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Effects of Transcatheter Pulmonary Valve Replacement on the Hemodynamic and Ventricular Response to Exercise in Patients With Obstructed Right Ventricle-to-Pulmonary Artery Conduits

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Objectives This study sought to investigate the effects of exercise on the right ventricle in patients with an obstructed right ventricular outflow tract (RVOT) conduit before and after transcatheter pulmonary valve replacement (TPVR).

Background Conventionally, assessment of the right ventricle in congenital heart disease patients with dysfunctional RVOT conduits is performed at rest. However, this does not reflect dynamic exercise changes.

Methods Exercise stress echocardiography (ESE) before and 6 months after TPVR was performed. ESE protocol included measurement of rest and immediate post-exercise RVOT maximal instantaneous gradients (MIGs), right ventricular (RV) systolic pressure, 2-dimensional fractional area change, and global longitudinal strain (GLS).

Results Twenty patients with RVOT conduit obstruction (median age, 18 years), the majority ($n = 14$) with tetralogy of Fallot, completed the study. Pre-TPVR, the median resting MIG across the RVOT was 53 mm Hg (23 to 95 mm Hg) and increased to 93 mm Hg (49 to 156 mm Hg; $p < 0.001$) with exercise. After TPVR, the median MIG at rest was 26 mm Hg (6 to 41 mm Hg, and after exercise, it was 45 mm Hg (9 to 102 mm Hg), both significantly lower than before TPVR ($p \leq 0.001$), but there was still a substantial increase in gradient with exercise in many patients. The RV fractional area change, RV GLS, and left ventricular GLS, both at rest and after exercise, were significantly greater after TPVR than before. A greater pre-TPVR exercise-related increase in RV function was associated with improvement in peak Vo_2 after TPVR ($p = 0.01$).

Conclusions In patients with obstructed RVOT conduits, TPVR resulted in significant improvement in conduit stenosis and RV function at both rest and at peak exercise and in exercise cardiopulmonary function. The ability to augment RV function at peak exercise before TPVR was associated with improved exercise capacity 6 months after TPVR. (J Am Coll Cardiol Intv 2014;7:530–42) © 2014 by the American College of Cardiology Foundation

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Right ventricular outflow tract (RVOT) conduits are often used for the treatment of complex congenital heart disease. Over their lifetime, stenosis, regurgitation, or both develop in most conduits (1–3). Until recently, treatment options for RVOT conduit dysfunction were limited to medical management, bare-metal stenting, or surgical conduit replacement. Transcatheter implantation of bare-metal stents predominantly to treat conduit stenosis is an effective alternative to surgery, but leaves a patient with free pulmonary valve regurgitation (4,5). Percutaneous transcatheter pulmonary valve replacement (TPVR), which allows for nonoperative treatment of RVOT obstruction and regurgitation, has emerged as an attractive alternative for extending the functional life span of surgical RVOT conduits (6,7).

Previous studies have evaluated the response of pressure- and volume-overloaded ventricles to TPVR at rest, and resting hemodynamic assessments are typically used to determine candidacy for RVOT intervention and TPVR (7–9). However, the physiological changes encountered during exercise may exacerbate the overloaded ventricular conditions (10,11), and, not surprisingly, patients with RVOT conduits typically manifest symptoms initially during activity. Accordingly, evaluation of hemodynamics and ventricular function in response to exercise may provide novel and important insights into the dynamic physiology of the right and left heart in these patients, as well as further our understanding of the benefits, indications, and limitations of TPVR therapy. However, there are limited data on the ventricular response to exercise in patients with congenital heart disease, and especially for the right heart, in patients with RVOT dysfunction.

Using exercise stress echocardiography (ESE), we sought to characterize the effects of exercise on cardiac performance, focusing on the right ventricle, in patients with congenital heart disease and an obstructed RVOT conduit and to assess the changes in the physiological responses to exercise stress after TPVR.

Methods

Patients and study design. This prospective study was performed at a single institution from March 2010 through August 2011 under a protocol that was approved by the Boston Children's Hospital Committee for Clinical Investigations. For logistical reasons, potential study patients were ascertained during evaluation for TPVR. Patients with a stenotic RVOT conduit (defined as a maximal Doppler gradient ≥20 mm Hg across the conduit on pre-TPVR echocardiogram), with or without pulmonary regurgitation (PR), who underwent ESE as part of the clinical evaluation within 3 months before TPVR, were considered eligible. Patients with a maximal continuous wave flow Doppler gradient <20 mm Hg across the conduit (i.e., those with predominant PR and minimal RVOT obstruction) or those in whom ESE was either not ordered or not possible due to poor imaging windows were excluded. Patients who were able to return to our center for follow-up evaluation and ESE within 4 to 6 months of TPVR were enrolled. All participants provided written informed consent.

Cardiac catheterization. Cardiac catheterization was performed with patients under general endotracheal anesthesia. Right ventricular (RV) systolic pressure and the peak systolic gradient across the RVOT conduit were obtained at the beginning of the procedure, before any intervention, and compared with pre-catheterization noninvasive parameters. TPVR was performed with the Melody valve (Medtronic Inc., Minneapolis, Minnesota) according to standard, previously reported techniques (6,7).

Cardiopulmonary exercise test. Maximal exercise testing was performed using a Bruce protocol on a treadmill or a ramp protocol on an electronically braked cycle ergometer. Equipment was calibrated to the manufacturer's specifications. Treadmill testing was preferred during the ESE protocols to facilitate quick and easy transition to the bed for peak exercise imaging. In patients who could not perform treadmill testing, bicycle ergometry was performed. To maintain consistency, patients were tested using the same exercise mode (treadmill or bicycle) at pre- and post-TPVR studies.

Expired gases were measured during rest and during the exercise protocol. Oxygen uptake (V_{O_2}), carbon dioxide elimination, and minute ventilation were measured. Peak V_{O_2} was defined as the highest V_{O_2} achieved by the subject during the test. The ventilatory anaerobic threshold was measured by the V-slope method when it could be accurately determined. The ventilatory equivalent of carbon dioxide (ratio of minute ventilation to carbon dioxide production) was measured at the anaerobic threshold, and the respiratory exchange ratio (ratio of carbon dioxide production to V_{O_2}) was measured continuously. Values for V_{O_2} and O_2 were indexed to body weight and expressed as a percentage of predicted values for healthy age- and sex-matched subjects, as reported previously (12).

ESE with 2-dimensional strain. Resting and ESE studies were acquired using commercially available ultrasound equipment as a part of the routine imaging evaluation before and after TPVR (Philips iE33, Koninklijke Philips Electronics, Eindhoven, the Netherlands). ESE studies were

Abbreviations and Acronyms

ESE = exercise stress echocardiography
FAC = fractional area change
GLS = global longitudinal strain
IVS = interventricular septum
LV = left ventricular
MIG = maximal instantaneous gradient
PR = pulmonary regurgitation
RV = right ventricular
RVOT = right ventricular outflow tract
TPV = transcatheter pulmonary valve
TPVR = transcatheter pulmonary valve replacement
TTS = time to peak
V_{O_2} = oxygen uptake