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NEW RESEARCH PAPERS

STRUCTURAL

Transfemoral Tricuspid Valve Replacement in Patients With Tricuspid Regurgitation

TRISCEND Study 30-Day Results

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ABSTRACT

OBJECTIVES The TRISCEND study (Edwards EVOQUE Tricuspid Valve Replacement: Investigation of Safety and Clinical Efficacy after Replacement of Tricuspid Valve with Transcatheter Device) is evaluating the safety and performance of transfemoral transcatheter tricuspid valve replacement in patients with clinically significant tricuspid regurgitation (TR) and elevated surgical risk.

BACKGROUND Transcatheter valve replacement could lead to a paradigm shift in treating TR and improving patient quality of life.

METHODS In the prospective, single-arm, multicenter TRISCEND study, patients with symptomatic moderate or greater TR, despite medical therapy, underwent percutaneous transcatheter tricuspid valve replacement with the EVOQUE system. A composite rate of major adverse events, echocardiographic parameters, and clinical, functional, and quality-of-life measures were assessed at 30 days.

RESULTS Fifty-six patients (mean age of 79.3 years, 76.8% female, 91.1% TR severe or greater, 91.1% atrial fibrillation, and 87.5% New York Heart Association functional class III or IV) were treated. At 30 days, TR was reduced to mild or less in 98%. The composite major adverse events rate was 26.8% at 30 days caused by 1 cardiovascular death in a patient with a failed procedure, 2 reinterventions after device embolization, 1 major access site or vascular complication, and 15 severe bleeds, of which none were life-threatening or fatal. No myocardial infarction, stroke, renal failure, major cardiac structural complications, or device-related pulmonary embolism were observed. New York Heart Association significantly improved to functional class I or II (78.8%; $P < 0.001$), 6-minute walk distance improved 49.8 m ($P < 0.001$), and Kansas City Cardiomyopathy Questionnaire score improved 19 points ($P < 0.001$).

CONCLUSIONS Early experience with the transfemoral EVOQUE system in patients with clinically significant TR demonstrated technical feasibility, acceptable safety, TR reduction, and symptomatic improvement at 30 days. The TRISCEND II randomized trial (NCT04482062) is underway. (J Am Coll Cardiol Intv 2022;15:471–480) © 2022 Published by Elsevier on behalf of the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

ECL = echocardiographic core laboratory

IVC = inferior vena cava

MAE = major adverse event(s)

NYHA = New York Heart Association

PVL = paravalvular leak

RA = right atrium/atrial

RV = right ventricle/ventricular

TEE = transesophageal echocardiography

TR = tricuspid regurgitation

TTE = transthoracic echocardiography

TTVR = transcatheter tricuspid valve replacement

TV = tricuspid valve

Numerous studies show an independent association with increasing tricuspid regurgitation (TR) severity and mortality,[1-5] yet optimal clinical management strategies for TR remain unclear. Medical therapies, including diuretic agents and therapies to treat the primary cause of heart failure, remain a Class IIa recommendation in the American College of Cardiology/American Heart Association guidelines for the management of valvular heart disease.[6] Isolated tricuspid valve (TV) surgery is a Class IIa recommendation in the setting of right heart failure and severe primary or secondary disease poorly responsive to medical therapy and a Class IIb recommendation in patients with prior left heart surgery in the absence of severe pulmonary hypertension or right ventricular (RV) dysfunction. Given that isolated TV surgery is associated with a high risk of in-hospital mortality of approximately 10% attributed to chronic right heart volume overload, many patients with severe symptomatic TR remain untreated.[1,7,8]

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Transcatheter solutions for TR, currently under investigation, may offer lower-risk therapeutic options for these patients.[9,10] Early studies with transcatheter leaflet repair devices have shown safety with acceptable efficacy,[11-13] yet challenges remain, including limited applicability in highly selected patients, significant residual TR in some patients, and technically difficult echocardiographic imaging. A multinational report of compassionate use of transcatheter TV replacement (TTVR) utilizing a transjugular or transatrial approach showed technical success and acute TR reduction but 10% in-hospital mortality rate, comparable to open heart surgery.[14] The EVOQUE TV replacement system (Edwards Lifesciences) utilizes a percutaneous, transfemoral transvenous approach and showed promising results in a 25-patient first-in-human experience.[15] In patients with severe TR, the procedure showed 92% technical success, 0% mortality, and significantly improved TR severity and New York Heart Association (NYHA) functional class at 30 days.

To confirm the favorable outcomes from this early, compassionate use experience, the TRISCEND study (Edwards EVOQUE Tricuspid Valve Replacement: Investigation of Safety and Clinical Efficacy after Replacement of Tricuspid Valve with Transcatheter Device) is underway.

METHODS

STUDY DESIGN. The prospective, single-arm, multicenter TRISCEND study is registered on ClinicalTrials.gov (NCT04221490) and was designed to evaluate safety and performance of the EVOQUE system in patients with symptomatic moderate or greater TR despite medical therapy or with prior heart failure hospitalization for TR. Study participation was approved by each site's local Institutional Review Board. Written informed consent was obtained from all enrolled patients in accordance with 21 Code of Federal Regulations Part 50, the principles of the Declaration of Helsinki, the relevant part of ICH/Good Clinical Practice, ISO 14155, and the local Institutional Review Board. The sponsor trained investigators and staff on proper device use according to the instructions for use.

STUDY OVERSIGHT. Each site's local heart team assessed initial patient eligibility requirements before submitting cases to the central screening committee. Comprised of physician investigators, the central screening committee determined final appropriateness for enrollment. An echocardiographic core laboratory (ECL), clinical events committee, and data safety monitoring board provided trial oversight. The ECL (Baylor Scott and White Research Institute) independently assessed all echocardiograms, approved study participation together with the central screening committee, and evaluated device performance throughout follow-up. The data safety monitoring board assessed safety, and the clinical events committee adjudicated prespecified endpoint-related major adverse events (MAEs) and hospitalizations for heart failure or TR; both groups are comprised of independent, noninvestigator physicians. The sponsor ensured protocol training, consistent data collection, protocol compliance, and patient confidentiality and also provided data management, review, monitoring, and quality control throughout the study.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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PATIENT ELIGIBILITY. Patients at least 18 years of age, with at least moderate functional or degenerative TR despite medical therapy, were eligible for enrollment. Medical therapy was at investigator discretion and included diuretic medications in stable doses unless a patient had a documented history of intolerance. Anticoagulation was recommended through 6 months postprocedure.

Patients were excluded from the study if they had unsuitable anatomy for device placement, prior TV repair or replacement that would interfere with EVOQUE valve implantation, severe pulmonary hypertension (pulmonary artery systolic pressure >70 mm Hg or >2/3 systemic with pulmonary vascular resistance >5 WU after vasodilator challenge), or severe RV dysfunction. Additional exclusion criteria were left ventricular ejection fraction <25%, severe renal insufficiency with estimated glomerular filtration rate ≤25 mL/min/1.73 m^2 or requiring chronic renal replacement therapy, along with comorbid condition(s) that, in the opinion of the investigator, could limit patient participation. Transthoracic echocardiography (TTE) images were recorded at baseline, discharge, and 30 days postprocedure. Transesophageal echocardiography (TEE) images were obtained at screening and intraprocedurally. For pacemaker-dependent patients, a plan was made prior to the procedure for alternative pacing options, including a coronary sinus lead or a leadless pacemaker.

DEVICE AND PROCEDURE. The EVOQUE system utilizes a transfemoral approach and consists of a 28-F percutaneous delivery system (Figure 1) compatible with all valve sizes; the EVOQUE valve implant (Figure 1) in 44-mm, 48-mm, and 52-mm diameters; a loading system; and a dilator kit. The delivery system has 3 planes of motion, which allow steerability and precise positioning. Primary and secondary flexion allow coaxial alignment with the TV, and depth of implantation is adjustable with the depth knob.

The EVOQUE valve consists of a trileaflet bovine pericardial tissue valve, nitinol frame, and fabric skirt. Nine anchors are positioned between the chordae tendineae to engage and capture native leaflets, while the valve frame and fabric skirt minimize the risk of paravalvular leak (PVL).

Once femoral access is obtained, a pre-shaped guidewire is inserted into the right atrium (RA) and advanced across the TV into the RV with TEE guidance critical throughout the procedure. The delivery system is inserted over the guidewire and positioned at the junction of the inferior vena cava (IVC) and RA before it is advanced and flexed across the TV; the delivery capsule is directed toward the RV and positioned below the TV. After position and trajectory are confirmed, anchors are exposed by retracting the capsule to ensure that anchors remain below the leaflet tips and above the papillary muscle heads. During further expansion, anchor tips are positioned below the annulus and leaflets are captured. After optimal anchor positioning and confirmed leaflet capture, the EVOQUE valve is fully deployed and released from the delivery system. Finally, the delivery system is removed, and the femoral access site is closed using standard techniques.

FIGURE 1 EVOQUE Tricuspid Valve Replacement System

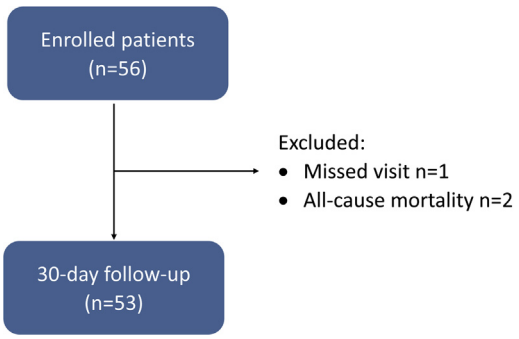
The EVOQUE valve design engages leaflets, chords, and annulus to achieve secure placement. The valves (sized 44 mm, 48 mm, and 52 mm) are delivered by a 28-F transfemoral delivery system.

ECHOCARDIOGRAPHIC ASSESSMENT. All echocardiograms were analyzed by the ECL following American Society of Echocardiography standards.[16] Chamber size, function, and valvular regurgitation were assessed using standard 2-dimensional color Doppler methods; TR effective regurgitant orifice and regurgitant volume were quantified using the proximal isovelocity surface area method.[17,18] TR severity was graded using a prespecified 5-class scheme previously described.[18-20]

STUDY ENDPOINTS. The safety endpoint was a composite rate of MAEs at 30 days postenrollment comprising cardiovascular mortality; myocardial infarction; stroke; renal complications requiring unplanned dialysis or renal replacement therapy; severe bleeding defined as fatal, life-threatening, extensive, or major bleeding according to the Mitral Valve Academic Research Consortium[21]; nonelective TV reintervention; major access site and vascular complications; major cardiac structural complications; and device-related pulmonary embolism.

Performance endpoints included device, procedural, and clinical success. Device success was assessed at exit from the catheterization laboratory and defined as device deployed and delivery system retrieved as intended. Procedural success was evaluated based on device success at exit from the catheterization laboratory without clinically significant PVL on TTE at discharge, as assessed by the ECL. Clinical success was defined as procedural success without any MAEs at 30 days. The echocardiographic endpoint was a reduction in TR grade from baseline to discharge. TR severity was assessed at baseline, discharge, and 30 days.

FIGURE 2 Patient Flowchart



Of the 56 enrolled patients, 53 had a 30-day follow-up visit.

Clinical, functional, and quality-of-life outcomes (NYHA functional classification, 6-minute walk distance, Kansas City Cardiomyopathy Questionnaire) were assessed at 30 days. Edema was assessed by patient questionnaire, ankle circumference measurements, and a standard pitting grading scale.

STATISTICAL ANALYSIS. Analysis was performed using SAS software version 9.4 (SAS Institute) and represents the intent-to-treat population. Patients with missing data were excluded from the denominator for endpoint calculations. For categorical data, results were summarized with patient count, percentage, and 95% CI by normal approximation, where appropriate. For continuous variables, results were summarized with the number of observations and mean ± SD, and median (minimum, maximum) for hospital length of stay and 95% CI by normal approximation were also included. Comparative statistics, including change from baseline to 30-day follow-up, were calculated with Wilcoxon signed rank test or paired Student's *t*-test.

RESULTS

Fifty-six consecutive patients (76.8% women) (Figure 2) with a mean age of 79.3 ± 7.7 years were treated at 9 U.S. investigational sites. Baseline clinical characteristics and laboratory values are shown in Table 1. Patients were deemed at high surgical risk with a mean Society of Thoracic Surgeons score (mitral valve repair) of 7.7 ± 5.3% and a EuroSCORE II (European System for Cardiac Operative Risk Evaluation II) of 5.6 ± 4.9%. A total of 91.1% presented with torrential, massive, or severe TR; most had functional TR (67.9%).

Most patients were in NYHA functional class III or IV (87.5%). Major comorbidities included atrial

TABLE 1 Baseline Characteristics (N = 56)

Age, y	79.3 ± 7.7
Female	43 (76.8)
EuroSCORE II	5.6 ± 4.9
STS score, mitral valve repair, %	7.7 ± 5.3
NYHA functional class III or IV	49 (87.5)
Tricuspid valve pathology	
Degenerative (primary)	6 (10.7)
Functional (secondary)	38 (67.9)
Mixed	10 (17.9)
Pacer related	1 (1.8)
Indeterminate	1 (1.8)
Comorbidities	
Systemic hypertension (treated)	49 (87.5)
Pulmonary hypertension (sPAP ≥30 mm Hg) in last 12 mo	45 (80.4)
Chronic obstructive pulmonary disease	10 (17.9)
Chronic kidney disease (eGFR 15-89 mL/min/1.73 m^2)	37 (66.1)
Diabetes	12 (21.4)
Dyslipidemia or hyperlipidemia	39 (69.6)
Ascites	12 (21.4)
Gastrointestinal or esophageal bleeding	11 (19.6)
Coronary artery disease (≥50% stenosis)	8 (14.3)
Cerebrovascular disease (stroke or TIA)	15 (26.8)
Prior myocardial infarction	2 (3.6)
Prior percutaneous coronary intervention/stent	8 (14.3)
Peripheral arterial disease	1 (1.8)
Coronary artery bypass grafting	9 (16.1)
Prior carotid stenting/surgery	1 (1.8)
Prior valve surgery/intervention (mitral/aortic/tricuspid)	22 (39.3)
Atrial fibrillation	51 (91.1)
RBBB	11 (19.6)
LBBB	6 (10.7)
Pacemaker	19 (33.9)
Prior heart failure hospitalization in last 12 months	20 (35.7)
Laboratory values	
Albumin, g/dL	4.0 ± 0.6
Alanine transaminase, U/L	22.2 ± 11.7
Aspartate transaminase, U/L	29.0 ± 10.1
Alkaline phosphatase, U/L	115.7 ± 62.5
Gamma-glutamyltransferase, U/L	86.5 ± 76.3
B-type natriuretic peptide	678.8 ± 1,813.8
Prothrombin time, s	18.8 ± 8.2
INR	1.6 ± 0.74
eGFR, mL/min/1.73 m^2	49.0 ± 12.9
Creatinine, mg/dL	1.2 ± 0.3
Uric acid, mg/dL	7.4 ± 2.9

Values are mean ± SD or n (%).

eGFR = estimated glomerular filtration rate; EuroSCORE = European System for Cardiac Operative Risk Evaluation; INR = international normalized ratio; LBBB = left bundle branch block; NYHA = New York Heart Association; RBBB = right bundle branch block; sPAP = systolic pulmonary artery pressure; STS = The Society of Thoracic Surgeons; TIA = transient ischemic attack.

TABLE 2 Procedural Characteristics and Clinical Success (N = 56)

Right femoral vein access	56/56 (100)
Device success[a]	55/56 (98.2)
Procedural success[b]	54/56 (96.4)
Clinical success[c]	41/56 (73.2)
Device time (implant insertion to release), min	70.1 ± 31.5 (56)
Fluoroscopy time, min	32.6 ± 14.3 (56)
Hospital length of stay, d	
Mean ± SD (n)	4.3 ± 4.3 (56)
Median (range)	3.0 (1.0-25.0)[d]
95% CI	3.2-5.5
Discharge location	
Home	48/56 (85.7)
Home with services	4/56 (7.1)
Skilled nursing facility	2/56 (3.6)
Other hospital	1/56 (1.8)
Other	1/56 (1.8)

Values are n/N (%) or mean ± SD (n), unless otherwise indicated. [a]Device is deployed and delivery system successfully retrieved as intended at the time of the patient's exit from the cardiac catheterization laboratory. [b]Device success and no clinically significant paravalvular leak on transthoracic echocardiogram (assessed by the echocardiographic core laboratory) at the time of discharge. [c]Procedural success and no MAEs at 30 days. [d]One patient required 25 days of hospitalization caused by valve embolization, subsequent emergent redo sternotomy, and notable post-surgical bleeding from the chest tube.

fibrillation (91.1%), systemic hypertension (87.5%), and pulmonary hypertension (80.4%).

Prior cardiac treatments included valve surgery or intervention (39.3%) and pacemaker or implantable cardioverter-defibrillator implantation (33.9%) with leads crossing the TV annulus in 32%. Heart failure hospitalization occurred in 35.7% within 12 months prior to enrollment, and 35.7% reported ankle swelling with a moderate to extreme impact on activity level.

Baseline RV function assessment demonstrated a mean tricuspid annular plane systolic excursion of 14.6 ± 4.2 mm and RV fractional area change of 37.1 ± 9.2%. Effective regurgitant orifice area was 0.76 ± 0.56 cm^2, regurgitant volume was 55.1 ± 29.4 mL, and vena contracta width measured via 2-dimensional TTE RV inflow or apical 4-chamber view was 8.7 ± 3.2 mm or 10.0 ± 4.3 mm, respectively.

ACUTE CLINICAL OUTCOMES. All patients received an EVOQUE valve via right femoral vein access with a mean implantation time of 70.1 ± 31.5 minutes. Median hospital length of stay postprocedure was 3 days (range: 1-25 days), and 92.9% were discharged directly home. Device success was achieved in 98.2% and procedural success was achieved in 96.4% (Table 2).

At discharge, 100% of patients had a reduction of 1 TR grade or more, and 98.1% showed an improvement of 2 or more grades. Overall, the reduction in TR severity by discharge showed significant improvement ($P < 0.001$) (Table 3).

TABLE 3 TR Grade at Baseline and Discharge

	Baseline	Discharge	*P* Value, Baseline vs Discharge[a]
TR severity			<0.001
0 = none/trace	0/55 (0)	35/55 (64)	
01 = mild	0/55 (0)	18/55 (33)	
02 = moderate	5/55 (9.1)	2/55 (4)	
03 = severe	25/55 (45.5)	0/55 (0)	
04 = massive	15/55(27.3)	0/55 (0)	
05 = torrential	10/55 (18.2)	0/55 (0)	

Values are n/N (%). [a]*P* value by Wilcoxon signed rank test comparing baseline with discharge.
TR = tricuspid regurgitation.

30-DAY CLINICAL OUTCOMES. Of enrolled patients, 53 completed 30-day follow-up (Figure 2). Clinical success occurred in 73.2%. The 30-day MAEs adjudicated by the clinical events committee are shown in Table 4. Fifteen (26.8%) patients experienced MAEs, with 1 cardiovascular death (1.8%), 2 nonelective TV reinterventions, 1 major access site or vascular complication, and 15 severe bleeding events (none life-threatening or fatal). No myocardial infarction, stroke, renal failure requiring dialysis, major cardiac structural complications, or device-related pulmonary embolism were observed.

The all-cause 30-day mortality rate was 3.6% (n = 2). These 2 deaths included the previously mentioned cardiovascular mortality and 1 noncardiovascular death in a patient who died from carcinoid syndrome in hospital. The cardiovascular death was related to the device and procedure and occurred in an 82-year-old patient with a history of congestive heart failure (NYHA functional class III at baseline). Intraprocedure TEE confirmed that the implant migrated, resulting in severe TR and moderate PVL. The patient underwent valve-in-valve implantation during the index procedure, did not improve clinically, and died of heart failure and RV dysfunction 20 days postprocedure.

Nonelective TV reinterventions occurred in 1 patient on postoperative day 1 (before discharge, partial embolization) and in another patient on day 2 (after discharge, embolization); both underwent surgical reintervention with a bioprosthetic valve. The severe bleeding events were extensive (n = 7) and major (n = 8); none were life-threatening or fatal (Table 4). They included 3 access site, 2 epistaxes, 3 gastrointestinal, 1 hematuria, 1 hemolytic anemia in a patient with a history of anemia of chronic disease, 2 perioperative blood losses during surgical tricuspid reintervention, and 3 vascular (nonaccess site) bleeds. Nine of these patients required transfusion of at least 1 unit of packed red blood cells. All patients who

TABLE 4 Clinical Events Committee–Adjudicated Safety Events at 30 Days (N = 56)

Cardiovascular mortality	1 (1.8)[a]
Myocardial infarction	0
Stroke	0
Renal complications requiring dialysis or renal replacement therapy	0
New need for renal replacement therapy	0
Severe bleeding[b]	15 (26.8)
Fatal	0
Life-threatening	0
Extensive	7 (12.5)
Major	8 (14.3)
Nonelective tricuspid valve reintervention	2 (3.6)
Major access site and vascular complications requiring intervention	1 (1.8)
Major cardiac structural complications	0
Device-related pulmonary embolism	0
Composite MAE rate	15 (26.8)

Values are as n (%) or n. [a]All-cause mortality included 1 cardiovascular and 1 noncardiovascular death. [b]Severe bleeding is defined as major, extensive, life-threatening, or fatal bleeding per Mitral Valve Academic Research Consortium criteria.

MAE = major adverse event(s).

experienced MAE bleeds were on anticoagulation or antiplatelet medication before the procedure; 73% were taking warfarin. Of 36 patients without a pacemaker prior to enrollment, 4 (11.1%) developed new conduction disturbances requiring permanent pacemaker implantation (site reported).

Clinical, functional, and quality-of-life outcomes significantly improved at 30 days (**Central Illustration**). Most patients (87.5%) were in NYHA functional class III or IV at baseline, and at 30 days, 78.8% were in NYHA functional class I or II ($P < 0.001$). The 6-minute walk distance increased a mean of 49.8 ± 80.5 m at 30 days ($P < 0.001$) from 199.1 ± 128.6 m at baseline to 248.9 ± 127.5 m. The Kansas City Cardiomyopathy Questionnaire score improved from 46.5 ± 23.1 points at baseline to 65.6 ± 21.6 points, a mean improvement of 19.0 ± 20.5 points at 30 days ($P < 0.001$). Edema assessed by standard pitting test significantly improved at 30 days ($P < 0.001$), and 13.7% reported ankle swelling with moderate to extreme activity limitations at 30 days compared with 35.7% at baseline. Ankle circumference improved (left: from 23.0 ± 3.8 cm to 21.8 ± 4.6 cm; $P = 0.003$; right: from 23.1 ± 3.7 cm to 21.9 ± 4.5 cm; $P = 0.002$), and body weight decreased (from 73.7 ± 18.6 kg to 71.6 ± 19.4 kg; $P = 0.008$).

30-DAY TTE RESULTS. At baseline, TR severity was torrential (15.4%), massive (25.0%), severe (50.0%), or moderate (9.6%), which reduced to none or trace or mild TR in 98.1% at 30 days ($P < 0.001$) (**Central Illustration**). At 30 days, 100% of patients had a reduction of one TR grade or more, and 98.1% improved by 2 or more grades (**Figure 3**). Pulmonary artery systolic pressure decreased from 40.1 ± 10.5 mm Hg to 32.2 ± 10.2 mm Hg ($P = 0.002$). Mean gradient was 3.4 ± 1.5 mm Hg at 30 days (**Table 5**).

Measures of right heart remodeling showed significant improvement at 30 days. RV end-diastolic and end-systolic areas significantly improved from 33.1 ± 7.2 cm^2 to 23.4 ± 7.1 cm^2 ($P < 0.001$) and from 20.5 ± 5.1 cm^2 to 17.6 ± 5.8 cm^2 ($P = 0.001$), respectively, and IVC diameter (expiration) reduced from 27.0 ± 7.1 mm to 21.3 ± 5.6 mm ($P < 0.001$). There was worsening of RV function between baseline and 30 days by tricuspid annular plane systolic excursion (14.9 ± 3.9 mm vs 13.0 ± 3.19 mm; $P = 0.035$) and RV fractional area change (37.6 ± 9.3% to 24.8 ± 9.9%; $P < 0.001$). RA systolic volume decreased from 154.1 ± 66.1 mL to 138.2 ± 61.8 mL ($P = 0.009$). Left ventricular ejection fraction significantly improved from 53.4 ± 10.2% to 58.2 ± 10.4% ($P = 0.014$).

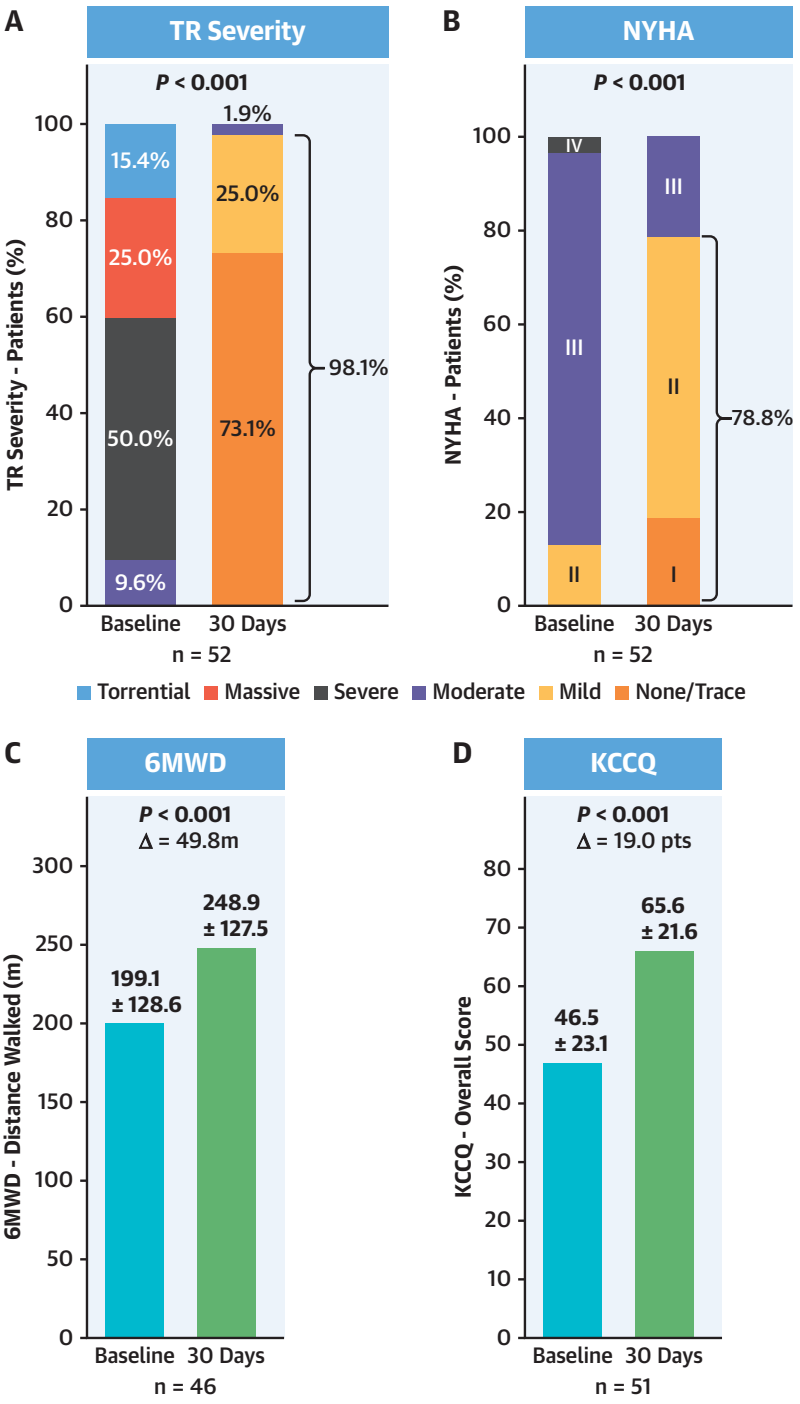
DISCUSSION

Here, we report initial results from the ongoing TRISCEND study, which is evaluating feasibility and safety of transfemoral TTVR with the EVOQUE system in patients with at least moderate TR. We saw high rates of device and procedural success (98.2% and 96.4%, respectively), with low mortality and significant TR reduction. Importantly, these acute outcomes were associated with significant improvements in functional status and quality of life at 30 days.

Current guidelines do not recommend surgery for isolated TR.[22,23] Most studies have demonstrated high surgical mortality of 9% to 11%,[8,24-26] with limited single-site reports showing lower in-hospital mortality between 3.1% and 3.7% for isolated TR redo surgery using minimally invasive techniques.[27-29] Results with a percutaneous transcatheter approach in the TRISCEND study compare favorably with an in-hospital mortality of 1.8% and a 30-day MAE rate of 26.8% in a more complex, high-surgical-risk patient population with advanced age and significant comorbidities. These results also compare favorably to the only other published series of TTVR, which utilized surgical cutdown and a transatrial approach in most patients and demonstrated significant TR reduction and symptomatic improvement but higher in-hospital mortality of 10%.[16] The lower mortality in the TRISCEND study is potentially caused by the percutaneous transfemoral approach.

Multiple lower-risk transcatheter treatment options for patients with symptomatic severe TR have recently been evaluated.[11,13,30] The most robust early

CENTRAL ILLUSTRATION **30-Day Results of the TRISCEND Study With the EVOQUE System**



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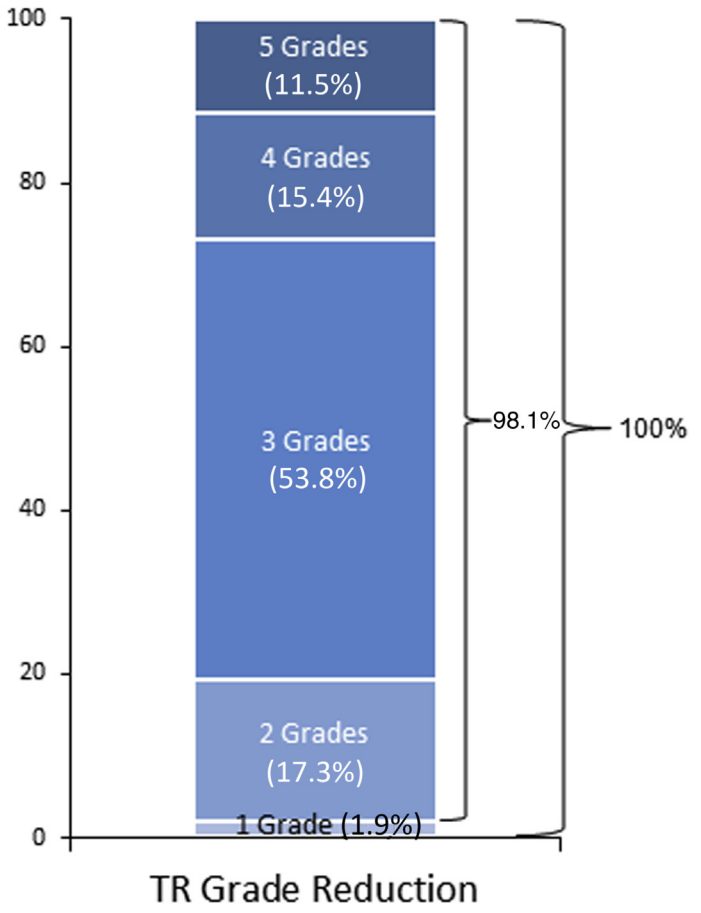
Transfemoral tricuspid valve replacement with the EVOQUE system showed reduced tricuspid regurgitation (TR) severity and improved clinical, functional, and quality-of-life outcomes. **(A)** The Baylor Scott and White Research Institute core laboratory assessed TR severity. *P* value from Wilcoxon signed rank test. **(B)** *P* value from Wilcoxon signed rank test. **(C)** *P* value from paired Student's *t*-test. **(D)** *P* value from paired Student's *t*-test. Values are mean ± SD. 6MWD = 6-minute walk distance; KCCQ = Kansas City Cardiomyopathy Questionnaire; NYHA = New York Heart Association; TRISCEND = Edwards EVOQUE Tricuspid Valve Replacement: Investigation of Safety and Clinical Efficacy after Replacement of Tricuspid Valve with Transcatheter Device.

FIGURE 3 Reduced Severity of TR at 30 Days



All patients with available data (n = 52) had at least 1 grade reduction, and 98.1% had at least 2 grades' reduction in tricuspid regurgitation (TR) severity between baseline and 30 days.

TABLE 5 Paired Baseline and 30-Day Follow-Up Echocardiographic Parameters

	n	Baseline	30 d	*P* Value[a]
PASP, mm Hg	31	40.1 ± 10.5	32.2 ± 10.2	0.002[b]
RV end-diastolic area, cm^2	45	33.1 ± 7.2	23.4 ± 7.1	<0.001[b]
RV end-systolic area, cm^2	45	20.5 ± 5.1	17.6 ± 5.8	0.001[b]
RV FAC, %	45	37.6 ± 9.3	24.8 ± 9.9	<0.001[b]
IVC diameter, expiration, mm	48	27.0 ± 7.1	21.3 ± 5.6	<0.001[b]
RA volume systolic, mL	52	154.1 ± 66.1	138.2 ± 61.8	0.009[b]
TAPSE, mm	24	14.9 ± 3.9	13.0 ± 3.2	0.035[b]
TV mean gradient, mm Hg	49	1.8 ± 1.1	3.4 ± 1.5	<0.001[b]
LVEF, %	47	53.4 ± 10.2	58.2 ± 10.4	0.014[b]

Values are mean ± SD. [a]*P* values calculated by Student's *t*-test for paired analysis. [b]Statistically significant.

FAC = fractional area change; IVC = inferior vena cava; LVEF = left ventricular ejection fraction; PASP = pulmonary artery systolic pressure; RA = right atrial; RV = right ventricular; TAPSE = tricuspid annular plane systolic excursion; TV = tricuspid valve.

feasibility data comes from 2 studies of transcatheter edge-to-edge repair with either the PASCAL transcatheter valve repair system (Edwards Lifesciences)[13] or the TriClip transcatheter TV repair system (Abbott).[31] These studies demonstrated safety and technical feasibility of these approaches, with significant reduction in TR and clinical improvement. However, they also highlighted technical challenges, including inadequate leaflet imaging, inability to treat large coaptation gaps, and interference of device placement by pacemaker leads. An analysis of transcatheter edge-to-edge repair patients in a TV repair registry (TriValve) demonstrated substantial residual TR, with 64% still experiencing moderate or greater TR at last follow-up (mean 290 days), potentially leading to worse long-term outcomes.[32] In addition, although infrequent, single leaflet detachments can occur, leading to recurrence of TR.

One challenge with transcatheter replacement is adequate anchoring given the asymmetric nature of the tricuspid annulus and lack of calcium. The EVOQUE system relies both on leaflet capture and annular oversizing for adequate fixation. Device embolization is a potentially catastrophic complication. In this study, there were 2 cases of device embolization (3.6%) and 1 device migration (1.8%) requiring reintervention. The cause of these embolizations is unclear, although a combination of factors (such as sizing and procedural considerations) likely contributed; further study is required to refine patient selection and procedural technique to reduce the incidence and improve device success.

Another concern with valve replacement is the ability of the RV to tolerate TR elimination, as it may increase RV afterload and lead to RV failure. Although quantitative measures showed some reduction in RV function post TTVR in this study, there was no clinical evidence of RV failure at 30 days despite 45% of patients having massive or torrential TR, except in the previously mentioned cardiovascular mortality caused by heart failure and RV dysfunction after an unsuccessful procedure. Whether RV function will return to baseline or even improve at longer-term follow-up remains to be seen. While there are limitations to quantifying and interpreting RV function, and despite it appearing to slightly worsen at 30 days, there were positive signs of RV remodeling with a reduction of RV, RA, and IVC dimensions in the TRISCEND study. Another recent study showed that after isolated TV intervention, patients who exhibited RV reverse remodeling (reduction in RV size with no more than mild RV dysfunction) within 18 months postoperatively had significantly improved survival.[33]

In the TRISCEND study, the MAE rate was primarily driven by severe bleeding events. Importantly, none were life-threatening or fatal, and the majority were

not access site or device related. Many of these events represent the challenges of treating an elderly comorbid population with atrial fibrillation necessitating anticoagulation. In addition, anticoagulation was required post-valve implantation to minimize valve thrombosis risks or thromboembolic events at the discretion of the treating physician. The association of TR with hepatic congestion and malnutrition may also make patients further coagulopathic. Prior studies demonstrate bleeding rates in patients with severe TR treated with guideline-directed medical therapy can be 15% per year,[34] and contemporary bleeding rates after TR surgery can exceed 35%.[26] Careful pre-, intra-, and post-procedural management is critical to minimizing bleeding in this elderly population. Site-reported new permanent pacemaker implantations (11.1%) were within expected range, considering rates as high as 21% after TV surgery.[35,36]

STUDY LIMITATIONS. This report represents currently available data with a limited number of patients and follow-up to 30 days for the ongoing TRISCEND study. The technology, procedural techniques, and patient selection methodology are novel and evolving, as are echocardiographic techniques, resulting in some parameters not being assessable by the ECL. We furthermore did not systematically evaluate changes in medication use over time.

CONCLUSIONS

Symptomatic, significant TR is currently undertreated, TV surgery carries high risks, and conservative medical therapy has unsatisfactory outcomes. Early experience with the transfemoral EVOQUE TV replacement system in the TRISCEND study shows safety and favorable performance, with a significant reduction in TR severity and associated improvements in clinical, functional, and quality-of-life measures. The EVOQUE system could provide an attractive alternative to surgery or conservative medical therapy for reduction of TR severity and improvement in patient outcomes. The TRISCEND study is ongoing, and a randomized pivotal trial (the TRISCEND II study [NCT04482062]) has commenced.

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PERSPECTIVES

WHAT IS KNOWN? Clinically relevant TR is frequently undertreated and associated with reduced quality of life and increased mortality. Transcatheter treatment options may be safe and improve long-term patient outcomes, and are being evaluated.

WHAT IS NEW? Thirty-day results of the TRISCEND study show promising safety and high procedural success with a percutaneous transcatheter valve replacement using the EVOQUE system. Patients had significant improvements in TR, NYHA functional class, 6-minute walk distance, and quality of life at 30 days.

WHAT IS NEXT? Patient follow-up in the TRISCEND study is ongoing to further understand the potential long-term benefits of treating moderate or greater TR with the transfemoral EVOQUE system. In addition, the randomized pivotal TRISCEND II trial is underway (NCT04482062).

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