Comprehensive Assessment of Right Ventricular Function in Patients with Pulmonary Hypertension with Global Longitudinal Peak Systolic Strain Derived from Multiple Right Ventricular Views

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Background: Right ventricular (RV) function is a strong predictor of mortality in pulmonary hypertension (PH), but two-dimensional (2D) echocardiography–derived assessments of RV function that could aid in risk assessment and management of patients with PH are of limited utility. RV longitudinal peak systolic strain (RVLS) derived from 2D speckle-tracking echocardiography is a relatively novel method for quantifying RV function but typically is derived from a single apical four-chamber view of the right ventricle and may have inherent limitations. The objective of this study was to determine the utility of regional and global RVLS calculated from multiple views of the right ventricle to comprehensively assess RV function in a cohort of patients with PH.

Methods: Regional and global RVLS were obtained from multiple views of the right ventricle (centered on the right ventricle–focused apical position) in 40 patients with PH, defined as a mean pulmonary artery pressure $\geq$ 25 mm Hg, most of whom also had pulmonary capillary wedge pressures $\leq$ 15 mm Hg and were thus defined as having pulmonary arterial hypertension. This was compared with other 2D echocardiography–derived parameters of RV function and functional parameters.

Results: Global RVLS calculated from multiple views had a superior correlation with 6-min walk distance compared with other parameters of RV function, including tricuspid annular plane systolic excursion, RV myocardial performance index, and fractional area change. Although global RVLS calculated from multiple views displayed a similar correlation with 6-min walk distance as global RVLS calculated from a single four-chamber view, analysis of regional strains provided by multiple views identified distinct patterns of RV dysfunction, consisting of global, free wall, or septal dysfunction, that were associated with specific clinical characteristics.

Conclusions: Global RVLS derived from multiple right ventricle–focused views yields a comprehensive quantitative assessment of regional and global RV function that correlates moderately with functional parameters and may be useful in the assessment of PH. Distinct patterns of regional RV dysfunction are associated with different clinical characteristics. (J Am Soc Echocardiogr 2014;■:■-■.)

Keywords: Pulmonary hypertension, Right ventricular function, Speckle-tracking echocardiography, Strain, 6-minute walk distance

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Pulmonary arterial hypertension (PAH), a subset of pulmonary hypertension (PH), is a disease of the pulmonary vasculature that leads to right ventricular (RV) dysfunction and failure. RV function is of critical importance in the prognosis of PAH. Hemodynamic parameters, including right atrial pressure and cardiac index, both reflecting RV function,[1] and pro–brain natriuretic peptide, associated with right heart failure, are all important prognostic biomarkers.[2] Patients with PAH are routinely followed using echocardiography, but the conventional two-dimensional (2D) echocardiographic assessment of the right ventricle does not include a clear quantitative assessment of function but rather a quantification of RV dimensions and a qualitative assessment of contractility.[3] This is due both to the complex geometry of the right ventricle and a poor understanding of its mechanical functioning compared with that of the left ventricle.[4] Quantitative assessments of

Abbreviations

AP4 = Four-chamber right ventricular equivalent view

AP3 = Three-chamber right ventricular equivalent view

AP2 = Two-chamber right ventricular equivalent view

FAC = Fractional area change

LV = Left ventricular

MPI = Myocardial performance index

PA = Pulmonary artery

PAAT = Pulmonary artery acceleration time

PAH = Pulmonary arterial hypertension

PH = Pulmonary hypertension

REVEAL = Registry to Evaluate Early and Long-Term Pulmonary Arterial Hypertension Disease Management

RV = Right ventricular

RVLS = Right ventricular longitudinal peak systolic strain

6MWD = 6-min walk distance

TAPSE = Tricuspid annular plane systolic excursion

2D = Two-dimensional

RV function would aid in clinical decision making, as echocardiographic assessments of RV function are routinely used to guide the level of aggressiveness of PAH therapy.[5]

To this end, a number of 2D echocardiography–derived parameters for RV functional assessment, such as tricuspid annular plane systolic excursion (TAPSE), RV fractional area change (FAC), and RV myocardial performance index (MPI), have been proposed, but all have inherent strengths and weaknesses[3] (Figure 1). RV longitudinal peak systolic strain (RVLS) is a relatively novel approach for quantifying RV function and, when calculated using 2D speckle-tracking echocardiography, is angle independent and yields a quantitative assessment of RV systolic function. Moreover, recent studies have demonstrated relationships between RVLS and outcomes and response to therapy in patients with PAH.[6-9] However, a continued limitation of RVLS from a single RV view is that it does not yield a truly "global" view of RV function.[3] Recently, an approach for a global assessment of RV function has been developed that uses 3 right ventricle–focused views analogous to their apical views of the left ventricle,[10] to allow a full reconstruction of the right ventricle in an 18-segment or a 17-segment model (Figure 2) with a calculation of a true "global RVLS." In this work, we compared global RVLS between normal controls and patients with PH, correlated global RVLS with other parameters of RV function (including TAPSE, MPI, and FAC) and with functional status as assessed by 6-min walk distance (6MWD), and identified patterns of regional RV dysfunction in patients with PH.

METHODS

Study Population

Clinically indicated echocardiographic studies incorporating the three views of the right ventricle (Figure 1) were performed on 42 consecutive patients at Duke University Medical Center (Durham, NC) with diagnoses of PH, defined as a mean pulmonary artery (PA) pressure ≥ 25 mm Hg, between May and December 2012. These patients had diagnoses of PAH (mean PA pressure ≥ 25 mm Hg and PCWP ≤ 15 mm Hg),[11] exercise-induced PAH (normal mean PA pressure at rest but mean PA pressure ≥ 30 mm Hg with exercise),[12] or PH out of proportion to diastolic dysfunction (mean PA pressure ≥ 25 mm Hg, PCWP > 15 mm Hg, and pulmonary vascular resistance significantly higher than 3 Wood units).[11] Of these patients, one did not have images of sufficient quality for strain calculations, while one underwent repeat heart catheterization that demonstrated no evidence of PH on no medical therapy. The remaining 40 patients with PH, along with a group of 40 previously described controls,[10] were included in our final analysis. This normal population was a cohort of young volunteers (mean age, 28.9 ± 9.1 years) without any history of cardiovascular disease, with a minimum age of 18 years at the time of the study, normal echocardiographic findings, including anatomy, left ventricular (LV) ejection fraction ≥ 50%, RV FAC ≥ 35%, and TAPSE ≥ 16 mm. Exclusion criteria for the control population included any abnormal echocardiographic findings or prolonged QRS duration. Subjects used as normal controls provided informed consent for research echocardiography. For patients with PH whose images were obtained during clinically indicated echocardiographic assessments, a waiver of consent was approved for the Duke Echocardiography Lab Database by the Duke University Medical Center Institutional Review Board. This study was approved by the Duke University Medical Center Institutional Review Board.

Echocardiography

All echocardiographic studies were performed using a Vivid E9 scanner with a 3.5-MHz probe (GE Vingmed Ultrasound AS, Horten, Norway). A full standard echocardiographic examination, including grayscale images optimized for 2D strain analysis (50–90 frames/sec) including three right ventricle–focused apical views,[10] was performed. The three apical RV views were equivalent to the imaging planes of the two-chamber, three-chamber, and four-chamber LV apical views with the transducer angled rightward (Figure 1). View optimization often required repositioning of the transducer toward the left anterior axillary line. The resulting four-chamber-equivalent view has four chambers (right atrium and ventricle, left ventricle and atrium), the two-chamber-equivalent view has three (right atrium, right ventricle, and RV outflow tract), and the three-chamber equivalent view has two chambers (right atrium and ventricle) (Figures 2A–2C).

All echocardiographic examinations were performed either on the same day as a 6-min walk test or within 3 months of 6-min walk test in patients with PH. Six-minute walk tests were not done in three patients with PH and were not performed in any of the normal controls. Right heart catheterization was typically not performed near the time of echocardiography, except in those patients with new diagnoses of PH. Offline analysis was performed using EchoPAC PC version BT11 (GE Vingmed Ultrasound AS) by a single experienced reader, and analysis was confirmed by a separate experienced reader; interreader variability for this methodology has been shown to be low, with intraobserver variability (2 ± 6%) and interobserver variability (1 ± 9%) for global peak strain (percentage mean difference [bias] ± coefficient of variation).[10]

2D Echocardiography–Derived Parameters of RV Function

TAPSE was determined from an M-mode through the lateral tricuspid annulus by calculating the amount of longitudinal motion of the annulus at peak systole[13] (Figure 1A). PA acceleration time (PAAT) was calculated from a spectral Doppler image obtained by placing a pulsed Doppler sample volume at the pulmonary valve annulus. PAAT was calculated as the time from the onset of systolic pulmonary arterial flow to peak flow velocity[14] (Figure 1B). RV MPI was calculated as the RV isovolumic time divided by the ejection time using the pulsed Doppler method.[3] Isovolumic time was calculated as the duration of tricuspid regurgitation from continuous-wave Doppler across the tricuspid valve minus the ejection time from a single representative beat. Ejection time was calculated as the duration of RV