Speckle-Tracking Echocardiographic Measures of Right Ventricular Function Correlate With Improvement in Exercise Function After Percutaneous Pulmonary Valve Implantation

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Background: Speckle-tracking echocardiographic (STE) measures of right ventricular (RV) function appear to improve after transcatheter pulmonary valve implantation (TPVI). Measures of exercise function, such as ventilatory efficiency (the minute ventilation [V_E]/carbon dioxide production [V_{CO_2}] slope), have been shown to be prognostic of mortality in patients who may require TPVI. The aim of this study was to evaluate the correlation between STE measures of RV function and changes in V_E/V_{CO_2} after TPVI.

Methods: Speckle-tracking echocardiography and cardiopulmonary exercise testing were performed at baseline and 6 months after TPVI in 24 patients from four centers. Conventional echocardiographic measures of RV function were also assessed. Echocardiographic and exercise stress test results were interpreted by single blinded observers at separate core laboratories.

Results: All patients demonstrated relief of pulmonary regurgitation and stenosis after TPVI. Improvements in RV longitudinal strain (−16.9 ± 3.5% vs −19.7 ± 4.3%, $P < .01$) and strain rate (−0.9 ± 0.4 vs. −1.2 ± 0.4 s^{-1}, $P < .01$) were noted. The V_E/V_{CO_2} slope improved (32.4 ± 5.7 vs 31.5 ± 8.8, $P = .03$). No other significant echocardiographic or exercise changes were found. On multivariate regression, the change in V_E/V_{CO_2} was independently associated with change in RV longitudinal early diastolic strain rate ($P < .001$) and tricuspid A velocity ($P < .001$). Preintervention RV longitudinal strain was found to be a predictor of change in V_E/V_{CO_2} after TPVI ($r = -0.60$, $P < .001$).

Conclusions: STE measures of RV function appear to hold the potential for use as predictors of improved outcomes in patients requiring TPVI. Future studies should directly assess the prognostic significance of STE measures of RV function in this population. (J Am Soc Echocardiogr 2015;28:1036-44.)

Keywords: Speckle-tracking echocardiography, Transcatheter pulmonary valve implantation, Congenital heart disease

Patients with congenital heart disease requiring right ventricular (RV)–to–pulmonary artery (PA) conduits frequently develop free pulmonary regurgitation, severely dilated right ventricles, and decreased ventricular function over time.[1] Measures of ventilatory efficiency derived from exercise testing, such as the minute ventilation [V_E]/carbon dioxide production [V_{CO_2}] slope, have been shown to be prognostic of mortality in these patients and are improved after pulmonary valve replacement secondary to improvement in effective stroke volume.[2-7]

The relationship between echocardiographic measures of ventricular function and these exercise derived surrogates of outcome are unknown. These patients show little improvement in ventricular function when assessed using traditional echocardiographic markers.[8] Speckle-tracking echocardiographic (STE) measures of ventricular function have been

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Abbreviations

AT = Anaerobic threshold

COMPASSION = Congenital Multicenter Trial of Pulmonic Valve Regurgitation Studying the SAPIEN Interventional Transcatheter Heart Valve

LV = Left ventricular

MRI = Magnetic resonance imaging

PA = Pulmonary artery

RV = Right ventricular

STE = Speckle-tracking echocardiographic

TPVI = Transcatheter pulmonary valve implantation

V_{CO_2} = Carbon dioxide production

V_E = Minute ventilation

V_{O_2} = Oxygen uptake

shown to be more sensitive than conventional measures in many disease processes, including in those patients undergoing transcatheter pulmonary valve implantation (TPVI).[9-12] However, the relationship between STE measures of RV function before and after TPVI and exercise measures is unknown in this population. The objective of this study was to determine the usefulness of assessing RV STE measures of function by assessing their relationships with changes in cardiopulmonary exercise function both before and after TPVI. We hypothesized that RV STE measures of cardiac function would correlate with changes seen in exercise function after TPVI.

METHODS

This was a retrospective, secondary analysis of data collected during the Congenital Multicenter Trial of Pulmonic Valve Regurgitation Studying the SAPIEN Interventional Transcatheter Heart Valve (COMPASSION) trial. COMPASSION is a prospective, nonrandomized, multicenter study whose aim is to assess the safety and efficacy of the SAPIEN transcatheter heart valve (Edwards Lifesciences, Irvine, California) for the treatment of dysfunctional RV-PA conduits. Early phase 1 results have shown good feasibility, effectiveness, and safety.[13] Patients included in COMPASSION were enrolled prospectively from four participating centers. Inclusion criteria were (1) weight $\geq$ 35 kg; (2) in situ conduit diameter of 16 to 24 mm; (3) moderate or severe pulmonary regurgitation, defined as grade 3+ pulmonary regurgitation on echocardiography and/or RV-PA conduit obstruction with a mean gradient of >35 mm Hg; and (4) peak oxygen uptake (V_{O_2}) or V_E/V_{CO_2} < 70% of the predicted value. Informed consent was obtained from all potential subjects and/or their legal guardians. The institutional review board at each participating institution approved the trial.

Procedure

The protocol for valve implantation has been reported previously and is summarized here for convenience.[13] Procedures were performed under general anesthesia with biplane fluoroscopic guidance. The minimum diameter of the conduit was assessed by angiography. Risk for coronary compression was assessed with aortic root angiography or selective coronary angiography with simultaneous inflation of a noncompliant balloon in the conduit. Prestenting of the conduit with a bare-metal stent was performed. A 23- or 26-mm SAPIEN transcatheter heart valve was then implanted over a stiff guidewire and expanded via balloon inflation.

Echocardiographic Protocol

Analysis of echocardiograms submitted to the COMPASSION core laboratory was performed. Echocardiograms were acquired by experienced sonographers at each center following a protocol that included a complete set of standardized views to evaluate ventricular function. The image acquisition protocol was developed by the echocardiography core laboratory. On-site or Web-based training to the local SAPIEN TPVI sites was provided. Echocardiograms used for this analysis were obtained at baseline before TPVI, before discharge after TPVI, at 30-day follow-up, and at 6-month follow-up. All studies were performed under baseline physiologic conditions, not under the influence of anesthesia. Measures were recorded at end-expiration with quiet respiration. Pre-TPVI echocardiograms were obtained $\leq$1 week before TPVI. Echocardiograms were in Digital Imaging and Communications in Medicine format. All measurements were made offline by a single reviewer and averaged over three beats. Pulmonary regurgitation was graded from 0 to 4 on the basis of the jet width/annulus ratio and flow reversal in the branch pulmonary arteries as follows: 0 = no regurgitation, 1 = jet width/annulus ratio < 0.25, 2 = jet width/annulus ratio between 0.25 and 0.5, 3 = jet width/annulus ratio between 0.5 and 0.7, and 4 = jet width/annulus > 0.7 with flow reversal in the branch pulmonary arteries.[14,15] Tricuspid valve regurgitant orifice area was calculated from the apical four-chamber and parasternal short-axis windows.

Two-Dimensional, Spectral, and Tissue Doppler Measures of Myocardial Function

From a standard apical four-chamber window, RV fractional area change was defined as [(end-diastolic area − end-systolic area)/end-diastolic area] × 100. Tricuspid annular plane systolic excursion was obtained, and indexed tricuspid annular plane systolic excursion was calculated as [(RV end-diastolic length − RV end-systolic length)/RV end-diastolic length]. Pulsed Doppler tissue imaging S′ velocities at the tricuspid valve annulus and interventricular septum were obtained from the apical four-chamber view.

To evaluate diastolic function, Doppler velocities of transtricuspid flow (E and A) were obtained from an apical four-chamber window. Tissue Doppler velocities of the tricuspid annulus and interventricular septum (E′ and A′) were obtained. Derived ratios (E/A and E/E′) were calculated.

STE Measures of Myocardial Function

Speckle-tracking was performed as a secondary analysis of echocardiograms submitted to the COMPASSION echocardiography core laboratory. A single, blinded observer performed offline analysis of Digital Imaging and Communications in Medicine images using vendor-independent software (2D Cardiac Performance Analysis version 3.0; TomTec Imaging Systems GmbH, Munich, Germany). Myocardial motion was tracked through the cardiac cycle, calculating myocardial deformation from echogenic speckles in the B-mode image. The endocardium and epicardium were manually traced in the right ventricle from the lateral tricuspid annulus to the septal component of the tricuspid annulus (Figure 1). The septum was included because of its importance to global RV function.[16] End-systole was defined as end-ejection of the pulmonic valve for the right ventricle and of the aortic valve for the left ventricle using spectral Doppler. Speckle-tracking measures of deformation from the apical four-chamber view included peak longitudinal strain, strain rate, and early diastolic strain rate. Left ventricular (LV) measures of deformation from the apical four-chamber view were also assessed. Global deformation measurements were calculated as averages of six segments. Tracking was visually assessed, and deformation curves were not