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# 6-Month Outcomes of the TricValve System in Patients With Tricuspid Regurgitation

## The TRICUS EURO Study

Rodrigo Estévez-Loureiro, MD, PhD,[a] Angel Sánchez-Recalde, MD, PhD,[b] Ignacio J. Amat-Santos, MD, PhD,[c] Ignacio Cruz-González, MD, PhD,[d] Jose A. Baz, MD,[a] Isaac Pascual, MD, PhD,[e] Julia Mascherbauer, MD, PhD,[f] Omar Abdul-Jawad Altisent, MD, PhD,[g] Luis Nombela-Franco, MD, PhD,[h] Manuel Pan, MD, PhD,[i] Ramiro Trillo, MD,[j] Raul Moreno, MD, PhD,[k] Georg Delle Karth, MD, PhD,[l] Luisa Salido-Tahoces, MD,[b] Sandra Santos-Martinez, MD,[c] Jean C. Núñez, MD,[d] Cesar Moris, MD, PhD,[e] Georg Goliasch, MD, PhD,[f] Pilar Jimenez-Quevedo, MD, PhD,[h] Soledad Ojeda, MD, PhD,[i] Belén Cid-Álvarez, MD, PhD,[j] Evelyn Santiago-Vacas, MD,[g] Santiago Jimenez-Valero, MD,[k] Ana Serrador, MD, PhD,[c] Javier Martín-Moreiras, MD, PhD,[d] Andreas Strouhal, MD,[l] Christian Hengstenberg, MD,[f] Jose Luis Zamorano, MD, PhD,[b] Rishi Puri, MBBS, PhD,[m] Andrés Íñiguez-Romo, MD, PhD[a]

## ABSTRACT

**BACKGROUND** Severe tricuspid regurgitation (TR) is frequently associated with significant morbidity and mortality; such patients are often deemed to be at high surgical risk. Heterotopic bicaval stenting is an emerging, attractive transcatheter solution for these patients.

**OBJECTIVES** The aim of this study was to evaluate the 30-day safety and 6-month efficacy outcomes of specifically designed bioprosthetic valves for the superior and inferior vena cava.

**METHODS** TRICUS EURO (Safety and Efficacy of the TricValve® Transcatheter Bicaval Valves System in the Superior and Inferior Vena Cava in Patients With Severe Tricuspid Regurgitation) is a nonblinded, nonrandomized, single-arm, multicenter, prospective trial that enrolled patients from 12 European centers between December 2019 and February 2021. High-risk individuals with severe symptomatic TR despite optimal medical therapy were included. The primary endpoint was quality-of-life (QOL) improvement measured by Kansas City Cardiomyopathy Questionnaire score and New York Heart Association (NYHA) functional class improvement at 6-month follow-up.

**RESULTS** Thirty-five patients (mean age 76 ± 6.8 years, 83% women) were treated using the TricValve system. All patients at baseline were in NYHA functional class III or IV. At 30 days, procedural success was 94%, with no procedural deaths or conversions to surgery. A significant increase in QOL at 6 months follow-up was observed (baseline and 6-month Kansas City Cardiomyopathy Questionnaire scores 42.01 ± 22.3 and 59.7 ± 23.6, respectively; $P = 0.004$), correlating with a significant improvement in NYHA functional class, with 79.4% of patients noted to be in functional class I or II at 6 months ($P = 0.0006$). The rates of 6-month all-cause mortality and heart failure hospitalization were 8.5% and 20%, respectively.

**CONCLUSIONS** The dedicated bicaval system for treating severe symptomatic TR was associated with a high procedural success rate and significant improvements in both QOL and functional classification at 6 months follow-up. (J Am Coll Cardiol Intv 2022;15:1366–1377) © 2022 by the American College of Cardiology Foundation.

From [a]Complejo Hospitalario Universitario Alvaro Cunqueiro, Vigo, Spain; [b]Hospital Universitario Ramon y Cajal, CIBERCV, Madrid, Spain; [c]CIBERCV, Hospital Clínico Universitario de Valladolid, Valladolid, Spain; [d]Hospital Clinico Universitario de Salamanca, CIBERCV, IBSAL, Salamanca, Spain; [e]Hospital Universitario Central de Asturias, Oviedo, Spain; [f]Division of Cardiology, Department for Internal Medicine II, Medical University of Vienna, Vienna, Austria; [g]Hospital Universitario Germans Trias i Pujol, Barcelona, Spain; [h]Cardiovascular Institute, Hospital Clínico San Carlos, IdISSC, Madrid, Spain; [i]Hospital Universitario Reina Sofia, Córdoba, Spain; [j]Hospital Clinico Universitario de Santiago de Compostela, CIBERCV, Santiago, Spain; [k]Hospital Universitario La Paz, Madrid, Spain; [l]Hospital Floridsdorf, Vienna, Austria; and the [m]Cleveland Clinic, Cleveland, Ohio, USA.

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Given the clinical relevance of severe symptomatic tricuspid regurgitation (TR),[1] significant efforts are under way to establish a range of effective transcatheter solutions that would obviate the need for high-risk surgical tricuspid valve (TV) surgery.[2,3] Left untreated, patients with severe TR face a dismal prognosis.[4-6] Current transcatheter TV interventions have largely focused on edge-to-edge repair or orthotopic replacement strategies.[7-9] The success of these therapies relies on both a suitable anatomy and effective periprocedural imaging guidance. Many patients with severe TR are deemed to be suboptimal candidates for these novel treatment approaches. Heterotopic bicaval stenting, or caval valve implantation (CAVI), has emerged as a possible transcatheter strategy for indirectly treating the systemic effects of severe TR.[10] This approach carries the inherent advantages of a streamlined fluoroscopic procedural work flow using familiar concepts akin to transcatheter aortic valve replacement. Following computed tomographic (CT) screening and procedural planning, the procedure is straightforward, avoiding the challenges of periprocedural navigation and guidance around the TV apparatus. However, nondedicated bicaval devices present significant limitations, such as the difficulty of sizing and anchoring, the necessity of prestenting in some cases, and the increased risk for embolization. Therefore, reproducible optimal outcomes have remained elusive.[11,12]

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To overcome these limitations, new specifically designed devices have been developed using the stent graft concept (Tricento, Trillium) or self-expanding valve implantation in both caval systems. The TricValve system (Products + Features) is a dedicated CAVI device consisting of 2 self-expanding Nitinol stents that harbor bovine pericardial leaflets, one specifically designed for the superior vena cava (SVC) and another for the inferior vena cava (IVC). TRICUS EURO (Safety and Efficacy of the TricValve® Transcatheter Bicaval Valves System in the Superior and Inferior Vena Cava in Patients With Severe Tricuspid Regurgitation; NCT04141137) was a Conformité Européenne mark trial testing the safety and efficacy of this dedicated CAVI system in patients with severe symptomatic TR deemed at high surgical risk. We report the 30-day safety and 6-month clinical results.

## METHODS

**TRIAL DESIGN, INCLUSION CRITERIA, AND PATIENT SELECTION.** TRICUS EURO was a nonblinded, nonrandomized, single-arm, multicenter, prospective trial enrolling patients from 12 institutions in Spain and Austria. The study enrolled adult individuals with symptomatic severe TR (grade ≥3 in a 5-grade classification) despite optimal medical therapy (symptoms and signs of right heart failure and New York Heart Association [NYHA] functional class III or IV). These findings needed to be demonstrated within 8 weeks prior to device implantation, with echocardiography demonstrating significant backflow in the IVC and/or SVC, with a v wave ≥25 mm Hg as demonstrated by right heart catheterization (measured in the IVC and/or SVC 2-4 cm above or below right atrial inflow). Patients required a left ventricular ejection fraction ≥40% and needed to be able to reach a 6-minute walk distance of ≥60 m. All patients needed to be ineligible for open heart surgery and were evaluated for clinical and anatomical suitability for CAVI by the local heart team as well as the TRICUS EURO eligibility committee.

The main exclusion criteria included severe right ventricular (RV) dysfunction (tricuspid annular plane systolic excursion [TAPSE] <13 mm) and/or the presence of severe pulmonary hypertension (systolic pulmonary pressure >65 mm Hg) and significant renal dysfunction (defined as serum creatinine >3.0 mg/dL) or use of any form of dialysis within the past 4 weeks and at time of screening. Other main exclusion criteria are noted in the Supplemental Appendix. The TRICUS EURO flowchart is summarized in **Figure 1**. Available valve sizes were 25/29 mm for the SVC and 31/35 mm for the IVC. The majority of exclusions were for anatomical reasons, mainly the limited range of diameters of the prosthesis available for the trial. The study was approved by the ethics committee of each of the recruiting centers. All patients gave informed consent.

**THE TRICVALVE SYSTEM.** The system comprises 2 self-expanding valves specifically designed for the

**ABBREVIATIONS AND ACRONYMS**

**CAVI** = caval valve implantation

**CT** = computed tomographic

**IVC** = inferior vena cava

**KCCQ** = Kansas City Cardiomyopathies Questionnaire

**NT-proBNP** = N-terminal pro-brain natriuretic peptide

**NYHA** = New York Heart Association

**QOL** = quality of life

**RV** = right ventricular

**SVC** = superior vena cava

**TAPSE** = tricuspid annular plane systolic excursion

**TR** = tricuspid regurgitation

**TV** = tricuspid valve

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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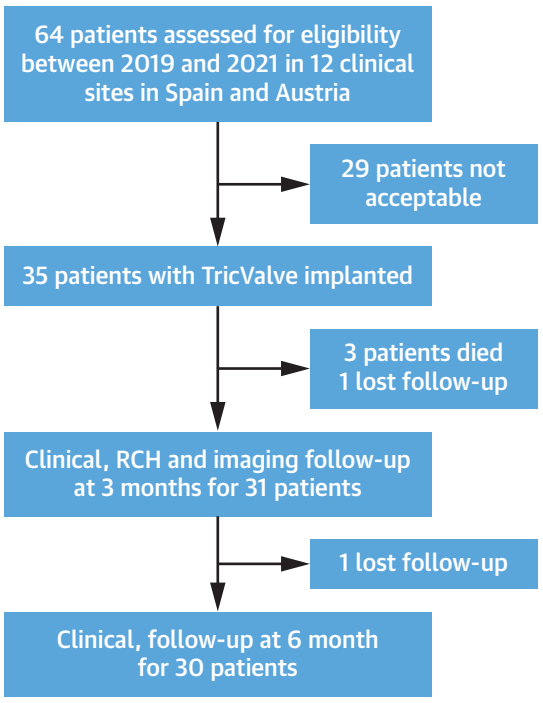
**FIGURE 1 Flowchart of Study**




Thirty-five high-risk patients with tricuspid regurgitation were treated using the TricValve system. RHC = right heart catheterization.

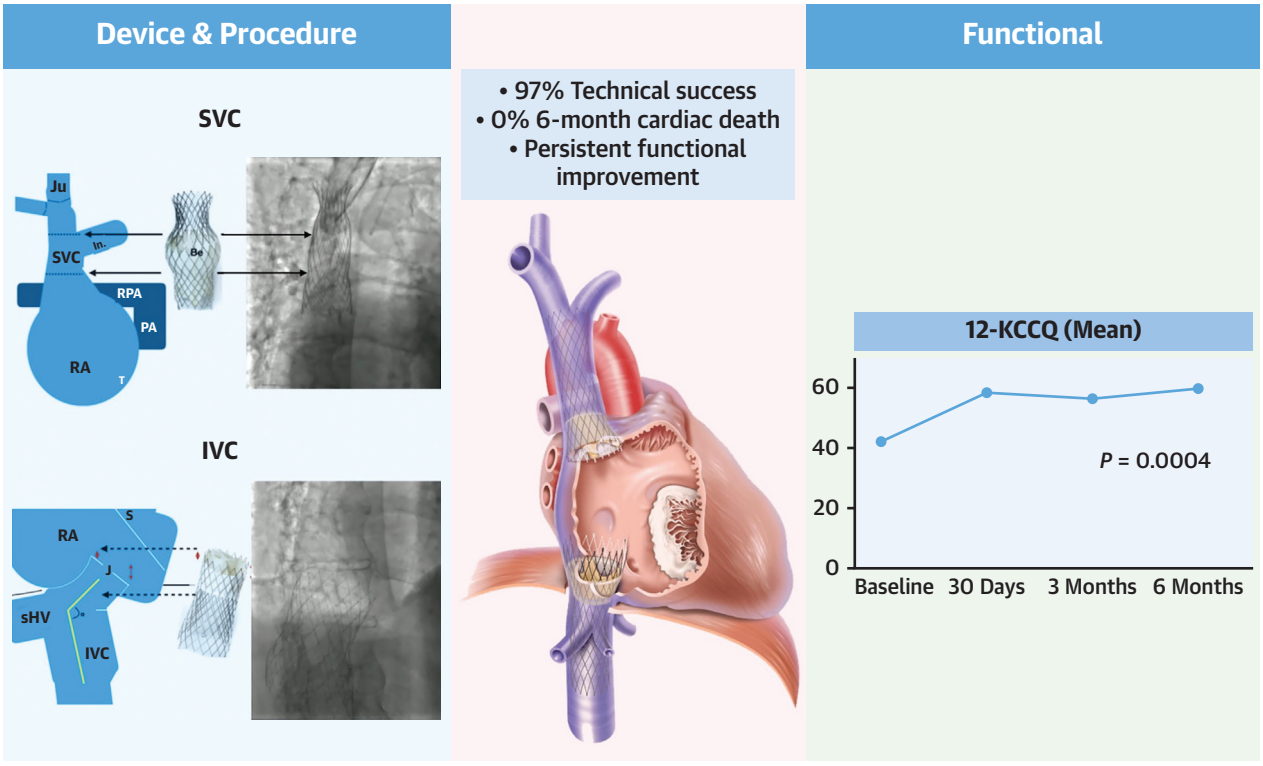
SVC and IVC (**Central Illustration**). Both devices are premounted in a 27.5-F delivery system. The prosthetic leaflets are processed with anticalcification treatments and chemically dehydrated to allow complete device pre-preloading and packaging, obviating the need for device loading at the time of procedure. Caval anchoring is based on stent design, radial force, and the degree of oversizing. The SVC prosthesis has a "belly design" in order to better accommodate the valve within the SVC to prevent dislodgement. It also harbors a long skirt covering the inferior half of the device in order to minimize paravalvular leak. The superior crown of the SVC prosthesis has low radial force, allowing valve stabilization and optimal SVC alignment. This part is uncovered to avoid interference with the venous drainage of the innominate system. The inferior prosthesis harbors a short skirt to avoid hepatic vein occlusion. It has high radial force within its superior segment, where the valve is fixed, and low radial force distally to allow soft interaction with the caval wall. Selection of valve sizing depends on CT measurements of both SVC and IVC. Multiple measurements are undertaken at different landmarks along the SVC and IVC. Length of the SVC and distance from the IVC to the origin of the hepatic veins are of high relevance to decide if the device can be accommodated in the SVC or IVC. Sizing information is included in Supplemental Figures 1 and 2.

**THE PROCEDURE.** Implantation requires 3 venous access sites: 1 right common femoral venous access sites for device deployment and 2 left common femoral venous access sites for pigtail control injections and a Swan-Ganz/multipurpose/JR catheter that is placed in the right pulmonary arterial branch to serve as a landmark during SVC valve deployment. Ideally the broad portion of the SVC valve should be placed just at the top of this landmark catheter.[13] Using the pigtail (plus a multipurpose catheter to serve as an additional marker within the innominate vein), an angiogram of the SVC is typically obtained to identify the optimal level of SVC valve deployment. A stiff wire placed in the right subclavian or internal jugular vein is recommended for valve deployment. Deployment should be performed slowly, starting in a high position with gentle downward device traction until it arrives at the target position. Valves are fully recapturable up to 80% of deployment.

For IVC deployment, a venogram of the hepatic veins centered on the confluence of the IVC and its junction with the right atrium is obtained, serving as a reference for deployment. The IVC prosthesis is deployed in a similar way to the SVC prosthesis, starting in a high position, toward the right atrium, while gently simultaneously retracting the system until the target position (proximal edge of the prosthesis landing between the right atrium and suprahepatic vein confluence). Transesophageal echocardiography or transthoracic echocardiography can be useful (although not mandatory), as the entrance or junction between the IVC and right atrium is usually well defined in the bicaval or subcostal view. An ideal IVC deployment usually involves <15-mm inflow protrusion into the right atrium. All procedural steps are performed under anticoagulation with unfractionated heparin, aiming for an activated clotting time of >300 seconds. Pacemaker leads are not a contraindication to the therapy. The SVC valve is deployed in the standard fashion, and the lead is trapped against the SVC wall. No lead dysfunction has been noted during procedures in the study. Normal lead function is assessed after implantation. A pictorial description of the procedure is shown in **Figure 2**.

**ENDPOINTS.** The primary endpoint was the assessment of change in NYHA functional class and change in quality of life (QOL) (measured using the 12-item

**CENTRAL ILLUSTRATION** **6-Month Outcomes of the TricValve System for Severe TR: TRICUS EURO Study (N = 35)**

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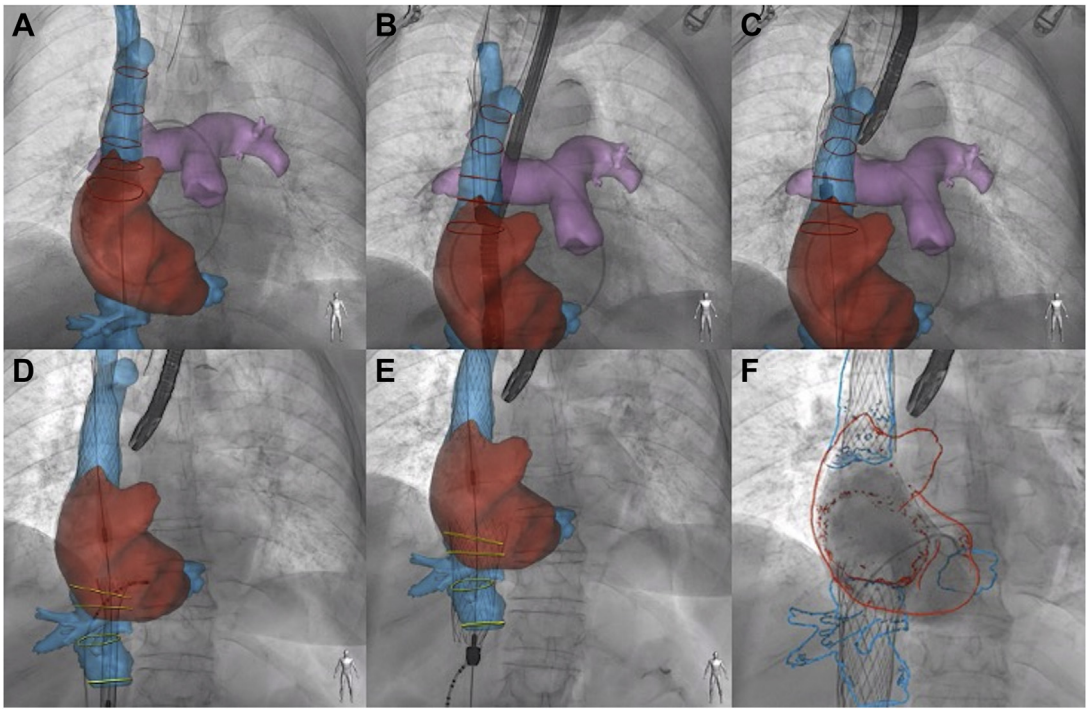
12-KCCQ = 12-item Kansas City Cardiomyopathy Questionnaire; Be = belly; In = innominate vein; IVC = inferior vena cava; J = juntion; JU = jugular vein; PA = pulmonary artery; RA = right atrium; RPA = right pulmonary artery; S = coronary sinus; sHV = suprahepatic vein; SVC = superior vena cava; T = tricuspid valve; TR = tricuspid regurgitation.

Kansas City Cardiomyopathy Questionnaire [KCCQ]) at 6 months after TricValve implantation. Secondary endpoints were as follows: 1) major adverse events, including death, myocardial infarction, cardiac tamponade, cardiac surgery for failed TricValve implantation, stroke, and major bleeding according to Valve Academic Research Consortium-2 criteria at 30-day and 6-month follow-up; 2) functional capacity assessed using the 6-minute walk test; 3) device implantation success (technical and procedural); 4) hemodynamic evaluation assessed on right heart catheterization at 3-month follow-up; 5) echocardiographic outcomes; and 6) laboratory parameters (liver enzymes, renal function, and N-terminal pro-brain natriuretic peptide [NT-proBNP])

An independent committee evaluated and adjudicated all safety and efficacy events. An independent echocardiography and computed tomography core laboratory assessed echocardiographic and CT outcomes during follow-up.

All clinical events were defined according to Valve Academic Research Consortium-2 criteria.[14] Device implantation success was defined as follows: 1) technical success, including successful percutaneous access and device positioning without periprocedural major adverse events; and 2) procedural success, defined as technical success plus the ability of the device to provide appropriate hemodynamic improvement in systemic venous backflow (evidenced by the fall of the v wave in the SVC and/or IVC immediately after intervention). QOL was assessed using the 12-item KCCQ,[15] which is a shorter version of the 23-item questionnaire assessing symptoms, function, and QOL that is more feasible to apply while preserving the instrument's psychometric properties.

**FIGURE 2 TricValve Procedure With Computed Tomographic Fusion Imaging**




**(A)** Both superior vena cava (SVC) and inferior vena cava (IVC) **(blue)** and right atrium (RA) **(red)**. Pulmonary artery (PA) in **violet**. A Swan-Ganz catheter is placed in right PA branch to serve as a landmark for SVC valve implantation. **(B)** SVC valve deployment. Free flow superior part is located in jugular vein. **(C)** Full deployment of SVC valve. Prosthesis "belly" is positioned above PA catheter. **(D)** Deployment of IVC valve. **(E)** Valve fully deployed with small protrusion in RA and correct positioning over the hepatic veins, without obstruction. **(F)** Right atrial angiogram showing abolishment of caval backflow.

**STATISTICAL ANALYSIS.** Descriptive data are presented as mean ± SD or median (IQR) depending on variable distribution. Categorical variables are described as frequencies and percentages. Changes in exercise capacity (6-minute walk distance), NYHA functional class, and QOL (KCCQ score) (prior to and following implantation) were evaluated using Student's paired *t*-test or the Wilcoxon test. Sensitivity analyses were carried out as well using the "last observation carried forward" method to evaluate the effect of missing values during follow-up in the main variables of the study, showing that missing data did not influence the results. All statistical tests used a 2-sided *P* value of 0.05 as a significance threshold. Statistical analysis was performed using IBM SPSS Statistics 25.

## RESULTS

**BASELINE CHARACTERISTICS.** From December 2019 to February 2021, 64 patients were screened for the study, of whom 35 met the inclusion criteria and were enrolled. Baseline characteristics of these 35 patients are shown in Table 1. The mean age was 76 ± 6.8 years, and 83% were women. All patients were highly symptomatic, most of them in NYHA functional class III, with a significant burden of comorbidities, such as atrial fibrillation (94%), prior pacemaker leads (23%), renal dysfunction (60%), and prior valve interventions (68%). The overall European System for Cardiac Operative Risk Evaluation II score was 5.8 ± 4.2. All patients presented symptoms and signs of right heart failure, such as lower limb edema, ascites, and pleural effusion.

Baseline echocardiographic characteristics are shown in Table 2. The mean left ventricular ejection fraction was 59.2%, with most patients demonstrating dilated right-sided chambers with preserved RV function. The tricuspid annulus was dilated as well, and hepatic vein backflow was present in 97% of patients.

Baseline hemodynamic assessment is shown in Supplemental Table 1. All patients demonstrated high right atrial, SVC, and IVC pressures, with mean

**TABLE 1 Baseline Clinical Characteristics (N = 35)**

| | |
|---|---|
| Age, y | 76 ± 6.8 |
| Male | 6 (17.1) |
| BMI, kg/m$^2$ | 26.3 ± 4.6 |
| Coronary artery disease | 4 (11.4) |
| Atrial fibrillation | 33 (94.2) |
| Pacemaker | 8 (22.8) |
| PAD | 1 (2.8) |
| COPD | 2 (5.7) |
| Estimated GFR <60 mL/min/1.73 m$^2$ | 21 (60.0) |
| GFR, mL/min/1.73 m$^2$ | 52 ± 16 |
| Diabetes mellitus | 7 (20.0) |
| Cancer | 5 (14.2) |
| Chronic liver disease | 3 (8.5) |
| Stroke/TIA | 3 (8.5) |
| Prior valve surgery | |
| Aortic valve | 7 (20.0) |
| Mitral valve | 12 (34.3) |
| Tricuspid valve | 5 (14.3) |
| EuroSCORE II, % | 5.8 ± 4.2 |
| AST, IU/L | 31 ± 11 |
| ALT, IU/L | 18 ± 8 |
| NT-proBNP, pg/mL | 2,654 ± 2,965 |

Values are mean ± SD or n (%).

ALT = alanine aminotransferase; AST = aspartate aminotransferase; BMI = body mass index; COPD = chronic obstructive pulmonary disease; EuroSCORE = European System for Cardiac Operative Risk Evaluation; GFR = glomerular filtration rate; NT-proBNP = N-terminal pro-brain natriuretic peptide; PAD = peripheral artery disease; TIA = transient ischemic attack.

**TABLE 2 Baseline and 6-Month Echocardiographic Analyses**

| | Preintervention | 6 Months | *P* Value Baseline vs 6 Months |
|---|---|---|---|
| LVEDV, mL | 51 ± 25 | 56 ± 21 | 0.555 |
| LVESV, mL | 21.5 ± 13 | 19 ± 9 | 0.279 |
| Left ventricular ejection fraction, % | 59.2 ± 8 | 64 ± 11 | 0.387 |
| Left ventricular end-diastolic diameter, mm | 41 ± 8 | 42 ± 6 | 0.829 |
| LA diameter, mm | 47 ± 12 | 49 ± 10 | 0.761 |
| RVEDA, cm$^2$ | 22.4 ± 7 | 23 ± 7 | 0.998 |
| RVESA, cm$^2$ | 11.5 ± 3 | 12 ± 5 | 0.445 |
| Right atrial diameter, major, mm | 68 ± 1 | 69 ± 12 | 0.505 |
| Right atrial diameter, minor, mm | 55 ± 7 | 55 ± 10 | 0.867 |
| RV fractional area change, % | 47.7 ± 8 | 47 ± 9 | 0.829 |
| TAPSE, mm | 18 ± 4 | 17 ± 4 | 0.368 |
| PASP, mm Hg | 42.3 ± 11.3 | 40 ± 9 | 0.309 |
| Tricuspid annulus, mm | 41 ± 9 | 41 ± 6 | 0.595 |
| Hepatic vein backflow present | 97.0% | 52.9% | <0.001 |
| TR grades 3-5 | 100.0% | 86.4% | 0.020 |
| TR vena contracta, mm | 11.4 | 11 ± 6 | 0.384 |
| EROA, cm$^2$ | 0.82 (0.44-1.36) | 0.78 (0.40-1.10) | 0.555 |

Values are mean ± SD, %, or median (IQR).

EROA = effective regurgitant orifice area; LA = left atrial; LVEDV = left ventricular end-diastolic volume; LVESV = left ventricular end-systolic volume; PASP = pulmonary artery systolic pressure; RV = right ventricular; RVEDA = right ventricular end-diastolic area; RVESA = right ventricular end-systolic area; TAPSE = tricuspid annular plane systolic excursion; TR = tricuspid regurgitation.

v-wave pressures of 24.27 ± 10.13, 23.03 ± 9.04, and 23.39 ± 7.69 mm Hg, respectively.

Median follow-up duration was 6 months (IQR: 5.8-6.2 months).

**PROCEDURAL OUTCOMES.** Results are shown in Table 3. Technical success was obtained in 97% of patients (34 of 35) and procedural success in 94% (33 of 35), with no procedural mortality or strokes. There was 1 case of SVC prosthesis migration into the right atrium, without embolization and without further clinical consequences, which was managed conservatively. The same patient needed a permanent pacemaker early after implantation of the device, which was carried out without any complications. There were no cases of cardiac tamponade or conversions to surgery. The median length of hospital stay for the cohort was 7 days (IQR: 3-9.5 days). The most common early postprocedural adverse event was transitory shoulder pain, which developed in 28.5% of patients and is likely related to phrenic nerve compression induced by the IVC prosthesis. All patients remained under anticoagulant treatment (warfarin or direct oral anticoagulant agents) at the time of discharge.

**PRIMARY OUTCOMES.** There was a significant increase in KCCQ score from 42.01 ± 22.3 points at baseline to 59.7 ± 23.6 at 6-month follow-up ($P$ = 0.004) (Figure 3). Likewise, a significant improvement in NYHA functional class was observed, with 79.4% of patients in functional class I or II at 6 months (vs 0% at baseline) (Figure 4). Sensitivity analyses showed no influence of missing data in the effect of the treatment in the primary outcomes.

**SECONDARY OUTCOMES.** Major adverse events at 30 days, 3 months, and 6 months are shown in Table 4. No device-related mortality was observed, and 3 patients (8.5%) had died at 6-month follow-up. None of the deaths was recorded as cardiovascular in nature (subdural hematoma, kidney and respiratory failure in a patient with prior severe lung and kidney disease, and pneumonia). No cases of myocardial infarction, cardiac tamponade, or cardiac surgery for

**TABLE 3 Procedural Characteristics**

| | |
|---|---|
| In-hospital mortality | 1 (2.8) |
| Stroke/TIA | 0 |
| Number of valves implanted | 70 |
| Technical success | 34 (97) |
| Procedural success | 33 (94) |
| Device embolization/migration | 1 (3) |
| Conversion to surgery | 0 (0) |
| Cardiac tamponade | 0 (0) |
| New pacemaker implantation | 1 (3) |
| Length of hospital stay, d | 7 (3.0-9.5) |

Values are n (%) or median (IQR).
TIA = transient ischemic attack.

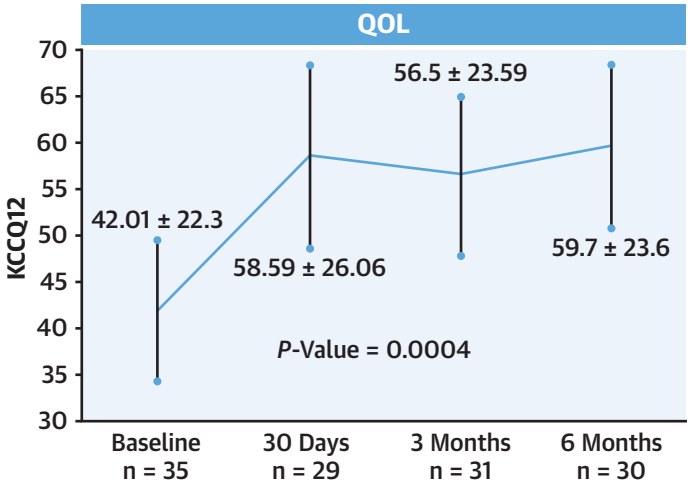
failed device implantation were recorded up to 6-month follow-up. The most frequent complication was major bleeding, which occurred in 17.1% of patients. We observed 2 cases of major bleeding due to access-site complications, but 4 cases occurred during follow-up, not related to access site (1 subdural hematoma, 1 renal hematoma, and 2 cases of gastrointestinal bleeding). The 2 gastrointestinal bleeding events were in the context of vitamin K antagonist overdose. All patients were receiving anticoagulation when bleeding occurred. The heart failure hospitalization readmission rate was 20% (7 patients), all of them predominantly right heart failure and mostly related to respiratory infections or renal function deterioration in a population with high comorbidity burden. Notwithstanding, after system implantation, complete resolution (58.6%) or partial improvement regarding fluid overload signs was observed in the 72.3% of patients.

Although the distance covered during the 6-minute walk test increased numerically, this difference did not reach clinical or statistical significance (245 ± 86 vs 276 ± 90 m, baseline vs 6 months; $P = 0.46$) (Figure 5). However, large improvements in 6-minute walk distance (>40 m) were evident in 24.1% of patients.

Hemodynamic parameters on follow-up are shown in Supplemental Table 1. Significant increases in right atrial pressures were noted following device implantation, which tended to decrease to baseline values by the 3-month mark. IVC pressures significantly decreased compared with baseline both immediately postprocedure and at the 3-month mark. No significant changes were observed in SVC pressures.

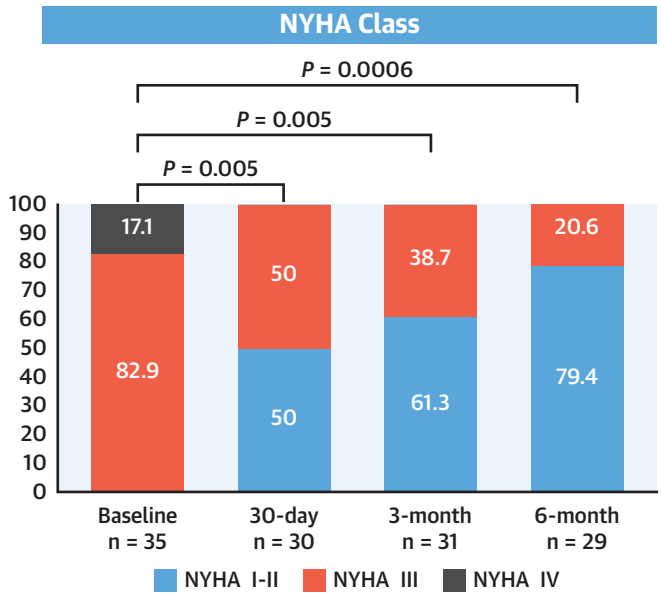
Echocardiography at 6 months showed nonsignificant changes compared with baseline in the majority of parameters (Table 2). Only hepatic vein backflow was absent in 52.9% of the patients, and a lower percentage of at least severe TR was noted. No loss in valve stent integrity was observed, and no intra- or

**FIGURE 3 QOL at Baseline and During Follow-Up**




Patients treated showed significant increases in quality of life (QOL) at 6-month follow-up compared with baseline. KCCQ12 = 12-item Kansas City Cardiomyopathy Questionnaire.

**FIGURE 4** NYHA Functional Class at Baseline and During Follow-Up




Patients treated showed significant improvements in New York Heart Association (NYHA) functional class at 6-month follow-up compared with baseline.

paravalvular leak was documented. No leaflet thrombosis or valve-related infection was detected.

In the CT analyses at 3 months, no perforation or structural damage to the valve stents was observed. There were 2 cases of device thrombosis, both in IVC prosthesis but outside the stent frame, toward the Eustachian valve. Both patients were receiving anticoagulation, and no clinical events were recorded.

No differences were observed in renal function or liver enzymes over time. However, at 3-month follow-up, significant increases in NT-proBNP values were noted (2,654 ± 2,965 pg/mL vs 3,056 ± 2,554 pg/mL, baseline vs 3-month follow-up; $P = 0.01$) (Supplemental Table 2). We observed decreases in weight at 6 months from baseline values, although this was not significant (65 ± 11 kg vs 62.5 ± 11 kg, baseline vs 6-month follow-up; $P = 0.695$). Likewise, significant reductions in the doses of loop diuretic agents were observed (84 ± 55 mg preprocedure vs 65 ± 38 mg at 6 months; $P = 0.036$), which is in concordance with the positive effect of the therapy in reducing congestion.

**TABLE 4** Major Adverse Cardiovascular Events

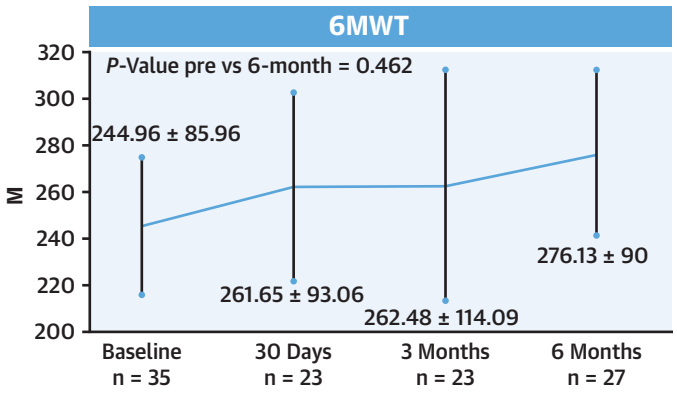
| | Procedural | 30 Days | 3 Months | 6 Months | Overall 6 Months |
|---|---|---|---|---|---|
| Death | 0 | 2 | 1 | 0 | 8.5% |
| Myocardial infarction | 0 | 0 | 0 | 0 | 0% |
| Cardiac tamponade | 0 | 0 | 0 | 0 | 0% |
| Conversion surgery | 0 | 0 | 0 | 0 | 0% |
| Stroke | 0 | 0 | 1 | 1 | 5.7% |
| Major bleeding | 1 | 3 | 2 | 0 | 17.1% |
| Transient shoulder pain | 7 | 3 | 0 | 0 | 28.5% |

## DISCUSSION

The TRICUS EURO Conformité Européenne mark trial demonstrated the safety and efficacy of the TricValve device for patients with severe symptomatic TR ineligible for surgery, with high procedural technical success, low periprocedural complication rates coupled with significant, sustained improvements in functional status and QOL metrics to 6 months. These findings underscore the utility of a dedicated CAVI device for successfully treating a high-risk population that typically harbors high short- to medium-term morbidity and mortality rates and very poor QOL.

In recent times, transcatheter edge-to-edge repair, annuloplasty devices and orthotopic TV replacement

**FIGURE 5** **6MWD at Baseline and During Follow-Up**




Patients treated showed a non-significant increase in 6-minute walk distance (6MWD) at 6-month follow-up compared with baseline.

have shown promising positive results in highly selected TR populations.[7,9,16-18] Aside from a relatively high screening failure rate to qualify for these devices, relatively long procedural times and the need for advanced periprocedural imaging techniques to visualize the TV and surrounding structures currently limit the broader application of these therapies.

CAVI therefore offers several advantages. First, it is not constrained by TV or RV anatomical considerations, with only the size and length of the caval system as potential anatomical exclusions. Exclusions due to a large vena cava were the most frequent in our study because only small prostheses were available for this study. However, larger valve sizes have now been developed that cover almost all dimensions of the vena cava.

Second, CAVI procedures are fluoroscopically guided, so advanced imaging is not necessary in the vast majority of cases implementing a familiar transcatheter aortic valve replacement-like work flow.

Third, general anesthesia is not mandatory, because patients can be treated under conscious sedation with transthoracic echocardiographic monitoring. Fourth, pacing leads pose no limitation to CAVI, with all direct TV therapeutic options remaining preserved should the future potential need arise. Although prior results with nondedicated CAVI systems were suboptimal,[11,19,20] the results of TRICUS EURO demonstrate excellent periprocedural performance and sustained functional gain, making this device appealing for patients with severe symptomatic TR.

The current target population of transcatheter therapies for severe TR is typically old and frail, with significant comorbidities and decreased QOL. In such individuals, the immediate goals of care are to improve QOL and reduce hospitalization rates.[21,22] TRICUS EURO demonstrated a significant, rapid QOL improvement at 30 days that was sustained at 6 months. The mean KCCQ score increase of 16 points observed in the present trial correlates with a significantly large QOL improvement, which is in line with prior observations with TV edge-to-edge repair or direct annuloplasty devices[7,23] and of greater magnitude than observed with cardiac resynchronization therapy in heart failure, transcatheter aortic valve replacement, or percutaneous mitral valve repair.[21,24-27] Although these comparisons likely relate to the differing disease substrates, medical management remains highly limited for patients with TR, and ameliorating the systemic TR effects typically leads to a rapid significant improvement in clinical status. In a recent comprehensive analysis of QOL metrics following TV edge-to-edge repair in 115 patients,[28] the treatment was associated with a significant improvement in SF-36 physical and mental summary scores. Importantly, an increase in the physical component score of >5 points was associated with a reduction in the composite event of all-cause mortality and hospital readmission for HF.

Therefore, although speculative, the TRICUS EURO results could be expected to ultimately associate with improvement in harder clinical events. This hypothesis requires formal evaluation in an appropriately powered prospective randomized trial. Although presently limited to 6-month follow-up, the mortality and heart failure readmission rates in TRICUS EURO appear favorable compared with the natural history of severe symptomatic TR.[1]

Mechanistically, implanting valved Nitinol stents in both caval systems reduces IVC pressures and might increase cardiac output, with the proviso that RV preload was increased in the context of normal RV function, as has been shown in animal models.[29,30] Caval backflow reduction translates into reduced liver congestion, improving liver and renal biochemical findings with subsequent reductions in abdominal congestion, ascites, and peripheral edema and eventually to a lower necessity of high-dose diuretic agents, as suggested by our data. Likewise, the reduction in caval regurgitant volume may increase RV stroke volume to the pulmonary circulation, thus potentially increasing cardiac output. The reduction in volume overload may induce a degree of reverse right heart remodeling.[19] Although still debatable,[31] the present study showed no obvious hemodynamic benefit of SVC implantation, as we did not observe reduction of SVC pressures. This finding may have several explanations but is likely to be related to measurement errors by assessing the SVC pressures from femoral access with multiholed catheters (pigtail or multipurpose) through the SVC valve. In our opinion, implantation of an SVC valve is desirable, as it can help avoid the deleterious effects of redirecting reflux into the superior venous system with unintended consequences such as SVC-like syndrome. The Tricento is the other dedicated CAVI device currently in common clinical use. This device consists of a stent graft that extends from the IVC to the SVC and that presents a lateral bicuspid valve that allows flow into the right atrium. The largest experience with the device, in 21 patients, was recently published.[32] The device was associated with a significant functional improvement and with few procedural adverse events. Although initial results have been promising, the device is custom made and presents greater exclusion features than the TricValve, which make it less generalizable. Likewise, the development of cases of stent fractures has led to the redesign of the stent frame.

Despite the positive clinical effects of the TricValve in TRICUS EURO, we observed in the follow-up period 2 features that warrant further longer-term evaluation: no right heart chamber inverse remodeling and increases in NT-proBNP levels. These findings likely relate to ventricularization of the right atrium and the observed rise in pressures in this cavity. This could be explained by the fact that in the early phases of developing CAVI systems, it was thought that the right atrium would act as a reservoir, accommodating the increase in pressures following CAVI.[10] However, the present study enrolled patients in an advanced state of disease (all in NYHA functional class III or IV with caval v waves ≥25 mm Hg while in a relatively euvolemic state). It is likely that in this situation, the adaptive capacity of the right heart chambers is overcome. In this sense, currently the threshold of the v wave for device selection has dropped to 15 mm Hg, offering enough margin to create a transprosthetic caval gradient and thus maintain valve function. Likewise, our study allowed the inclusion of patients with TAPSE >13 mm. It is currently recognized that TAPSE provides less accurate correlation with the prognosis of patients undergoing transcatheter tricuspid interventions than RV ejection fraction,[33] and it is therefore conceivable that we included patients with significant RV dysfunction. As RV function is essential for pulsatile backflow into the caval system, special attention must be paid to patient selection in order to maximize the benefit of CAVI.[10] Finally, our current imaging follow-up is limited to 6 months, which might be too early to assess the effects on right heart chamber structure and function. Longer imaging follow-up may unravel reverse remodeling that was observed in some prior studies.[10,19]

**STUDY LIMITATIONS.** TRICUS EURO represents an initial experience with this system, and longer follow-up is required to assess clinical benefit and mechanistic effects upon right-sided cardiac chamber hemodynamic status and remodeling. TRICUS EURO was conducted during the coronavirus disease 2019 pandemic, with patients in lockdown. Therefore, the positive effects of the therapy could have been hindered by a restriction in physical activity during these periods. Despite these shortcomings, this study represents the first comprehensive short- to mid-term analysis of a dedicated CAVI system for treating patients with severe symptomatic TR deemed not suitable for TV surgery.

## CONCLUSIONS

The dedicated TricValve CAVI system for treating severe symptomatic TR is safe and effective in producing rapid and sustained mid-term QOL and functional benefits in patients with severe symptomatic TR, with Conformité Européenne mark labeling achieved on the basis of the present results. Although longer term clinical and imaging follow-up will be required to enhance our understanding of the effects of CAVI systems, a pivotal randomized trial of CAVI vs standard medical therapy is warranted to better establish the role of CAVI in the emerging transcatheter TV paradigm.

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Dr Estévez-Loureiro has received speaker fees from ~~P+F.~~ Dr Puri serves as a consultant to P+F and V-Dyne. Drs Sánchez-Recalde, Amat-Santos, Cruz-González, and Altisent have received proctor and speaker fees from P+F. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

**ADDRESS FOR CORRESPONDENCE:** Dr Rodrigo Estévez-Loureiro, Department of Cardiology, University Hospital Alvaro Cunqueiro, C/ Clara Campoamor 341, 36213 Vigo, Spain. E-mail: roiestevez@hotmail.com.

## CLINICAL PERSPECTIVES

**WHAT IS KNOWN?** Severe symptomatic TR is associated with a grave prognosis and is rarely treated.

**WHAT IS NEW?** The TricValve, a novel dedicated CAVI system, is safe to implant and is associated with rapid and sustained clinical improvement.

**WHAT IS NEXT?** Larger studies are required to confirm these findings and to identify the ideal candidates for this therapy. A randomized trial comparing CAVI with standard medical therapy is warranted.

## REFERENCES

**1.** Topilsky Y, Maltais S, Medina Inojosa J, et al. Burden of tricuspid regurgitation in patients diagnosed in the community setting. *J Am Coll Cardiol Img*. 2019;12:433–442.

**2.** Curio J, Demir OM, Pagnesi M, et al. Update on the current landscape of transcatheter options for tricuspid regurgitation treatment. *Interv Cardiol Rev*. 2019;14:54–61.

**3.** Taramasso M, Alessandrini H, Latib A, et al. Outcomes after current transcatheter tricuspid valve intervention: mid-term results from the international TriValve registry. *J Am Coll Cardiol Intv*. 2019;12:155–165.

**4.** Nath J, Foster E, Heidenreich PA. Impact of tricuspid regurgitation on long-term survival. *J Am Coll Cardiol*. 2004;43:405–409.

**5.** Topilsky Y, Nkomo VT, Vatury O, et al. Clinical outcome of isolated tricuspid regurgitation. *J Am Coll Cardiol Img*. 2014;7:1185–1194.

**6.** Wang N, Fulcher J, Abeysuriya N, et al. Tricuspid regurgitation is associated with increased mortality independent of pulmonary pressures and right heart failure: a systematic review and meta-analysis. *Eur Heart J*. 2019;40:476–484.

**7.** Lurz P, Stephan von Bardeleben R, et al. Transcatheter edge-to-edge repair for treatment of tricuspid regurgitation. *J Am Coll Cardiol*. 2021;77:229–239.

**8.** Fam NP, Braun D, von Bardeleben RS, et al. Compassionate use of the PASCAL transcatheter valve repair system for severe tricuspid regurgitation: a multicenter, observational, first-in-human experience. *J Am Coll Cardiol Intv*. 2019;12:2488–2495.

**9.** Hahn RT, Kodali S, Fam N, et al. Early multinational experience of transcatheter tricuspid valve replacement for treating severe tricuspid regurgitation. *J Am Coll Cardiol Intv*. 2020;13:2482–2493.

**10.** Lauten A, Dreger H, Laule M, Stangl K, Figulla HR. Caval valve implantation. *Interv Cardiol Clin*. 2018;7:57–63.

**11.** Laule M, Mattig I, Schöbel C, et al. Inferior caval valve implantation versus optimal medical therapy for severe tricuspid regurgitation. *J Am Coll Cardiol*. 2019;74:473–475.

**12.** Dreger H, Mattig I, Hewing B, et al. Treatment of Severe Tricuspid Regurgitation in Patients With Advanced Heart Failure With Caval Vein Implantation of the Edwards SAPIEN XT Valve (TRI-CAVAL): a randomised controlled trial. *EuroIntervention*. 2020;15:1506–1513.

**13.** Abdul-Jawad Altisent O, Benetis R, Rumbinaite E, et al. Caval valve implantation (CAVI): an emerging therapy for treating severe tricuspid regurgitation. *J Clin Med*. 2021;10:4601.

**14.** Kappetein AP, Head SJ, Généreux P, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. *Eur Heart J*. 2012;33:2403–2418.

**15.** Spertus JA, Jones PG. Development and validation of a short version of the Kansas City Cardiomyopathy Questionnaire. *Circ Cardiovasc Qual Outcomes*. 2015;8:469–476.

**16.** Fam NP, von Bardeleben RS, Hensey M, et al. Transfemoral transcatheter tricuspid valve replacement with the EVOQUE system: a multicenter, observational, first-in-human experience. *J Am Coll Cardiol Intv*. 2021;14:501–511.

**17.** Kodali S, Hahn RT, Eleid MF, et al. Feasibility study of the transcatheter valve repair system for severe tricuspid regurgitation. *J Am Coll Cardiol*. 2021;77:345–356.

**18.** Kitamura M, Fam NP, Braun D, et al. 12-Month outcomes of transcatheter tricuspid valve repair with the PASCAL system for severe tricuspid regurgitation. *Catheter Cardiovasc Interv*. 2021;97:1281–1289.

**19.** Lauten A, Ferrari M, Hekmat K, et al. Heterotopic transcatheter tricuspid valve implantation: First-in-man application of a novel approach to tricuspid regurgitation. *Eur Heart J*. 2011;32:1207–1213.

**20.** Lauten A, Figulla HR, Unbehaun A, et al. Interventional treatment of severe tricuspid regurgitation: early clinical experience in a multicenter, observational, first-in-man study. *Circ Cardiovasc Interv*. 2018;11:e006061.

**21.** Lewis EF. Assessing the impact of heart failure therapeutics on quality of life and functional capacity. *Curr Treat Options Cardiovasc Med*. 2013;15:425–436.

**22.** Stevenson LW, Hellkamp AS, Leier CV, et al. Changing preferences for survival after hospitalization with advanced heart failure. *J Am Coll Cardiol*. 2008;52:1702–1708.

**23.** Nickenig G, Weber M, Schüler R, et al. Tricuspid valve repair with the Cardioband system: two-year outcomes of the multicentre, prospective Tri-Repair study. *EuroIntervention*. 2021;16:E1264–E1271.

**24.** Cleland JGF, Calvert MJ, Verboven Y, Freemantle N. Effects of cardiac resynchronization therapy on long-term quality of life: an analysis

from the Cardiac Resynchronisation-Heart Failure (CARE-HF) study. *Am Heart J*. 2009;157:457–466.

**25.** Lewis EF, Claggett BL, McMurray JJV, et al. Health-related quality of life outcomes in PARADIGM-HF. *Circ Heart Fail*. 2017;10:e003430.

**26.** Reynolds MR, Magnuson EA, Wang K, et al. Health-related quality of life after transcatheter or surgical aortic valve replacement in high-risk patients with severe aortic stenosis: results from the PARTNER (Placement of Aortic Transcatheter Valve) trial (Cohort A). *J Am Coll Cardiol*. 2012;60:548–558.

**27.** Feldman T, Foster E, Glower DD, et al. Percutaneous repair or surgery for mitral regurgitation. *N Engl J Med*. 2011;364:1395–1406.

**28.** Kitamura M, Kresoja KP, Balata M, et al. Health status after transcatheter tricuspid valve repair in patients with functional tricuspid regurgitation. *J Am Coll Cardiol Intv*. 2021;14:2545–2556.

**29.** Lauten A, Figulla HR, Willich C, et al. Percutaneous caval stent valve implantation: Investigation of an interventional approach for treatment of tricuspid regurgitation. *Eur Heart J*. 2010;31:1274–1281.

**30.** Boudjemline Y, Agnoletti G, Bonnet D, et al. Steps toward the percutaneous replacement of atrioventricular valves: an experimental study. *J Am Coll Cardiol*. 2005;46:360–365.

**31.** O'Neill BP. Caval valve implantation: are 2 valves better than 1? *Circ Cardiovasc Interv*. 2018;11:e006334.

**32.** Wild MG, Lubos E, Cruz-Gonzalez I, et al. Early clinical experience with the Tricento bicaval valved stent for treatment of symptomatic severe tricuspid regurgitation: a multicenter registry. *Circ Cardiovasc Interv*. 2022;15:e011302.

**33.** Kresoja KP, Rommel KP, Lücke C, et al. Right ventricular contraction patterns in patients undergoing transcatheter tricuspid valve repair for severe tricuspid regurgitation. *J Am Coll Cardiol Intv*. 2021;14:1551–1561.

**KEY WORDS** CAVI, right heart failure, tricuspid regurgitation

**APPENDIX** For inclusion and exclusion criteria as well as supplemental tables and figures, please see the online version of this paper.