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EDITORIAL COMMENT

Noninvasive Methods to Track Cardiovascular Hemodynamic Changes in Pregnancy

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Cardiovascular adaptive changes during normal pregnancy have been well studied and include a reduction in systemic vascular resistance and blood pressure and an increase in cardiac output, heart rate, and plasma volume.[1] Changes in myocardial contractility that occur during each trimester and in the postpartum period[1-3] are not as well understood. Unfortunately, there is no easy way to measure contractility clinically. It is well known that left ventricular (LV) ejection fraction (EF) is influenced by changes in preload, afterload, and contractility, which can be further assessed by measuring LV volumes and geometry.

Echocardiography is the principal means of studying cardiovascular structure and function in all patients, regardless of pregnancy status. Adaptive cardiac changes that are easily seen on echocardiography include an increase in chamber size, LV mass, and cardiac output. However, LVEF, fractional shortening, and most parameters of diastolic function do not appear to change significantly during pregnancy.[4,5] Accordingly, a few studies have employed deformation imaging such as strain and strain rate during pregnancy with the goal of detecting subclinical LV dysfunction before an observed decline in LVEF to provide opportunities for early clinical intervention.[6] Similarly, while 3 dimensional (3D) measurements have continuously proven superior to 2 dimensional methods for volume quantitation, in experienced hands,[7] these newer techniques have experienced slow adoption into clinical practice for all patients.

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Strain uses speckle tracking to "track" myocardial deformation during contraction and relaxation. "Speckles" are acoustic markers generated by the myocardium and followed in their displacement during the cardiac cycle. Negative strain values indicate shortening or compression, while positive values indicate elongation. By averaging various regional strains, the global longitudinal strain (GLS) can be calculated, which can detect early subendocardial longitudinal damage such as in ischemia. Normal GLS values range from −18% to 25% in healthy individuals, with variability in software and suppliers, as well as age and sex.[8,9] Even less information and more variability are observed regarding normative values of GLS throughout gestation and in the postpartum period.

Strain rate measures the deformation change over time and assesses contractility while strain analyzes regional EF. Increased preload increases strain at all levels of wall stress, while increased afterload reduces strain. In contrast, strain rate is thought to be less impacted by changes in preload and afterload.

Any assessment of systolic function must take systolic arterial pressure into account. Arterial applanation ("to flatten") tonometry ("measuring of pressure") is a noninvasive, reproducible method to evaluate aortic pressure. This was inspirated by ocular tonometry to indirectly assess intraocular pressure by compressing a specified area of the cornea. Radial artery applanation (AT) is performed by placing a hand-held tonometer (strain gauge pressure sensor) over the radial artery and applying mild pressure to partially flatten the artery to assess central pulse pressure.[10]

Aortic stiffness can be determined by pulse wave velocity (PWV) to assess central aortic pressures. PWV is the pulse wave distance between the carotid and femoral arteries divided by the time delay

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between the recorded pulse waves. PWV can measure the stiffness in the carotid-radial (muscular) and carotid-femoral (elastic) parts of the arterial tree. An increase of PWV results in earlier reflection of the pulse wave reaching the heart in late systole, increasing systolic blood pressure (increasing cardiac workload) and is referred to as augmentation and expressed as augmentation index.[11] Few studies have explored the clinical application of this noninvasive tool to assess hemodynamic changes during pregnancy. A cross-sectional study by Macedo et al[12] of 193 females with normal singleton pregnancies compared to 23 nonpregnant controls found pregnant women to have lower mean arterial pressure and augmentation index reaching its nadir at mid pregnancy. The pulse wave velocity did not change significantly with gestation.

In view of the above, in this issue of *JACC: Advances* Naqvi et al[13] set out to evaluate normal cardiovascular adaptive changes using echocardiography and applanation tonometry in 45 healthy, predominantly Hispanic pregnant patients. Serial 2 dimensional and 3D echocardiography including speckle tracking strain and radial artery AT were performed during each trimester of pregnancy and again postpartum. The authors found that the LV and right ventricular end diastolic and systolic volumes in each trimester increased when compared to studies performed postpartum. Left atrial volume increased in the 2nd and 3rd trimesters, left atrial contraction velocity increased in the 3rd trimester, and pulmonary vein systolic filling velocity, throughout pregnancy. Most notably, they found that several markers increased during pregnancy, including left ventricular, right ventricular, and left atrial strain rates. Using arterial AT, they demonstrated an increase in vascular compliance likely due to vasodilatation of peripheral vessels and expansion of blood volume and reduced aortic systolic augmentation index resulting in a decrease in afterload. All the above changes reversed postpartum.

Can the techniques of speckle imaging and AT provide insight into those patients most at risk for adverse pregnancy outcomes and future maternal cardiovascular disease? The use of strain for prognostic information was performed prospectively in 89 female patients in the Investigations of Pregnancy Associated Consortium; a reduced GLS was associated with an increase in the composite outcome of death, heart transplant, left ventricular assist device, and persistent LVEF $<$50% at 1 year.[14] Bortnick et al[15] evaluated 53 patients with peripartum cardiomyopathy; 11 of 13 with strain imaging had persistently mild and severely abnormal GLS even when LVEF recovered. In a study of 191 high-risk pregnant patients using arterial AT, 14 (7.3%) developed preeclampsia. First-trimester 1 m/s increase in carotid-femoral PWV was associated with 64% increased odds for preeclampsia, and a 1-millisecond increase in time to wave reflection was associated with 11% decreased odds for preeclampsia.[16] The area under the curve of arterial stiffness, blood pressure, ultrasound indices, and angiogenic biomarkers was 0.83 (95% CI: 0.74-0.92), 0.71 (95% CI: 0.57-0.86), 0.58 (95% CI: 0.39-0.77), and 0.64 (95% CI: 0.44-0.83), respectively. With a 5% false-positive rate, blood pressure had a sensitivity of 14% for preeclampsia and 35% for arterial stiffness. Suggesting perhaps that female patients who develop hypertensive disorders of pregnancy may have increased arterial stiffness, as detected by PWV, before demonstrating any clear signs of hypertensive disorders of pregnancy.

This important study by Naqvi et al[13] reports the practical use and possible normative values of more sophisticated markers of cardiac systolic function, contractility, and systemic vascular resistance in healthy, pregnant individuals. Strain rate offers a promising approach for the detection of cardiac dysfunction earlier in pregnancy, which may allow for closer surveillance and intervention to prevent adverse pregnancy outcomes. Similarly, routine use of radial AT tonometry to monitor systemic vascular resistance may provide early insight into whether a pregnant individual's cardiovascular system is adapting to the pregnancy as expected. This noninvasive and safe technology can be applied to the widely available existing infrastructure of echocardiography to broaden the opportunities to detect abnormal cardiovascular adaptation to pregnancy and, in turn, provide earlier intervention.

One limitation of the study by Naqvi et al[13] is the cohort size, although this limitation is quite common in original investigations in cardio-obstetrics. Another limitation is the number of subjects lost to follow-up. In addition, the baseline left ventricular strain and baseline right ventricular strain were less negative than expected, which may limit the internal validity of the study. As the authors mention, 3D techniques and strain and strain rate measurements are not incorporated in the standard protocol in all echocardiography labs, and likewise, AT is not a widely used tool, which may limit the external applicability of these results. However, the study provides support for expanding the use of these techniques.

An important next step is to assess these same echocardiographic and tonometry measurements in those individuals who experience cardiovascular complications of pregnancy, such as hypertensive disorders of pregnancy, peripartum cardiomyopathy, and gestational diabetes, which are all known to negatively impact maternal cardiovascular health.[17] Perhaps improved screening with these measures resulting in earlier treatment and intervention could prevent some of the long-term implications of these disorders. This article offers a critical foundation of normative data from which to launch the investigation of multiple important questions to continue to broaden the understanding of cardiovascular disease during pregnancy.

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