Pregnancy is a physiological state that allows characterization of cardiac morphological and physiological adaptation of the human heart to chronic increase in preload and afterload. In addition, this characterization allows clinicians to detect pathological cardiac disease during early stages. Prior echocardiographic studies have described an increase in cardiac dimensions and changes in systolic and diastolic function during normal human pregnancy; however, the studies have been limited by cross-sectional design. It is important to develop uniformity in echocardiographic methodology, gestational age, and equipment and data collection when evaluating serial changes in pregnancy. Owing to the strong influence of age, ethnicity, and height on cardiac output and echo Doppler parameters, including tissue Doppler velocities, it is important to study serial changes in these parameters in the same cohort at each trimester of pregnancy and then in the postpartum state, to evaluate changes in cardiac structure and function during pregnancy and if and when the physiologic adaptation of the heart returns to normal. The high dropout rate during serial evaluation in pregnancy, especially during the postpartum state, makes such studies more challenging. Normal pregnancy-induced cardiovascular changes include an increase in stroke volume, cardiac output, and a decrease in peripheral vascular resistance. In this issue of Circulation: Cardiovascular Imaging, Savu et al1,2 ought to be congratulated on their collaborative effort at 2 centers in collecting important data in a prospective study of normal pregnant women defining normal morphological changes in the heart during normal pregnancy. The authors still had a 38% dropout rate for the postpartum scan and compensated for this by collecting data on 10 age- and sex-matched controls. Dropout rate postpartum as high as 73% occurred in earlier studies of similar nature.

The article by Savu et al provides additional insights into physiological and morphological adaptive changes that occur in the human heart during normal pregnancy. The authors used comprehensive measures of cardiac function with conventional as well as newer methods of assessment by echocardiography. They determined longitudinal segmental myocardial function during pregnancy with tissue Doppler strain and strain rate imaging and radial and circumferential myocardial function by 2D speckle tracking. As described previously, the authors found increases in left ventricular (LV) and right ventricular chamber size as well as in left atrial size and increased LV volumes during both systole and diastole. These changes led to no overall change in LV ejection fraction or in fractional shortening during pregnancy; however, cardiac stroke volume, cardiac output, and stroke work increased and peripheral vascular resistance decreased during gestation. There was an increase in cardiac globularity as measured by sphericity index, as well as in eccentric hypertrophy and LV mass. Significant echocardiographic changes started in the second trimester, and all peaked in the third trimester. These changes recovered in the postpartum state. There was a significant reduction in global and segmental longitudinal deformation both of the left and right ventricle. Unlike changes in cardiac dimensions, mass, and globularity, which became manifest in the second trimester, decrease in longitudinal deformation only occurred in the third trimester, when cardiac volume increase was the highest and normalized in the postpartum state.

Similar changes of decreased long axis LV function at rest; normal LV ejection fraction; increased cardiac output; increased LV wall thickness, size and volumes; and an increase in left atrial size, related to elevation in brain (B-type) natriuretic peptide levels, along with an elevation in E/E′ are described in patients with alcoholic and nonalcoholic cirrhosis: a pathological state sharing increased preload increase of pregnancy. There is also limited data on reversal of these echocardiographic changes, including cardiac index, stroke volume index, LV wall thickness, and chamber size after liver transplantation. Other studies in a canine model and in humans post dialysis have shown load dependency of tissue Doppler velocities. These similar findings reported by Savu et al as well as in other volume overloaded states may suggest that the heart has a universal adaptation response to a chronic volume-overloaded state characterized by an increase in chamber dimensions, an increase in cardiac output, no change in LV ejection fraction, a decrease in LV longitudinal deformation to compensate for an increase in cardiac volumes, and an increase in E/E′ ratio from volume overload.

Tissue Doppler strain and strain rate showed a reduction in global and segmental strain and strain rate in the third trimester. The high dropout rate during serial evaluation in pregnancy, especially during the postpartum state, makes such studies more challenging. The high dropout rate during serial evaluation in pregnancy, especially during the postpartum state, makes such studies more challenging.

Editorial

Serial Echocardiographic Assessment of the Human Heart in Normal Pregnancy

Tasneem Z. Naqvi, MD, FRCP, FACC, FASE; Uri Elkayam, MD, FACC

The article by Savu et al provides additional insights into physiological and morphological adaptive changes that occur in the human heart during normal pregnancy. The authors used comprehensive measures of cardiac function with conventional as well as newer methods of assessment by echocardiography. They determined longitudinal segmental myocardial function during pregnancy with tissue Doppler strain and strain rate imaging and radial and circumferential myocardial function by 2D speckle tracking. As described previously, the authors found increases in left ventricular (LV) and right ventricular chamber size as well as in left atrial size and increased LV volumes during both systole and diastole. These changes led to no overall change in LV ejection fraction or in fractional shortening during pregnancy; however, cardiac stroke volume, cardiac output, and stroke work increased and peripheral vascular resistance decreased during gestation. There was an increase in cardiac globularity as measured by sphericity index, as well as in eccentric hypertrophy and LV mass. Significant echocardiographic changes started in the second trimester, and all peaked in the third trimester. These changes recovered in the postpartum state. There was a significant reduction in global and segmental longitudinal deformation both of the left and right ventricle. Unlike changes in cardiac dimensions, mass, and globularity, which became manifest in the second trimester, decrease in longitudinal deformation only occurred in the third trimester, when cardiac volume increase was the highest and normalized in the postpartum state.

Similar changes of decreased long axis LV function at rest; normal LV ejection fraction; increased cardiac output; increased LV wall thickness, size and volumes; and an increase in left atrial size, related to elevation in brain (B-type) natriuretic peptide levels, along with an elevation in E/E′ are described in patients with alcoholic and nonalcoholic cirrhosis: a pathological state sharing increased preload increase of pregnancy. There is also limited data on reversal of these echocardiographic changes, including cardiac index, stroke volume index, LV wall thickness, and chamber size after liver transplantation. Other studies in a canine model and in humans post dialysis have shown load dependency of tissue Doppler velocities. These similar findings reported by Savu et al as well as in other volume overloaded states may suggest that the heart has a universal adaptation response to a chronic volume-overloaded state characterized by an increase in chamber dimensions, an increase in cardiac output, no change in LV ejection fraction, a decrease in LV longitudinal deformation to compensate for an increase in cardiac volumes, and an increase in E/E′ ratio from volume overload.

Tissue Doppler strain and strain rate showed a reduction in global and segmental strain and strain rate in the third
trimester that returned to normal post pregnancy. While authors’ explanation of reduction in longitudinal deformation being secondary to geometric changes of chamber enlargement, increased volumes, and globularity are plausible, such reduction in longitudinal function in pregnancy may be related to loading changes, given that the deformation is maximum when volume changes are the highest. Usually, changes in cardiac motion in 1 direction are associated with compensatory changes in cardiac motion in the other plane. In this regard, compensatory changes in circumferential or radial direction or in cardiac torsion would be expected. The latter has been shown to increase in diastolic dysfunction of the aging to maintain cardiac output, as well as in first stage of diastolic dysfunction.

Recent developments allow angle-independent assessment of myocardial function by speckle tracking echocardiography that overcomes the limitation of angle dependency of the Doppler derived indices. The authors performed speckle tracking radial and circumferential strain in the radial direction; however, they provided no data on radial strain measurements. We are informed that there were no changes in the radial or circumferential strain during pregnancy. The radial strain and strain rate data varies depending on the type of ultrasound equipment used, as well as off-line software used for analysis. It is important that the authors used the same software (GE Vivid 7 or Vivid 9 and Echo Pac) for measuring radial and circumferential strain as they did for measuring longitudinal strain. There is more consistency in longitudinal measures of 2D myocardial strain among different ultrasound systems.

Another limitation of the study includes lack of reporting of LV diastolic function despite collection of data on mitral inflow and mitral annular tissue Doppler. Prior studies have shown a reduction in mitral inflow E and A ratio and in mitral annular E’, suggesting a mild impairment in LV relaxation during pregnancy.

It is to be noted that, unlike prior studies that have examined women in the third trimester at 33 to 38 weeks of gestation, in this study, the authors studied patients during the third trimester only, during 32 to 33 weeks of gestation. Although the reason for limiting to this time window may have been logistic, they missed out on the more pronounced changes likely to occur in the last 5 to 6 weeks of gestation. Another potential reason could have been the limitation of 2D echocardiographic imaging, particularly that of foreshortening of the heart in late stages of gestation. Even at 32 weeks, some of the shape changes that were observed could have been related to elevation of hemidiaphragm causing LV foreshortening: a problem inherent in 2D imaging that can be overcome by 3D imaging.

The ethnicities of the subjects enrolled in this study is not provided, although it is likely that the majority of study subjects were white. Another limitation is the use of peripheral blood pressure to calculate peripheral vascular resistance and stroke work. Central aortic pressure, as well as vascular stiffness measured noninvasively, that the authors have alluded to in their article, could have been a better measure of blood pressure, peripheral vascular resistance, and of stroke work.

**Future Studies**

We have now begun to understand the complex 3D motion of the heart, which includes circumferential contraction and radial and longitudinal displacement, as well as the wringing motion of cardiac rotation, with the base moving clockwise and the apex moving counterclockwise. Changes in loading conditions have been shown to affect LV torsion, as well as tissue Doppler velocities. More importantly, new methods such as 3D speckle tracking technology have now become available to evaluate the complex motion of the heart in a single beat. This technology is ideally suited to evaluate cardiac motion during pregnancy, wherein changes in motion in 1 direction may be offset by compensatory changes in another direction. Although the data from the current study adds a useful resource for the pregnancy-related changes in the population studied, effects of study population heterogeneity related to race on cardiac changes means that such data should be collected in multiple ethnic populations to develop population-based norms in pregnancy. Ultimately, such data from multiple ethnic populations will prove to be a useful source of reference for the physician in being able to separate out physiological versus pathological changes in pregnancy. Given the high dropout rate expected to occur during and, in particular, after pregnancy, institutional resources to assist with child care and incentives to study subjects may improve dropout rates. Challenges inherent in conducting studies in pregnant women require that investigators from multiple centers partner to conduct larger scale studies in normal and pathological states of pregnancy.

**Disclosures**

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