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CLINICAL RESEARCH
Clinical trials

Transfemoral tricuspid valve replacement and one-year outcomes: the TRISCEND study

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Abstract

Background and Aims For patients with symptomatic, severe tricuspid regurgitation (TR), early results of transcatheter tricuspid valve (TV) intervention studies have shown significant improvements in functional status and quality of life associated with right-heart reverse remodelling. Longer-term follow-up is needed to confirm sustained improvements in these outcomes.

Methods The prospective, single-arm, multicentre TRISCEND study enrolled 176 patients to evaluate the safety and performance of transcatheter TV replacement in patients with ≥moderate, symptomatic TR despite medical therapy. Major adverse events, reduction in TR grade and haemodynamic outcomes by echocardiography, and clinical, functional, and quality-of-life parameters are reported to one year.

Results Enrolled patients were 71.0% female, mean age 78.7 years, 88.0% ≥ severe TR, and 75.4% New York Heart Association classes III–IV. Tricuspid regurgitation was reduced to ≤mild in 97.6% ($P < .001$), with increases in stroke volume (10.5 ± 16.8 mL, $P < .001$) and cardiac output (0.6 ± 1.2 L/min, $P < .001$). New York Heart Association class I or II was achieved in 93.3%

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(*P* < .001), Kansas City Cardiomyopathy Questionnaire score increased by 25.7 points (*P* < .001), and six-minute walk distance increased by 56.2 m (*P* < .001). All-cause mortality was 9.1%, and 10.2% of patients were hospitalized for heart failure.

Conclusions In an elderly, highly comorbid population with ≥moderate TR, patients receiving transfemoral EVOQUE transcatheter TV replacement had sustained TR reduction, significant increases in stroke volume and cardiac output, and high survival and low hospitalization rates with improved clinical, functional, and quality-of-life outcomes to one year. Funded by Edwards Lifesciences, TRISCEND ClinicalTrials.gov number, NCT04221490.

Structured Graphical Abstract

Key Question

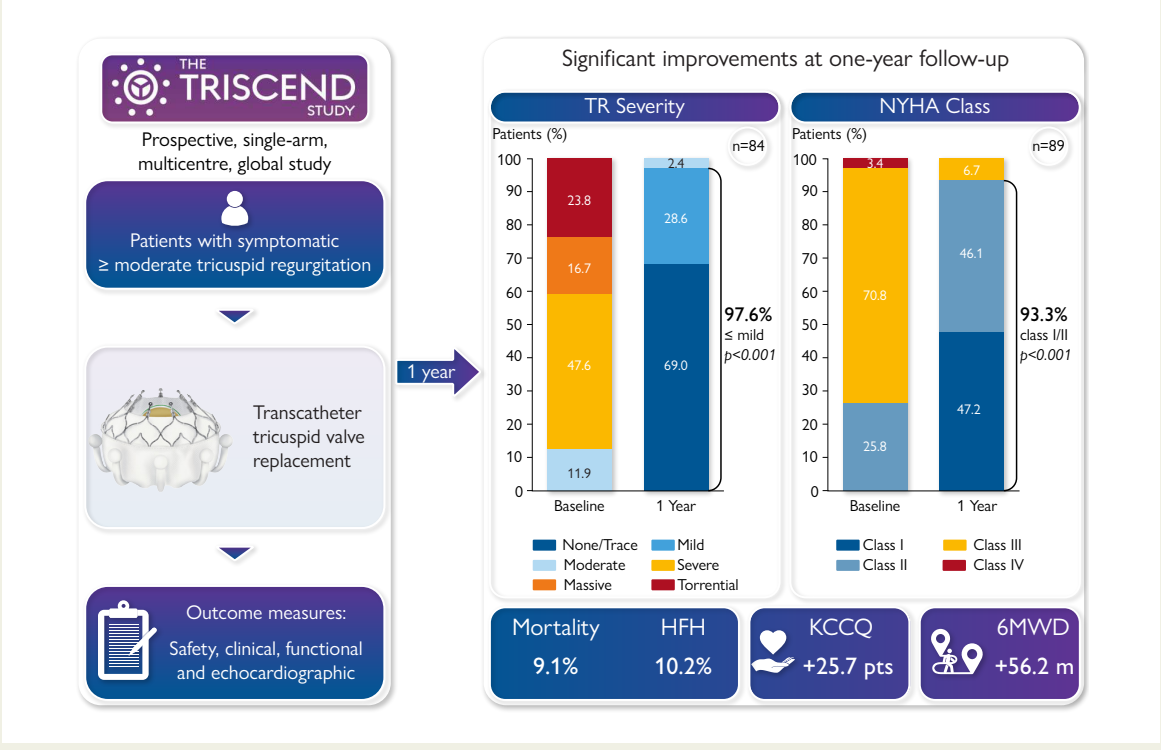
What are the one-year outcomes of EVOQUE transcatheter tricuspid valve replacement in treating patients with ≥ moderate tricuspid regurgitation (TR)?

Key Finding

At one year, TR was ≤ mild in 97.6%, with significant improvements in stroke volume, cardiac output, New York Heart Association class, Kansas City Cardiomyopathy Questionnaire score, and six-minute walk distance. All-cause mortality was 9.1% and heart failure hospitalization 10.2%.

Take Home Message

Patients with ≥ moderate TR receiving EVOQUE transcatheter tricuspid valve replacement had sustained TR reduction as well as significant improvement of hemodynamic parameters and quality-of-life at one-year follow-up.



One-year results of transcatheter tricuspid valve replacement in patients with ≥ moderate tricuspid regurgitation. The TRISCEND study demonstrated the following for patients treated with the EVOQUE system: 9.1% all-cause mortality and 10.2% HF hospitalization; significant TR reduction to grade ≤ mild in 97.6% of patients; and marked improvement in functional and quality-of-life outcomes, including a 25.7-point increase in KCCQ, 56.2-m increase in 6MWD, and 93.3% of patients in NYHA class I/II. 6MWD, six-minute walk distance; HFH, heart failure hospitalization; KCCQ, Kansas City Cardiomyopathy Questionnaire; NYHA, New York Heart Association; TR, tricuspid regurgitation.

Keywords Transcatheter tricuspid valve replacement • TTVR • Tricuspid regurgitation • EVOQUE

Introduction

Moderate or greater tricuspid regurgitation (TR) affects ~4% of elderly adults,[1–4] with increasingly severe TR associated with higher morbidity and mortality.[5–8] However, treatment options are limited: surgery is rarely elected due to high in-hospital mortality of 10%–12% for isolated tricuspid valve (TV) surgery,[9,10] and medical treatment fails to stem long-term disease progression.[11–13]

Transcatheter TV interventions (TTVI) have grown exponentially to accommodate the unmet need of patients with symptomatic, severe TR.[14] A reduction in TR severity may result in right-heart reverse remodelling and improvements in forward stroke volume and survival.[15] To that end, tricuspid transcatheter edge-to-edge repair (TEER) devices received commercial approval in Europe and led to positive changes in ESC/EACTS guideline recommendations for use of TTVI.[16] Tricuspid TEER remains an important treatment option. However, rates of residual TR ≥ severe range from 43%–48%[17,18] and may contribute to adverse outcomes in some patients.[19,20] Thus, the prospect of eliminating TR has led to development of transcatheter TV replacement (TTVR) to further expand treatment options.

Early experiences with TTVR devices have demonstrated significant TR reduction to 98% ≤ mild[21] and associated improvements in functional status and quality of life.[21–24] To address a paucity of longer-term data in larger cohorts, we report interim one-year clinical and echocardiographic outcomes of the EVOQUE TV replacement system (Edwards Lifesciences, Irvine, CA) from the global, multicentre, prospective, single-arm TRISCEND study.

Methods

Patient selection and study conduct

The TRISCEND study evaluates the safety and performance of the EVOQUE system in patients with ≥moderate symptomatic TR despite medical therapy who are deemed appropriate for TTVR by the multidisciplinary local heart team and confirmed by a central screening committee and echocardiographic core laboratory (core lab).

Key exclusion criteria were TV anatomy precluding device placement or function, haemodynamic instability, severe pulmonary hypertension [pulmonary artery systolic pressure (PASP) > 70 mmHg or >2/3 systemic with pulmonary vascular resistance > 5 WU after vasodilator challenge], severe right ventricular (RV) dysfunction, refractory heart failure (HF) requiring advanced intervention, and need for emergent surgery or planned cardiac surgery within the next 12 months. Additional exclusion criteria were left ventricular (LV) ejection fraction < 25% and severe renal insufficiency with estimated glomerular filtration rate ≤ 25 mL/min/1.73 m^2 or requiring chronic renal replacement therapy.

Patients who had a transtricuspid valve pacing lead implanted in the last three months were excluded from the study. Patients who had a lead implanted more than three months prior could be enrolled, although those who were pacemaker dependent needed to qualify for an alternative pacing option in case of lead failure post-procedure. Removing leads prior to the procedure was not required, although lead location across the annulus was factored into procedure planning to avoid adverse interactions between the lead and the device. Transoesophageal echocardiography (TEE), transthoracic echocardiography (TTE), and computed tomography (CT) were used for anatomic and functional screening and baseline assessments. Transoesophageal echocardiography was required for intraprocedural guidance, and TTE was assessed at discharge and follow-up. Clinical and echocardiographic follow-up were conducted at 30 days, six months, and one year, and will continue annually to five years.

The TRISCEND study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments, Good Clinical Practice principles, and ISO 14155. The protocol was approved by the Institutional Review Board or Ethics Committee at each participating centre. All patients provided written informed consent. Per protocol, the sponsor funded all trial-related activities and performed site selection, data collection and monitoring, and statistical analysis. The principal investigator monitored all aspects of on-site trial conduct and had access to source data. An echocardiographic core lab (Baylor Scott and White Research Institute Cardiac Imaging Core Laboratory, Dallas, TX) analysed all echocardiograms. A data safety monitoring board and clinical events committee oversaw and adjudicated events, respectively. Edwards Lifesciences sponsored the study, registered at ClinicalTrials.gov (NCT04221490).

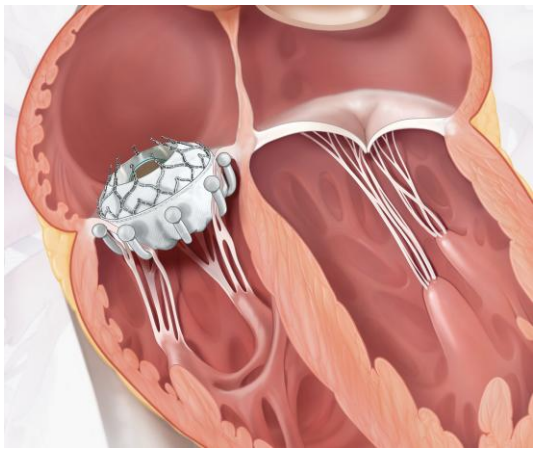


Figure 1 The Edwards EVOQUE transcatheter tricuspid valve replacement system.

EVOQUE tricuspid valve replacement system

The transcatheter EVOQUE system (*Figure 1*, Supplementary data online, *Video S1*) comprises a trileaflet bovine pericardial tissue valve implant available in 44 mm, 48 mm, and 52 mm diameters; a 28 Fr percutaneous delivery system; a dilator kit; and a loading system, stabilizer, stabilizer base, and stabilizer plate. The implant features a nitinol frame, nine anchors for implantation stability, and a sealing skirt to minimize paravalvular leak. The 28 Fr delivery system has three planes of flexion for precise steering and positioning.

The EVOQUE valve is delivered to the right ventricle via transfemoral venous access and positioned within the native TV under real-time TEE visualization. Once in position, the anchors are exposed to engage the native leaflets, subvalvular anatomy, and annulus in a procedure previously described.[21]

Study endpoints

The safety endpoint was a 30-day composite of major adverse events (MAEs): cardiovascular mortality, stroke, myocardial infarction, renal complications requiring unplanned dialysis or renal replacement therapy, severe bleeding (major, extensive, life threatening, or fatal as defined by the Mitral Valve Academic Research Consortium[25]), non-elective TV re-intervention, major access site and vascular complications, major cardiac structural complications, and device-related pulmonary embolism.

Performance endpoints were device success (analysed per device and defined as successful device deployment and delivery system retrieval at the patient's exit from the catheterization laboratory), procedural success (analysed per patient and defined as device success without clinically significant paravalvular leak by TTE at discharge as determined by the core lab), and clinical success (analysed per patient and defined as procedural success without MAEs at 30 days).

The echocardiographic endpoint was reduction in TR grade from screening or baseline TTE compared with discharge TTE. Two-dimensional TTE with Doppler was performed to assess TR using the five-grade scheme proposed by Hahn and Zamorano.[26] Additional TTE parameters included TV mean gradient, cardiac output, stroke volume, right atrial volume, LV ejection fraction, inferior vena cava (IVC) diameter and respiratory variations, RV end-diastolic diameter, PASP, tricuspid annular plane systolic excursion (TAPSE), RV fractional area change (FAC), and hepatic vein flow reversal.

Clinical, functional, and quality-of-life endpoints were assessed at baseline, 30 days, six months, and one year, and will continue annually to five years. These include New York Heart Association (NYHA) classification, Kansas City Cardiomyopathy Questionnaire (KCCQ), Short Form Health

Table 1 Baseline characteristics ($n = 176$)[a]

Variable	
Age, years	78.7 ± 7.33
Female sex	71.0 (125)
TR grade ≥ severe	88.0 (154/175)
TR aetiology	
Primary	9.7 (17)
Secondary	68.2 (120)
Mixed	14.2 (25)
Pacer related	2.8 (5)
Indeterminate	5.1 (9)
STS mortality score, %	
MV repair	7.4 ± 5.8 (174)
MV replacement	10.0 ± 5.3 (127)
EuroSCORE II, %	5.1 ± 4.0
NYHA classes III–IV	75.4 (132/175)
Katz ADL score	5.7 ± 0.7
Hypertension (treated)	84.1 (148)
Dyslipidaemia/hyperlipidaemia	65.3 (115)
Renal insufficiency	58.5 (103)
Diabetes	20.5 (36)
Coronary artery disease ≥ 50% stenosis	20.5 (36)
Coronary artery bypass grafting	16.5 (29)
Prior myocardial infarction	8.0 (14)
Carotid artery stenting/surgery	1.7 (3)
Prior stroke	13.6 (24)
Peripheral arterial disease	6.3 (11)
Cancer/malignancy	28.4 (50)
Cirrhosis	13.1 (23)
Ascites	22.2 (39)
LVEF, %	55.3 ± 10.4 (158)
Cardiomyopathy	10.2 (18)
Heart failure hospitalization in last 12 months	40.9 (72)
Pulmonary hypertension within past year	75.0 (132)
Valve surgery/intervention	37.5 (66)
Aortic valve	18.8 (33)
Mitral valve	26.1 (46)
Tricuspid valve	1.7 (3)
Atrial fibrillation	92.0 (162)
Pacemaker	32.4 (57)
Right bundle branch block	22.2 (39)
Left bundle branch block	3.4 (6)
Gastrointestinal or oesophageal bleeding	16.5 (29)
Laboratory values	
Albumin, g/dL	4.0 (3.7, 4.2)
Alanine transaminase, U/L	18.0 (13.0, 25.0)
Aspartate transaminase, U/L	26.0 (20.0, 35.0)
Alkaline phosphatase, U/L	110.0 (81.0, 146.0)
Gamma-glutamyl transferase, U/L	75.0 (36.0, 137.0)
Brain natriuretic peptide, pg/mL	332.0 (189.0, 580.0)
Prothrombin time, s	16.6 (14.4, 22.2)
INR	1.4 (1.2, 2.0)
eGFR, mL/min/1.73 m^2	52.0 (39.5, 60.0)
NT-proBNP, pg/mL	1465.0 (972.0, 2495.0)
Creatinine, mg/dL	1.1 (0.9, 1.4)
Uric acid, mg/dL	7.0 (5.3, 9.2)

Values are given as % (*n*), mean ± SD (*n*), or median (interquartile range).
ADL, activities of daily living; eGFR, estimated glomerular filtration rate; INR, international normalized ratio; MV, mitral valve; NT-proBNP, N-terminal pro-brain natriuretic peptide; NYHA, New York Heart Association; PASP, pulmonary artery systolic pressure; STS, Society of Thoracic Surgeons; TR, tricuspid regurgitation; LVEF, left ventricular ejection fraction.
[a]$n = 176$ unless otherwise noted.

Survey (SF-36) version 2, and six-minute walk distance (6MWD). All-cause mortality, HF hospitalization, and non-elective TV re-intervention were assessed at one year and will continue annually to 5 years.

Echocardiographic assessment

The independent core lab analysed all echocardiograms, including screening echocardiograms for inclusion and exclusion criteria, using American Society of Echocardiography standards.[27] Two-dimensional Doppler echocardiography was used to assess chamber size and function and valvular regurgitation, and proximal isovelocity surface area method (PISA) was used to measure effective regurgitant orifice area (EROA) and regurgitant volume.

Medical therapy

Medical therapy was administered at the investigator's discretion, with diuretic medications at stable doses for 30 days prior to the procedure unless the patient had a documented history of intolerance. Study guidelines recommended maintaining patients on a pre-procedure diuretic regimen for three months post-implant. Anticoagulation was recommended for up to six months post-procedure.

Statistical analysis

Continuous variables are reported as mean ± standard deviation or median [interquartile range (IQR)], with *P*-values calculated by paired Student's *t*-test. Categorical variables are summarized with patient count and percentage, with paired change from baseline *P*-values calculated by Wilcoxon signed rank test. Event rate denominators for MAEs (including cardiovascular mortality) include patients who had been in the trial for at least the specified timepoint or had an event. All-cause mortality and HF hospitalization observed rates are calculated using the denominator of all patients enrolled in the study, and

Kaplan–Meier estimates for time to first event are reported. Annualized HF hospitalization compares site-reported data from 12 months before implant to clinical events committee-adjudicated hospitalization 12 months after implant. SAS software version 9.4 (SAS Institute) was used for statistical analysis.

Results

Baseline characteristics

Among 176 patients enrolled at 20 centres in North America and Europe, 71.0% were female, mean age 78.7 years, Society of Thoracic Surgeons mortality scores of 7.4% (mitral valve repair) and 10.0% (mitral valve replacement), and EuroSCORE II 5.1% (*Table 1*). Tricuspid regurgitation grade was ≥severe in 88.0%, with aetiologies of secondary (68.2%), mixed (14.2%), primary (9.7%), indeterminate (5.1%), and pacer related (2.8%). Three-quarters (75.4%) of patients were in NYHA class III or IV, and significant comorbidities included atrial fibrillation (92.0%), hypertension (84.1%), pulmonary hypertension (75.0%), dyslipidaemia or hyperlipidaemia (65.3%), renal insufficiency or failure (58.5%), and ascites (22.2%). At baseline, 32.4% had a pre-existing cardiac implantable electronic device, 37.5% had a history of valve surgery or intervention, and 16.5% had prior coronary artery bypass grafting (*Table 1*). Baseline medications included diuretics (92.0%), anticoagulants (84.1%), beta blockers (72.7%), and antiplatelets (40.3%).

Procedural outcomes

Successful femoral access was achieved in 99.4% of patients (one case was aborted due to stenosis in right and left iliac veins), with a right-femoral-vein approach used in 93.8% of cases and pre-dilatation performed in 84.7%. The mean time from skin incision to closure was 121.4 ± 65.7 min, with 71.6 ± 31.4 min from delivery system insertion to removal and 34.4 ± 15.2 min of fluoroscopy. The median length of hospital stay was 3.0 (IQR: 2.0, 7.0) days, and 91.1% of patients were discharged to home (4.7% with organized home-health services). Device success was 94.4%, procedural success 93.0%, and clinical success 77.1%.

Safety outcomes

Thirty-day results

At 30 days, the composite MAE rate was 18.6% (*Table 2*). Cardiovascular mortality was 1.7%, and non-elective TV re-interventions occurred in 2.3%. These were a valve-in-valve implant during the index procedure after unsuccessful implantation due to challenging anatomy; two surgical explants for valve embolization, as previously reported;[21] and a valve-in-valve intervention for a partially detached valve. No patient required RV mechanical support following TTVR.

New permanent pacemakers (not included in the pre-defined composite MAE definition) were implanted in 15 patients (13.3% of patients without a pre-existing pacemaker), all within 9 days post-procedure. No patients received a new pacemaker after 30 days. Of those receiving new pacemakers, 14 had baseline atrial fibrillation, eight with additional conduction disturbances (i.e. left bundle branch block, right bundle branch block, prolonged QT interval, and atrioventricular block).

One-year results

Major adverse event rates at one year are presented in *Table 2*. The all-cause cause mortality rate ($n = 176$) was 9.1%, and the rate of hospitalization for HF was 10.2%. Kaplan–Meier estimates for all-cause mortality and HF hospitalization were 9.9 ± 2.3% and 11.6 ± 2.6%, respectively (*Figure 2*), and there was a 74.9% relative reduction in the rate of HF hospitalization in the 12 months before vs. after the procedure ($P < .001$; *Figure 3*).

Table 2 Major adverse events adjudicated by the clinical events committee at 30 days and one year

CEC-adjudicated MAEs	30 days ($n = 172$)[a]	1 year ($n = 149$)[a]
Cardiovascular mortality	1.7 (3)	9.4 (14)
Myocardial infarction	0.0 (0)	0.0 (0)
Stroke	0.6 (1)	1.3 (2)
Major cardiac structural complications	0.0 (0)	0.0 (0)
Renal complications requiring unplanned dialysis or renal replacement therapy	1.7 (3)	3.4 (5)
Non-elective tricuspid valve re-intervention	2.3 (4)	4.0 (6)
Major access site and vascular complications	2.3 (4)	2.7 (4)
Severe bleeding[b]	16.9 (29)[c]	25.5 (38)[d]
Major	8.1 (14)	10.7 (16)
Extensive	7.0 (12)	10.7 (16)
Life threatening	1.7 (3)	4.7 (7)
Fatal	0.6 (1)	0.7 (1)
Device-related pulmonary embolism	0.0 (0)	0.0 (0)
Composite MAEs	**18.6 (32)[e]**	**30.2 (45)[e]**

Values are given as % (*n*).
CEC, clinical events committee; MAEs, major adverse events.
[a]Denominator includes patients who have been in the trial for at least the specified timepoint or have had an MAE, and number of patients who have had an event is shown.
[b]Severe bleeding as defined by the Mitral Valve Academic Research Consortium.
[c]Most common causes of bleeding up to 30 days were access/puncture-site related ($n = 11$) and gastrointestinal ($n = 8$).
[d]Most common cause of bleeding after 30 days was gastrointestinal ($n = 8$).
[e]Composite (bold) MAE *n* is counted as the number of patients experiencing at least one MAE. One-year counts are cumulative.

Echocardiographic outcomes

In paired analysis from baseline to one year, 97.6% of implanted patients had TR ≤ mild, with 69.0% having no or trace TR ($P < .001$) (*Figure 4*). All patients (100%) experienced at least one grade reduction in TR severity, 97.6% had ≥two grade reductions, and 33.3% ≥four grade reductions. The majority (88.2%) of patients had no or trace paravalvular leak, with 10.6% mild and 1.2% moderate. Changes from baseline to one-year follow-up TTE (*Table 3*) included reductions in RV mid-ventricular end-diastolic diameter (−6.3 ± 9.5 mm, $P < .001$) and IVC diameter at end-expiration (−7.2 ± 5.9 mm, $P < .001$). In the setting of a stable LV ejection fraction ($P = .197$), there were significant increases in LV outflow tract stroke volume (10.5 ± 16.8 mL, $P < .001$) and cardiac output (0.6 ± 1.2 L/min, $P < .001$). Several parameters associated with RV systolic function decreased, including RV FAC (−8.4 ± 13.8%, $P < .001$) and TAPSE (−2.8 ± 6.5 mm, $P = .006$). Pulmonary artery systolic pressure also decreased (−6.8 ± 13.6 mmHg, $P = .003$). The TAPSE/PASP ratio was 0.48 mm/mmHg at baseline with an insignificant decrease at one year (−0.07 ± 0.36 mm/mmHg, $P = .439$).

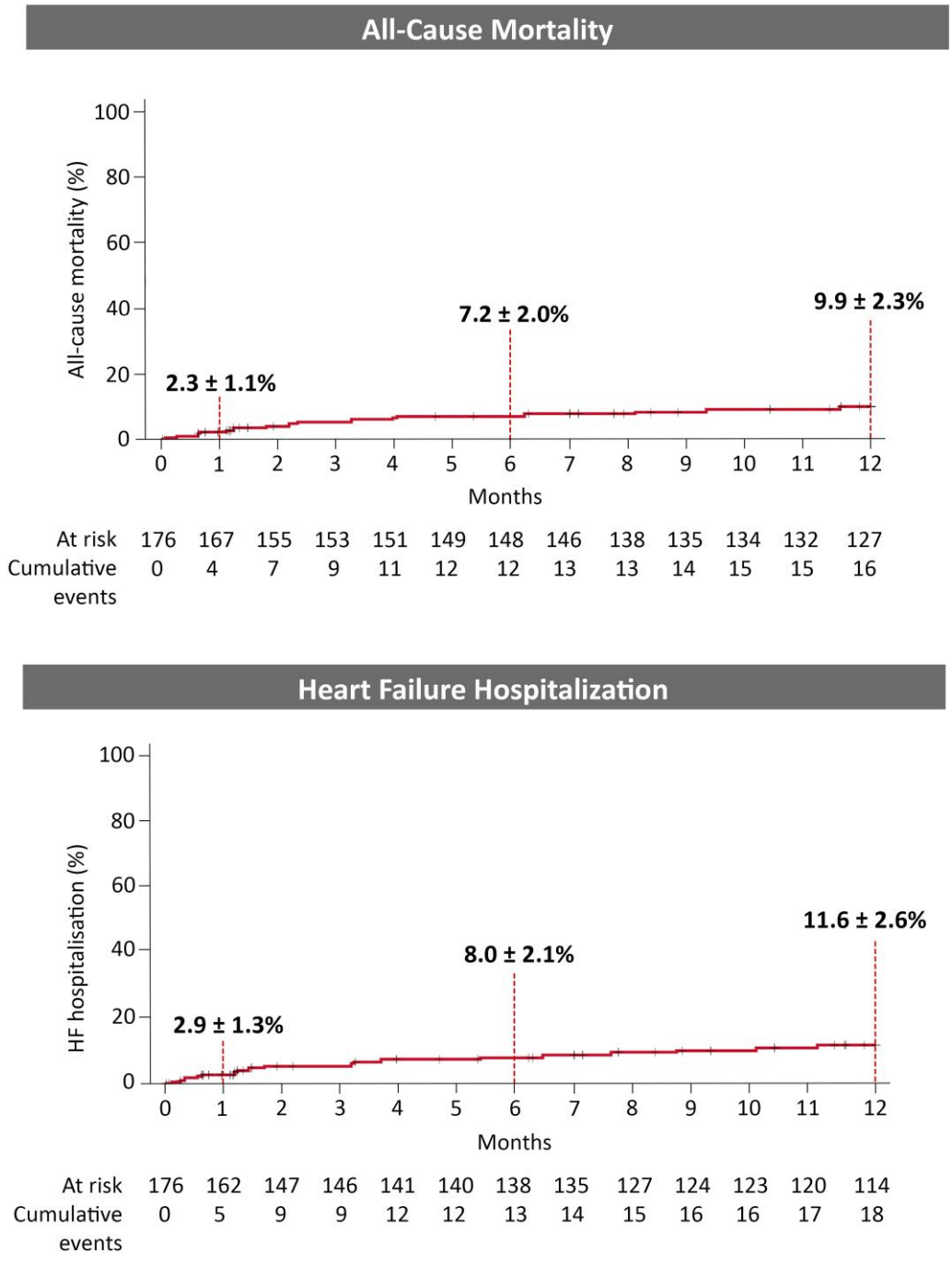


Figure 2 Kaplan–Meier estimates for all-cause mortality and heart failure (HF) hospitalizations to one year. Kaplan–Meier curves show time to first events.

Clinical, functional, and quality-of-life outcomes

Patients experienced significant and sustained improvements in clinical, functional, and quality-of-life outcomes in paired analyses compared with baseline (*Figure 4*). At one year, 93.3% of patients were in NYHA class I or II, compared with 25.8% at baseline ($P < .001$). The mean KCCQ overall summary score increased from 46.0 ± 21.8 points to 71.7 ± 22.0 points ($P < .001$), with 54.9% of patients improving by at least 20 points and 21.6% by 10–19 points; 50.0% had scores in the range of 75 to 100 points at one year. SF-36 mental scores improved by 5.7 ± 12.4 points ($P < .001$) and physical scores by 7.4 ± 9.5 points ($P < .001$) (*Figure 5*). There was also a significant improvement in mean 6MWD, which increased by 56.2 ± 117.0 m ($P < .001$). Patients lost body weight by a mean of 1.8 ± 6.3 kg ($P = .005$), and the proportion of patients with absent or grade 1 + oedema (assessed by standard pitting) improved from 63.9% at baseline to 86.6% at one year ($P < .001$). Changes in right and left ankle circumference were insignificant.

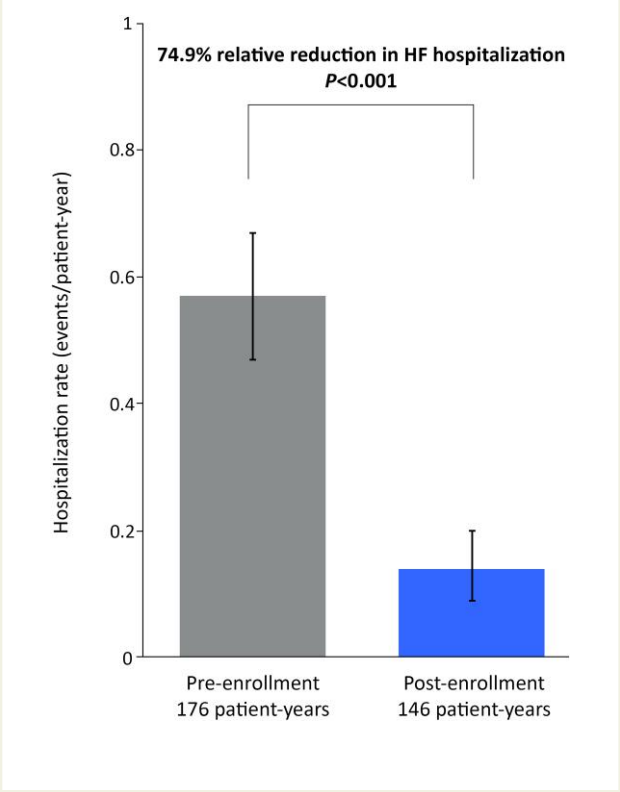


Figure 3 Patients experienced a 74.9% annualized reduction in heart failure hospitalizations between the 12 months before and 12 months after EVOQUE implantation. HF, heart failure.

Discussion

This study represents the largest cohort with one-year follow-up of patients undergoing TTVR for symptomatic TR. At one year, the TRISCEND study demonstrated the following for patients treated with the EVOQUE system: (i) device and procedural success of 94.4% and 93.0%, respectively; (ii) 9.1% all-cause mortality; (iii) 10.2% HF hospitalization rate with 74.9% annualized reduction; (iv) sustained TR reduction to grade ≤ mild in 97.6% of patients; (v) right-heart reverse remodelling with improvement in forward stroke volume and cardiac output; and (vi) marked improvement in functional and quality-of-life outcomes (*Structured Graphical Abstract*).

To place these results into context, recent natural history studies of comparable patients with symptomatic severe TR despite optimal medical therapy have shown one-year mortality rates between 36% and 42%, compared with 9.1% in this study.[5,28] The TriValve Registry showed that, compared with propensity-matched medically treated patients, TTVI in selected high-risk patients with symptomatic severe TR is associated with lower one-year mortality (23 ± 3% vs. 36 ± 3%; $P = .001$) and hospitalization rates (26 ± 3% vs. 47 ± 3%; $P < .0001$).[28] Surgical replacement carries a 10%–12% in-hospital mortality rate,[10,29] and other TTVR therapies have reported short-term mortality rates of 13%–17%.[22,24] The one-year mortality and HF hospitalization rates in the TRISCEND study are the lowest reported for transcatheter replacement therapies in this otherwise high-risk, comorbid population. The estimated 74.9% reduction in annualized HF hospitalization, if confirmed by randomized controlled trials, is not only impactful for patients but also for healthcare systems.

The MAE rate in this study was primarily driven by severe bleeding events. Of these, all but one patient were on an antiplatelet and/or anticoagulation regimen at baseline, elevating the risk for bleeding complications. Moreover, patients had multiple comorbidities that increase the risk for bleeding, including renal insufficiency, liver dysfunction, and past medical history of bleeding.[30,31] In medically managed TR patients, of whom >80% are on chronic anticoagulation and >20% have cirrhosis, gastrointestinal bleeding rates are reportedly high, exceeding 15 per 100 patient-years.[32] Bleeding rates in the TRISCEND study are thus consistent with the patient population and may not be device specific. Although not defined as an MAE, 15 patients required new pacing; however, the 13.3% rate of new pacemaker implants at 30 days is similar to the reported rates of 10%–14% following TV surgery.[10,33]

Of the attempted device implants, 5.6% were unsuccessful, with half of these procedures aborted due to insufficient imaging and/or unfavourable patient anatomy. Intraprocedural imaging should improve with increased experience and the development of formal acquisition protocols and advanced imaging tools for TV replacement.[34] This early experience with TTVR provided insights into potential anatomical challenges, including sizing, RV dimensions and function, and IVC-to-annulus offset, that are important to consider when planning interventions. Future learnings will help elucidate best approaches for diverse patient anatomies.

A general concern with TTVR therapies is an anticipated reduction in RV function and RV stroke volume when TR is alleviated.[35–37] A recent meta-analysis of TTVI studies suggests that, for any transcatheter device therapy, a reduction in TR is associated with a reduction in echocardiographic measures of RV function yet is also associated with right-heart reverse remodelling with an increase in forward stroke volume.[15] The echocardiographic findings from the TRISCEND study are consistent with evidence of right-heart reverse remodelling (i.e. reduction in mid-RV dimensions and IVC diameter) and increases in both stroke volume and cardiac output, despite a reduction in standard measures of RV function. Right ventricular-pulmonary artery coupling, which indexes RV function to afterload, may be a more physiologic measure of RV function and has been shown to predict outcomes in transcatheter device therapies.[35,38] Baseline high RV-pulmonary artery coupling, as well as a decline in coupling measurements (suggesting RV-pulmonary artery coupling 'reserve'), are independently associated with reduced all-cause mortality following TTVI.[35] Patients in the TRISCEND study had a high baseline ratio of TAPSE/PASP and a decline at one year (although insignificant), consistent with normal RV-pulmonary artery coupling at baseline, and RV functional reserve at one year. Importantly, TAPSE/PASP at both baseline and one year suggest that RV function remains appropriately coupled to the increase in effective afterload associated with TR reduction.

The recent publication of the TRILUMINATE Pivotal trial[39] on TEER raises questions about the clinical benefit of TR reduction. TRILUMINATE randomized patients to tricuspid TEER or medical therapy with a 12-month primary hierarchical outcome of (i) mortality or TV surgery, (ii) HF hospitalization, and (iii) quality-of-life improvement ≥ 15 points assessed using the KCCQ. The primary endpoint results favoured the TEER group ($P = .02$), driven mainly by significant improvement in KCCQ, without a difference in mortality, TV surgery, or HF hospitalization, despite significant reduction in TR after the TEER implant. Interestingly, patients who derived the most benefit in symptomatic improvement had the greatest reduction in TR, suggesting that degree of TR reduction is important in transcatheter therapy. The reasons for lack of differences in these important endpoints are unknown and deserve further investigation.

There are important differences in TRILUMINATE and TRISCEND patient populations. Patients in the TRISCEND study likely had more

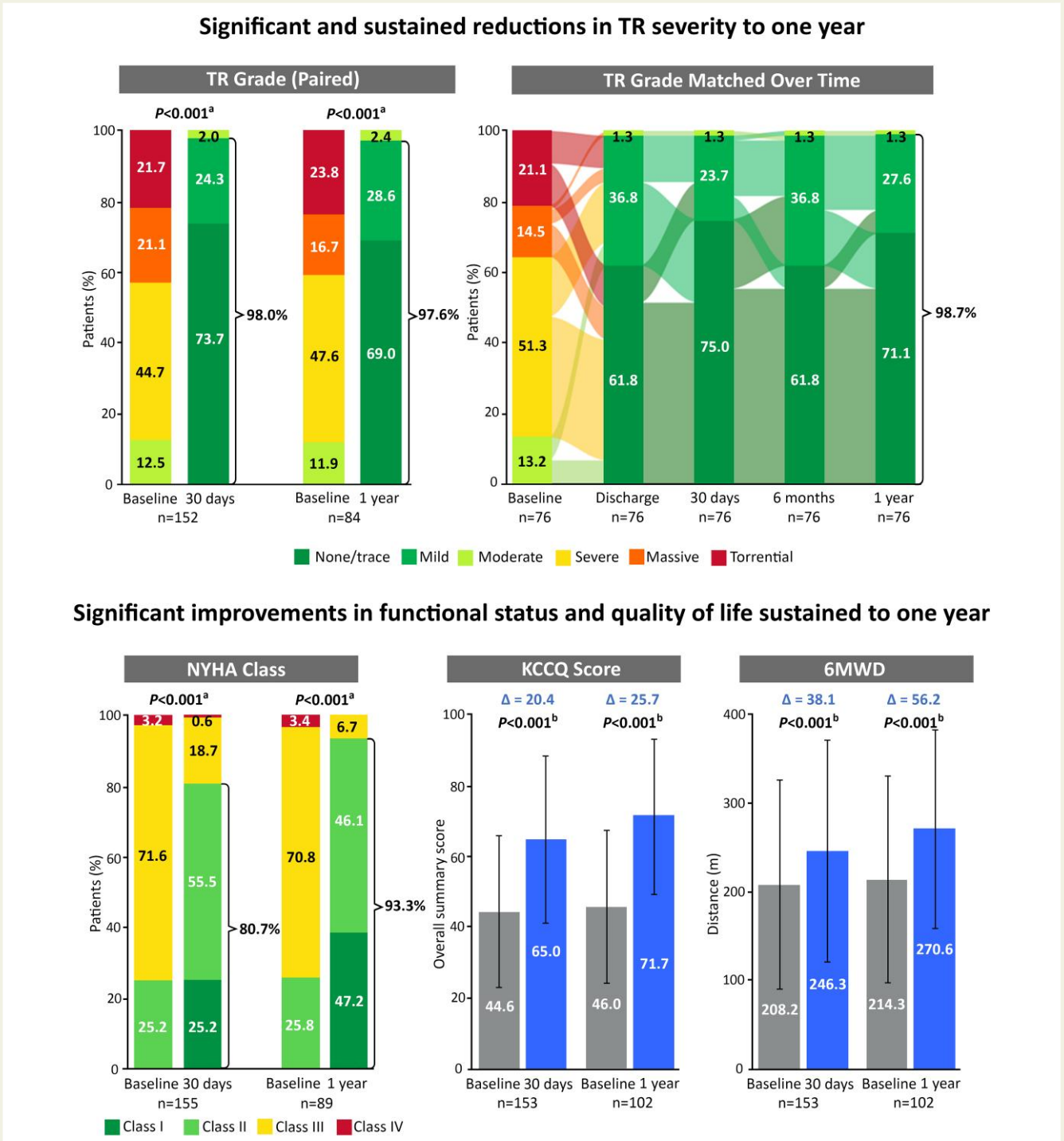


Figure 4 One-year results of transfemoral tricuspid valve replacement with the EVOQUE valve showed significant improvements in tricuspid regurgitation severity, New York Heart Association (NYHA) functional class, Kansas City Cardiomyopathy Questionnaire (KCCQ) score, and six-minute walk distance (6MWD) in paired analysis. The Sankey diagram, top right, shows the flow of TR grade changes among patients who completed every echocardiographic follow-up visit; the width of the arcs between time points represents the proportion of patients who experienced a specific grade change (e.g. severe to none/trace). [a]*P*-values calculated by Wilcoxon signed rank test. [b]*P*-values calculated by paired *t*-test. Error bars show standard deviation. TR, tricuspid regurgitation.

advanced disease with more patients presenting in NYHA class III/IV (75.4% in TRISCEND vs. 59.4% in TRILUMINATE), with renal disease (58.5% vs. 35.4%), and with prior year HF hospitalization (40.9% vs. 25.1%). The TRILUMINATE trial showed a graded response of the KCCQ overall score to TR reduction, and the nearly complete elimination of TR in the TRISCEND study [2.4% residual moderate TR (0.0% ≥ severe) in TRISCEND vs. 50.3% residual moderate or greater TR in TRILUMINATE] may be why, compared to TEER, TTVR resulted

Table 3 Paired changes observed on transthoracic echocardiogram at baseline and one-year follow-up

	Baseline	One year	Δ One year—baseline *P*-value[a]
RV end-diastolic mid diameter, mm	41.4 ± 8.8 (69)	35.0 ± 7.4 (69)	−6.3 ± 9.5 −6.0 (−12.0, .0) **P < .001**
RV fractional area change, %	38.7 ± 10.1 (59)	30.3 ± 10.6 (59)	−8.4 ± 13.8 −10.0 (−17.0, −2.0) **P < .001**
TAPSE, mm	15.3 ± 5.2 (46)	12.5 ± 4.2 (46)	−2.8 ± 6.5 −2.0 (−5.0, 1.0) **P = .006**
RA volume systolic, mL	144.4 ± 54.1 (73)	140.5 ± 53.8 (73)	−3.9 ± 42.3 −2.0 (−27.8, 25.0) P = .434
IVC diameter (expiration), mm	27.6 ± 7.7 (76)	20.4 ± 5.1 (76)	−7.2 ± 5.9 −7.0 (−11.0, −3.0) **P < .001**
LVEF, %	54.1 ± 11.2 (70)	55.6 ± 10.9 (70)	1.5 ± 9.7 2.0 (−5.0, 7.0) P = .197
Cardiac output (LVOT), L/min	4.0 ± 1.1 (81)	4.5 ± 1.1 (81)	.6 ± 1.2 .4 (−.1, 1.2) **P < .001**
Stroke volume (LVOT), mL	54.8 ± 15.8 (81)	65.3 ± 17.6 (81)	10.5 ± 16.8 9.0 (1.0, 14.0) **P < .001**
RA pressure systolic, mmHg	12.0 ± 4.8 (75)	8.7 ± 4.7 (75)	−3.3 ± 5.9 .0 (−7.0, .0) **P < .001**
IVC respiratory variation (derived), %	30.2 ± 16.9 (74)	40.5 ± 17.3 (74)	10.3 ± 24.2 10.0 (−5.0, 28.0) **P < .001**
PASP, mmHg	39.3 ± 12.8 (40)	32.5 ± 11.0 (40)	−6.8 ± 13.6 −5.2 (12.9, 1.8) **P = .003**
TAPSE/PASP	0.48 ± 0.26 (22)	0.41 ± 0.21 (22)	−.07 ± .36 −.04 (−.3, .1) P = .439
TV mean gradient, mmHg	1.7 ± 1.0 (82)	3.4 ± 1.4 (82)	1.7 ± 1.6 1.7 (.8, 2.8) **P < .001**
LVOT VTI	18.0 ± 4.3 (81)	18.9 ± 4.2 (81)	.9 ± 4.3 1.0 (−2.0, 2.6) P = .054
Hepatic vein flow reversal	*n* = 49	*n* = 49	**P < .001**[b]
S-dominant	0 (0)	26.5 (13)	
D-dominant	4.1 (2)	63.3 (31)	
S-reversal	95.9 (47)	10.2 (5)	

Results reported that data are given as mean ± SD (*n*), % (*n*), or median (IQR).
IVC, inferior vena cava; LV, left ventricle; LVEF, LV ejection fraction; LVOT VTI, LV outflow tract velocity time integral; PASP, pulmonary artery systolic pressure; RA, right atrium; RV, right ventricle; TAPSE, tricuspid annular plane systolic excursion; TV, tricuspid valve.
[a]*P*-values calculated by paired *t*-test, unless otherwise noted.
[b]*P*-values calculated by Wilcoxon signed rank test.
Bold values are statistically significant.

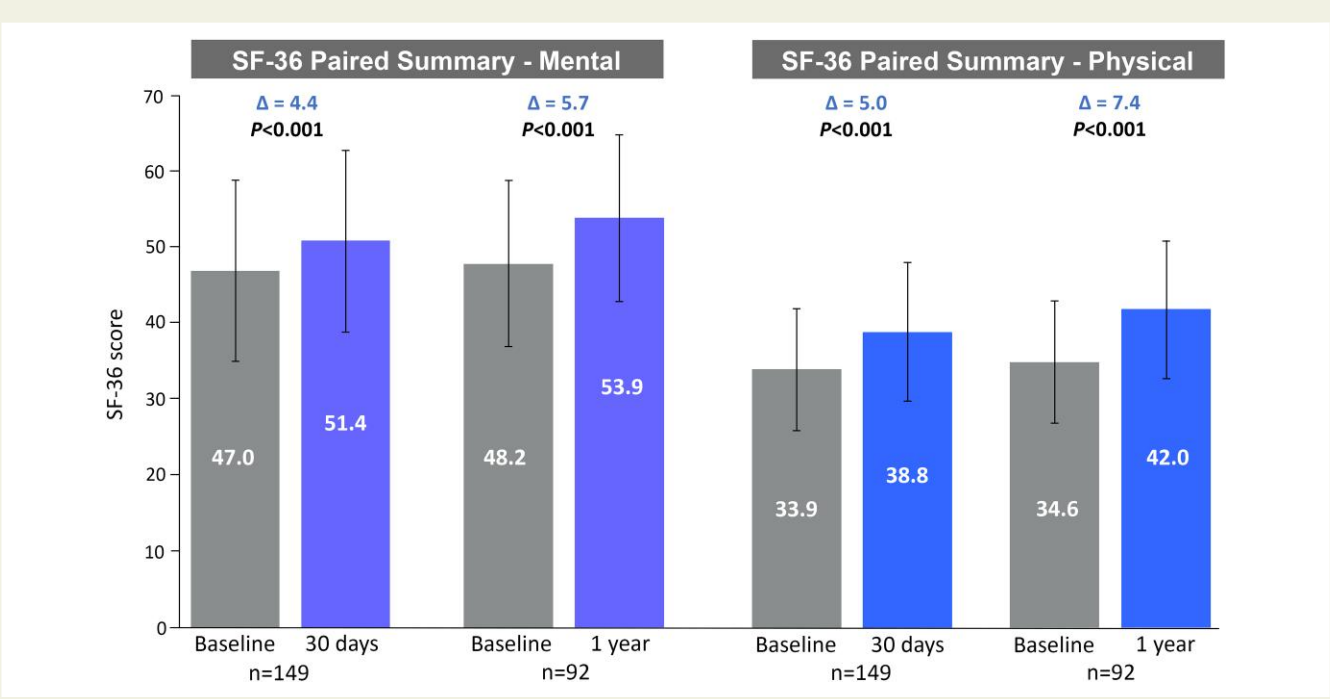


Figure 5 Short Form Health Survey (SF-36) scores improved significantly for mental and physical domains on paired analysis. *P*-values calculated by paired *t*-test; error bars represent standard deviation.

in marked improvement in the KCCQ (25.7 points vs. 12.3 points) and 6MWD (+56.2 m vs. −8.1 m).[39] Because the signs and symptoms of severe chronic TR are related to low cardiac output, the sustained reduction in TR and the improvement in forward stroke volume after TTVR likely explains the marked improvement in NYHA class, KCCQ, and 6MWD at one year. Indeed, the magnitude of improvements in symptoms, quality of life, and functional metrics are among the largest reported for any transcatheter valve therapy trials.[17,40–42]

Limitations

The main limitation of this study is the single-arm design without comparison to standard of care, which is under investigation in a randomized pivotal trial. In addition, these results reflect the treatment of a highly selected patient cohort in specialized centres with extensive experience in transcatheter valve intervention, and outcomes may not be generalizable. Additionally, as an interim analysis, not all enrolled patients had yet reached their one-year follow-up. Moreover, echocardiographic data were incomplete due to unmeasurable variables on some echocardiograms—a sign of the inherent challenges of TV imaging. Finally, TTVR is an evolving field and standardized criteria for data collection and clinical trial definitions continue to develop.

Conclusions

In patients with significant, symptomatic TR, TTVR with the transfemoral EVOQUE system in the TRISCEND study demonstrated high procedural success and sustained TR reduction to mild or none at one year. A high burden of comorbidities contributed to risk of bleeding and new pacemakers and underscore both the challenges and need for treatment options for this high-risk group of patients. In this study representing the largest one-year follow-up of patients undergoing TTVR for symptomatic TR, patients experienced marked improvements in symptoms and functional and quality-of-life outcomes with low mortality and reduced hospitalization rates. The TRISCEND II randomized pivotal trial is currently enrolling (ClinicalTrials.gov, NCT04482062).

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Supplementary data

Supplementary data are available at *European Heart Journal* online.

Declarations

Disclosure of Interest

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Data Availability

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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Ethical Approval

The TRISCEND study was conducted in compliance with the Declaration of Helsinki (2008), was approved by Institutional Review Boards of all participating sites, and all patients provided written informed consent. Study oversight included an independent clinical events committee, a data safety monitoring board, and an echocardiography core laboratory.

Pre-registered Clinical Trial Number

The pre-registered clinical trial number is ClinicalTrials.gov/NCT04221490.

References

1. Topilsky Y, Maltais S, Medina Inojosa J, Oguz D, Michelena H, Maalouf J, *et al.* Burden of tricuspid regurgitation in patients diagnosed in the community setting. *JACC Cardiovasc Imaging* 2019;**12**:433–42. https://doi.org/10.1016/j.jcmg.2018.06.014
2. Vieitez JM, Monteagudo JM, Mahia P, Perez L, Lopez T, Marco I, *et al.* New insights of tricuspid regurgitation: a large-scale prospective cohort study. *Eur Heart J Cardiovasc Imaging* 2021;**22**:196–202. https://doi.org/10.1093/ehjci/jeaa205
3. Yang L, Chen H, Pan W, Guan L, Zhang X, Zhang L, *et al.* Analyses for prevalence and outcome of tricuspid regurgitation in China: an echocardiography study of 134,874 patients. *Cardiology* 2019;**142**:40–6. https://doi.org/10.1159/000496601
4. Condello F, Gitto M, Stefanini GG. Etiology, epidemiology, pathophysiology and management of tricuspid regurgitation: an overview. *Rev Cardiovasc Med* 2021;**22**:1115–42. https://doi.org/10.31083/j.rcm2204122
5. Offen S, Playford D, Strange G, Stewart S, Celermajer DS. Adverse prognostic impact of even mild or moderate tricuspid regurgitation: insights from the national

echocardiography database of Australia. *J Am Soc Echocardiogr* 2022;**35**:810–7. https://doi.org/10.1016/j.echo.2022.04.003
6. Topilsky Y, Nkomo VT, Vatury O, Michelena HI, Letourneau T, Suri RM, *et al.* Clinical outcome of isolated tricuspid regurgitation. *JACC Cardiovasc Imaging* 2014;**7**:1185–94. https://doi.org/10.1016/j.jcmg.2014.07.018
7. Chorin E, Rozenbaum Z, Topilsky Y, Konigstein M, Ziv-Baran T, Richert E, *et al.* Tricuspid regurgitation and long-term clinical outcomes. *Eur Heart J Cardiovasc Imaging* 2020;**21**:157–65. https://doi.org/10.1093/ehjci/jez216
8. Benfari G, Antoine C, Miller WL, Thapa P, Topilsky Y, Rossi A, *et al.* Excess mortality associated with functional tricuspid regurgitation complicating heart failure with reduced ejection fraction. *Circulation* 2019;**140**:196–206. https://doi.org/10.1161/CIRCULATIONAHA.118.038946
9. Dreyfus GD, Essayagh B. Transcatheter treatment options for severe tricuspid regurgitation: and the winner is valve replacement? *JACC Cardiovasc Interv* 2021;**14**:512–4. https://doi.org/10.1016/j.jcin.2021.01.012
10. Scotti A, Sturla M, Granada JF, Kodali SK, Coisne A, Mangieri A, *et al.* Outcomes of isolated tricuspid valve replacement: a systematic review and meta-analysis of 5,316 patients from 35 studies. *EuroIntervention* 2022;**18**:840–51. https://doi.org/10.4244/eij-d-22-00442
11. Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin JP, Gentile F, *et al.* 2020 ACC/AHA guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association joint committee on clinical practice guidelines. *Circulation* 2021;**143**:e35–71. https://doi.org/10.1161/CIR.0000000000000932
12. Spinka G, Bartko PE, Heitzinger G, Prausmüller S, Pavo N, Frey MK, *et al.* Natural course of nonsevere secondary tricuspid regurgitation. *J Am Soc Echocardiogr* 2021;**34**:13–9. https://doi.org/10.1016/j.echo.2020.08.018
13. Fender EA, Zack CJ, Nishimura RA. Isolated tricuspid regurgitation: outcomes and therapeutic interventions. *Heart* 2018;**104**:798–806. https://doi.org/10.1136/heartjnl-2017-311586
14. Praz F, Muraru D, Kreidel F, Lurz P, Hahn RT, Delgado V, *et al.* Transcatheter treatment for tricuspid valve disease. *EuroIntervention* 2021;**17**:791–808. https://doi.org/10.4244/eij-d-21-00695
15. Sannino A, Ilardi F, Hahn RT, Lancellotti P, Lurz P, Smith RL, *et al.* Clinical and echocardiographic outcomes of transcatheter tricuspid valve interventions: a systematic review and meta-analysis. *Front Cardiovasc Med* 2022;**9**:919395. https://doi.org/10.3389/fcvm.2022.919395
16. Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J, *et al.* 2021 ESC/EACTS guidelines for the management of valvular heart disease. *Eur Heart J* 2022;**43**:561–632. https://doi.org/10.1093/eurheartj/ehab395
17. Nickenig G, Weber M, Lurz P, von Bardeleben RS, Sitges M, Sorajja P, *et al.* Transcatheter edge-to-edge repair for reduction of tricuspid regurgitation: 6-month outcomes of the TRILUMINATE single-arm study. *Lancet* 2019;**394**:2002–11. https://doi.org/10.1016/S0140-6736(19)32600-5
18. Kodali S, Hahn RT, Eleid MF, Kipperman R, Smith R, Lim DS, *et al.* Feasibility study of the transcatheter valve repair system for severe tricuspid regurgitation. *J Am Coll Cardiol* 2021;**77**:345–56. https://doi.org/10.1016/j.jacc.2020.11.047
19. Besler C, Orban M, Rommel KP, Braun D, Patel M, Hagl C, *et al.* Predictors of procedural and clinical outcomes in patients with symptomatic tricuspid regurgitation undergoing transcatheter edge-to-edge repair. *JACC Cardiovasc Interv* 2018;**11**:1119–28. https://doi.org/10.1016/j.jcin.2018.05.002
20. Sugiura A, Tanaka T, Kavsur R, Öztürk C, Vogelhuber J, Wilde N, *et al.* Leaflet configuration and residual tricuspid regurgitation after transcatheter edge-to-edge tricuspid repair. *JACC Cardiovasc Interv* 2021;**14**:2260–70. https://doi.org/10.1016/j.jcin.2021.07.048
21. Kodali S, Hahn RT, George I, Davidson CJ, Narang A, Zahr F, *et al.* Transfemoral tricuspid valve replacement in patients with tricuspid regurgitation: TRISCEND study 30-day results. *JACC Cardiovasc Interv* 2022;**15**:471–80. https://doi.org/10.1016/j.jcin.2022.01.016
22. Hahn RT, Kodali S, Fam N, Bapat V, Bartus K, Rodés-Cabau J, *et al.* Early multinational experience of transcatheter tricuspid valve replacement for treating severe tricuspid regurgitation. *JACC Cardiovasc Interv* 2020;**13**:2482–93. https://doi.org/10.1016/j.jcin.2020.07.008
23. Webb JG, Chuang AM, Meier D, von Bardeleben RS, Kodali SK, Smith RL, *et al.* Transcatheter tricuspid valve replacement with the EVOQUE system: 1-year outcomes of a multicenter, first-in-human experience. *JACC Cardiovasc Interv* 2022;**15**:481–91. https://doi.org/10.1016/j.jcin.2022.01.280
24. Lu FL, An Z, Ma Y, Song ZG, Cai CL, Li BL, *et al.* Transcatheter tricuspid valve replacement in patients with severe tricuspid regurgitation. *Heart* 2021;**107**:1664–70. https://doi.org/10.1136/heartjnl-2020-318199
25. Stone GW, Adams DH, Abraham WT, Kappetein AP, Généreux P, Vranckx P, *et al.* Clinical trial design principles and endpoint definitions for transcatheter mitral valve repair and replacement: part 2: endpoint definitions: a consensus document from the mitral valve academic research consortium. *J Am Coll Cardiol* 2015;**66**:308–21. https://doi.org/10.1016/j.jacc.2015.05.049
26. Hahn RT, Zamorano JL. The need for a new tricuspid regurgitation grading scheme. *Eur Heart J Cardiovasc Imaging* 2017;**18**:1342–3. https://doi.org/10.1093/ehjci/jex139
27. Hahn RT, Abraham T, Adams MS, Bruce CJ, Glas KE, Lang RM, *et al.* Guidelines for performing a comprehensive transesophageal echocardiographic examination: recommendations from the American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists. *J Am Soc Echocardiogr* 2013;**26**:921–64. https://doi.org/10.1016/j.echo.2013.07.009
28. Taramasso M, Benfari G, van der Bijl P, Alessandrini H, Attinger-Toller A, Biasco L, *et al.* Transcatheter versus medical treatment of patients with symptomatic severe tricuspid regurgitation. *J Am Coll Cardiol* 2019;**74**:2998–3008. https://doi.org/10.1016/j.jacc.2019.09.028
29. Dreyfus J, Flagiello M, Bazire B, Eggenspieler F, Viau F, Riant E, *et al.* Isolated tricuspid valve surgery: impact of aetiology and clinical presentation on outcomes. *Eur Heart J* 2020;**41**:4304–17. https://doi.org/10.1093/eurheartj/ehaa643
30. O'Brien EC, Simon DN, Thomas LE, Hylek EM, Gersh BJ, Ansell JE, *et al.* The ORBIT bleeding score: a simple bedside score to assess bleeding risk in atrial fibrillation. *Eur Heart J* 2015;**36**:3258–64. https://doi.org/10.1093/eurheartj/ehv476
31. Lip GY, Frison L, Halperin JL, Lane DA. Comparative validation of a novel risk score for predicting bleeding risk in anticoagulated patients with atrial fibrillation: the HAS-BLED (Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly, Drugs/Alcohol Concomitantly) score. *J Am Coll Cardiol* 2011;**57**:173–80. https://doi.org/10.1016/j.jacc.2010.09.024
32. Cai S, Bowers N, Dhoot A, Ho EC, Ong G, Eckstein J, *et al.* Natural history of severe tricuspid regurgitation: outcomes after transcatheter tricuspid valve intervention compared to medical therapy. *Int J Cardiol* 2020;**320**:49–54. https://doi.org/10.1016/j.ijcard.2020.07.018
33. Gammie JS, Chu MWA, Falk V, Overbey JR, Moskowitz AJ, Gillinov M, *et al.* Concomitant tricuspid repair in patients with degenerative mitral regurgitation. *N Engl J Med* 2022;**386**:327–39. https://doi.org/10.1056/NEJMoa2115961
34. Hahn RT, Saric M, Faletra FF, Garg R, Gillam LD, Horton K, *et al.* Recommended standards for the performance of transesophageal echocardiographic screening for structural heart intervention: from the American Society of Echocardiography. *J Am Soc Echocardiogr* 2022;**35**:1–76. https://doi.org/10.1016/j.echo.2021.07.006
35. Brener MI, Lurz P, Hausleiter J, Rodés-Cabau J, Fam N, Kodali SK, *et al.* Right ventricular-pulmonary arterial coupling and afterload reserve in patients undergoing transcatheter tricuspid valve repair. *J Am Coll Cardiol* 2022;**79**:448–61. https://doi.org/10.1016/j.jacc.2021.11.031
36. Brener MI, Masoumi A, Ng VG, Tello K, Bastos MB, Cornwell WK III, *et al.* Invasive right ventricular pressure-volume analysis: basic principles, clinical applications, and practical recommendations. *Circ Heart Fail* 2022;**15**:e009101. https://doi.org/10.1161/circheartfailure.121.009101
37. Rommel KP, Besler C, Noack T, Blazek S, von Roeder M, Fengler K, *et al.* Physiological and clinical consequences of right ventricular volume overload reduction after transcatheter treatment for tricuspid regurgitation. *JACC Cardiovasc Interv* 2019;**12**:1423–34. https://doi.org/10.1016/j.jcin.2019.02.042
38. Cahill TJ, Pibarot P, Yu X, Babaliaros V, Blanke P, Clavel MA, *et al.* Impact of right ventricle-pulmonary artery coupling on clinical outcomes in the PARTNER 3 trial. *JACC Cardiovasc Interv* 2022;**15**:1823–33. https://doi.org/10.1016/j.jcin.2022.07.005
39. Sorajja P, Whisenant B, Hamid N, Naik H, Makkar R, Tadros P, *et al.* Transcatheter repair for patients with tricuspid regurgitation. *N Engl J Med* 2023;**388**:1833–42. https://doi.org/10.1056/NEJMoa2300525
40. Nickenig G, Weber M, Schuler R, Hausleiter J, Nabauer M, von Bardeleben RS, *et al.* Tricuspid valve repair with the Cardioband system: two-year outcomes of the multicentre, prospective TRI-REPAIR study. *EuroIntervention* 2021;**16**:e1264–71. https://doi.org/10.4244/EIJ-D-20-01107
41. Stone GW, Lindenfeld J, Abraham WT, Kar S, Lim DS, Mishell JM, *et al.* Transcatheter mitral-valve repair in patients with heart failure. *N Engl J Med* 2018;**379**:2307–18. https://doi.org/10.1056/NEJMoa1806640
42. Baron SJ, Magnuson EA, Lu M, Wang K, Chinnakondepalli K, Mack M, *et al.* Health status after transcatheter versus surgical aortic valve replacement in low-risk patients with aortic stenosis. *J Am Coll Cardiol* 2019;**74**:2833–42. https://doi.org/10.1016/j.jacc.2019.09.007