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# The International Multicenter TriValve Registry

## Which Patients Are Undergoing Transcatheter Tricuspid Repair?

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## ABSTRACT

**OBJECTIVES** This study sought to develop a large, international registry to evaluate the diffusion of these approaches and investigate patient characteristics and initial clinical results.

**BACKGROUND** Several transcatheter tricuspid valve therapies are emerging as therapeutic options for patients with severe symptomatic tricuspid regurgitation (TR), generally a high-risk surgical population.

**METHODS** The TriValve (Transcatheter Tricuspid Valve Therapies) registry included 106 high-risk patients (76 ± 9 years of age; 60.4% women; European System for Cardiac Operative Risk Evaluation II 7.6 ± 5.7%) from 11 cardiac centers, with severe TR.

**RESULTS** A total of 35% of the patients had prior left heart valve intervention (surgical in 29 of 106 and transcatheter in 8 of 106 patients). Right ventricular (RV) dysfunction (tricuspid annular plane systolic excursion <17 mm) was present in 56.3% of the patients; 95% of the patients were in New York Heart Association functional class III to IV. The etiology of TR was functional in 95.2%, and the mean tricuspid annulus was 45.4 ± 11 mm. In 76.9% of the patients, the main location of the regurgitant jet was central; pre-procedural systolic pulmonary artery pressure was 39.7 ± 13.8 mm Hg; and the inferior vena cava was severely dilated in most of the patients (27.4 ± 6.8 mm). Implanted devices included MitraClip (n = 58), Trialign (n = 17), TriCinch (n = 15), FORMA (n = 7), Cardioband (n = 5), and caval valve implantation (n = 3). One case had combined Trialign + MitraClip. Patients treated with the different techniques were similar in terms of European System for Cardiac Operative Risk Evaluation II and degree of RV dysfunction. In 68% of the cases the tricuspid intervention was performed as an isolated procedure. Procedural success was achieved in 62% of cases. At 30-day follow-up, all-cause mortality was 3.7%, with an overall incidence of major adverse cardiac and cerebrovascular events of 26%; 58% of the patients were New York Heart Association functional class I or II at 30 days.

**CONCLUSIONS** Patients currently undergoing transcatheter tricuspid valve therapy are mostly high risk, with a functional etiology and very severe central regurgitation, and do not have severely impaired RV function. Initial results suggest that transcatheter tricuspid valve therapy is feasible with different techniques, but clinical efficacy requires further investigation. (J Am Coll Cardiol Intv 2017;10:1982–90) © 2017 by the American College of Cardiology Foundation.

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Different transcatheter tricuspid valve (TV) therapies have been recently emerging as therapeutic options for patients with a severe symptomatic functional tricuspid regurgitation (TR), which conventionally represent a high-risk surgical population (1–3). Preliminary small series showed the feasibility of percutaneous TV repair with a number of devices (4–7). However, at the initial stage of development of these therapies, several clinical, anatomic, and technical issues have to be addressed and overcome before assessing their efficacy.

Most of the patients treated today are compassionate end-stage heart failure patients, with right ventricular (RV) dysfunction and severe comorbidities. In this context, it can be extremely difficult to assess the potential clinical benefits of transcatheter TV therapies and to assess which patients could really benefit from an interventional treatment. Fluctuations of TR in response to loading conditions and medical therapies further compound this problem.

SEE PAGE 1991

In particular, the dissemination of the different approaches, interventional timing, and proper clinical and anatomical patients' selection are currently unknown (8,9).

The International TriValve (Transcatheter Tricuspid Valve Therapies) registry was established to address these issues and is the first international registry to collect data regarding patients undergoing TV interventions with currently available devices.

The objectives of the study are to investigate the usage of transcatheter TV therapies and their initial clinical results in a high number of patients using a large, worldwide registry. In particular, the study sought to examine the anatomic and clinical characteristics of patients undergoing transcatheter tricuspid interventions, as well as the dissemination of the different devices, and report the initial feasibility and safety outcomes.

## METHODS

**REGISTRY DESIGN.** The TriValve registry was initiated in November 2016. The registry is not supported by any external funding and was designed to collect data from centers across the world that had experience with transcatheter TV therapies with different devices: MitraClip (Abbott Vascular, Santa Clara, California) in tricuspid position, FORMA (Edwards Lifescience, Irvine, California) spacer, Cardioband (Edwards Lifescience) tricuspid, TriCinch (4TECH, Galway, Ireland), Trialign (Mitraling, Tewksbury, Massachusetts), and caval valve implantation (CAVI) (**Figure 1**). The comprehensive description of the different procedures were reported elsewhere (4–6,10–15).

A total of 11 centers from Europe and North America had contributed the registry. Continued communication with involved centers (M.T.) was initiated. Data were collected with the use of a dedicated dataset. All inconsistencies were resolved directly with local investigators and on-site data monitoring. For each patient, we collected the baseline pre-procedural clinical and echocardiographic characteristics. Early post-procedural hemodynamic analysis included data from intraprocedural and pre-discharge echocardiographic data. Baseline clinical, anatomic, and echocardiographic data were collected for all the patients included in the registry. Because the main objective of this report is to investigate the usage of tricuspid therapies and which type of patients are being treated today, the study currently only reports outcomes of patients not included in ongoing unpublished trials, to avoid any potential conflict.

**ABBREVIATIONS AND ACRONYMS**

**CAVI** = caval valve implantation

**NYHA** = New York Heart Association

**RV** = right ventricular

**TAPSE** = tricuspid annular plane systolic excursion

**TR** = tricuspid regurgitation

**TV** = tricuspid valve

**VC** = vena contracta

on the Speakers Bureau for Abbott Vascular; on the scientific advisory board for Millipede; and as a consultant for 4Tech, Mitralign, and Millipede. Dr. Braun has received speaker honoraria from Abbott Vascular. Dr. Brochet has received speaker fees from Abbott Vascular. Dr. Denti has served as a consultant for Abbott Vascular, 4Tech, and InnovHeart. Dr. Deuschl has served as a proctor and consultant for Valtech/Edwards (Cardioband). Dr. Hausleiter has received speaker honoraria from Abbott Vascular and Edwards Lifesciences. Dr. Kuck has served as a consultant for Abbott Vascular, St. Jude Medical, Biotronik, Medtronic, Edwards Lifesciences, and Mitralign; and is cofounder of Cardiac Implants. Dr. Nietlispach has served as a consultant for Abbott Vascular, Medtronic, and Edwards Lifesciences; and owns stock in Edwards Lifesciences. Dr. Schäfer has received lecture fees, study honoraria, travel expenses from, and is member of the advisory board of Abbott. Dr. Tang has served as a consultant, advisory board member, and faculty trainer for Abbott Structural Heart. Dr. Vahanian has served as a consultant for Abbott Vascular, Edwards Lifesciences, and Mitral Tech. Dr. Webb has received research support from Edwards Lifesciences; and served as a consultant for Abbott Vascular, Edwards Lifesciences, and St. Jude Medical. Dr. Maisano has served as a consultant for Abbott Vascular, Edwards Lifesciences, and Medtronic; and is cofounder of 4Tech. Dr. Leon has served as a nonpaid member of the Scientific Advisory Board of Edwards Lifesciences and consultant for Abbott Vascular and Boston Scientific. All other authors have reported that they have no relationships relevant to the contents of this paper. Drs. Taramasso and Hahn contributed equally this work.

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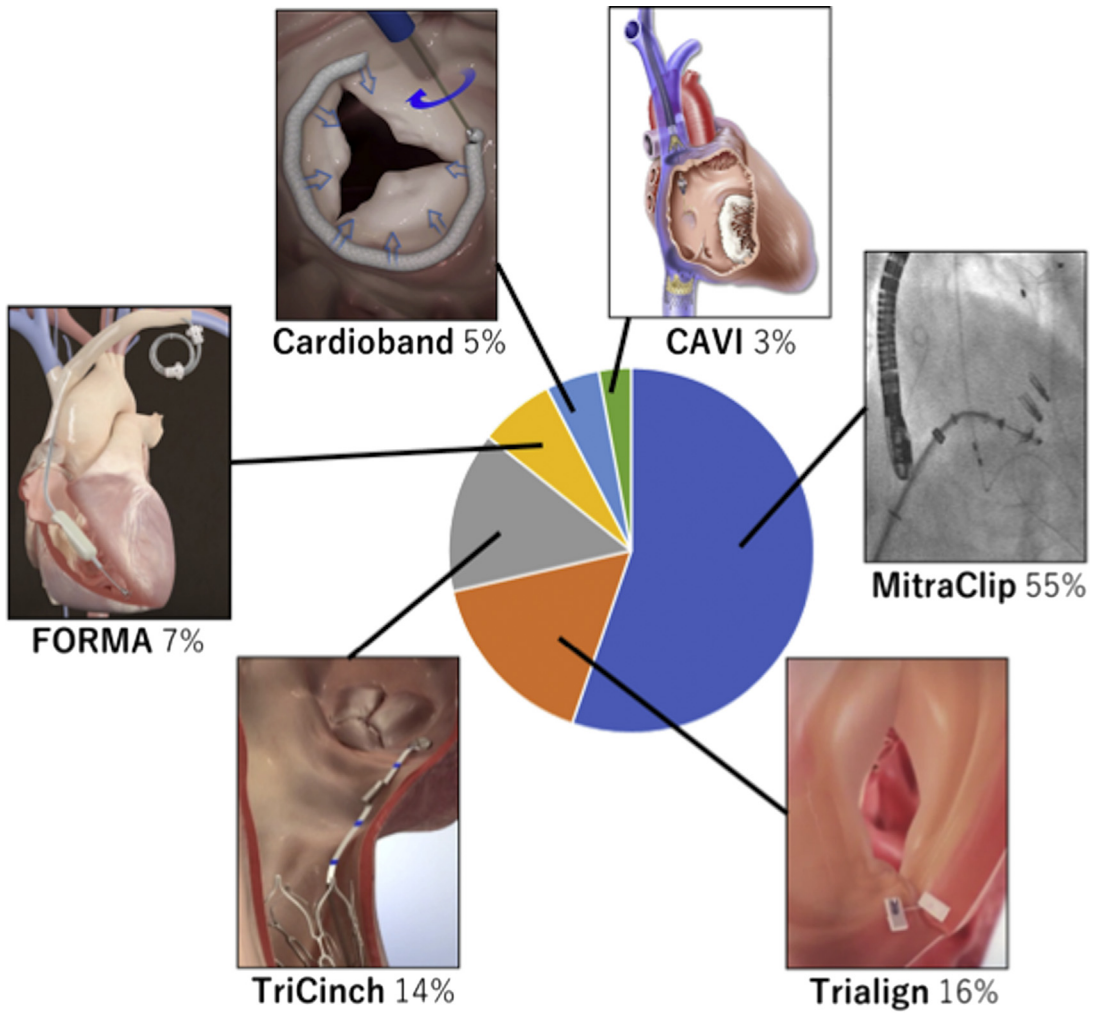
**FIGURE 1 Distribution of the Different Devices Used in the Registry**




CAVI = caval valve implantation.

The inclusion of patients in this registry was approved in each center by a local ethical committee or per local practice for the collection of retrospective data.

**DEFINITIONS.** All the patients included in the registry met the criteria for tricuspid intervention according to the European or American guidelines for the management of heart valve disease or were treated according to local multidisciplinary team decision (16,17). Grading of the severity of TR was assessed using a combination of semiquantitative and quantitative assessment (18), as described by the American Society of Echocardiography guidelines as well as the European Association of Echocardiography guidelines (19,20).

In the absence of a consensus position regarding TV interventions, periprocedural adverse events were defined according to the Mitral Valve Academic Research Consortium criteria (21). Procedural success was defined as patient alive at the end of the procedure, with the device successfully implanted and delivery system retrieved, with a residual TR ≤2+.

Follow-up data were collected for patients at 30 days and then according to the time frame elapsed from the index procedure to data lock for present analysis.

**STATISTICAL ANALYSIS.** Statistical analysis was performed with the use of JMP version 8.0 software (SAS Institute Inc, Cary, North Carolina). Results are

presented as mean ± SD for continuous variables with normal distribution (tested by the Shapiro-Wilk normality test), as median and interquartile range (interquartile range [25th, 75th percentiles]) for continuous variables without normal distribution, and as percentages for categorical data. One-way analysis of variance and paired *t* test were used to compare normally distributed continuous variables, and the Kruskal-Wallis test was used for non-normally distributed data. Chi-square and Fisher exact tests were used to compare categorical variables. A 2-sided p value ≤0.05 was considered statistically significant.

## RESULTS

**PATIENT DEMOGRAPHICS AND CLINICAL PROFILE.** Between January 2014 and December 2016, 106 patients with severe symptomatic TR underwent transcatheter TV repair in 11 different centers (Europe, United States, and Canada) and were included in the TriValve registry.

Patients mean age was 76 ± 9 years, with a 60.4% prevalence of women. Expected surgical risk for mortality assessed with European System for Cardiac Operative Risk Evaluation II was 7.6 ± 5.7%.

Overall, 35% of the patients had previous left-sided valve intervention: in 29 (27.4%) patients, this was an open-heart surgical operation, whereas in 8 (7.5%) patients, this was a transcatheter procedure (MitraClip in 7 cases, transcatheter aortic valve replacement in 1 case). In 25 (23.5%) patients, a transvalvular tricuspid pacemaker lead was present, and 83 (78.3%) patients had a history of longstanding persistent atrial fibrillation.

Most patients were severely symptomatic for dyspnea: 95% were in New York Heart Association (NYHA) functional class III to IV, whereas mean duration of severe RV failure symptoms before the procedure was 9 months.

At the time of the procedure, 27.3% of the patients (n = 29) had ascites, 81.1% (n = 86) had peripheral edema despite the maximal tolerated diuretic therapy and 56.6% (n = 60) were admitted at least once within the last 6 months, due to RV failure. Baseline median N-terminal pro-B-type natriuretic peptide was 2,253 (IQR: 1,416 to 5,252) pg/ml.

Table 1 summarizes the baseline clinical profile of the patients included in the registry.

**TABLE 1 Baseline Clinical Profile of the Overall Study Population (N = 106)**

| | |
|---|---|
| Age, yrs | 76.3 ± 8.9 |
| Female | 64 (60.4) |
| Body mass index, kg/m$^2$ | 26.3 ± 5.0 |
| EuroSCORE II, % | 7.6 ± 5.7 |
| TR etiology | |
| Functional | 101 (95.0) |
| Degenerative | 1 (1.0) |
| Mixed | 2 (2.0) |
| Pacemaker induced | 2 (2.0) |
| Previous left side valve intervention (surgical/transcatheter) | 26.0/7.5 |
| Peripheral artery disease | 12 (11.5) |
| Transtricuspid pacing lead | 25 (23.5) |
| Atrial fibrillation | 83 (79.0) |
| Previous myocardial infarction | 18 (17.5) |
| COPD | 15 (14.4) |
| Cerebrovascular disease | 39 (37.0) |
| Diabetes | 25 (24.0) |
| eGFR, ml/min | 43 ± 15 |
| AST/ALT, IU/l | 30/19 |
| NT-proBNP, pg/ml | 2,523 (1,416-5,252) |
| Hemodynamic instability | 4 (3.8) |
| Ascites | 29 (27.3) |
| Peripheral edema | 86 (81.0) |
| NYHA functional class III-IV | 101 (95.0) |
| Previous admission for RV failure | 60 (56.6) |
| Baseline hemoglobin (g/dl) | 11.6 ± 2.0 |
| Medical therapy | |
| Torasemide (n = 57), mg | 25 (15-40) |
| Furosemide (n = 45), mg | 80 (25-160) |
| Spironolactone | 44 (45.0) |

Values are mean ± SD, n (%), or median (interquartile range).

ALT = alanine aminotransferase; AST = aspartate aminotransferase; COPD = chronic obstructive pulmonary disease; eGFR = estimated glomerular filtration rate; EuroSCORE = European System for Cardiac Operative Risk Evaluation; IU = international units; NT-pro-BNP = N-terminal pro-B-type natriuretic peptide; NYHA = New York Heart Association; RV = right ventricular; TR = tricuspid regurgitation.

**ECHOCARDIOGRAPHIC PROFILE.** All patients included in the registry underwent preoperative transthoracic and transesophageal echocardiographic assessment. The etiology of TR was functional in 95.6% of the cases. Mean vena contracta (VC) width of the tricuspid jet was 1.1 ± 0.55 cm, with a regurgitant volume of 62.9 ± 27 ml. Tricuspid annulus (measured in 2-dimensional apical 4-chamber transthoracic view) was severely dilated in most of the patients (45.4 ± 11 mm; range 29 to 124.9 mm). Coaptation depth of the TV was 11.9 ± 5 mm. The regurgitant jet was mainly central in 76.9% of the cases.

RV dysfunction (defined as tricuspid annular plane systolic excursion [TAPSE] <17 mm) was present in 56.3% of the patients (mean 16 ± 4 mm). The right atrium (120.2 ± 79.0 ml) and the inferior vena cava (27.4 ± 6.8 mm) were severely enlarged. Left ventricular ejection fraction was 50.8 ± 12.6%; concomitant mitral regurgitation ≥3+ was present in 27 patients (25%), with a pre-procedural systolic pulmonary artery pressure of 39.7 ± 13.8 mm Hg. Table 2

**TABLE 2 Baseline Echocardiographic Profile (N = 106)**

| | |
|---|---|
| Right atrial volume, ml | 120 ± 79 |
| LVEF, % | 50.8 ± 12.6 |
| LV end-diastolic diameter, mm | 48.7 ± 9.0 |
| Concomitant MR ≥3+ | 27 (25) |
| TR jet location | |
| Central | 81 (77) |
| Anteroseptal | 17 (15) |
| Anteroposterior | 5 (5) |
| Posteroseptal | 3 (3) |
| Tricuspid vena contracta, cm | 1.10 ± 0.55 |
| Tricuspid regurgitant volume, ml | 62.9 ± 27.0 |
| Tricuspid anteroseptal diameter, mm | 45.4 ± 11.0 |
| Tricuspid EROA, $cm^2$ | 0.87 ± 0.56 |
| TAPSE, mm | 16.2 ± 4.0 |
| S-TDI, cm/s | 9.7 ± 3.0 |
| Tenting area, $cm^2$ | 4.1 ± 2.3 |
| Coaptation depth, mm | 11.9 ± 5.0 |
| Systolic pulmonary artery pressure, mm Hg | 39.7 ± 13.9 |
| IVC diameter, cm | 27.4 ± 6.8 |

Values are mean ± SD or n (%).

EROA = effective regurgitant orifice area; IVC = inferior vena cava; LV = left ventricle; LVEF = left ventricular ejection fraction; MR = mitral regurgitation; S-TDI = systolic tissue Doppler imaging; TAPSE = tricuspid annular plane systolic excursion; TR = tricuspid regurgitation.

shows the echocardiographic characteristics of the patients.

**PERIPROCEDURAL AND EARLY OUTCOMES.** Implanted devices included MitraClip (n = 58), Trialign (n = 17), TriCinch (n = 15), FORMA (n = 7), Cardioband (n = 5), and CAVI (n = 3). One case had combined Trialign and MitraClip.

All patients but one (who received a TriCinch repair in conscious sedation using intracardiac echocardiography guidance) (22) were treated under general anesthesia, using transesophageal echocardiographic and fluoroscopic guidance.

In 68% of the cases (n = 72), the tricuspid intervention was performed as an isolated procedure, whereas in 32%, it was performed concomitantly with a transcatheter mitral procedure. Patients with concomitant mitral procedure had comparable systolic pulmonary artery pressure (37.2 ± 13.6 mm Hg vs. 39.8 ± 14.5 mm Hg) but lower ejection fraction (40.8 ± 14% vs. 54.2 ± 10%; p < 0.001).

Table 3 compares the profile of the patients treated with the different devices.

Patients treated with the different techniques had similar European System for Cardiac Operative Risk Evaluation II and degree of RV dysfunction. Patients who received CAVI had significantly more dilated tricuspid annuli and inferior venae cavae (both p < 0.05 compared with the other approaches). MitraClip was the device most frequently used in patients with a transvalvular pacing lead (38% of the cases).

Procedural and periprocedural outcomes were available for 95 patients. Procedural success (defined as patient alive at the end of the procedure with the device successfully implanted, delivery system retrieved, and a residual TR grade ≤2) was achieved in 62% of cases, without any differences in patients who had concomitant mitral intervention. Post-procedural adverse events included 8 patients requiring blood transfusion of >1 blood units, 10 acute kidney injury, 1 conversion to open surgery, and 1 pericardial effusion requiring drainage. No cases of stroke or acute myocardial infarction were observed. Median post-procedural length of stay was 7 (IQR: 4 to 10) days. Figures 2 and 3 show RV function and TR change at pre-discharge echocardiography compared with baseline in the total population. Prevalence of TR ≤2+ at discharge was higher in patients who had concomitant mitral intervention (73% vs. 38%; p = 0.01).

At 30-days follow-up (available for 81 patients), all-cause mortality was 3.7% (total 3 patients [1 with isolated TV intervention and 2 with concomitant

**TABLE 3 Profile of the Patients Treated With Different Devices**

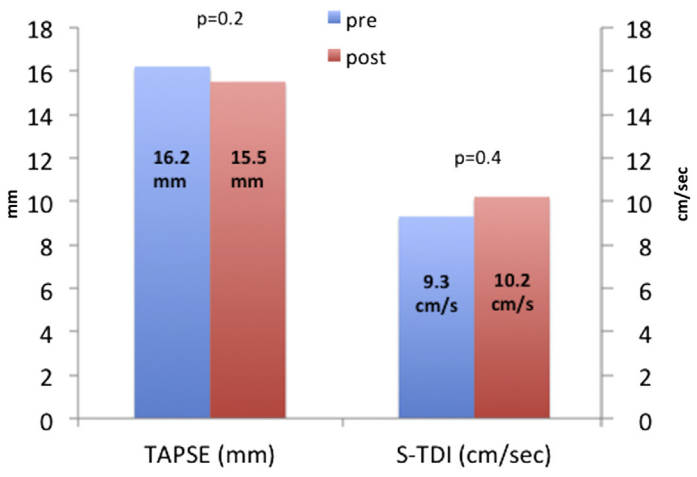
| | MitraClip (n = 58) | Trialign (n = 18) | Cardioband (n = 5) | TriCinch (n = 15) | FORMA (n = 7) | CAVI (n = 3) | p Value* |
|---|---|---|---|---|---|---|---|
| Previous left side intervention | 12 (20) | 9 (50) | 2 (40) | 7 (47) | 6 (86) | 1 (33) | 0.09 |
| EuroSCORE II, % | 7.8 ± 6.0 | 9.6 ± 9.0 | 4.5 ± 3.0 | 5.6 ± 3.0 | 7.9 ± 4.0 | 3.4 ± 1.0 | 0.50 |
| LVEF, % | 48 ± 14 | 53 ± 10 | 52 ± 7 | 56 ± 8 | 55 ± 8 | 54 ± 11 | 0.30 |
| TAPSE, mm | 16 ± 4 | 16 ± 5 | 15 ± 3 | 16 ± 4 | 15 ± 4 | 16 ± 7 | 0.90 |
| Central TR jet, % | 24 (42) | 18 (100) | 2 (40) | 11 (78) | 7 (100) | 3 (100) | 0.20 |
| Annular diameter, mm | 42 ± 8 | 49 ± 26 | 44 ± 6 | 45 ± 6 | 50 ± 6 | 58 ± 1 | 0.020 |
| IVC diameter, cm | 27 ± 6 | 26 ± 6 | 25 ± 12 | 26 ± 7 | 32 ± 6 | 38 ± 12 | 0.040 |
| Transvalvular lead | 22 (38) | 0 (0) | 1 (20) | 0 (0) | 1 (14) | 1 (33) | 0.0005 |

Values are n (%) or mean ± SD. *Comparisons performed with 1-way analysis of variance.

CAVI = caval valve implantation; other abbreviations as in Tables 1 and 2.

mitral procedure]: 1 from sepsis, 1 from heart failure, and 1 after tricuspid surgery). Overall incidence of major adverse events was 22.2% (n = 18) including: 2 bleeding (2.4%), 7 rehospitalization for heart failure (8.6%), 1 stroke (1.2%), 2 tricuspid surgery (2.4%; both due to failure of the procedure and residual unchanged TR), 1 respiratory failure (1.2%), 1 arrhythmic event (ventricular tachycardia successfully direct current shocked, 1.2%), and 4 device failures (4.9%). At 30 days, 59% of the patients were NYHA functional class I or II (p = 0.003 compared with baseline) (Figure 4). The proportion of patients with ascites was reduced to 13% (p = 0.006 compared with baseline) and that of patients with peripheral edema to 41.9% (p = 0.002 compared with baseline), with no significant differences between patients with isolated TV intervention and concomitant mitral intervention. Dosage of diuretics was significantly reduced compared with baseline (84% reduction of furosemide and 54.5% reduction of torasemide compared with baseline; p = 0.04 and 0.005, respectively) (Figure 5). Thirty days echocardiography (available for 40 patients) showed TR ≤2+ in 49% of the patients (p = 0.003 compared with baseline; 66% in patients with concomitant mitral intervention and 43% in patients with isolated TV intervention; p = 0.02), with a TAPSE of 16.2 ± 3.3 mm (p = 0.4 compared with baseline, no difference between isolated and concomitant intervention).

**FIGURE 2** RV Function at Baseline Compared With Discharge Echocardiographic Assessment




No significant changes have been observed. RV = right ventricular; S-TDI = systolic tissue Doppler imaging; TAPSE = tricuspid annular plane systolic excursion.

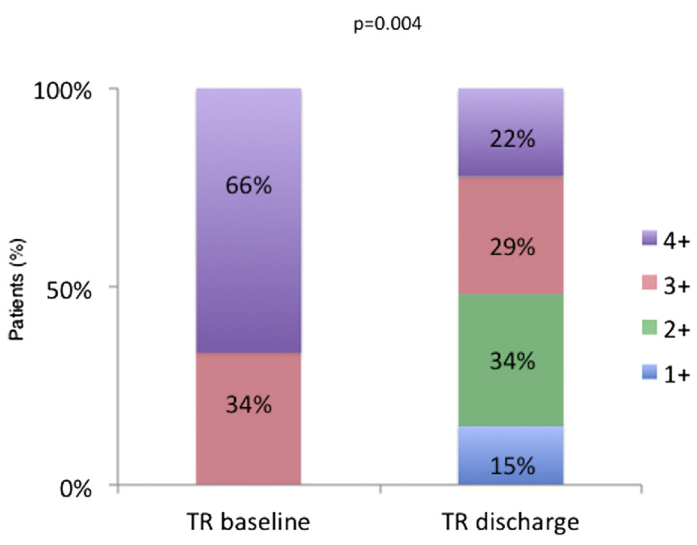
## DISCUSSION

The present study is the first large, comprehensive evaluation of the transcatheter approaches for the treatment of native TV regurgitation. The main objective of this first report is to explore which type of patients are today treated worldwide and to give an overall insight into the feasibility of transcatheter TV therapy using different devices. Currently, with more than 100 patients included so far, this series represents the largest real-life registry of patients treated with transcatheter TV interventions. The main results are that transcatheter TV intervention is feasible with different devices, with a high safety profile and, despite suboptimal anatomic results in some cases, it is associated with promising short-term clinical benefits.

**EPIDEMIOLOGY AND CLINICAL PROFILE OF THE PATIENTS.** The results reported here showed that the patients undergoing transcatheter TV treatment today are mostly high-risk patients with functional TR.

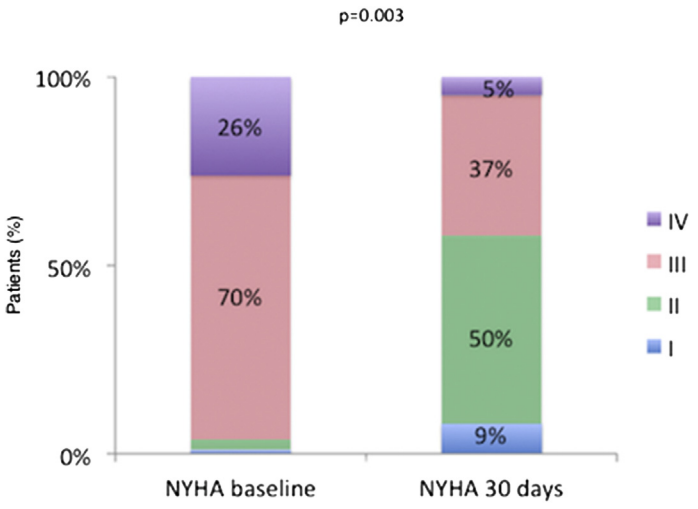
It has been shown that the presence of severe TR in patients with advanced heart failure does not increase morbidity and mortality, whereas severe TR is an independent mortality risk factor in patients with less advanced disease (23), suggesting that in patients with end-stage heart failure, the presence of TR is more an epiphenomenon rather an incremental

**FIGURE 3** TR Grade at Baseline Compared With Discharge Echocardiographic Assessment




TR = tricuspid regurgitation.

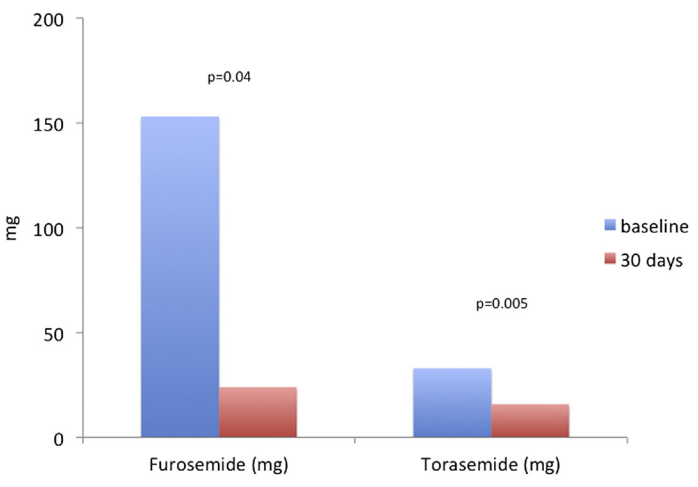
**FIGURE 4 NYHA Functional Class at Baseline Compared With 30 Days**




NYHA = New York Heart Association.

risk factor that could eventually be corrected and impact the natural course of the disease (<60% of the patients had TAPSE <17 mm) and may be a population expected to benefit from tricuspid repair. In fact, severe RV dysfunction is an exclusion criteria for current feasibility trials with the different devices in which a substantial proportion of the patients of this registry are included. Whether the exclusion of these patients is appropriate has not been determined. To understand which patients are the ideal candidates to benefit the most from these interventions, a better characterization of RV function using advanced methods should be the focus of future investigation.

**FIGURE 5 Diuretic Dosage at Baseline Compared With 30 Days**




Another interesting finding is that only 35% of the patients included in this registry had late TR after previous left-sided valve intervention (28% surgical, 7% transcatheter). In the surgical literature, late TR after left valve surgery is more frequently encountered (24). This difference can be the result of a number of referral biases. First, there are no Class I indications in the current guidelines for isolated tricuspid surgery. Second, patients with prior left heart surgery may not be referred for further interventions.

**TR ETIOLOGY AND ANATOMY.** The large majority of the patients included in the registry had functional TR (more than 95%). This reflects the epidemiology of TR in Western countries (functional in about 90% of the cases) (25). However, functional etiology of TR is an inclusion criteria for all the feasibility devices trials, and this could have biased the large prevalence of functional TR in this registry. Transvalvular pacing leads, a potential cause of TR, were present in about 24% of the patients. This etiology is often listed as a "primary" cause of TR because the lead will often result in adhesion to or pinning of the leaflet. This may not always be associated with annular dilatation and functional TR and the benefit of these transcatheter devices requires formal investigation.

Integral areas of research in transcatheter TV interventions include patient selection (which patients will benefit from a reduction in TR), which approach (annular versus leaflet) is most appropriate for a patient's given anatomy, and the appropriate timing of intervention.

A large number of patients in this registry have atrial fibrillation and in this setting, markedly dilated tricuspid annulus (anteroseptal diameter 45.4 ± 11 mm). The patients in the registry also exhibited severe leaflet tethering (coaptation depth 11.9 ± 5 mm). Studies have shown that recurrence of TR following valve repair can be predicted by leaflet tethering (26,27), so the benefit of tricuspid annular devices in this setting may be suboptimal. Indeed, as in surgery, these patients may require either multiple repair devices (annuloplasty and leaflet plasty) or even transcatheter TV replacement to ensure efficacious TR reduction.

**NEED FOR NEW DEFINITIONS AND PROCEDURAL CONSIDERATIONS: FEASIBILITY, SAFETY, AND EFFICACY.** Grading the severity of TR in this patient population is problematic. Annular dilatation with marked tethering of the leaflets resulted in central malcoaptation and a large central jet in about 75% of the cases. According to guidelines, severe

TR corresponds to a VC of >0.7 cm and a regurgitant volume of >45 ml (19,20). In this series, the average VC is 1.1 cm and regurgitant volume about 63 ml, which is ~1.5 times the criteria for "severe" and is sometimes referred to as "torrential" or "free" TR. It seems clear that given the extreme severity of regurgitation in many patients, the current grading schemes are inadequate to the wide spectrum of severe TR and need to be redefined.

In reporting outcomes of transcatheter TV treatments in the future, it will be extremely important to have a precise quantification of the entity of TR before and after any intervention. In this study, in absence of recommendations and definition on how to report outcomes after tricuspid procedures, procedural success was defined as "patient alive at the end of the procedure with the device successfully implanted and a residual TR ≤2+," for uniformity with the mitral valve procedures. According to this definition, this outcome was achieved in only 62% of the patients, according to current grading schemes for TR. However, patients consistently report improvements in quality-of-life measures despite only modest reductions in TR. The initial results of the registry confirm this observation: 30 days after the procedure, significant clinical improvements were observed in terms of NYHA functional class and RV failure symptoms compared with baseline. Given the discordance between TR reduction and clinical improvement, it is evident that we cannot use definitions of procedural success for the TV that have been used for the aortic and mitral valves. Moreover, a reduction from torrential to severe TR may still be beneficial for the patient by reducing anasarca and intestinal edema and improving the efficacy of medical therapy in patients with right heart failure. This observation raises another issue in the burgeoning field of interventional TV therapies: the needs define appropriate outcomes in this patient population and develop standard definitions on how to evaluate and report these outcomes.

These initial results importantly showed that TV repair is feasible with different technologies. The devices implanted in the registry reflect the worldwide usage of the different therapies. The most common device is the MitraClip (more than 50% of the patients of the registry) likely related to its approval by governing bodies for use on the mitral valve and thus its ready availability and operator familiarity (14).

Major clinical differences were not observed in patients treated with the different devices. The exception being patients treated with CAVI who had larger tricuspid annulus and inferior vena cava dimensions, suggesting a more advanced disease. However, as only 3% of the included patients had CAVI, no strong conclusions can be derived. The overall incidence of adverse events and 30-day mortality is low, especially considering the high-risk profile of the patients and the pathology, confirming the safety of TV interventions.

TV intervention was performed concomitantly with a mitral intervention in about 30% of the cases. Although this combined approaches mimics the surgical paradigm, given the high safety profile of the transcatheter approaches, staged procedures may mitigate the risk associated with simultaneous combined valves interventions.

**STUDY LIMITATIONS.** This study has several limitations, partially related to the typology of the registry itself. First, it is a prospective nonrandomized study, without a control group. The number of patients with severe TR who were not treated during the same period is not available. Second, this is a real-world registry reporting the clinical practice in different centers and countries; therefore, echocardiographic and clinical outcomes have been reported by the different sites and investigators, without core-lab adjudication. For the same reason, the modalities of follow-up are different within the different centers. Third, because the registry is relatively new, long-term outcomes are not available yet. Last, as specified in the Methods, definitions of procedural success and outcomes have been established by the investigators, because they have not been standardized yet.

## CONCLUSIONS

This multinational registry of patients with severe, symptomatic TR confirms that multiple devices for transcatheter TV therapy are currently being utilized in high-risk patients with functional etiology and advanced TV disease. Initial results suggest that transcatheter TV therapy is feasible and safe with different techniques with early clinical efficacy, despite seemingly suboptimal procedural results according to the standard definition. Further investigations are required to better define optimal patient selection, timing of intervention, disease severity, and device efficacy, creating an urgent need for standardized endpoint definition in this emerging field.

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## PERSPECTIVES

**WHAT IS KNOWN?** Different devices are under preliminary clinical evaluation for transcatheter TV treatment. Because clinical experience with the different techniques is at this stage really preliminary, several clinical, anatomic, and technical issues have to be addressed. The usage and penetration of the different devices as well as proper patient selection are largely unknown.

**WHAT IS NEW?** We developed the first large, international registry to evaluate the diffusion of the different transcatheter tricuspid repair approaches, and sought to investigate patient characteristics and initial clinical results. The preliminary results from the registry showed that patients currently undergoing transcatheter TV therapy are mostly high risk, with a functional etiology and very severe central regurgitation, and do not have severely impaired RV function.

**WHAT IS NEXT?** Initial results suggest that transcatheter TV therapy is feasible with different techniques, but clinical efficacy requires further investigation.

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**KEY WORDS** transcatheter tricuspid repair, tricuspid regurgitation, tricuspid valve