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

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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

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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.

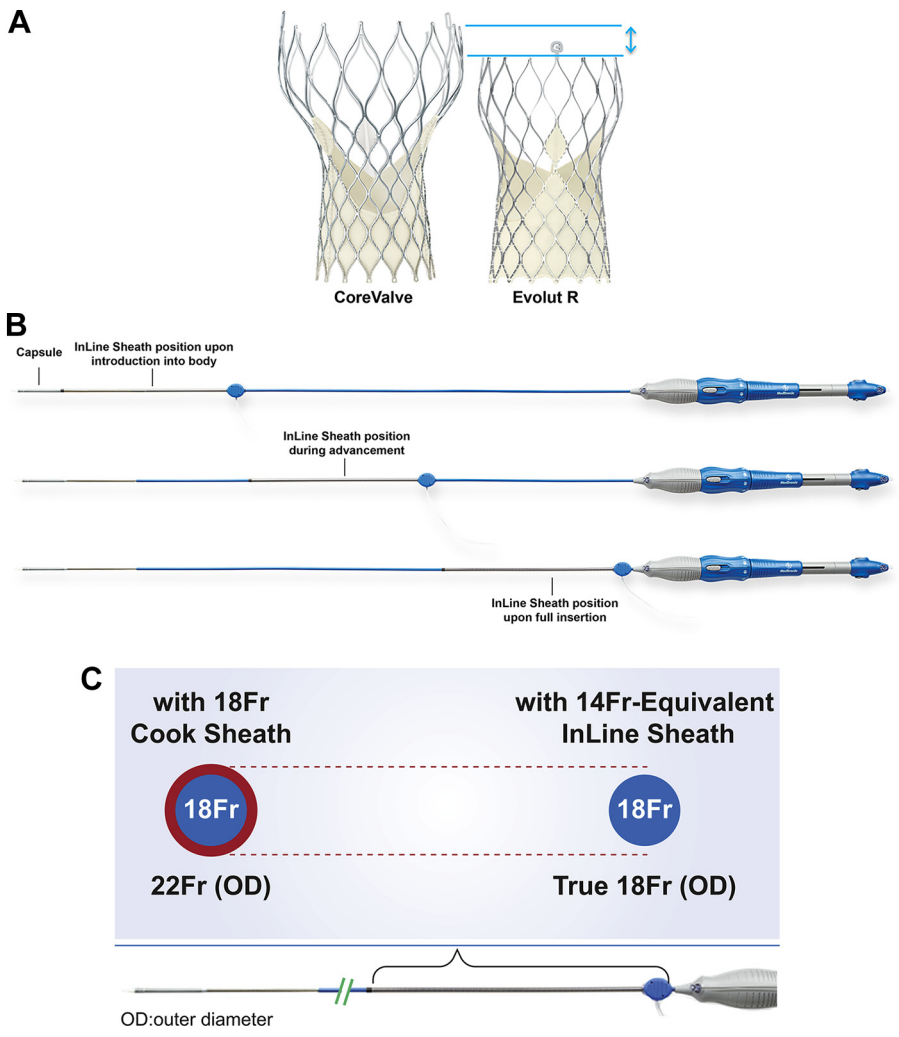
PATIENT SELECTION. All eligible patients had symptomatic (New York Heart Association [NYHA] functional class ≥II) aortic stenosis defined as an aortic valve (AV) area of <1.0 cm^2 (or AV index of <0.6 cm^2/m^2) and a mean AV gradient >40 mm Hg or maximal velocity of >4.0 m/s by resting echocardiogram. 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

FIGURE 1 Medtronic CoreValve Evolut R System



(A) Evolut R valve compared with CoreValve. The frame height of Evolut R has been reduced by 10% and is more conformable. The skirt has been extended at the in-flow aspect **(arrow)**. **(B)** EnVeo Delivery System with InLine sheath. The InLine sheath is opposed to the capsule during delivery into the femoral artery. Once the InLine sheath is in the femoral artery, the valve is advanced "sheathless" through the iliac artery toward the aortic valve. **(C)** The EnVeo Delivery System compared with the current 18-F sheath system. By advancing "sheathless," a true outer diameter reduction from 22-F (current) to 18-F (14-F outer diameter [OD] equivalent) will be observed. ©2015 Medtronic, Inc. Printed with permission. CoreValve is a registered trademark of Medtronic CV Luxembourg S.a.r.l. Evolut, EnVeo, and InLine are trademarks of Medtronic, Inc.

annular perimeter (26 mm: 62.8 to 72.3 mm; 29 mm: 72.3 to 81.6 mm), as per the manufacturer's instructions for use.

STUDY PROCEDURE. Before patient enrollment, the study sponsor trained all investigative teams on the study methods, procedures, and requirements. All implanting physicians were trained on the use of the investigational TAVR system through didactic and simulator sessions. Throughout the study period, any newly learned procedural techniques were disseminated to the other investigators.

The choice of performing the procedure under general or local anesthesia was at the discretion of the implanting team. Although the EnVeo DCS with the InLine sheath allows for the valve to be delivered "sheathless," implantation using standard techniques (pre-positioning of an 18-F access sheath) was allowed on the basis of the manufacturer's instructions for use. Once all arterial and venous

accesses were achieved, intravenous unfractionated heparin was administered to achieve a recommended activated clotting time of ≥250 s.

The "sheathless" technique required distinct steps before advancement of the TAVR system into the patient. Once access was obtained and pre-closure sutures deployed, a 14-F 30-cm standard sheath was advanced into the patient. This access was used to cross the AV, followed by positioning of a pre-shaped stiff support wire in the LV. The manufacturer's instructions for use recommended balloon aortic valvuloplasty (BAV) before positioning of the valve. Once BAV was completed, the 14-F sheath was carefully removed, maintaining wire position in the LV. The EnVeo DCS with the InLine sheath, mounted with the Evolut R valve, was then advanced "sheathless" into the patient and implanted at the annulus. Following successful valve implantation, the EnVeo DCS was removed, and while maintaining wire position, the 14-F sheath was re-introduced. Following this, post-TAVR hemodynamics and angiographic and echocardiographic assessments were completed.

During the TAVR procedure, an electrocardiogram (ECG) was recorded at key procedural steps (pre-TAVR, pre-BAV, post-BAV, immediately post-deployment, and at completion) to prospectively assess if or when a rhythm change may have occurred.

During valve delivery, the Evolut R can be repositioned by either resheathing or recapturing to optimally place the valve. Resheathing was defined as when only part of the valve was retrieved back into the DCS capsule, and recapture was defined as when the valve was completely retrieved back into the DCS with the intent to re-cross the AV (if the valve fully migrated into the ascending aorta during deployment) or, if necessary, to completely remove the system from the patient safely. Repositioning to achieve an implant depth between 1 and 5 mm was recommended.

Following successful TAVR, the use of dual antiplatelet therapy was at the discretion of the implanting team. Generally, the best practice recommendation for the CoreValve system was used, with dual antiplatelet therapy continued for 3 months, followed by single antiplatelet therapy for life.

Follow-up evaluation included clinical assessment, echocardiography, and 12-lead ECG at discharge and 30 days, and is planned through 2 years post-procedure. Transthoracic echocardiography was performed pre-implant and at 24 h to 7 days after the implant to calculate device success. In addition, cardiac enzymes were monitored through 30 days, and creatine kinase-MB was collected if elevation in creatine kinase was detected. Modified Rankin scores (MRS) are documented at baseline, discharge, 30 days, 6 months, and 1 year, as well as at 1 and 3 months following any stroke events.

STUDY ENDPOINTS. There were 2 primary safety endpoints: the rate of all-cause mortality and the rate of any stroke at 30 days. The primary clinical performance endpoints were the device success rate, as defined by the VARC-2 (Valve Academic Research Consortium-2) (23), at 24 h to 7 days and the percent of patients with no more than mild aortic regurgitation at the early post-procedure echocardiogram (24 h through 7 days).

The secondary safety endpoints were: 1) the rates of the VARC-2 composite early safety endpoint, which includes death, all stroke (disabling and nondisabling), life-threatening bleeding, acute kidney injury at stage 2 or 3 (including renal replacement therapy), coronary artery obstruction requiring intervention, major vascular complication, and valve-related dysfunction requiring repeat procedure (BAV, TAVR, or SAVR); and 2) the individual components at 30 days. Secondary clinical performance endpoints included the rate of successful recapture (if tried) and valve function by Doppler echocardiography at 30 days.

STATISTICAL METHODS. The analysis cohort for this report comprised all 60 patients implanted with the Evolut R transcatheter aortic valve (TAV). Baseline categorical variables are presented as percents and continuous variables as mean ± SD. Event rates are reported as Kaplan-Meier estimates.

The clinical performance endpoints of device success and the percent of patients with no more than mild aortic regurgitation were summarized with 2-sided 95% exact binomial confidence intervals. The comparisons for valve hemodynamic data (mean AV gradient and AV area) between baseline and early post-procedure were conducted using the paired t-test. All statistical analyses were performed using Statistical Analysis Systems software, version 9.2 (SAS Institute, Cary, North Carolina).

RESULTS

PATIENTS. A total of 60 patients (66.7% female; mean age 82.8 ± 6.1 years) underwent TAVR with the CoreValve Evolut R system at 6 centers in the United Kingdom, Australia, and New Zealand between October 2013 and July 2014 (Online Appendix A). The study cohort included each implanter's first experience with the Evolut R System. The overall study

compliance for the 30-day follow-up visit was 98.3% (Figure 2).

The mean STS score and logistic EuroSCORE were 7.0 ± 3.7% and 20.5 ± 12.5%, respectively. The most prevalent STS factors at baseline were chronic lung disease in 26 (43.3%), atrial fibrillation or flutter in 22 (36.7%), and prior coronary artery bypass grafting in 17 (28.3%) patients. At baseline, 68.3% of patients had NYHA functional class III or IV symptoms, with 41 patients (68.3%) considered to be frail (Table 1).

PROCEDURAL OUTCOMES. The majority of cases were performed under general anesthesia (63.3%), with transfemoral being the predominant TAVR access route (98.3%) (Table 2). The EnVeo DCS was advanced sheathless using the InLine sheath in the majority of cases without difficulty. Pre-dilation of the native AV was performed in 96.7% of cases, and a 20-mm balloon was used in 60.3% of cases. The Evolut R TAVR system was advanced to the native AV annulus in all patients without difficulty.

The 29-mm valve was implanted in 68.3% of patients, and post-implant dilation was performed in 21.7% of cases. Valve repositioning was successfully performed 22 times in 15 patients by either resheathing or recapturing to optimize valve position (Table 2). There were no instances in which the valve needed to be completely retrieved, and there was no valve-related dysfunction requiring a repeat procedure. One patient required a second Evolut R valve implantation due to the first valve being deployed supra-annularly, causing marginal aortic migration of the valve upon full release and resulting in severe PVL. This patient was discharged without complication, with a 30-day echocardiogram showing mild PVL.

CLINICAL OUTCOMES. There was no death or stroke observed up to 30 days (Table 3). Symptom relief post-TAVR was observed, with 76.3% of patients improving by at least 1 NYHA functional class and 39.0% improving by at least 2 NYHA functional classes from baseline to 30 days. No patient had coronary occlusion, annulus rupture, or ventricular perforation during TAVR.

Major vascular complication was observed in 5 patients (8.3%). Two patients required access intervention following TAVR: 1 patient experienced a dissection of the right common femoral artery, treated successfully with angioplasty with no further sequelae, and the other had a failed percutaneous closure device leading to bleeding and hematoma, treated with blood products and left femoral artery stenting. Access groin hematoma was noted in the other 3 patients, with 2 requiring blood products.

FIGURE 2 Study Flow and Compliance Up to 30 Days

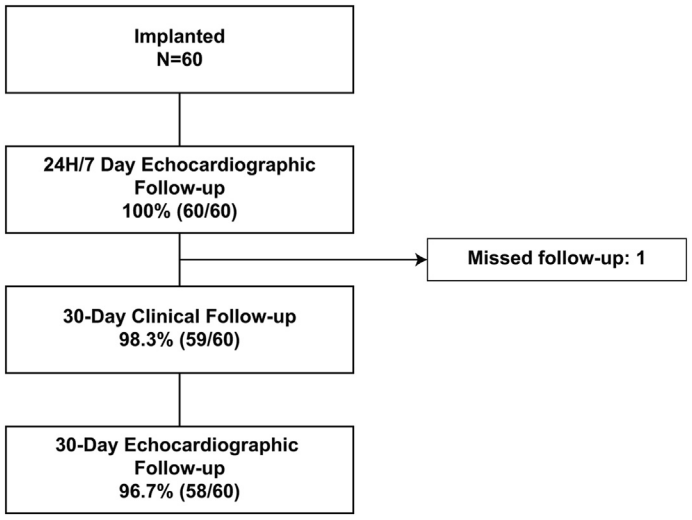


TABLE 1 Baseline Characteristics of Patients (n = 60)

Age, yrs	82.8 ± 6.1
Female	66.7 (40)
Logistic EuroSCORE, %	20.5 ± 12.5
Society of Thoracic Surgeons score, %	7.0 ± 3.7
New York Heart Association functional class	
II	31.7 (19)
III	60.0 (36)
IV	8.3 (5)
Society of Thoracic Surgeons factors	
Diabetes	26.7 (16)
Serum creatinine >2 mg/dl	1.7 (1)
Dialysis	0.0 (0)
Chronic lung disease (COPD)	43.3 (26)
Peripheral vascular disease	16.7 (10)
Cerebrovascular disease	13.3 (8)
Previous coronary artery bypass grafting	28.3 (17)
Previous percutaneous coronary intervention	13.3 (8)
Previous myocardial infarction	13.3 (8)
Atrial fibrillation/atrial flutter	36.7 (22)
Other comorbidities and medical history	
Severely atherosclerotic aorta	1.7 (1)
Frailty*	68.3 (41)
Abnormal chest wall anatomy	3.3 (2)
Evidence of radiation damage	1.7 (1)
Pre-existing permanent pacemaker or defibrillator	11.7 (7)

Values are mean ± SD or % (n). *Defined as slowness, weakness, exhaustion, wasting and malnutrition, poor endurance and inactivity, and loss of independence as assessed by the heart team. Frailty measurements include: 5-m walking time, handgrip strength test using a handgrip dynamometer, body mass index <20 kg/m^2 and or weight loss of 5 kg/yr; serum albumin <3.5 g/dl, and cognitive impairment or dementia.

COPD = chronic obstructive pulmonary disease; EuroSCORE = European System for Cardiac Operative Risk Evaluation.

TABLE 2 Procedural Outcomes Through 30 Days (n = 60)

Procedure time, min	83.7 ± 26.7
Total fluoroscopy time, min (n = 58)	24.1 ± 9.3
General anesthesia	63.3 (38)
Access	
Iliofemoral	98.3 (59)
Direct aortic	1.7 (1)
Pre-TAVR balloon valvuloplasty	96.7 (58)
Successful valve repositioning, if attempted (n = 15)*	100 (22/22)
Valve resheathing, n	10
Valve recapture, n	12
Valve size implanted	
26-mm	31.7 (19)
29-mm	68.3 (41)
Post-TAVR balloon valvuloplasty	21.7 (13)
New permanent pacemaker implantation†	11.7 (7)
Implant depth, mm‡	
Noncoronary sinus	3.9 ± 3.0
Left coronary sinus	4.9 ± 3.0
Length of stay, days	5.0 ± 2.5

Values are mean ± SD or % (n). *22 attempts in 15 patients. †Patients with a pacemaker or implantable cardioverter-defibrillator at baseline are included. ‡Center-reported measurements.
TAVR = transcatheter aortic valve replacement.

TABLE 3 Clinical Outcomes at 30 Days (n = 60)

All-cause mortality	0.0 (0)
All stroke	0.0 (0)
Life-threatening or disabling bleeding	5.0 (3)
Acute kidney injury: stage 2 or 3	1.7 (1)
Coronary artery obstruction	0.0 (0)
Annular rupture/dissection	0.0 (0)
Left ventricular perforation	0.0 (0)
Major vascular complication	8.3 (5)
Valve-related dysfunction requiring repeat procedure	0.0 (0)
VARC-2 composite safety endpoint	13.3 (8)

Values are Kaplan-Meier rates (n).
VARC-2 = Valve Academic Research Consortium-2.

Life-threatening or disabling bleeding was observed in 3 patients, occurring at the access site, permanent pacemaker site, or induced by the endotracheal tube.

At 30 days, a new permanent pacemaker implantation was required in 11.7% of patients. Six patients had third-degree atrioventricular block, and 1 had second-degree atrioventricular block post-procedure. All permanent pacemaker implants occurred between 1 and 5 days post-TAVR. Pre-procedure ECG abnormalities were present in 4 patients: 2 had first-degree atrioventricular block, 1 had right bundle branch block (RBBB), and 1 had both RBBB and first-degree atrioventricular block. When the depth of implant was reviewed, the average depth for those who received a pacemaker (left coronary cusp [LCS] 9.4 ± 3.1 mm; noncoronary cusp [NCS] 8.1 ± 3.5 mm) was significantly deeper than that of patients who did not receive a new pacemaker (LCS 4.3 ± 2.5 mm; NCS 3.3 ± 2.5 mm; $p < 0.0001$ for both comparisons).

The VARC-2 overall device success rate was 78.6% post-procedure (Table 4). In 5 patients, the effective orifice area (EOA) could not be determined to calculate the patient-prosthesis mismatch (PPM).

ECHOCARDIOGRAPHIC OUTCOMES. The Evolut R TAV effectively reduced the mean AV gradient from 49.1 ± 13.0 mm Hg at baseline to 9.2 ± 3.9 mm Hg early post-procedure ($p < 0.0001$). The AV area was also significantly improved from 0.6 ± 0.2 cm^2 at baseline to 1.9 ± 0.5 cm^2 early post-procedure ($p < 0.0001$).

Figure 3 shows valve hemodynamics through 30 days. Mild or less PVL occurred post-TAVR in 96.6% of patients; 2 patients had moderate and none had severe PVL at 30 days (Figure 4).

DISCUSSIONS

This prospective, multicenter, first-in-man study has demonstrated that the resheathable Medtronic CoreValve Evolut R TAVR system is safe, with good clinical performance at treating high-risk symptomatic patients with severe aortic stenosis. No death or stroke were observed up to 30 days, and the overall VARC-2-defined device success rate at 24 h to 7 days post-procedure was 78.6%, with 93.2% of patients having mild or less PVL. The PVL improved at 30 days, with 96.6% having mild or less, 3.4% having moderate, and none having severe PVL.

Although study design, patient selection, and TAVR experience may differ, the 30-day mortality and stroke rates observed in this study compare favorably to those reported in other studies using first-generation (10,11,24,25) or next-generation (26-29) devices. Despite patients in this study having an STS score of 7.0 ± 3.7%, the absence of primary clinical events at 30 days may in part be due to the use of MSCT (for sizing and assessment of coronary ostia), careful adherence to best practices learned from global use of the Medtronic CoreValve device, appropriate patient selection, the self-expanding nature of the TAVR system, and the resheathable feature of the Evolut R system.

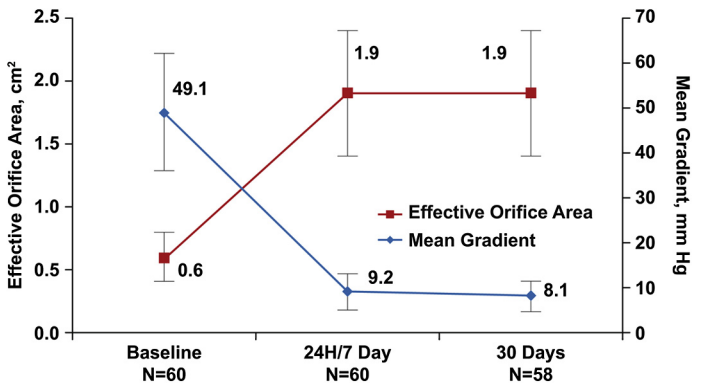
Stroke, coronary occlusion, annular rupture, and LV perforation during TAVR significantly affects patient outcomes post-TAVR. The low stroke rate observed in this study is consistent with that reported (0% to 4%) from other studies (26-29). Female sex, use of the balloon-expandable TAVR system, previous bioprosthetic AV, and low-lying coronary ostia

TABLE 4 VARC-2-Defined Device Success (n = 60)

Absence of procedural mortality	100 (60/60)
Correct position of 1 valve in the proper location	98.3 (59/60)
Mean gradient <20 mm Hg or peak velocity <3 m/s	98.3 (59/60)
Absence of moderate or severe regurgitation	93.3 (56/60)
Absence of patient-prosthesis mismatch*	83.6 (46/55)
Overall device success	78.6 (44/56)

Values are % (n/N). *The effective orifice area could not be determined in 5 patients to calculate patient-prosthesis mismatch.
VARC-2 = Valve Academic Research Consortium-2.

FIGURE 3 Mean Echocardiographic Hemodynamic Measurements



Error bars represent SDs.

are risk factors for coronary occlusion (30). Severe annular calcification, the use of a balloon-expandable TAVR system, and aggressive post-dilation are associated with annular rupture (31,32). None of these complications were observed in this study.

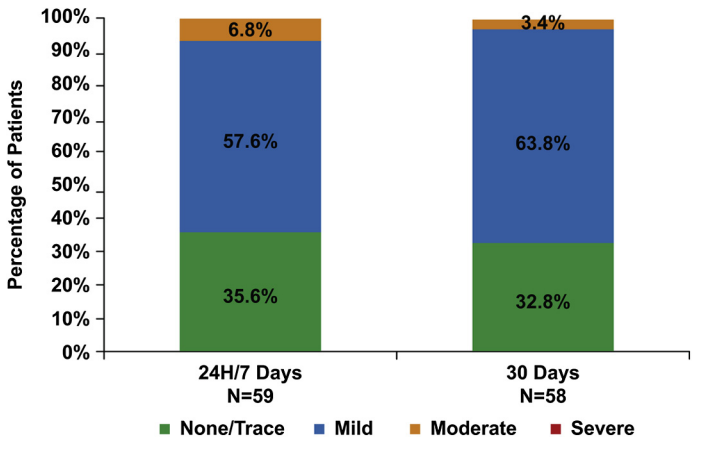
Device success, as intended by VARC-2, requires a composite of: 1) absence of procedural mortality; 2) correct position of a single prosthetic valve; and 3) intended performance of the prosthetic valve (no PPM mean valve gradient <20 mm Hg or peak velocity <3 m/s, and no moderate or severe prosthetic regurgitation). Failure to meet any 1 of these 3 parameters will categorize the device a failure. The device success rate for this study was lower than expected (Table 4) and was driven predominantly by the presence of calculated PPM in 9 patients. The challenges with calculating PPM are recognized, especially when transthoracic rather than transesophageal echocardiography is used to measure LV outflow tract diameter. Furthermore, these data were not available in 5 patients, further affecting the device success rate. Importantly, the mean EOA at 24 h to 7 days and at 30 days was good (1.9 ± 0.5 cm^2), with low mean gradients of 9.2 ± 3.9 mm Hg and 8.1 ± 3.3 mm Hg, respectively.

REPOSITIONABILITY AND SAFETY. Repositioning with the Evolut R was performed 22 times in 15 patients safely and without difficulty to optimize final valve implant position. Repositioning in these 15 patients enabled an average final implant depth of 5.9 ± 3.4 mm for NCS and 6.3 ± 4.1 mm for LCS. The ability to resheath and reposition in turn contributed to the overall good clinical outcomes, with no death or stroke, low to moderate PVL rates, and low permanent pacing rates observed in this study.

The novel distal portion of the capsule (containing the crimped valve [Figure 1B]) expands to facilitate valve resheathing and recapturing of a partially released Evolut R valve, which reduces friction and mechanical stress encountered during repositioning, thereby reducing agitation of friable native valve tissue and potentially contributing to the absence of clinical stroke observed.

PERMANENT PACEMAKER IMPLANTATION. The rate of permanent pacemaker implantation was 11.7% in our study. The rate of permanent pacemaker implantation post-TAVR with the CoreValve device ranges between 11% and 40% (33,34) and for the Edwards SAPIEN between 3% and 8% (35). More recently, the multicenter ADVANCE II (CoreValve Prospective International Post-Market Advance II Study) study, investigating the effect of best practice on rhythm disturbances with the CoreValve device, reported pacing rates of 13.3% (36). Similar low rates of pacing were also observed with other new TAVR devices (27–29); however, the Lotus system reported a pacing

FIGURE 4 Post-Procedure Echocardiographic Paravalvular Leak Assessments



rate of 28.6% (26). Although the cause is multifactorial, pre-existing RBBB (37), final device depth, and oversizing are suggested triggers.

The lower pacing rate in this study could be attributed to: 1) the redesigned delivery system (with resheath and recapture capability) enabling more accurate positioning; and 2) the modified, more conformable nitinol frame design resulting in a more uniform outward force and reduced stiffness at the inflow portion of the valve, thus potentially reducing trauma to the conduction system as compared with the CoreValve system. Of the 7 patients who received a permanent pacemaker through 30 days, 4 had pre-existing conduction abnormalities and all had significantly lower final deployment depth as compared with the study average.

PARAVALVULAR LEAK. Moderate to severe PVL post-TAVR is associated with a poor prognosis (38,39). Potential causes include suboptimal positioning, undersizing, and eccentric calcification. A more conformable frame, MSCT-based sizing, and repositionability may mitigate some of these challenges, as observed in this study. The observed rates for PVL mild or less (96.6%) and moderate (3.4%) with the Evolut R compare favorably to the CoreValve (mild or less: 91%; moderate to severe: 9%) (11), and appear similar to SAPIEN S3 (mild or less: 96.6%; moderate: 3.4%) at 30 days (29).

HEMODYNAMIC PERFORMANCE. Aortic valve pressure gradient and valve area were significantly improved following Evolut R TAV implantation (**Figure 3**). Absence of PPM at the early post-implant echocardiogram (in 55 evaluable patients) was 83.6%. Despite the challenges and inconsistency with deriving these data, they appear to be better than that reported in the Reprise II (60.7%) (26) or the PARTNER (40% to 56%) (40) studies. This may, in part, be due to the supra-annular function of the Evolut R valve. Furthermore, the mean gradient and EOA at 30 days for the Evolut R were equivalent to those reported for the CoreValve bioprosthesis in the CoreValve US Extreme Risk (8.7 ± 4.2 mm Hg and 1.86 ± 0.56 cm^2) (25) and High Risk (8.9 ± 3.9 mm Hg and 1.95 ± 0.56 cm^2) (11) studies.

VASCULAR COMPLICATIONS. The rates of major vascular complications (MVC) (8.3%) and life-threatening bleeding events (5.0%) are consistent with rates reported for the CoreValve system. The CoreValve Extreme Risk (25) and High Risk (11) studies reported MVC rates of 8.2% and 5.9%, respectively, and life-threatening bleeding events of 12.7% and 13.6%, respectively. Patients with MVC in our study had a slightly higher body mass index when compared with those who did not (28.2 ± 5.0 kg/m^2 vs. 26.8 ± 4.8 kg/m^2; p = 0.53), which may have contributed to the access-related events.

STUDY LIMITATIONS. This was a first-in-man study of the use of the Evolut R TAV in patients at high or prohibitive risk of SAVR. The study size was relatively small, with a short (30-day) follow-up. Longer-term follow-up to 2 years is planned. Although all patients had MRS assessments pre- and post-TAVR, formal neurological assessments were not performed unless a change in MRS was observed. The absence of clinical neurological events may also be in part due to the small study numbers. Larger studies are required to further evaluate clinical outcomes.

CONCLUSIONS

This study confirms the clinical safety and performance of the next-generation Evolut R repositionable TAVR system in treating high-risk or surgically inoperable symptomatic aortic stenosis patients. Future studies will further help to validate the favorable outcomes observed in this study.

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PERSPECTIVES

WHAT IS KNOWN? High-risk or inoperable patients with symptomatic severe aortic stenosis are increasingly treated by TAVR; however, challenges such as death, stroke, paravalvular leak, and need for permanent pacing exist.

WHAT IS NEW? TAVR with the 14-F–equivalent, repositionable Medtronic Evolut R system results in reduced event rates.

WHAT IS NEXT? Larger studies are required to evaluate and confirm the findings of this small pivotal study.

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KEY WORDS aortic valve stenosis, self-expanding heart valve, transcatheter aortic valve replacement

APPENDIX For additional study information and subject selection criteria, please see the online version of this article.