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Treatment of Symptomatic Severe Aortic Stenosis With a Novel Resheathable Supra-Annular Self-Expanding Transcatheter Aortic Valve System

Ganesh Manoharan, MBBCH, MD,* Antony S. Walton, MBBS,† Stephen J. Brecker, MBBS, MD,‡ Sanjeevan Pasupati, MBCHB,§ Daniel J. Blackman, MD,‖ Hongyan Qiao, PHD,¶ Ian T. Meredith, AM, MBBS, PHD#

ABSTRACT

OBJECTIVES The purpose of this study was to prospectively evaluate the safety and clinical performance of the CoreValve Evolut R transcatheter aortic valve replacement (TAVR) system (Medtronic, Inc., Minneapolis, Minnesota) in a single-arm, multicenter pivotal study in high- or extreme-risk patients with symptomatic aortic valve stenosis.

BACKGROUND Although outcomes following TAVR are improving, challenges still exist. The repositionable 14-F equivalent CoreValve Evolut R TAVR system was developed to mitigate some of these challenges.

METHODS Suitable patients (n = 60) underwent TAVR with a 26- or 29-mm Evolut R valve. Primary safety endpoints were mortality and stroke at 30 days. Primary clinical performance endpoints were device success per the VARC-2 (Valve Academic Research Consortium-2) and the percent of patients with mild or less aortic regurgitation 24 h to 7 days post-procedure.

RESULTS Patients (66.7% female; mean age 82.8 ± 6.1 years; Society of Thoracic Surgeons Score 7.0 ± 3.7%) underwent TAVR via the transfemoral route in 98.3%, using a 29-mm valve in 68.3% of patients. All attempts at repositioning were successful. No death or stroke was observed up to 30 days. The VARC-2 overall device success rate was 78.6%. Paravalvular regurgitation post TAVR was mild or less in 96.6%, moderate in 3.4%, and severe in 0% at 30 days. Major vascular complications occurred in 8.3%, and permanent pacemaker implantation was required in 11.7% of patients.

CONCLUSIONS The repositionable 14-F equivalent Evolut R TAVR system is safe and effective at treating high-risk symptomatic aortic stenosis patients. Repositioning was successful when required in all patients, with low rates of moderate or severe paravalvular aortic regurgitation and low permanent pacemaker implantation. (The Medtronic CoreValve™ Evolut R™ CE Mark Clinical Study; NCT01876420) (J Am Coll Cardiol Intv 2015;8:1359–67)

The prevalence of patients presenting with aortic stenosis increases with age (1,2), and untreated symptomatic patients have a poor prognosis (3–5). Transcatheter aortic valve replacement (TAVR) is now an accepted treatment strategy for patients who are considered to be high risk or unsuitable for surgery (6–11).

Despite studies demonstrating good outcomes following TAVR, challenges such as vascular access complications (12,13), the need for permanent

From the *Regional Cardiology Department, Royal Victoria Hospital, Belfast, United Kingdom; †Victorian Heart Centre, Epworth Hospital, Melbourne, Australia; ‡Cardiology and Interventional Cardiology Services, St. George's Hospital, London, United Kingdom; §Department of Cardiology, Waikato Hospital, Hamilton, New Zealand; ‖Department of Cardiology, Leeds General Infirmary, Leeds, United Kingdom; ¶Statistical Services, Medtronic, Inc., Minneapolis, Minnesota; and the #Monash Cardiovascular Research Centre, MonashHEART, Monash Health, and Department of Medicine, Monash University, Melbourne, Australia.
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ABBREVIATIONS AND ACRONYMS

BAV = balloon aortic valvuloplasty

DCS = delivery catheter system

LV = left ventricle

MRS = Modified Rankin score

MSCT = multislice computer tomography

NYHA = New York Heart Association

PPM = patient-prosthesis mismatch

PVL = paravalvular leak

SAVR = surgical aortic valve replacement

STS = Society of Thoracic Surgeons

TAV = transcatheter aortic valve

TAVR = transcatheter aortic valve replacement

pacemaker post-TAVR (14,15), paravalvular leak (PVL) (16,17), stroke (18,19), and procedure-related complications (20,21) still remain. Technological advancements, with conformable valve frames and more accurate valve positioning, may improve outcomes.

The Medtronic CoreValve Evolut R System (Medtronic, Inc., Minneapolis, Minnesota) (**Figure 1**) was designed to mitigate some of these difficulties. Detailed design characteristics have been described previously (22). In brief, this system comprises the Evolut R valve and the EnVeo R Delivery Catheter System (DCS) with the InLine sheath. The trileaflet valve and sealing skirt are made out of porcine pericardial tissue, sutured in a supra-annular position on a compressible and self-expandable nitinol frame (**Figure 1A**). The Enveo R DCS enables the valve to be fully repositionable and recapturable before full release by turning the delivery handle (**Figure 1B**). The built-in InLine sheath allows for the whole system to be inserted into a patient without the need for a separate access sheath, reducing the overall profile of the system (**Figure 1C**), equivalent to the outer diameter of a 14-F sheath.

The objectives of this prospective, single-arm, multicenter pivotal study were to evaluate the safety and clinical performance of the CoreValve Evolut R TAVR system in patients with severe symptomatic aortic valve stenosis who are at high or extreme risk for surgical aortic valve replacement (SAVR). The 30-day outcomes are presented in this paper.

METHODS

STUDY DESIGN. This prospective, single-arm, multicenter study was conducted at 6 centers in the United Kingdom, Australia, and New Zealand (Online Appendix A). The study was funded by Medtronic, and the protocol was developed in collaboration with the study investigators.

The study was conducted in accordance with the Declaration of Helsinki and was consistent with Good Clinical Practice and the applicable local regulatory requirements. Local ethics committee approval was obtained, and signed informed consent was obtained from each patient who met all study inclusion criteria and had no exclusion criteria (Online Appendix B) before enrollment and before performing any study-related investigations.

The study methods included the following measures to minimize potential sources of bias:

- An external clinical event committee, comprising a cardiologist, a cardiothoracic surgeon, and a neurologist, adjudicated all serious adverse events in the study.
- A data safety monitoring board provided oversight of all safety aspects of the study.
- All sites followed a standardized protocol for acquisition of echocardiographic endpoint data.
- An echocardiography core laboratory (Mayo Clinic, Rochester, Minnesota) evaluated all echocardiograms and echocardiographic study endpoint results.
- All study-related data were collected electronically, and independent full source data verification was periodically conducted at each site.

PATIENT SELECTION. All eligible patients had symptomatic (New York Heart Association [NYHA] functional class ≥II) aortic stenosis defined as an aortic valve (AV) area of <1.0 cm^2 (or AV index of <0.6 cm^2/m^2) and a mean AV gradient >40 mm Hg or maximal velocity of >4.0 m/s by resting echocardiogram. Patients with low flow/low gradient aortic stenosis were permitted if they had documented dobutamine or exercise stress echocardiography demonstrating a mean gradient >40 mm Hg or a maximal valve velocity >4 m/s and an AV area <1.0 cm^2 (or AV area index <0.6 cm^2/m^2).

Risk assessment was determined on the basis of a Society of Thoracic Surgery (STS) score ≥8.0% or documented heart team agreement of high or extreme risk for SAVR due to frailty or comorbidities.

Primary clinical exclusion criteria were any contraindication for placement of a bioprosthetic valve, clinically significant untreated coronary artery disease, severe left ventricular (LV) function (ejection fraction <20%), end-stage renal disease, liver failure, bare-metal stent placement within 30 days or drug-eluting stent within 6 months before assessment, myocardial infarction within the past 30 days, severe dementia, or any condition that would preclude anticoagulation. Key anatomical exclusion criteria were a pre-existing prosthetic heart valve in any position, mixed AV disease (stenosis and regurgitation), severe mitral or tricuspid regurgitation, moderate or severe mitral stenosis, or bicuspid or unicuspid AV.

Multislice computed tomography (MSCT) of suitable patients was used to analyze the aortic annulus and peripheral vasculature to assess anatomic suitability. This information assigned patients to undergo TAVR via the transfemoral or an alternative access route (direct aortic or subclavian artery). Two valve sizes were available in this study (26 or 29 mm), and valve choice was determined by the MSCT-derived