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Clinical Research

Percutaneous Implantation of the Edwards SAPIEN Transcatheter Heart Valve for Conduit Failure in the Pulmonary Position

Early Phase 1 Results From an International Multicenter Clinical Trial

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Objectives The purpose of this study was to evaluate the safety and effectiveness of the Edwards SAPIEN transcatheter heart valve (Edwards Lifesciences LLC, Irvine, California) in the pulmonary position in patients with moderate to severe pulmonary regurgitation with or without stenosis.

Background Transcatheter pulmonary valve replacement is evolving, but to date, experience has been limited to the Melody valve (Medtronic Inc., Minneapolis, Minnesota).

Methods Eligible patients with dysfunctional right ventricle-to-pulmonary artery conduits were screened if body weight was ≥35 kg and the in situ conduit diameter was ≥16 mm and ≤24 mm. Standardized implantation and follow-up protocols were used.

Results Thirty-six patients from 4 centers were recruited between April 2008 and May 2010. Mean body weight was 73.4 ± 22.9 kg. Successful valve deployment was achieved in 33 of 34 attempts (97.1%). Valve migration occurred in 3 patients, with 2 requiring surgical retrieval; however, 1 patient underwent successful perventricular valve implantation. Further intraprocedure complications included pulmonary hemorrhage (n = 2), ventricular fibrillation (n = 1), and stent migration (n = 1). Pullback gradient across the conduit decreased from 26.8 ± 18.4 mm Hg to 11.7 ± 8.0 mm Hg ($p < 0.001$). The right ventricular/aortic pressure ratio decreased from 0.6 ± 0.2 to 0.4 ± 0.1 ($p < 0.001$). Peak Doppler gradient across the right ventricular outflow tract decreased from 41.9 ± 27.9 mm Hg to 19.1 ± 13.3 mm Hg ($p < 0.001$). At 6-month follow-up, all patients were alive. The number of patients with New York Heart Association functional class I increased from 5 at baseline to 27 at follow-up. Pulmonary regurgitation was ≤2+ in 97% of patients. Freedom from reintervention was 97% with 1 patient undergoing elective placement of a second valve due to conduit-induced distortion of the initial implant.

Conclusions Transcatheter pulmonary valve replacement using the Edwards SAPIEN transcatheter heart valve is safe and effective in patients with dysfunctional right ventricle-to-pulmonary artery conduits. (J Am Coll Cardiol 2011; 58:2248–56) © 2011 by the American College of Cardiology Foundation

From the *Rush University Medical Center, Chicago, Illinois; †Cedars-Sinai Medical Center, Los Angeles, California; ‡Duke Family Medicine Center, Durham, North Carolina; §The Heart Hospital, London, United Kingdom; ‖Medical University of South Carolina, Charleston, South Carolina; ¶Children's Hospital of Philadelphia, Philadelphia, Pennsylvania; #Yale-New Haven Hospital, New Haven, Connecticut; and **Edwards Lifesciences, Irvine, California. The trial was sponsored and funded through Edwards Lifesciences LLC. Dr. Hijazi is a consultant to Edwards Lifesciences. Dr. Kar has received research grants from Abbott Vascular; and has received honoraria from and is a consultant for Medtronic. Dr. Mullen is a proctor for Edwards Lifesciences. Dr. Makkar has received consultancy fees, grant support, and lecture fees from Abbott, Medtronic, and Lilly; and grant support from Johnson & Johnson and St. Jude Medical. Dr. Shirali is a consultant to, recipient of research grants from, and a member of the advisory board of Philips Medical Systems; and has received research grants from Edwards Lifesciences. Dr. Fogel has received grants from Edwards Lifesciences for the COMPASSION study; has received grants from Siemens; and payment as medical monitor for Kereos. Christopher Cain was an employee of Edwards Lifesciences during the trial. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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Transcatheter pulmonary valve replacement (tPVR) provides a less invasive alternative to surgery in patients with right ventricular-to-pulmonary artery (RV-PA) conduit dysfunction. Since the original report using a bovine jugular vein within a balloon-expandable stent was described in an ovine model more than 10 years ago (1), several clinical trials using this valve (Melody valve, Medtronic Inc., Minneapolis, Minnesota) in both Europe and the United States have demonstrated effective immediate restoration of valvular competence with significant reductions in conduit pressure gradients (2,3). Concerns have been raised, however, regarding the performance of this device with early stent fracture rates leading to potential valve dysfunction in more than 25% of cases (4). The Edwards SAPIEN transcatheter heart valve (THV) (Edwards Lifesciences LLC, Irvine, California) was initially introduced as a transcatheter alternative to surgical valve replacement in elderly patients with severe aortic stenosis (5). Since then, favorable safety and efficacy have been reported in a large randomized clinical trial involving elderly inoperable patients and high-risk surgical patients with severe aortic valve stenosis (6). Reports describing implantation in the pulmonary position for right ventricular outflow tract conduit dysfunction, mirroring valve efficacy and durability in the aortic position have followed (7); however, to date, formal studies evaluating valve effectiveness in the pulmonary position have not been conducted.

The COMPASSION (COngenital Multicenter trial of Pulmonic vAlve regurgitation Studying the SAPIEN interventional) THV was designed as a prospective, nonrandomized, multicenter study to assess the safety and efficacy of the SAPIEN THV for the treatment of dysfunctional RV-PA conduits with moderate to severe pulmonary regurgitation with or without stenosis. In this paper, we report the results of phase 1 U.S. Food and Drug Administration–approved clinical trial, with particular emphasis on restoration of valve competency and impact on conduit stenosis. The institutional review board of each participating institution approved the trial.

Methods

Patients. Between April 2008 and May 2010, 36 patients from 4 centers (3 in the United States and 1 in Europe) were recruited (Fig. 1). Patients with a dysfunctional RV-PA conduit, defined as ≥3+ pulmonary regurgitation by transthoracic echocardiography (TTE) or pulmonary regurgitant fraction ≥40% by cardiac magnetic resonance imaging (MRI) with or without stenosis, were considered eligible for inclusion in the trial provided that body weight was ≥35 kg and the in situ conduit diameter was ≥16 mm and ≤24 mm. After eligibility screening, informed consent was obtained from all potential subjects and/or their legal guardians. Pre-procedure baseline assessment included standard laboratory testing as well as computed tomography (CT) angiography and cardiac MRI. Exercise testing was also conducted using a standardized protocol. The primary endpoint for the trial was freedom from device failure or procedure-related death and/or reoperation at 1 year. Secondary endpoints included freedom from major adverse cardiac and cerebral events at 6 months and evidence of functional improvement as assessed by improvement in degree of pulmonary regurgitation and stenosis on TTE, pulmonary regurgitation on MRI, symptoms assessed by New York Heart Association (NYHA) classification, and exercise tolerance as assessed by cardiopulmonary exercise testing. Follow-up protocol included assessment at 30 days, 6 months, 1 year, and annually thereafter up to 5 years (Fig. 2). Standardized protocols for echocardiography, exercise testing, CT, and MRI were used. Cardiopulmonary exercise testing was performed using a ramp workload protocol. Anaerobic threshold was determined by use of the modified V-slope method. All study echocardiograms, MRI, and exercise stress tests were interpreted in centralized (Core) facilities.

Abbreviations and Acronyms

CT = computed tomography
MRI = magnetic resonance imaging
NYHA = New York Heart Association
RV-PA = right ventricle to pulmonary artery
THV = transcatheter heart valve
tPVR = transcatheter pulmonary valve replacement
TTE = transthoracic echocardiogram

Valve and delivery system. The SAPIEN Pulmonic THV is a radiopaque, stainless steel, balloon-expandable support structure (frame), with an integrated, unidirectional, trileaflet bovine tissue valve and a polyethylene terephthalate

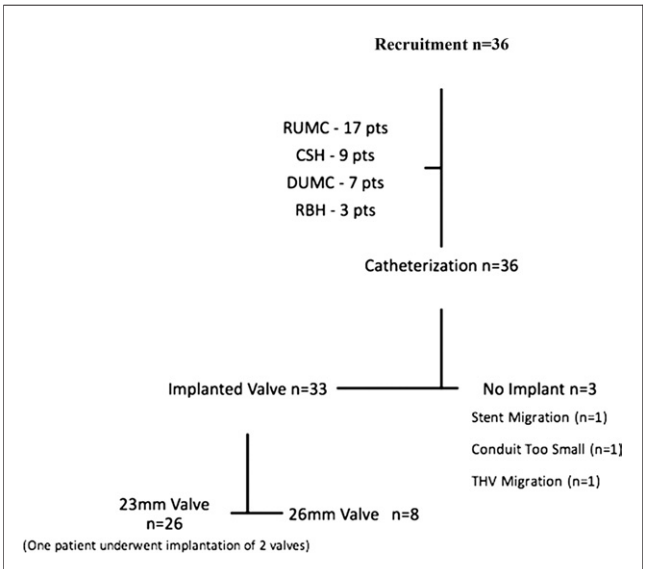

Figure 1 Flow Diagram Outlining Numbers of Patients Recruited and Subsequent Valve Implantation Outcome

CSH = Cedar Sinai Hospital; DUMC = Duke University Medical Center; RBH = Royal Brompton Hospital; RUMC = Rush University Medical Center; THV = transcatheter heart valve.