6.073 ± 1.310	0.178
PV S (cm/s)	54.673 ± 13.704	53.259 ± 9.443	53.608 ± 9.419	42.128 ± 14.732	<0.001
PV D (cm/s)	53.210 ± 13.785	54.238 ± 10.928	53.976 ± 11.585	45.856 ± 16.338	0.039
PV AR (cm/s)	30.176 ± 21.556	32.707 ± 14.419	41.453 ± 19.936	25.140 ± 12.458	0.005
PV a dur (msec)	111.064 ± 19.257	117.467 ± 18.874	122.493 ± 22.382	116.584 ± 20.083	0.129

Data as mean ± SD. *P* value comparing pregnancy stages using mixed model regression analysis.
LV = left ventricle; PV = pulmonary vein; RV = right ventricle.

cross-sectional design.[2,6,21] Studies that have been prospective performed conventional 2D, M mode, and spectral Doppler techniques for cardiac assessment. Speckle tracking echo is angle independent and less load dependent than tissue Doppler method. Few studies that have assessed cardiac deformation have shown a reduction in LV longitudinal strain in the third trimester both by speckle tracking[10,27] and by tissue Doppler.[28] These studies did not evaluate LV deformation in all planes or the atrial strain. LV motion is complex and occurs in the longitudinal, circumferential, and radial planes along with twisting motion. It is possible that decline in deformation in one direction is compensated by an increase in another plane. We used the angle-independent method of 2D speckle tracking for measuring LV strain in longitudinal, radial, and circumferential directions. We also used strain rate, which measures the rate of rise in deformation in multiple planes and is less load dependent than tissue Doppler and 2D speckle tracking strain. Like earlier studies, we also observed a decrease in LV, RV, LA, and RA strain

TABLE 4 Left Ventricular Volumes by 2D and 3D Echocardiography and Right Ventricular Volumes by 3D Echocardiography

	1st Trimester (n = 45)	2nd Trimester (n = 36)	3rd Trimester (n = 31)	Postpartum (n = 28)	*P* Value[a]
3D					
LV end diastolic volume	83.672 ± 14.022	91.512 ± 14.620	97.581 ± 19.864	85.163 ± 13.960	0.001
LV end systolic volume	34.583 ± 6.946	39.405 ± 7.345	45.994 ± 15.180	36.077 ± 7.116	<0.001
LV stroke volume	48.495 ± 8.032	51.727 ± 8.348	54.833 ± 10.127	48.577 ± 7.950	0.009
LV ejection fraction	58.172 ± 3.110	57.112 ± 3.359	55.652 ± 1.970	57.257 ± 3.328	0.008
RV end diastolic volume	77.074 ± 14.875	86.871 ± 16.783	92.926 ± 18.083	78.267 ± 15.047	<0.001
RV end systolic volume	30.690 ± 6.194	35.390 ± 6.847	40.929 ± 15.178	30.740 ± 6.911	<0.001
RV stroke volume	46.264 ± 9.711	51.212 ± 10.962	55.145 ± 10.562	47.410 ± 9.928	0.002
RV ejection fraction	59.741 ± 3.516	58.644 ± 3.273	58.935 ± 3.890	59.837 ± 3.905	0.412
2D					
LV EDV (ml)	81.506 ± 14.624	87.071 ± 14.964	88.361 ± 16.065	90.457 ± 17.160	0.748
LV ESV (ml)	31.860 ± 6.592	34.917 ± 7.600	36.359 ± 7.478	36.991 ± 7.418	0.805
LV SV (ml)	49.647 ± 9.171	52.156 ± 8.453	52.003 ± 10.052	53.468 ± 10.725	0.776
LV EF (%)	61.197 ± 3.728	60.227 ± 3.436	58.889 ± 4.069	58.935 ± 3.296	0.781

Data as mean ± SD. [a]Indicates *P* value comparing pregnancy stages using mixed model regression analysis.
EDV = end diastolic volume; ESV = end systolic volume; LV = left ventricle; RV = right ventricle; SV = stroke volume; EF = ejection fraction; 3D = three-dimensional; 2D = two-dimensional.

TABLE 5 Cardiac Deformation by Speckle Tracking Strain During Pregnancy

	1st Trimester (n = 45)	2nd Trimester (n = 36)	3rd Trimester (n = 31)	Postpartum (n = 28)	*P* Value
Average strain (%)					
LV circumferential strain	−20.772 ± 4.349	−21.541 ± 4.174	−21.198 ± 3.581	−21.331 ± 3.588	0.855
LV longitudinal strain	−17.505 ± 3.359	−17.993 ± 2.584	−16.479 ± 3.419	−16.572 ± 2.668	0.107
LV radial strain	39.824 ± 15.786	42.259 ± 21.726	41.778 ± 17.724	35.209 ± 10.942	0.363
RV longitudinal strain	−20.993 ± 3.670	−19.718 ± 3.770	−18.992 ± 4.744	−19.655 ± 4.582	0.221
LA strain	33.423 ± 10.738	34.924 ± 11.970	29.184 ± 11.525	29.812 ± 9.752	0.084
RA strain	46.603 ± 13.483	45.947 ± 18.886	41.561 ± 12.238	41.063 ± 13.706	0.293
Average strain rate (s^{-1})					
LV circumferential strain rate	−1.679 ± 0.470	−1.810 ± 0.375	−1.714 ± 0.460	−1.595 ± 0.354	0.231
LV longitudinal strain rate	−1.242 ± 0.350	−1.194 ± 0.181	−1.231 ± 0.263	−1.068 ± 0.218	0.040
LV radial strain rate	3.089 ± 1.061	3.145 ± 1.235	3.000 ± 0.921	2.540 ± 0.855	0.094
RV longitudinal strain rate	−1.612 ± 0.314	−1.540 ± 0.284	−1.281 ± 0.748	−1.361 ± 0.306	0.008
LA strain rate (atrial systole)	1.735 ± 0.461	1.687 ± 0.540	1.588 ± 0.526	1.414 ± 0.325	0.035
RA strain rate	2.389 ± 0.582	2.264 ± 0.741	2.241 ± 0.793	1.861 ± 0.600	0.021

Data as mean ± SD. Each column in the table depicts absolute strain values during each pregnancy trimester and in the postpartum period. The values of longitudinal strain and strain rate and circumferential strain and strain rate are negative (decrease between 2 points due to shortening of LV longitudinal and circumferential fibers during systole), and more negative the value, the better is strain and strain rate. Radial strain and strain rate are positive numbers (due to lengthening between 2 points in the LV radial plane from thickening of muscle in systole), and more positive the value, better is the radial strain and strain rate. *P* value comparing pregnancy stages using mixed model regression analysis adjusting for gestational age in weeks.

LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle.

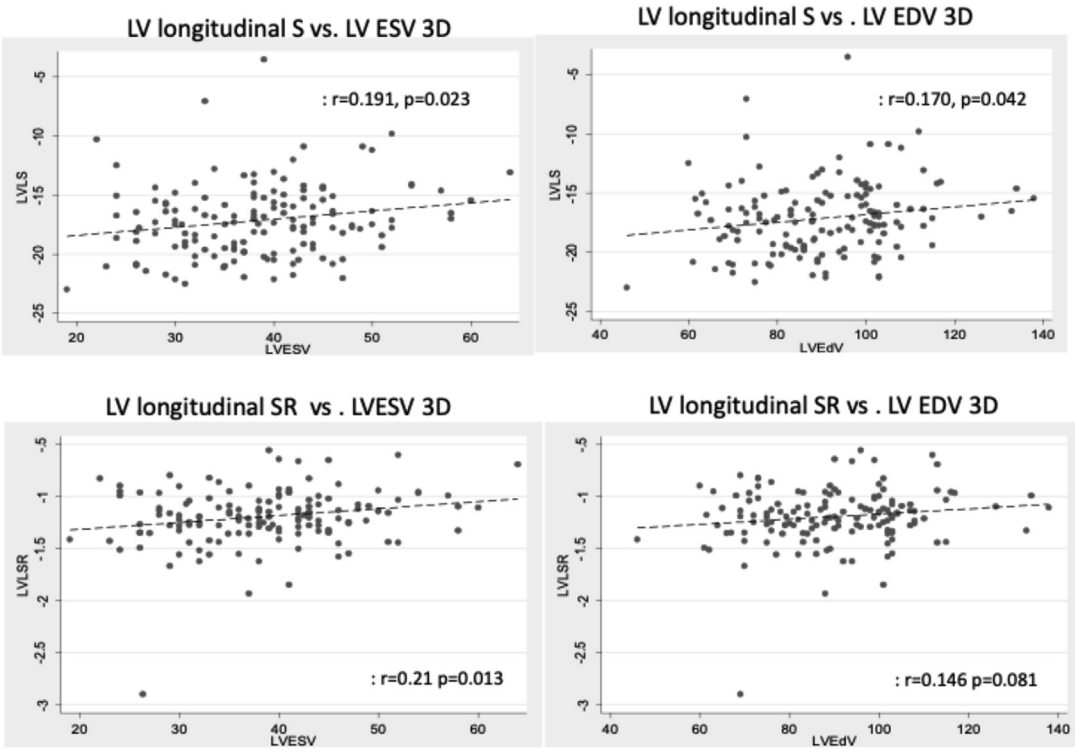
during the 3rd trimester; however, strain rate of all chambers remained increased even in late pregnancy except for RV. Besides load-dependent decline in longitudinal strain in cardiac chambers in the third trimester, another reason for a lower strain in the third trimester may be related to smaller changes needed in volume overloaded chambers to produce a given forward volume. Our findings also suggest that increased preload, most marked in the late trimester, affects strain but not strain rate, which is a better load-independent marker of cardiac function than strain.

There was a trend for an increase in IVS wall thickness, in LV mass and LV end diastolic diameter during pregnancy as well as postpartum, and no change in posterior wall thickness during pregnancy. While not statistically significant, mild increase in IVS thickness in end diastole allows the compensatory processes in response to increased volumetric burden or diastolic overload to help maintain contractile forces, including radial and circumferential efficiency, and counteracts the increased ventricular wall stress from increased LV volume. Posterior systolic wall thickening did not change significantly while IVS end systolic wall thickening increased, thereby reducing a significant increase in LV end systolic wall stress. Using only the PW thickness in end systole in the formula for end systolic wall stress, there would be a significant increase in LV wall stress in late pregnancy.

Two-dimensional echo was unable to detect significant changes in LV volumes or LVEF. Given the weaker correlation we found between 2D and 3D measurements in the third trimester compared to first trimester and postpartum measurements, we postulate this to be due to LV foreshortening from elevated diaphragm from the gravid uterus in later stages of pregnancy. Foreshortened views also likely explain why linear anteroposterior atrial dimension and atrial volumes were different in the third trimester. To overcome the geometric limitations of 2D echo, we measured LV and RV volumes and EF using 3D echo, which is more reproducible, and its measured cardiac volumes are comparable to magnetic resonance imaging volumes.[29] There was a progressive increase in LVEDV, LVESV, and LV stroke volume during pregnancy, as well as a slight but significant decline in LVEF in the third trimester by 3D measurements. Three-dimensional echo was able to detect the increase in RV EDV, ESV, and stroke volume during pregnancy, whereas most of RV dimensions measured by 2D echo failed to detect an increase in RV size except in mid RV region. Superior volumetric measurement accuracy of 3D compared to 2D was also shown by a stronger relationship with speckle tracking strain and strain rate measurements.

Increased LA strain and strain rate were accompanied by an increase in forward LA velocity of contraction. Increased pulmonary vein systolic flow into left atrium was likely secondary to a robust

FIGURE 1 Relationship Between LV Longitudinal Deformation With LV 3D Variables



Correlation between LV longitudinal strain and strain rate with 3D LV end systolic and end diastolic volumes. EDV = end diastolic volume; ESV = end systolic volume; LV = left ventricle; SR = strain rate; 3D = three-dimensional.

left atrial relaxation.[9] Other studies have shown that in the presence of a heightened atrial preload, as occurs with fluid loading, atrial contractility increases, manifested by an increase in pulmonary vein atrial velocity and increased A velocity on mitral inflow[11-13,31] or mitral annulus [11] without alternation in intrinsic LV diastolic properties.[31] We found a significant increase in pulmonary vein S-wave, in atrial reversal velocity, and in forward atrial velocity, along with increased LA strain and strain rate. We propose that these reflect more robust LA contraction as well as relaxation causing above changes rather than a manifestation of abnormal LV relaxation. Similar to other studies, we found no change in E/e' ratio.[7,12] Putting together changes in diastolic function including an increase in LA size and function, an early augmentation of e' suggests an improvement in diastolic function, while a late reduction in e' velocities and no significant change in average E/e' near term are likely secondary to volume overload [30,31] and not be secondary to LV diastolic dysfunction. A reduction in SEVR% may be related to shortening of diastolic filling time due to increased heart rate during pregnancy, thereby allowing for increased systolic ejection time during pregnancy. Robust LV relaxation and atrial contraction in our young cohort likely compensated for the relative reduction in diastolic filling time.

Changes in compliance of both central and peripheral blood vessels have been elegantly demonstrated by Poppas et al.[5] Using PW Doppler measurements at the aorta and carotid artery, they showed that the magnitude of peripheral wave reflections at the aorta was reduced in pregnancy. We demonstrated a reduction in pulse wave reflection by a simpler method of radial artery tonometry and its relation with LV filling parameters. Studies have also shown reduction in AIx_{75} in normal pregnancy[32] and an increase in pre-eclampsia[33]; however, these studies did not show the link between pulse wave reflection and diastolic function in pregnancy. A tighter relationship between LV diastolic function and AIx_{75} was found in nonpregnant diabetics compared to our study.[14] Influence of volume

TABLE 6 Differences Among Echo and Radial Artery Tonometry Variables During Pregnancy and Postpartum

2D/Doppler	
Hear rate (beats/min)	8.63 (3.99-13.28)
Stroke volume (ml)	1.71 (−4.72 to 8.13)
Cardiac output (L/min)	0.60 (0.10-1.10)
E/ave'	0.31 (−0.35 to 0.98)
Average e' (cm/s)	0.34 (−0.49 to 1.18)
3D echo	
LV-end diastolic volume (ml)	4.62 (−2.78 to 12.01)
LV-end systolic volume (ml)	3.67 (−0.32 to 7.76)
Strain rate	
LV longitudinal strain rate (s^{-1})	−0.77 (−2.12 to 0.58)
RV longitudinal strain rate (s^{-1})	−0.12 (−0.29 to 0.04)
Right atrial strain rate a (s^{-1})	−0.37 (−0.07 to −0.66)
Left atrial strain rate a (s^{-1})	−0.13 (−0.07 to −0.35)
Radial artery tonometry	
Augmentation pressure (mm Hg)	−4.17 (−6.05 to −2.29)
SEVR (%)	−21.67 (−33.70 to −9.67)
LV ejection duration (%)	3.25 (1.30-5.21)

Values are mean difference (95% CI). Values during the 3 pregnancy trimesters were averaged and compared against postpartum values.

LV = left ventricle; RV = right ventricle; SEVR = subendocardial viability ratio; 3D = 3-dimensional; 2D = 2-dimensional.

overload of pregnancy on indices of diastolic function may explain the weaker relationship we observed.

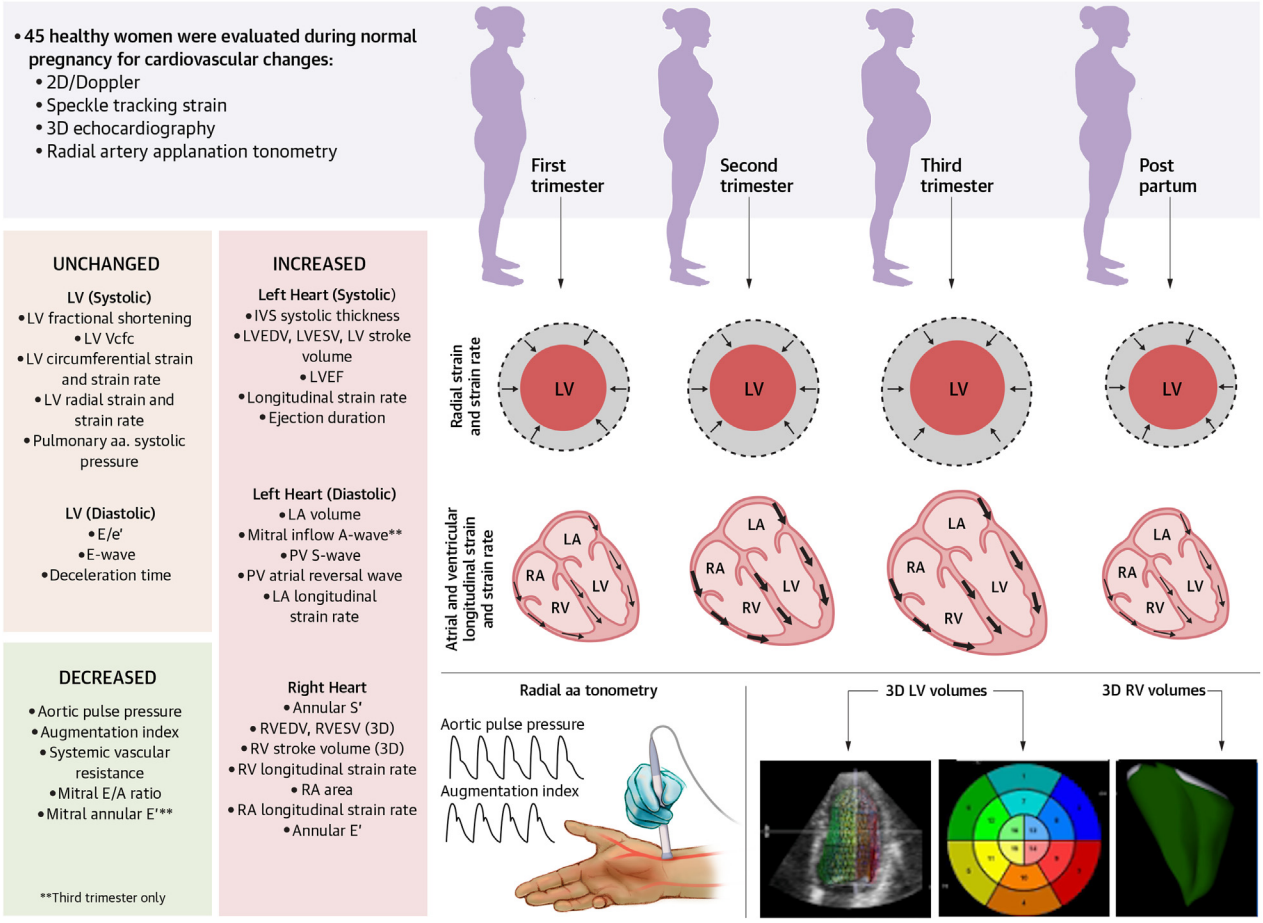
We observed more pronounced changes in central systolic BP compared to brachial artery BP. In addition, AI_{x75} correlated with central systolic BP, diastolic BP, pulse pressure, and LV end wall stress and weakly with peripheral BP, indicating that central BP provides a better assessment of LV afterload. Negative correlations between AIx_{75} and mitral E/A ratio and average e' also confirm a direct relationship between changing vascular compliance and changing diastolic function during pregnancy. As arterial stiffness increases, manifested by an increase in AIx_{75} toward the third trimester, a reduction in LV relaxation velocities is observed. Our data confirms prior observations on serial changes in arterial function in relation to physiological changes in cardiac systolic and diastolic function during normal pregnancy.

STRENGTHS AND LIMITATIONS. The strengths of the study are its prospective nature with predominantly Hispanic population on whom limited data is available. We used 3D and speckle tracking to evaluate cardiac volumes and function. Unlike other studies, we also evaluated strain rate of all 4 cardiac chambers. These techniques demonstrated limitations of 2D and spectral Doppler techniques in a volume-overloaded state that may provide conflicting results. At the same time, we evaluated central BP and augmentation index besides peripheral BP and showed relationship between augmentation index and some parameters of LV diastolic function. Our findings show that 3D and speckle tracking, besides 2D echo Doppler, permit reproducible measurements on repeated occasions throughout pregnancy. The study subject self-control design and consistency of examiner minimized the variability of data. The study has some limitations including a small sample size. Not all subjects returned for all study time points, despite study incentives for transportation and meals. This attrition may have influenced our study results and estimated differences we observed between pregnancy and postpartum state. Study dropout in pregnancy research studies has been reported in other prospective longitudinal studies studies in pregnancy,[3,28,31] and our cohort was enrolled in a county hospital with predominantly Hispanic women. We did not obtain preconception values, which would be more optimal to compare against values during pregnancy and postpartum to ascertain true return of parameters to baseline. The postpartum follow-up time may not have allowed complete normalization to baseline state. LV mass may take up to 6 months to return to baseline.[6] Our study involved predominantly Hispanic women, and findings may not apply to other ethnic groups. The average height of the population in this series is 5 feet 2 inches, which may have led to smaller cardiac volumes in our study.

CONCLUSIONS

Use of advanced ultrasound imaging using 3D echocardiography, speckle tracking, vascular compliance, and central aortic pressure assessment by applanation tonometry along with conventional 2D echo and echo Doppler in normal pregnancy allowed comprehensive assessment of cardiovascular adaptation in normal pregnancy. There was cardiac remodeling with four-chamber enlargement, increased LV and RV cardiac volumes by 3D echo, increased atrial contraction velocity, and improved LV relaxation in early pregnancy and in LV, RV, LA, and RA longitudinal strain rate and early to mid-pregnancy, leading to efficient cardiac pump function and diastolic function despite an increase in heart rate and preload. There was a decrease in LV, RV, LA, and RA longitudinal strain and a slight but significant decrease in LVEF in the third trimester. There was a reduction in central more than peripheral BP, reduction in cardiac augmentation index indicating increased vascular compliance, and increased heart rate, all resulting in increased stroke volume with

CENTRAL ILLUSTRATION Physiologic Cardiovascular Changes in Normal Pregnancy



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Physiologic changes during normal pregnancy compared to postpartum were studied using echocardiography and radial artery tonometry. Two-dimensional and 3D echocardiographic imaging during each trimester and in postpartum state in 45 women with normal pregnancy showed cardiac remodeling with four-chamber enlargement, increased 3D LV and RV cardiac volumes, and improved LV, RV, LA, and RA longitudinal strain rate throughout pregnancy. LV radial strain rate also trended higher. There was a reduction in LV, RV, LA and RA longitudinal strain in the third trimester. Radial artery tonometry demonstrated a reduction in aortic augmentation index with increased vascular compliance and reduced peripheral vascular resistance. These changes, along with increased heart rate and stroke volume throughout, allowed increased cardiac output during pregnancy. This cardiovascular adaptation reversed during the postpartum period. EDV = end diastolic volume; EF = ejection fraction; ESV = end systolic volume; IVS = inter ventricular septum; LA = left atrium; LV = left ventricle; PV = pulmonary vein; RA = right atrium; RV = right ventricle; Vcfc = velocity of circumferential fibre contraction; 3D = 3-dimensional.

increased ejection duration and cardiac output. These changes reversed during the postpartum period.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: Our report provides information on cardiovascular changes at different stages of normal pregnancy assessed by transthoracic echocardiography and measurement of peripheral and central blood pressure. Incremental benefit of using three dimensional and speckle tracking echocardiography and measurement of central blood pressure by radial artery tonometry is demonstrated. The findings in this report can help the medical providers improve their medical knowledge on normal cardiovascular adaption during pregnancy. Understanding these changes can help provide better patient care as many physiologic pregnancy changes can mimic findings observed in disease states such as heart failure.

TRANSLATIONAL OUTLOOK IMPLICATIONS: Our study highlights cardiovascular adaptation during normal pregnancy using echocardiography including speckle tracking and three dimensional echocardiogram and central aortic pressure measurment using radial artery tonometry. Competency in performing and interpreting these techniques may allow earlier detection of abnormalities in cardiovascular function during pregnancy. Barriers to clinical translation include use of state of art equipment and training on advanced imaging techniques. Additional research should incorporate multicenter studies including different ethnicities to understand variations in cardiovascular adaptation in normal pregnancy against which abnormal changes can be compared.

REFERENCES

1. Robson SC, Hunter S, Boys RJ, Dunlop W. Serial study of factors influencing changes in cardiac output during human pregnancy. *Am J Physiol*. 1989;256(4 Pt 2):H1060-H1065.

2. Rubler S, Damani PM, Pinto ER. Cardiac size and performance during pregnancy estimated with echocardiography. *Am J Cardiol*. 1977;40:534-540.

3. Monte SM, Sanders SP, Colan SD. Control mechanisms for physiological hypertrophy of pregnancy. *Circulation*. 1996;94:667-672.

4. Geva T, Mauer MB, Striker L, Kirshon B, Pivarnik JM. Effects of physiologic load of pregnancy on left ventricular contractility and remodeling. *Am Heart J*. 1997;133:53-59.

5. Poppas A, Shroff SG, Korcarz CE, et al. Serial assessment of the cardiovascular system in normal pregnancy. Role of arterial compliance and pulsatile arterial load. *Circulation*. 1997;95:2407-2415.

6. Simmons LA, Gillin AG, Jeremy RW. Structural and functional changes in left ventricle during normotensive and preeclamptic pregnancy. *Am J Physiol Heart Circ Physiol*. 2002;283:1627-1633.

7. Bamfo JE, Kametas NA, Nicolaides KH, Chambers JB. Maternal left ventricular diastolic and systolic long-axis function during normal pregnancy. *Eur J Echocardiogr*. 2007;8:360-368.

8. Katz R, Karliner JS, Resnik R. Effects of a natural volume overload state (pregnancy) on left ventricular performance in normal human subjects. *Circulation*. 1978;58:434-441.

9. Mabie WC, DiSessa TG, Crocker LG, Sibai BM, Arheart KL. A longitudinal study of cardiac output in normal human pregnancy. *Am J Obstet Gynecol*. 1994;170:849-856.

10. Cong J, Fan T, Yang X, et al. Structural and functional changes in maternal left ventricle during pregnancy: a three-dimensional speckle-tracking echocardiography study. *Cardiovasc Ultrasound*. 2015;13:6.

11. Fok WY, Chan LY, Wong JT, Yu CM, Lau TK. Left ventricular diastolic function during normal pregnancy: assessment by spectral tissue Doppler imaging. *Ultrasound Obstet Gynecol*. 2006;28:789-793.

12. Mesa A, Jessurun C, Hernandez A, et al. Left ventricular diastolic function in normal human pregnancy. *Circulation*. 1999;2:511-517.

13. Valensise H, Novelli GP, Vasapollo B, et al. Maternal cardiac systolic and diastolic function: relationship with uteroplacental resistances. A Doppler and echocardiographic longitudinal study. *Ultrasound Obstet Gynecol*. 2000;15:487-497.

14. Monaghan MJ. Role of real time 3D echocardiography in evaluating the left ventricle. *Heart*. 2006;92:131-136.

15. Grewal J, Majdalany D, Syed I, Pellikka P, Warnes CA. Three-dimensional echocardiographic assessment of right ventricular volume and function in adult patients with congenital heart disease: comparison with magnetic resonance imaging. *J Am Soc Echocardiogr*. 2010;23:127-133.

16. Kuhl HP, Schreckenberg M, Rulands D, et al. High-resolution transthoracic real-time three-dimensional echocardiography: quantitation of cardiac volumes and function using semi-automatic border detection and comparison with cardiac magnetic resonance imaging. *J Am Coll Cardiol*. 2004;43:2083-2090.

17. Van der Zwaan HB, Geleijnse ML, McGhie JS, et al. Right ventricular quantification in clinical practice: two-dimensional vs. three-dimensional echocardiography compared with cardiac magnetic resonance imaging. *Eur J Echocardiogr*. 2011;12:656-664.

18. Heimdal A, Stoylen A, Torp H, Skjaerpe T. Real-time strain rate imaging of the left ventricle by ultrasound. *J Am Soc Echocardiogr*. 1998;11:1013-1019.

19. Blessberger H, Binder T. Two dimensional speckle tracking echocardiography: basic principles. *Heart*. 2010;96:716-722.

20. Roos CJ, Auger D, Djaberi R, et al. Relationship between left ventricular diastolic function and arterial stiffness in asymptomatic patients with diabetes mellitus. *Int J Cardiovasc Imag*. 2013;29:609-616.

21. Khalil A, Jauniaux E, Cooper D, Harrington K. Pulse wave analysis in normal pregnancy: a prospective longitudinal study. *PLoS One*. 2009;4:e6134.

22. Lang RM, Bierig M, Devereux RB, et al. Recommendations for chamber quantification: a report from the American society of echocardiography's guidelines and standards committee and the chamber quantification writing group, developed in conjunction with the European association of echocardiography, a branch of the European

society of cardiology. *J Am Soc Echocardiogr*. 2005;18:1440-1463.

23. Quiñones MA, Otto CM, Stoddard M, Waggoner A, Zoghbi WA. Recommendations for quantification of Doppler echocardiography: a report from the Doppler quantification task force of the nomenclature and standards committee of the American society of echocardiography. *J Am Soc Echocardiogr*. 2002;15:167-184.

24. Rudski LG, Lai WW, Afilalo J, et al. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American society of echocardiography. *J Am Soc Echocardiogr*. 2010;23:685-713.

25. Kelly R, Hayward C, Avolio A, O'Rourke M. Noninvasive determination of age-related changes in the human arterial pulse. *Circulation*. 1989;80:1652-1659.

26. Chen CH, Nevo E, Fetics B, et al. Estimation of central aortic pressure waveform by mathematical transformation of radial tonometry pressure. Validation of generalized transfer function. *Circulation*. 1997;95:1827-1836.

27. Estensen ME, Beitnes JO, Grindheim G, et al. Altered maternal left ventricular contractility and function during normal pregnancy. *Ultrasound Obstet Gynecol*. 2013;41:659-666.

28. Savu O, Jurcuţ R, Giuşcă S, et al. Morphological and functional adaptation of the maternal heart during pregnancy. *Circ Cardiovasc Imaging*. 2012;5:289-297.

29. Jenkins C, Chan J, Bricknell K, Strudwick M, Marwick TH. Reproducibility of right ventricular volumes and ejection fraction using real-time three-dimensional echocardiography: comparison with cardiac MRI. *Chest*. 2007;131:1844-1851.

30. Stoddard MF, Pearson AC, Kern MJ, Ratcliff J, Mrosek DG, Labovitz AJ. Influence of alteration in preload on the pattern of left ventricular diastolic filling as assessed by Doppler echocardiography in humans. *Circulation*. 1989;79:1226-1236.

31. Firstenberg MS, Greenberg NL, Main ML, et al. Determinants of diastolic myocardial tissue Doppler velocities: influences of relaxation and preload. *J Appl Physiol*. 2001;90:299-307.

32. Smith SA, Morris JM, Gallery EDM. Methods of assessment of the arterial pulse wave in normal human pregnancy. *Am J Obstet Gynecol*. 2004;190:472-476.

33. Ronnback M, Lampinen K, Groop P, Kaaja R. Pulse wave velocity in currently and previously preeclamptic women. *Hypertens Pregnancy*. 2005;24:171-180.

KEY WORDS arterial compliance, pregnancy, strain imaging, three-dimensional echocardiography

APPENDIX For a supplemental appendix with the echo calculations and the applanation tonometry measures, please see the online version of this paper.