Journal of the American College of Cardiology
© 2011 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 57, No. 6, 2011
ISSN 0735-1097/$36.00
doi:10.1016/j.jacc.2010.07.056

Early Versus Late Functional Outcome After Successful Percutaneous Pulmonary Valve Implantation

Are the Acute Effects of Altered Right Ventricular Loading All We Can Expect?

Philipp Lurz, MD,*†‡ Johannes Nordmeyer, MD,*†§ Alessandro Giardini, MD, PHD,† Sachin Khambadkone, MD,† Vivek Muthurangu, MD,* Silvia Schievano, PHD,* Jean-Benoit Thambo, MD,†‖ Fiona Walker,¶ Seamus Cullen,¶ Graham Derrick,† Andrew M. Taylor, MD,*† Philipp Bonhoeffer, MD*

London, United Kingdom; Leipzig and Berlin, Germany; and Pessac, France

Objectives The purpose of this study was to assess the potential of late positive functional remodeling after percutaneous pulmonary valve implantation (PPVI) in right ventricular outflow tract dysfunction.

Background PPVI has been shown to impact acutely on biventricular function and exercise performance, but the potential for further late functional remodeling remains unknown.

Methods Sixty-five patients with sustained hemodynamic effects of PPVI at 1 year were included. Patients were divided into 2 subgroups based on pre-procedural predominant pulmonary stenosis (PS) (n = 35) or predominant pulmonary regurgitation (PR) (n = 30). Data from magnetic resonance imaging and cardiopulmonary exercise testing were compared at 3 time points: before PPVI, within 1 month (early) and at 12 months (late) after PPVI.

Results There was a significant decrease in right ventricle end-diastolic volume early after PPVI in both subgroups of patients. Right ventricle ejection fraction improved early only in the PS group (51 ± 11% vs. 58 ± 11% and 51 ± 12% vs. 50 ± 11%, $p < 0.001$ for PS, $p = 0.13$ for PR). Late after intervention, there were no further changes in magnetic resonance parameters in either group (right ventricle ejection fraction, 58 ± 11% in the PS group and 52 ± 11% in the PR group, $p = 1.00$ and $p = 0.13$, respectively). In the PS group at cardiopulmonary exercise testing, there was a significant improvement in peak oxygen uptake early (24 ± 8 ml/kg/min vs. 27 ± 9 ml/kg/min, $p = 0.008$), with no further significant change late (27 ± 9 ml/kg/min, $p = 1.00$). In the PR group, no significant changes in peak oxygen uptake from early to late could be demonstrated (25 ± 8 ml/kg/min vs. 25 ± 8 ml/kg/min vs. 26 ± 9 ml/kg/min, $p = 0.48$).

Conclusions In patients with a sustained hemodynamic result 1 year after PPVI, a prolonged phase of maintained cardiac function is observed. However, there is no evidence for further positive functional remodeling beyond the acute effects of PPVI. (J Am Coll Cardiol 2011;57:724–31) © 2011 by the American College of Cardiology Foundation

The acute physiological responses to percutaneous pulmonary valve implantation (PPVI) are different in patients with predominant right ventricular outflow tract (RVOT) obstruction compared with those with significant pulmonary regurgitation (PR). After reduction of RV afterload, patients showed an immediate improvement in right ventricle (RV) function and maximal exercise capacity (1–3); however, this is not seen in patients after restoration of PR (3,4). Data on late physiological outcome after percutaneous restoration of RVOT function are scarce. It is unknown whether percutaneous restoration of RVOT function can promote cardiac remodeling beyond the early period after

From the *Cardiovascular Unit, University College London Institute of Child Health, London, United Kingdom; †Cardiorespiratory Unit, Great Ormond Street Hospital for Children, London, United Kingdom; ‡Department of Internal Medicine/Cardiology and Grown Up Congenital Heart Disease, University of Leipzig-Heart Center, Leipzig, Germany; §Department of Congenital Heart Disease and Pediatric Cardiology, German Heart Institute Berlin, Berlin, Germany; ‖Hopital Cardiologique du Haut Leveque, Pessac, France; and the ¶Grown Up Congenital Heart Unit, The Heart Hospital NHS Trust, London, United Kingdom. Dr. Bonhoeffer is a consultant to Medtronic and NuMed and has received honoraria and royalties for the device described. Dr. Taylor has received speaker honoraria for Medtronic and has a research agreement with Siemens. All other authors have reported that they have no relationships to disclose. Drs. Lurz and Nordmeyer contributed equally to this work.

Manuscript received March 25, 2010; revised manuscript received June 16, 2010, accepted July 17, 2010.

intervention, thus improving cardiac function and exercise capacity in the midterm, or whether it simply interrupts the downward spiral of worsening cardiac function, leading to a stabilization of biventricular performance and exercise tolerance.

The aim of this study was to analyze the immediate and 1-year physiological responses to PPVI. In particular, we sought to analyze whether further changes in biventricular function and exercise performance (functional remodeling) occurred after the immediate post-interventional period. For this purpose, we enrolled patients into a prospective study protocol that included magnetic resonance (MR) imaging and cardiopulmonary exercise (CPEX) testing. To avoid a significant confounding effect of restenosis or occurrence of PR, only patients with a sustained hemodynamic result 1 year after PPVI were included in this study.

Methods

Patients and study protocol. To assess the acute and late effects of PPVI on biventricular function and exercise performance, MR imaging and CPEX testing were performed at 3 time points: first, within 1 month before PPVI (before PPVI); second, within 1 month after PPVI (early after PPVI); and third, 12 months after PPVI (late after PPVI).

Patients underwent PPVI according to the clinical and morphological criteria that have been published previously (5–7) and were enrolled in this study from May 2004 through June 2008. For initial inclusion into the study, patients had to fulfill the following criteria: no contraindications to MR imaging or CPEX testing, adequate MR image quality for assessment of ventricular volumes and great vessel blood flow, and symptom-limited maximal CPEX results with a respiratory exchange ratio ≥1.09. To avoid confounding of the data related to nonsustained efficacy of the procedure, patients had to show a sustained hemodynamic result 1 year after PPVI as assessed by echocardiography (no increase in peak RVOT gradient >15 mm Hg and no increase in PR). Only patients with a complete MR imaging and CPEX testing data set at all 3 assessment stages were analyzed. In total, 65 of 107 screened patients met these inclusion criteria. Figure 1 summarizes reasons for exclusion from the study.

Patients were divided into 2 groups according to PR fraction measured on MR imaging to separate patients with predominant pulmonary stenosis (PR fraction ≤25%, n = 35) from those with predominant PR (PR fraction >25%, n = 30). The New York Heart Association (NYHA) functional class was assessed at the same clinical contacts in all patients.

Written informed consent was obtained from patients and parents as appropriate. The ethics committees at the 2 contributing institutions approved the study protocol (Great Ormond Street Hospital for Children and The Heart Hospital, London, United Kingdom).

Abbreviations and Acronyms

- **CPEX** = cardiopulmonary exercise
- **EDV** = end-diastolic volume
- **EF** = ejection fraction
- **ESV** = end-systolic volume
- **MR** = magnetic resonance
- **NYHA** = New York Heart Association
- **PPVI** = percutaneous pulmonary valve implantation
- **PR** = pulmonary regurgitation
- **PS** = pulmonary stenosis
- **RV** = right ventricle
- **RVOT** = right ventricular outflow tract

PPVI. The protocol for valve implantation (Melody, Medtronic, Inc., Minneapolis, Minnesota) has been reported before (5,8–10) and is summarized here briefly for convenience. All implants were performed under general anesthesia. Vascular access was achieved through the femoral vein and artery. Standard right heart catheterization, including pressure measurements and RVOT angiography, was undertaken. Invasive systemic pressures were monitored. Aortic root angiography was performed routinely to assess the proximity of the coronary arteries to the RVOT to avoid possible coronary compression resulting from PPVI. Simultaneous balloon inflation in the RVOT and coronary angiography was performed in patients at risk for coronary obstruction (5,11–13). Very stenotic, tortuous conduits were pre-dilated with high-pressure Mullins balloons (NuMed, Hopkinton, New York) or pre-stented with IntraStent Max LD stents (ev3 Intravascular, Plymouth, Minnesota). After PPVI, pressure measurements and RVOT angiography were performed. Post-dilatation with high-pressure Mullins balloons was performed after PPVI where appropriate.

Echocardiography. All transthoracic echocardiographic studies were performed on a Vivid 7 GE machine (Vingmed, Milwaukee, Wisconsin). As an estimate of RV systolic pressure, the RV-to-right atrium pressure gradient was calculated from the tricuspid regurgitant jet (without addition of right atrial pressure). The peak RVOT gradient was calculated from the continuous-wave Doppler velocity across the RVOT (14). PR was defined qualitatively by color flow Doppler (15).

CPEX testing. CPEX testing was performed on a bicycle ergometer. The work rate increased with a ramp protocol of 10 to 20 W/min to reach exhaustion after approximately 10 min of exercise. Tests were considered to be maximal when they were interrupted because of symptoms like fatigue or dyspnea and a respiratory exchange ratio ≥1.09 was achieved. A 12-lead electrocardiography test was monitored continuously and blood pressures were recorded every 2 min during CPEX testing. Breath-by-breath respiratory gas exchange measurements were recorded throughout the test. Peak oxygen uptake was defined as the average of the values obtained in the last 20 s of exercise. Anaerobic threshold was determined by the modified V-slope method (16). Ventilatory efficiency, defined as the slope between minute ventilation and carbon dioxide elimination (ventilatory efficiency slope, or VE/VCO_2 slope) was obtained by linear