

Subclinical Right Ventricular Dysfunction by Strain Analysis Refining the Targets of Echocardiographic Imaging in Systemic Sclerosis

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The peculiar shape of the right ventricle (RV), its position within the chest, and the thinness of its free wall have always represented a formidable challenge for the assessment of RV size and function by conventional 2-dimensional echocardiography. Over time, a large number of 2D echocardiography and Doppler parameters have been proposed to describe RV geometry and function.^{1,2} However, most of them are limited by geometric assumptions about RV shape, load dependency, or suboptimal reproducibility, resulting in a limited contribution of conventional echocardiography to the understanding of the role played by the RV in many clinical conditions.

See Article by Mukherjee et al

In the last decade, the advent of 2D speckle-tracking echocardiography (2DSTE) has fueled the application of strain imaging to measure the RV myocardial deformation, particularly for an early detection of subclinical myocardial dysfunction, when global ventricular function indices are still normal. The possibility to derive strain parameters from conventional gray-scale images with excellent reproducibility and the relative ease of use of the technique have encouraged researchers to apply 2DSTE for elucidating the extent of RV involvement in a wide variety of cardiac and noncardiac conditions. A PubMed search found >800 articles published on RV strain imaging by echocardiography since 2008.

In this issue of *Circulation: Cardiovascular Imaging*, Mukherjee et al³ from the Johns Hopkins University School of Medicine report on the ability of 2DSTE longitudinal strain to detect occult abnormalities in regional and global myocardial function of RV free wall in patients with systemic sclerosis (SSc). Conventional 2DE parameters of RV function (eg, tricuspid annular plane systolic excursion and fractional area change) were similar in patients with SSc versus age- and sex-matched controls, whereas RV free wall longitudinal strain (RVFWLS) was found to be significantly impaired in patients with SSc, regardless of pulmonary systolic pressure and SSc phenotype. Moreover, the investigators identified a peculiar

regional strain pattern in SSc group, with decreased strain magnitude in the apical and mid segments and increased strain magnitude in the basal segments of the RV free wall. Thus, RVFWLS seems promising in allowing clinicians to identify subclinical RV myocardial impairment in patients with SSc. If these results are confirmed by future studies, evidence of occult RV dysfunction by RVFWLS assessment may prompt for a more intense cardiological follow-up or early treatment of patients with SSc, to avoid or delay the development of overt RV failure.

However, the anatomic substrate and the pathophysiology of impaired RVFWLS with altered regional pattern in patients with SSc remain to be clarified. One may hypothesize 2 major contributions to RV impaired performance in patients with SSc: higher pulmonary load because of vessel stiffness/sclerosis or primary intrinsic myocardial dysfunction. Mukherjee et al³ deserve credit for evaluating RVFWLS together with RV systolic pressure and pulmonary vascular resistance, as noninvasive indices of RV afterload. However, pulmonary vascular resistance reflects the afterload to a steady flow, not to pulsatile flow. Other parameters, including both static and dynamic pulsatile components (such as pulmonary impedance and compliance), may be useful to rule out early alterations in pulmonary vascular stiffness in SSc patients with pulmonary vascular resistance and pulmonary pressures within normal ranges. Yet, these parameters require invasive measurements, and their echocardiographic assessment is infrequent and less robust. Hemodynamic data suggested that RV impairment in SSc may be actually because of intrinsic myocardial dysfunction, rather than enhanced pulmonary vascular resistive and pulsatile loading, and reflects RV inability to compensate for the increased afterload.⁴ Delayed enhancement cardiac magnetic resonance imaging would help to identify the presence of structural abnormalities of the RV free wall myocardium (such as fibrosis) that may explain the abnormal regional strain pattern in patients with SSc.

In general, RVFWLS is regarded as an index of RV myocardial function only. In healthy subjects, left ventricular longitudinal strain and right atrial longitudinal strain were identified as correlates of RV longitudinal strain, suggesting the capability of 2DSTE to evaluate the functional coupling of the RV with the left ventricle or right atrium.⁵ It would be extremely interesting to verify if the same relationships occur also in systemic conditions such as SSc, known to potentially affect both RV and left ventricular myocardium.

An important aspect is the generalizability of the results of this study. Despite the fact that RV myocardial deformation analysis by 2DSTE has demonstrated prognostic value in different cardiovascular conditions,⁶⁻⁸ the technique is far from being standardized. To date, different ultrasound

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manufacturers and software developers have used different approaches (ie, definitions of the region of interest and of strain parameters) to 2DE image postprocessing to obtain strain and strain-rate values. The RVFWLS values reported by Mukherjee et al³ in their control subjects are significantly lower than those reported in the literature.^{5,9} However, they used a novel vendor-independent software package (EchoInsight, Epsilon Imaging, Ann Arbor, MI) to measure RVFWLS, whereas the large majority of investigators who applied RVFWLS for RV analysis used a different software (EchoPac, GE Vingmed, Horten, Norway).^{2,5,9} In addition, technical details such as the acquisition of the RV view (standard apical 4-chamber versus RV-focused apical 4-chamber view) and the way RV longitudinal strain is defined and calculated (ie, including or not including the interventricular septum) may significantly affect its values.⁵ Because RV longitudinal strain measured by 2DSTE is emerging as a powerful tool to detect subclinical RV myocardial dysfunction and assess patient prognosis in a variety of cardiac and noncardiac conditions,¹⁰ the European Association of Cardiovascular Imaging/American Society of Echocardiography/Industry Task Force to standardize deformation imaging^{11,12} has undertaken the initiative of standardizing the 2DSTE technique and parameters for RV analysis.

Finally, RV longitudinal strain is a parameter, which measures only the shortening of the RV along the base-to-apex direction, which is a consequence of the contraction of the longitudinal myocardial fibers in the subendocardial layer. However, RV free wall contains also a superficial layer of myocardial fibers that are circumferential and contribute to RV pump function. Indeed, there are multiple mechanisms involved in the overall RV pump function: (1) contraction of the longitudinal fibers, which draws the tricuspid valve toward the apex; (2) inward movement of the RV free wall that produces a bellows effect; (3) bulging of the interventricular septum into the RV during left ventricular contraction; and (4) circumferential contraction of the RV outflow tract. In spite of the fact that the longitudinal excursion is much larger (around 20–22 mm) than the transversal displacement (around 4–5 mm), the latter involves the large surface of the RV free wall and contributes significantly to RV output. Moreover, previous studies have shown that the relative contributions of these mechanisms to global RV pump function vary under different conditions. For example, in patients with RV pressure overload, the hypertrophied RV myocardial fibers change their spatial orientation and become more circumferential.^{13,14} As a consequence, in patients with pulmonary hypertension, circumferential and radial shortening increase their contribution to the RV pump function compared with normal subjects.^{15,16} Ideally, a comprehensive assessment of the different components of RV myocardial deformation would improve our understanding of the pathophysiology of RV dysfunction in different cardiac conditions. However, this is challenging, if not impossible, to achieve using conventional echocardiography.

The development of 3-dimensional echocardiography enabled the simultaneous assessment of RV mechanics in different dimensions (ie, longitudinal, radial, circumferential, and a combination of longitudinal and circumferential

shortening called area strain) by echocardiography, similar to cardiac magnetic resonance.^{17,18} In patients with pulmonary hypertension, significant correlation with RV ejection fraction was demonstrated for 3D RV longitudinal strain¹⁸ and RV area strain.¹⁹ Importantly, the latter was a strong independent predictor of death, suggesting the superiority of 3D echocardiography–derived area strain over the other parameters of RV deformation.¹⁹ However, only small populations have been investigated to date using 3D echocardiography–derived RV strain parameters, and their reference values are currently unknown.

The study by Mukherjee et al³ adds another important piece to the mounting evidence on the superiority of 2DSTE-derived strain as a sensitive marker of subclinical myocardial dysfunction, which conventional echocardiographic measures are unable to identify. The clinical importance of the subtle changes in RV myocardial function for an early diagnosis and outcome of patients with SSc remains to be established.

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