JACC: CARDIOVASCULAR INTERVENTIONS VOL. 17, NO. 16, 2024

ORIGINAL RESEARCH

STRUCTURAL

Transjugular Transcatheter Tricuspid Valve Replacement

Early Compassionate Use Outcomes

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ABSTRACT

BACKGROUND Data on procedural and early outcomes after transjugular transcatheter tricuspid valve replacement (TTVR) are limited.

OBJECTIVES This study sought to evaluate first-in-man procedural and clinical outcomes after transjugular TTVR with a special focus on patients who received large device sizes in whom TTVR outcomes have been questioned.

METHODS The retrospective registry included patients who underwent TTVR using the LuX-Valve Plus system (Jenscare Biotechnology Co Ltd) for symptomatic tricuspid regurgitation (TR) from January 2022 until February 2024 at 15 international centers in a compassionate use setting. The endpoints were procedural TR reduction, in-hospital death, adverse events, and 1-month survival. We further stratified results according to the size of the implanted device (<55 vs ≥55 mm).

RESULTS The registry included a total of 76 patients at a median age of 78 years (Q1-Q3: 72-83 years, 47.4% women). TR was reduced to ≤2+ and ≤1+ in 94.7% and 90.8% of patients (75.0% of patients received TTVR devices ≥55 mm) with well-sustained results at 1-month follow-up (TR ≤2+ in 95.0% and ≤1+ 86.8%). Residual TR was paravalvular in all cases. In-hospital death occurred in 4 patients (5.3%). Four patients (5.3%) underwent cardiac surgery during index hospitalization. Major in-hospital bleeding events occurred in 5 patients (6.6%). New in-hospital pacemaker implantation was required in 3.9% of patients in the overall cohort (5.7% in "pacemaker-naive" individuals). No cases of valve thrombosis, stroke, myocardial infarction, or pulmonary embolism were observed. At 1-month follow-up, survival was 94.4%, and NYHA functional class significantly improved. One further patient received a pacemaker, 1 further bleeding event occurred, and 2 patients underwent reintervention or surgery within the first 30 days after TTVR. No differences in procedural outcomes or adverse events were observed after stratification for valve size.

CONCLUSIONS Transjugular TTVR appears to be a safe and effective treatment option for patients with severe TR with comparable outcomes in very large tricuspid anatomies. (JACC Cardiovasc Interv. 2024;17:1936-1945)

ISSN 1936-8798 https://doi.org/10.1016/j.jcin.2024.06.014

Tricuspid regurgitation (TR) is a global health burden associated with significant morbidity and mortality.[1] The first randomized trial in the field of interventional TR treatment demonstrated superiority of transcatheter tricuspid valve edge-to-edge repair (T-TEER) over diuretic therapy in terms of quality of life improvement at 1-year follow-up.[2] TR is known to be a heterogenous disease presenting with various anatomical and clinical phenotypes.[3] A significant number of TR patients are ineligible for T-TEER because of large gap sizes, unfavorable tricuspid valve (TV) anatomy, interacting cardiac implantable electronic device leads, or poor echocardiographic visualization, among others. Therefore, transcatheter tricuspid valve replacement (TTVR) might be an emerging treatment alternative, and several devices are currently under clinical investigation.[4-6]

One increasingly used TTVR device is the LuX-Valve Plus system (Jenscare Biotechnology Co Ltd). In contrast to the existing transfemoral TTVR systems, the LuX-Valve Plus device is implanted using a transjugular approach.[4] The existing data suggest effective and safe TR reduction and an improvement in heart failure symptoms after TTVR using the LuX-Valve system,[7] but those data are limited to small sample sizes and/or early experience patients with surgical transatrial valve implantation.[4,8,9] The device covers valve sizes up to 65 mm, which is considerably larger compared to other currently available TTVR systems (eg, the EVOQUE [Edwards Lifesciences] valve, which has recently received the CE mark and Food and Drug Administration approval for 3 valve sizes up to 52 mm). Until today, outcome data for patients undergoing TTVR using valve sizes ≥55 mm are completely lacking, and it has been questioned if very large tricuspid anatomies with considerably enlarged right atrial and ventricular dimensions will be associated with comparable favorable outcomes after TTVR compared to smaller sizes. To add further evidence to the existing body of literature, we retrospectively collected patients who underwent transjugular TTVR in an international multicenter setting. The aim of this report was to evaluate procedural and early follow-up outcomes after transjugular TTVR with a special focus on patients who received large device sizes (≥55 mm).

ABBREVIATIONS AND ACRONYMS

DOAC = direct oral anticoagulant

RV = right ventricular

TR = tricuspid regurgitation

T-TEER = tricuspid valve transcatheter edge-to-edge repair

TTVR = transjugular tricuspid valve replacement

TV = tricuspid valve

TVARC = Tricuspid Valve Academic Research Consortium

METHODS

OVERALL COHORT AND VARIABLES. This analysis retrospectively registered all consecutive patients who underwent TTVR using the LuX-Valve Plus device for symptomatic TR from January 2022 until February 2024 at 15 international centers in a compassionate use program (Supplemental Table 1). Because of this retrospective design, no inclusion or exclusion criteria for treatment with this device were defined. Patients were treated according to each center's standard of care practice. Patients provided written informed consent and were treated after approval from the corresponding national regulatory board. Each patient underwent detailed echocardiographic evaluation and received cardiac computed tomography for further treatment planning. An interdisciplinary heart team discussed each patient

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Nicole Karam, MD, served as Guest Editor for this paper. H. Vernon "Skip" Anderson, MD, served as Guest Editor-in-Chief for this paper.

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.

Manuscript received February 21, 2024; revised manuscript received June 6, 2024, accepted June 11, 2024.

JACC: CARDIOVASCULAR INTERVENTIONS VOL. 17, NO. 16, 2024
AUGUST 26, 2024:1936–1945

and opted for transjugular TTVR as the therapy of choice.

Procedural details of TTVR using the LuX-Valve system have previously been described.[4] Briefly summarized, the device is implanted under fluoroscopic and echocardiographic guidance by a transjugular access route.[4] After advancing the delivery system through the jugular vein, the capsule containing the valve is adjusted in the center and perpendicular to the tricuspid annulus. For valve anchoring, 2 leaflet graspers are extended under the anterior and posterior leaflet before expansion of the ventricular valve component, respectively.[4] After deployment of the atrial disc and fixation of the septal anchor, the delivery catheter is removed.[4]

Echocardiographic analyses were performed by experienced physicians at each center according to recent recommendations,[10,11] and all data are site reported. The collected clinical baseline characteristics included demographic, laboratory, and medical data as well as relevant comorbidities. Cardiorenal and cardiohepatic syndromes were defined as an estimated glomerular filtration rate <60 mL/min and as elevation of 2 of 3 laboratory cholestasis parameters (bilirubin, gamma glutamyl transferase, and alkaline phosphatase), respectively, as previously described.[12,13] The assessment of heart failure symptoms comprised NYHA functional class, peripheral edema, jugular vein distension, pleural effusion, and ascites. Echocardiographic evaluation included left and right ventricular (RV) function and dimensions, the TR effective regurgitant orifice area, the TR regurgitant volume, and the mean TV inflow gradients (the TV mean pressure gradient). The analysis was conducted with the principles outlined in the Declaration of Helsinki.

ENDPOINTS: IN-HOSPITAL AND 1-MONTH FOLLOW-UP. The endpoints were intraprocedural success according to the Tricuspid Valve Academic Research Consortium (TVARC) consensus statement,[14] procedural TR reduction, procedural complications, in-hospital death, need for unplanned surgery, conduction disturbance requiring new pacemaker implantation, major bleeding complications, myocardial infarction, pulmonary embolism, stroke, new-onset dialysis, and device thrombosis. The endpoints at 1-month follow-up were 30-day clinical success assessed according to the TVARC criteria, TR reduction, changes in NYHA functional class, and heart failure symptoms. Additionally, 1-month survival was assessed.

STATISTICAL ANALYSIS. Data were depicted using IQRs. One-month survival rates were depicted using Kaplan-Meier curves. Differences between 2 independent samples were evaluated using the Mann-Whitney *U* test. Dependent samples were compared by applying the Wilcoxon test or the McNemar test as appropriate. A 2-sided *P* value <0.05 yielded statistical significance. The exact numerator and denominator for all percentages throughout the paper are presented in Tables 1 to 5. All analyses were performed using R version 4.0.4 (R Foundation for Statistical Computing) and SPSS version 25 (IBM Corp).

RESULTS

BASELINE CHARACTERISTICS. Seventy-six patients from 15 centers at a median age of 78 years (Q1-Q3: 72-83 years, 47.4% women) were included. TR was massive or torrential in 75.0% of patients. The median TR effective regurgitant orifice area and regurgitant volume were 65.5 mm^2 (Q1-Q3: 50.0-88.8 mm^2) and 52.0 mL (Q1-Q3: 46.8-89.3 mL). Although most patients presented with preserved left ventricular function (55.0% [Q1-Q3: 50.0%-60.3%]), RV function was borderline according to tricuspid annular plane systolic excursion (17.0 mm [Q1-Q3: 14.0-20.0 mm]) and RV fractional area change (35.1% [Q1-Q3: 28.5%-43.4%]). Overall, the right ventricle was significantly dilated (RV end-diastolic area = 30.5 cm^2 [Q1-Q3: 21.4-37.5 cm^2], tricuspid annulus diameter = 47.0 mm [Q1-Q3: 42.0-52.0 mm], and RV midventricular diameter = 42.5 mm [Q1-Q3: 48.0-48.8 mm]). The prevalence of cardiovascular comorbidities was high (atrial fibrillation = 90.7%, arterial hypertension = 73.0%, dyslipidemia = 64.9%, and diabetes mellitus = 24.3%). Cardiorenal and cardiohepatic syndromes were prevalent in 73.0% and 44.9% of patients, respectively. A transvalvular lead was present in 30.3% of patients. Right heart catheterization indicated mild postcapillary pulmonary hypertension (median mean pulmonary arterial pressure = 25.0 mm Hg [Q1-Q3: 18.0-32.1 mm Hg], pulmonary capillary wedge pressure = 16.0 mm Hg [Q1-Q3: 10.8-23.0 mm Hg]). Surgical risk was elevated as represented by a median TRI-SCORE of 6 points (Q1-Q3: 4-9 points)[15] and a median EuroSCORE II of 4.5% (Q1-Q3: 2.4%-8.7%). Detailed baseline characteristics are outlined in Tables 1 and 2.

Patients suffered from severe signs and symptoms of right heart failure, with NYHA functional class ≥III in 90.7%. Peripheral edema, ascites, and pleural effusion were observed in 85.5%, 44.6%, and 37.4%, respectively. Diuretic agents included a large dosage of loop diuretic agents in 89.2% of patients (furosemide equivalence dosage = 80 mg/d [Q1-Q3:

TABLE 1 Baseline Characteristics

Clinical characteristics (N = 76)	
Age, y	78 (72-83)
Female	36 (47.4)
BMI, kg/m^2	24.9 (21.2-28.8)
BSA, m^2	1.8 (1.6-2.0)
Dyslipidemia	48 (64.9)
Arterial hypertension	54 (73.0)
Myocardial infarction	8 (15.4)
COPD	15 (19.7)
Diabetes mellitus	17 (24.3)
Stroke	11 (15.5)
Cardiac surgery	35 (46.0)
AVR	2 (2.6)
TVr	2 (2.6)
CABG	9 (11.8)
CABG + AVR	3 (3.9)
MVR + AVR	3 (3.9)
MVR + AVR + TVr	1 (1.3)
MVr	2 (2.6)
HTx	6 (7.9)
NA	7 (9.2)
TV lead	23 (30.3)
Afib/flutter	68 (90.7)
Coronary artery disease	27 (36.0)
Dialysis	7 (9.6)
EuroSCORE II, %	4.5 (2.4-8.7)
TRI-SCORE	6 (4-9)
Heart failure symptoms	
Edema	65 (85.5)
Ascites	33 (44.6)
Pleural effusion	19 (37.4)
NYHA functional class	
I	0 (0.0)
II	7 (9.3)
III	54 (72.0)
IV	14 (18.7)
Medication data	
MRA	21 (42.9)
Loop diuretic	66 (89.2)
Loop diuretic dosage, mg/d	80 (40-120)
Thiazide	8 (19.0)
Beta blocker	36 (73.5)
RAS-I	22 (44.9)
ASS	4 (8.2)
Clopidogrel	4 (8.5)
Prasugrel	0 (0.0)
DOAC	34 (73.9)
Vitamin K antagonist	11 (22.4)
Laboratory parameters	
eGFR, mL/min	42.0 (28.8-61.3)
Creatinine, mg/dL	1.2 (0.8-1.6)
Bilirubin, mg/dL	0.8 (0.6-1.3)
AST, U/L	29.0 (22.0-37.0)
ALT, U/L	17.5 (12.8-26.0)
GGT, U/L	68.0 (42.0-188.0)
Alkaline phosphatase, U/L	17.5 (12.8-26.0)
Hb, g/dL	11.7 (10.9-12.9)
NT-proBNP, ng/mL	2,237 (1,109-4,487)
Right heart catheterization	
PA pressure systolic, mm Hg	36.0 (27.8-46.0)
PA pressure diastolic, mm Hg	17.5 (11.8-24.0)
PA pressure mean, mm Hg	25.0 (18.0-32.1)
PCWP, mm Hg	16.0 (10.8-23.0)
RA V-wave, mm Hg	18.5 (13.0-27.8)

Continued in the next column

Values are median (Q1-Q3) or n (%).

Afib = atrial fibrillation; ALT = alanine aminotransferase; ASS = aspirin; AST = aspartate aminotransferase; AVR = aortic valve replacement; BSA = body surface area; BMI = body mass index; CABG = coronary artery bypass graft; COPD = chronic obstructive pulmonary disease; DOAC = direct oral anticoagulation; eGFR = estimated glomerular filtration rate; GGT = gamma glutamyltransferase; Hb = hemoglobin; HTx = heart transplantation; MRA = mineralocorticoid receptor antagonist; MVr = mitral valve repair; MVR = mitral valve replacement; NA = not applicable; NT-proBNP = N-terminal pro–B-type natriuretic peptide; PCWP = pulmonary capillary wedge pressure; PA = pulmonary artery; RAS-I = renin angiotensin system inhibitor; TV = tricuspid valve; TVr = tricuspid valve repair.

40-120 mg/d]). On admission, 96.3% of patients received oral anticoagulation (73.9% direct oral anticoagulants [DOACs] and 22.4% vitamin K antagonist).

PROCEDURAL CHARACTERISTICS AND OUTCOMES. Intraprocedural success according to the TVARC consensus statement criteria was achieved in 93.4% of patients. The median procedure time was 140 minutes (Q1-Q3: 97-160 minutes). According to intraprocedural echocardiography, TR was reduced to ≤2+ in 94.7% of patients, ≤1+ in 90.8%, and 0+ in 65.8% of patients (**Central Illustration**). Residual TR ≥3+ was observed in 4 patients (5.2%). Residual TR was paravalvular in all cases.

Conversion to TV surgery was necessary in 4 cases (1 malpositioning of the valve, 1 device embolization, 1 anchor detachment with subsequent pericardial tamponade, and 1 pericardial effusion before device deployment). In 1 patient, the procedure was aborted because of insufficient extension of the leaflet graspers. One patient underwent surgery for access site complications. Bleeding complications that required blood transfusions occurred in 6.6% of patients. We observed no cases of in-hospital pulmonary embolism, stroke, or myocardial infarction. New in-hospital conduction disturbances that required permanent pacemaker implantation occurred in 3 (3.9%) patients (5.7% [3 of 53 patients] in pacemaker "naive" patients; 3 patients during in-hospital stay). Two patients received a transvalvular lead, and 1 patient received left bundle brunch pacing. Two patients (2.6%) suffered acute renal failure requiring new-onset dialysis. In total, 4 patients died within the index hospitalization (2 following emergency surgery, 1 from gastrointestinal bleeding following the procedure, and 1 from right heart failure).

TABLE 2 Echocardiographic Baseline Data

LVEF, %	55 (50.0-60.3)
LVEDV, mL	89.0 (58.2-142.9)
LVESV, mL	35.0 (21.2-52.2)
LA volume, mL	80 (55.7-113.0)
TR EROA, mm^2	65.5 (50.0-88.8)
TR RegVol, mL	52.0 (46.8-89.3)
TR VC, mm	10.0 (5.0-14.0)
TV mean PG, mm Hg	1.0 (0.9-1.5)
RV FAC, %	35.1 (28.5-43.4)
RV EDA, cm^2	30.5 (21.4-37.5)
RV ESA, cm^2	18.0 (11.9-23.1)
RV mid-diameter, mm	42.5 (48.0-48.8)
RV base diameter, mm	51.0 (47.0-56.8)
RV length, mm	71.0 (61.4-84.5)
TV annular diameter, mm	47.0 (42.0-52.0)
RA area, cm^2	32.2 (26.9-39.7)
RA volume, mL	134.3 (108.2-160.0)
TAPSE, mm	17.0 (14.0-20.0)
TR maximum PG, mm Hg	23.0 (13.3-32.0)
sPAP (echo), mm Hg	37.0 (27.0-47.0)
TR severity	
0+	0 (0.0)
1+	0 (0.0)
2+	2 (2.6)
3+	17 (22.4)
4+	19 (25.0)
5+	38 (50.0)

Values are median (Q1-Q3) or n (%).

EDA = end-diastolic area; EROA = effective regurgitant orifice area; ESA = end-systolic area; FAC = fractional area change; LA = left atrium; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume; PG = pressure gradient; RA = right atrial; RegVol = regurgitant volume; RV = right ventricular; sPAP = systolic pulmonary artery pressure; TAPSE = tricuspid annular plane systolic excursion; TR = tricuspid regurgitation; TV = tricuspid valve; VC = vena contracta.

TABLE 3 Procedural Outcomes (N = 76)

Intraprocedural success according to TVARC	71 (93.4)
Device and procedural complications	5 (6.6)
Embolization of the device	1 (1.3)
Malposition of the device	1 (1.3)
Anchor detachment	1 (1.3)
Pericardial effusion before valve deployment	1 (1.3)
Incomplete extension of anterior leaflet graspers	1 (1.3)
In-hospital death	4 (5.3)
Right heart failure	2 (2.6)
Cardiac tamponade	1 (1.3)
GI bleeding	1 (1.3)
Need for heart surgery	4 (5.3)
TVR because of malposition/embolization	2 (2.6)
Cardiac tamponade/pericardial effusion	2 (2.6)
Need for access site surgery	
Access site complication	1 (1.3)
Requirement of pacemaker implantation	
Related to all patients	3 (3.9)
Related to pacemaker-naive patients	3 (5.7)
In-hospital bleeding	5 (6.6)
In-hospital myocardial infarction	0 (0.0)
In-hospital stroke	0 (0.0)
In-hospital new-onset dialysis	2 (2.6)
In-hospital valve thrombosis	0 (0.0)
TV mean PG postprocedural, mm Hg	2.0 (1.8-3.4)
TV mean PG discharge, mm Hg	2.0 (1.1-2.1)
Procedure time, min	140 (97-160)
TR severity postprocedural	
0+	50 (65.8)
1+	19 (25.0)
2+	3 (3.9)
3+	2 (2.6)
4+	2 (2.6)
5+	0 (0.0)

Values are n (%) or median (Q1-Q3).

GI = gastrointestinal; TVARC = Tricuspid Valve Academic Research Consortium; TVR = tricuspid valve replacement; other abbreviations as in Table 2.

The median postprocedural TV inflow gradients were 2.0 mm Hg (Q1-Q3: 1.8-3.4 mm Hg). There was no evidence of valve thrombosis at discharge. All patients were discharged with oral anticoagulation therapy (57% DOACs and 43% vitamin K antagonist).

1-MONTH FOLLOW-UP. Four patients died within the first month after the procedure (1 following surgery for malpositioning of the device, 1 following cardiac tamponade after detachment of the septal anchor, 1 following right heart failure, and 1 from gastrointestinal bleeding), leading to a 30-day survival rate of 94.4% (Figure 1). Sixty-seven patients were eligible for the 1-month follow-up (4 patients died <30 days, and 6 patients were not able to attend the 30-day follow-up because the date of TTVR was <30 days before database closure). Clinical 1-month follow-up was available in 91.0% of eligible patients (n = 61/67) at a median time of 45 days (Q1-Q3: 28-50 days). TR remained reduced to ≤2+ in 95.0% of patients and ≤1+ in 86.8% of patients (Central Illustration). TR ≥3+ was observed in 3 patients (4.9%). Follow-up echocardiography revealed detachment of the septal anchor in 2 patients. One patient underwent subsequent heterotopic tricuspid valve replacement, and 1 patient underwent surgical tricuspid valve replacement. Between discharge and the 1-month follow-up, 1 further bleeding event occurred, and 1 further patient underwent pacemaker implantation (leadless pacemaker). The overall 30-day pacemaker rate was 5.2% (4 of 76) among all patients and 7.5% (4 of 53) among those without a pre-existing pacemaker. There was no evidence of valve thrombosis at 1-month follow-up. The median TV inflow gradient was 2.0 mm Hg (Q1-Q3: 1.2-2.1 mm Hg). Clinical success at 30 days according to the TVARC consensus statement was 91.8% among

patients with eligible follow-up. Symptomatic status significantly improved as indicated by NYHA functional class ≤II in 85.4% of patients (Central Illustration).

OUTCOMES STRATIFIED BY DEVICE SIZE. A device size ≥55 mm was implanted in 75.0% of patients (40 mm: 5.3%; 45 mm: 1.3%; 50 mm: 19.7%; 55 mm: 30.3%; 60 mm: 23.7%; and 65 mm: 19.7%). Large valves were more commonly implanted in men (59.6% vs 31.6% in valves <55 mm). Even though not achieving statistical significance, patients who received large valves showed a trend toward more severe biventricular and biatrial dilation as a sign of more advanced heart failure (Supplemental Table 2). Nevertheless, symptomatic status and heart failure symptoms were comparable between patients with valve sizes <55 and ≥55 mm. Beyond that, we did not observe significant differences in the prevalence of procedural complications, NYHA functional class improvement, and TR reduction after stratification by device size (Figure 2, Supplemental Table 3).

TABLE 4 Clinical 1-Month Outcomes (N = 61)

Clinical success according to TVARC at 30 days	56 (91.8)
Major bleeding	1 (1.6)
Myocardial infarction	0 (0.0)
Stroke	0 (0.0)
Pulmonary embolism	0 (0.0)
Reintervention/surgery	2 (3.3)
TricValve (Products & Features) after detachment of septal anchor	1 (1.6)
TVR	1 (1.6)
Pacemaker implantation	1 (1.6)
New-onset dialysis	0 (0.0)
Valve thrombosis	0 (0.0)
TR severity follow-up	
0+	29 (47.5)
1+	24 (39.3)
2+	5 (8.2)
3+	1 (1.6)
4+	2 (3.3)
5+	0 (0.0)
NYHA functional class	
I	24 (43.6)
II	23 (41.8)
III	4 (7.3)
IV	4 (7.3)

Values are n (%). 61 patients were eligible for the 1-month follow-up.
Abbreviations as in Tables 2 and 3.

DISCUSSION

GENERAL CONSIDERATIONS. This retrospective multicenter registry is the largest to report outcomes of patients who underwent TTVR using the LuX-Valve Plus system in a compassionate use setting. In contrast to previous publications on TTVR outcomes, it exclusively included patients who were treated using a transjugular approach, and it reports outcomes for a considerable percentage of patients with very large tricuspid anatomies. The main findings of this analysis were as follows:

1. Transjugular TTVR was linked with acceptable in-hospital complication rates for a new technology in a highly selected group of high or prohibitive surgical risk patients.
2. Transjugular TTVR resulted in an effective TR reduction up to 1 month after the procedure with approximately 13% of patients presenting with a predominantly mild paravalvular leakage of unknown clinical significance.
3. At 1 month, survival was 94.4%, and a substantial improvement in heart failure symptoms and exertional dyspnea was observed.
4. No significant differences in terms of procedural outcomes and adverse events were observed in patients requiring <55 or ≥55 mm valve sizes.

TR REDUCTION IN THE CONTEXT OF CURRENT LITERATURE. Several years of experience have shown that T-TEER is associated with TR reduction rates to ≤2+ between 87% in the setting of a randomized trial[2] and 83% under real-world conditions.[3] Compassionate use EVOQUE data reported 30-day TR

TABLE 5 Laboratory and Echocardiographic Follow-Up Data

	Baseline	Follow-Up	*P* Value	n
Laboratory data				
eGFR, mL/min	48 (31.5-63.0)	44 (29.6-60.5)	0.520	29
Bilirubin, mg/dL	0.8 (0.5-1.3)	0.7 (0.4-1.1)	0.106	24
AST, U/L	29.0 (24.5-35.5)	31.0 (24.5-39.8)	0.195	20
ALT, U/L	18.5 (13.8-24.8)	17.0 (13.0-22.5)	0.465	26
GGT, U/L	74.0 (37.0-203.0)	70.0 (37.5-169.0)	0.041	17
Alkaline phosphatase, U/L	105.0 (78.0-188.0)	137.0 (87.0-187.0)	0.583	23
Hb, g/dL	11.5 (11.0-12.7)	10.9 (9.9-12.0)	0.042	26
NT-proBNP, ng/mL	2,061 (1,083-4,374)	2,118 (1,021-6,206)	0.327	24
Echocardiographic data				
LVEF, %	55.0 (50.0-62.4)	60.0 (50.8-65.0)	0.138	38
TAPSE, mm	18.0 (14.8-21.0)	15.0 (12.8-17.5)	0.034	30
RV mid-diameter, mm	42.0 (37.5-49.5)	39.0 (35.4-46.5)	0.096	25
RV base diameter, mm	49.0 (45.7-56.5)	47.0 (43.0-56.0)	0.031	25
RA area, cm^2	30.2 (26.3-36.0)	28.0 (26.0-32.2)	0.006	24
RA volume, mL	120.0 (102.4-149.0)	96.0 (75.5-126.2)	0.013	25
sPAP (echo), mm Hg	37.0 (27.5-48.0)	35.0 (29.0-41.0)	0.239	25
Heart failure symptoms				
Edema	50 (83.3)	15 (25.0)	<0.001	60
Ascites	23 (39.0)	2 (3.4)	<0.001	59
Pleural effusion	12 (32.4)	3 (8.1)	0.013	37

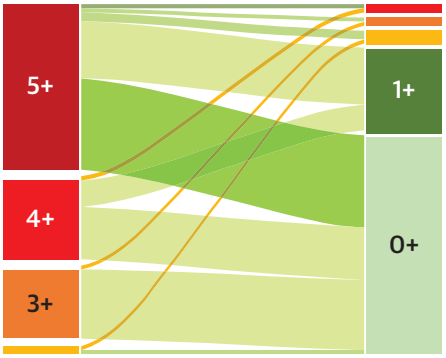
Values are median (Q1-Q3) or n (%).
Abbreviations as in Tables 1 and 2.

JACC: CARDIOVASCULAR INTERVENTIONS VOL. 17, NO. 16, 2024
AUGUST 26, 2024:1936-1945

CENTRAL ILLUSTRATION **LuX-Valve Plus For Transcatheter Tricuspid Valve Replacement**

Transcatheter Tricuspid Valve Replacement Using the LuX-Valve Plus System: Early Compassionate Use Outcomes in 2022-2024, N = 76

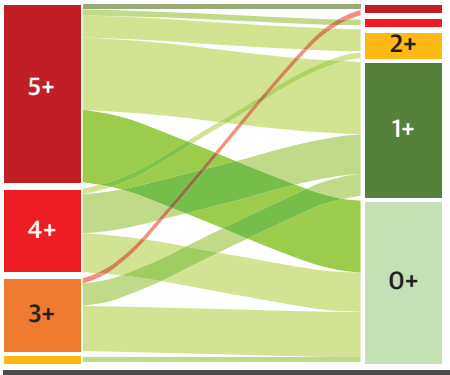
A In-Hospital Outcomes



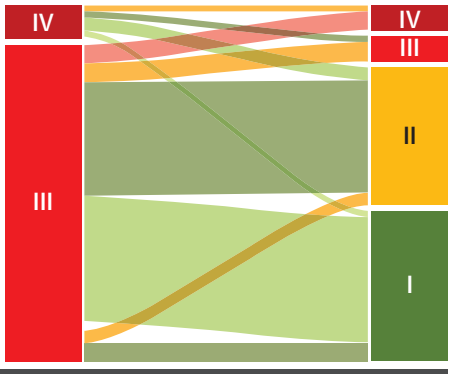
- 94.7% with TR reduction to ≤2+
- 5.3% conversion to cardiac surgery
- 5.7% had new PPM implantation
- 6.6% had major bleeding events
- 5.3% in-hospital death
- No valve thrombosis, MI, or PE

B 1-Month Outcomes

Tricuspid Regurgitation



NYHA Functional Class



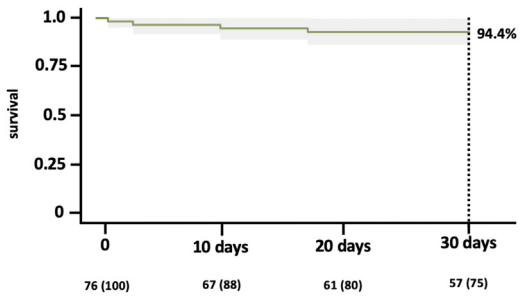
At 1-month follow-up with the LuX-Valve Plus System:

- Infrequent need for additional surgery or repeat intervention
- Durable TR reduction to ≤2+ in 95.0% of patients
- Significantly improved NYHA functional class (85.4% NYHA functional class ≤II vs 9.3% at baseline)
- No differences in outcomes or adverse events after stratification for valve size (≥55 vs <55 mm)

Stolz L, et al. JACC Cardiovasc Interv. 2024;17(16):1936-1945.

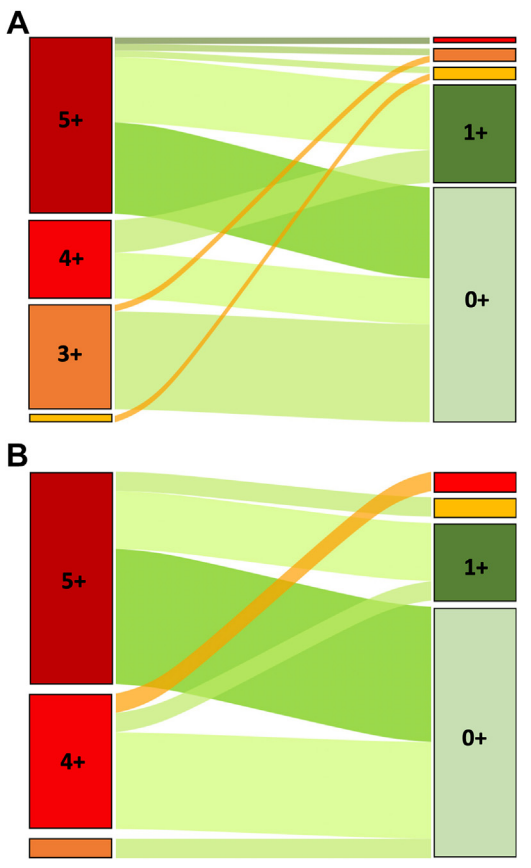
MI = myocardial infarction; PE = pulmonary embolism; PPM = permanent pacemaker; TR = tricuspid regurgitation.

FIGURE 1 1-Month Survival Following TTVR Using the LuX-Valve



1-month survival after transcatheter tricuspid valve replacement (TTVR) using the LuX-Valve system was 93.1%.

FIGURE 2 TR Reduction Stratified by Implanted Valve Size



Tricuspid regurgitation (TR) reduction was comparable in patients who received small (<55 mm) (A) vs large (≥55 mm) (B) valve sizes.

reduction rates to ≤1+ in 88% of patients.[6,16] At the same time, relevant residual TR ≥3+ has been associated with increased mortality in multiple T-TEER registries.[13,17] The degree of TR reduction may also play an important role in the extent of hemodynamic improvement after the procedure. RV reverse remodeling as well as quality of life improvement have been shown to predominantly occur in T-TEER patients with successful TR reduction.[18-20]

Our analysis revealed TR reduction to ≤2+ in all patients who underwent transjugular TTVR, which was sustained in 95.0% of patients at 1-month follow-up. All cases of residual TR after transjugular TTVR were of paravalvular nature, mostly mild (1+) in a posteroseptal location. The underlying mechanism for residual paravalvular leakage with the LuX-Valve might be manifold, including suboptimal, too atrial device positioning, device anchoring, device sizing, and pre-existing transvalvular leads (present in 30.3% of patients), among others. The unique anchoring mechanisms might require less device oversizing at the level of the tricuspid annulus than other TTVR devices, which might result in less sealing forces, but also in a lower compression of the atrioventricular node, which might be associated with a lower need for subsequent pacemaker implantations. The clinical relevance of mild (1+) or even moderate (2+) residual paravalvular TR is currently unknown and might differ from left-sided aortic or mitral paravalvular leakages because no cases of relevant hemolysis were observed and patients showed substantial symptomatic improvement.

IN-HOSPITAL AND 1-MONTH ADVERSE EVENTS. Mortality and need for reintervention or surgery. The results of this study must be interpreted against the background of a compassionate use setting. Those patients usually presented in a progressive disease state with multiple comorbidities and an increased surgical risk, which might explain the 5.3% in-hospital mortality rate. On the other hand, those patients probably are well selected for treatment with a new device. Two patients were in cardiogenic shock requiring preimplant inotropic support, 1 died of ongoing right heart failure and the other following emergency cardiac surgery because of malpositioning of the device. In 1 patient, device implantation was aborted because of incomplete extension of the leaflet graspers. One patient died following gastrointestinal bleeding. Another patient had a delayed pericardial tamponade and cardiac arrest. Detachment of the septal anchor occurred during cardiopulmonary resuscitation, and the patient subsequently died post-emergency surgery. Detachment of the septal anchor

occurred in 2 further cases at the 1-month follow-up. One patient underwent heterotopic TTVR and the other surgical TV replacement. The procedural learning curve may play a role in these events. In addition, a small device iteration to adjust the angulation and configuration of the septal anchor has been made during the enrollment phase of this study. Further data are needed to evaluate the effectiveness of the respective design changes of the device.

Bleeding and thrombosis. With 4 bleeding events during hospital stay (6.6%) and 1 further case within the 1-month follow-up, the overall bleeding rate was lower compared to previous studies (up to 16.9% at the 1-month follow-up). TTVR patients are prone to bleeding complications because of advanced age, anticoagulation therapy, hepatic dysfunction, and other comorbid conditions. Almost all patients received oral anticoagulation therapy for atrial fibrillation before TTVR. The optimal anticoagulation strategy after TTVR (DOACs vs vitamin K antagonist) is unknown but certainly needs to balance the risk of bleeding and valve thrombosis. The latter is of special importance because the hemodynamic low-flow/low-pressure characteristics of the right side of the heart may predispose to thrombus formation. Of note, in the present analysis, no case of device thrombosis was observed until the 1-month follow-up. In the present analysis, only 1 patient suffered access site complication that required surgical treatment (1.3%), which appears favorable considering the transjugular access and the large sheath size for vascular access.

Conduction disturbances and need for pacemaker implantation. With its close anatomical relationship to important structures of the conduction system, TTVR can cause conduction disturbances, which might require pacemaker implantation. Previous studies reported pacemaker implantation rates up to 13.3%.[5] Of note, all relevant conduction disturbances occurred within 9 days after the procedure.[5] In the present registry, 5.2% (4/76) of all patients and 7.5% (4/53) of those without a pre-existing pacemaker underwent permanent pacemaker implantation after TTVR. This rate might be lower compared to other TTVR devices because of differences in the anchor mechanisms and a lower need for device oversizing in relation to the tricuspid annulus with LuX-Valve devices.

AVAILABLE VALVE SIZES. In contrast to all currently available data on TTVR, the present registry reports outcomes for patients who received TTVR devices ≥55 mm in a considerable percentage of cases (75%). The largest valve that has been implanted in the TRISCEND I (Edwards EVOQUE Tricuspid Valve Replacement: Investigation of Safety and Clinical Efficacy After Replacement of Tricuspid Valve With Transcatheter Device) study and other published compassionate use EVOQUE reports measured 52 mm in diameter,[5,6,16,21,22] and a considerable proportion of patients with larger anatomies were screened out because of this limitation. Therefore, larger orthotopic replacement options may be an important asset to the toolbox of TR treatment, especially for patients with excessive annular dilation. As shown previously, there was no difference in the rate of adverse events in patients who received valves sized ≥55 mm compared to smaller ones, whereas TR reduction was comparable. It will be important to confirm this finding in larger studies that are powered for the detection of potential differences in outcomes.

STUDY LIMITATIONS. Even though not being subjected to core laboratory supervision, all site-reported data have been collected by experienced physicians and echocardiographers at each study center according to recent guidelines and recommendations. Of note, the study design is retrospective and included compassionate use cases only. Follow-up data beyond 30 days are pending. Finally, the study does not provide data regarding the 6-minute walking test distance of the study cohort.

CONCLUSIONS

Transjugular TTVR is a treatment option for patients with severe TR and large tricuspid anatomies. Although TR reduction was sustained until the 1-month follow-up, mild or moderate paravalvular leaks were observed, but the clinical relevance of this finding is currently unclear. Results of the prospective TRINITY (A Study to Evaluate the Safety and Performance of LuX-Valve Plus System for Tricuspid Replacement; NCT05436028) are highly anticipated in order to confirm the aggregated, favorable, compassionate use results.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

Dr Stolz has received speaker honoraria from Edwards Lifesciences. Dr Cheung has received speaker honoraria from Edwards Lifesciences, Abbott Vascular, and Medtronic; and has served as an eligibility committee member for the TRINITY trial. Dr Boone has served as a consultant for Edwards Lifesciences and Abbott. Dr Fam has served as a consultant for Edwards Lifesciences, Abbott, and Cardiovalve. Dr Villablanca has served as a consultant for Edwards Lifesciences, Medtronic, Angiodynamic, Telflex, and Abiomed. Dr De Backer has received institutional research grants and consulting fees from Abbott, Boston Scientific, and Medtronic. Dr Tchétché has served as consultant for Abbott, Edwards Lifesciences, Boston Scientific, and Medtronic. Dr So has served as a proctor for Abbott, Boston Scientific, Edwards Lifesciences, and Medtronic. Dr Latib has

served on the Advisory Board for Medtronic, Abbott Vascular, Boston Scientific, Edwards Lifesciences, Shifamed, NeoChord Inc, V-dyne, and Philips. Dr Scotti has served as a consultant for NeoChord and Edwards Lifesciences. Dr Estévez-Loureiro has served as a consultant to Abbott Vascular, Edwards Lifesciences, Boston Scientific, Venus Medtech, and Jenscare. Dr Leurent has received speaker and proctoring honoraria from Edwards Lifesciences and Abbott Medical. Dr Hausleiter has received research support and speaker honoraria from Edwards Lifesciences.

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PERSPECTIVES

WHAT IS KNOWN? The LuX-Valve device is increasingly used for TTVR in patients ineligible for T-TEER.

WHAT IS NEW? This is the largest registry to report effective TR reduction up to 1 month after LuX-Valve TTVR. This analysis is the first to report favorable outcomes of patients who receive TTVR devices ≥55 mm in diameter.

WHAT IS NEXT? Prospective studies are needed to confirm these compassionate use data. Therefore, the results of the currently ongoing TRINITY study are highly anticipated.

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KEY WORDS transcatheter tricuspid valve replacement, transjugular, tricuspid regurgitation, TTVI, TTVR

APPENDIX For supplemental tables, please see the online version of this paper.