

Clinical Research

Clinical Profile and Outcomes of Patients Deemed Ineligible for Transcatheter Tricuspid Valve Intervention

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See editorial by Kim and Fam, pages 1967-1970 of this issue.

ABSTRACT

Background: Transcatheter tricuspid valve intervention (TTVI) has expanded therapeutic options for tricuspid regurgitation (TR); however, a substantial proportion of patients remain ineligible because of anatomical and clinical constraints. We sought to characterize patients screened out from TTVI and evaluate their clinical outcomes.

Methods: In this single-centre retrospective cohort study (January 2021 to May 2025), we included consecutive patients with symptomatic severe TR referred for TTVI evaluation who were deemed ineligible by a multidisciplinary heart team. Patients were identified through institutional logs and clinical trial screening databases. Baseline clinical, echocardiographic, and hemodynamic data were collected. Outcomes included 1-year all-cause mortality, heart failure hospitalization (HFH), and their composite.

Results: Among 205 patients evaluated, 83 (40.5%) were deemed ineligible. The mean age was 72.2 years, with a high burden of comorbidities. Severe or torrential TR was present in 84.4% of patients. The most frequent reasons for exclusion were unfavourable anatomy, including significant tricuspid annular dilation (69.5%) and a coaptation gap ≥ 7 -10 mm (59.8%). Patients who died within 1 year had higher right-sided filling pressures on invasive hemodynamic

RÉSUMÉ

Contexte : Les interventions valvulaires tricuspides par voie trans-cathéter (IVTT) ont élargi les options thérapeutiques pour l'insuffisance tricuspide (IT); cependant, une proportion importante de patients reste inéligible en raison de contraintes anatomiques et cliniques. Nous avons cherché à caractériser les patients écartés de l'IVTT et à évaluer leurs résultats cliniques.

Méthodologie : Dans cette étude de cohorte rétrospective monocentrique (janvier 2021 – mai 2025), nous avons inclus des patients consécutifs présentant une IT sévère symptomatique, orientés vers une évaluation en vue d'une IVTT et jugés non éligibles par une équipe cardiaque multidisciplinaire. Les patients ont été identifiés à partir des registres institutionnels et des bases de données de sélection pour essais cliniques. Les données cliniques, échocardiographiques et hémodynamiques de base ont été recueillies. Les critères d'évaluation comprenaient la mortalité toutes causes confondues à 1 an, l'hospitalisation pour insuffisance cardiaque (HIC) et leurs critères composites.

Résultats : Parmi les 205 patients évalués, 83 (40,5 %) ont été jugés inéligibles. L'âge moyen était de 72,2 ans, avec un lourd fardeau de comorbidités. Une IT sévère ou torrentielle était présente chez 84,4 % des patients. Les motifs d'exclusion les plus fréquents étaient une

Keywords: Tricuspid valve repair; transcatheter tricuspid edge-to-edge repair; tricuspid valve replacement; tricuspid regurgitation; heart failure

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Tricuspid regurgitation (TR) is a prevalent and progressive valvular disorder, particularly in aging and comorbid populations.¹ Although historically under-recognized compared with left-sided valvular diseases, untreated severe TR has been increasingly acknowledged as a major contributor to poor clinical outcomes, including diminished quality of life, recurrent heart failure hospitalization (HFH), and increased mortality—especially among patients with advanced right ventricular (RV) dysfunction or end-organ damage.²⁻⁵ Although surgical correction of TR can improve clinical status, many patients are not referred for surgery because of high operative risk—particularly in the setting of advanced

assessment. At 1 year, all-cause mortality was 20.5%, HFH occurred in 31.3%, and the composite end point in 51.8%. Kaplan-Meier estimates showed survival of 77.5% and freedom from HFH of 58.3% at 12 months.

Conclusions: Patients deemed ineligible for TTVI represent a high-risk cohort with substantial morbidity and mortality at 1 year. These findings underscore the importance of earlier referral, optimized screening strategies, and continued device innovation to expand treatment eligibility.

right-sided heart failure, in whom the potential benefit of intervention might be limited.⁶ Contemporary series report in-hospital mortality rates of up to 9% for isolated tricuspid valve surgery.⁶

Over the past decade, transcatheter tricuspid valve intervention (TTVI) has emerged to address what is viewed as an unmet clinical need. Techniques such as transcatheter tricuspid valve replacement (TTVR), transcatheter tricuspid edge-to-edge repair (T-TEER), tricuspid annuloplasty, and caval valve implantation have demonstrated procedural safety and symptomatic benefit.⁷ Trials including the **TRILUMINATE** Pivotal (TRILUMINATE; NCT03904147), and the Edwards **CLASP TR EFS** (CLASP TR EFS; NCT03745313), among others, have shown meaningful reductions in TR severity, improved New York Heart Association functional class, 6-minute walk distance, and quality-of-life scores, with encouraging RV remodelling and reduced HFH.^{8,9} However, definitions of procedural success in these early studies might be overestimated because of methodological limitations, including selection bias, exclusion of failed cases, and limited long-term follow-up. Moreover, anatomical complexities often preclude intervention.^{10,11}

Despite technological advancements, a substantial proportion of patients are deemed unsuitable for current transcatheter approaches. Registry data suggest that screening failure rates for TTVI exceeds 40%-60% in select registries and might be even higher for investigational replacement therapies.^{12,13}

In this study we aimed to provide a comprehensive evaluation of patients referred for TTVI who were deemed ineligible. Herein, we describe the anatomical and clinical characteristics that contribute to ineligibility, summarize their hemodynamic profiles, and track outcomes over time. By highlighting the unmet needs and high event rates in this population, we aim to refine referral strategies, refine screening criteria, and support innovation in device design tailored to complex right heart anatomy.

Methods

Study design and patient screening

This was a single-centre, retrospective observational cohort study conducted at a high-volume tertiary structural

anatomie défavorable, notamment une dilatation significative de l'anneau tricuspide (69,5 %) et un défaut de coaptation $\geq 7-10$ mm (59,8 %). Les patients décédés dans l'année présentaient des pressions de remplissage droites plus élevées lors de l'évaluation hémodynamique invasive. À 1 an, la mortalité toutes causes confondues était de 20,5 %, une HIC survenait chez 31,3 % des patients et le critère d'évaluation composite était atteint chez 51,8 % d'entre eux. Les estimations de Kaplan-Meier montraient une survie de 77,5 % et une absence d'HIC de 58,3 % à 12 mois.

Conclusion : Les patients jugés inéligibles à l'IVTT constituent une cohorte à haut risque, présentant une morbidité et une mortalité importantes à 1 an. Ces résultats soulignent l'importance d'une orientation précoce, de stratégies de dépistage optimisées et d'une innovation continue en matière de dispositifs médicaux afin d'élargir l'éligibilité au traitement.

heart centre between January 2021 and May 2025. We included all consecutive patients ineligible for surgical tricuspid valve intervention and referred for evaluation of TTVI, who were ultimately deemed ineligible for the procedure.

Eligible patients had symptomatic severe TR and underwent comprehensive screening by a multidisciplinary heart team consisting of interventional cardiologists, cardiac surgeons, and advanced cardiac imaging specialists. Patients were identified through institutional screening logs. Only patients who were formally evaluated for enrollment in the following clinical trials were included: **TRILUMINATE**⁸ (NCT03904147), **TRILUMINATE** Continued Access Study (TRILUMINATE CAS), Edwards **CLASP TR EFS** (CLASP TR EFS; NCT03745313), and **TriCaval** biCaval Valve System for Severe Tricuspid Regurgitation (TRICAV-I; NCT06137807).¹⁴

Of the 225 patients assessed across the 3 trials, 103 (45.8%) failed screening. After excluding 20 patients who were screened for multiple trials, a final cohort of 83 unique screen failure patients was included in this analysis (Fig. 1).

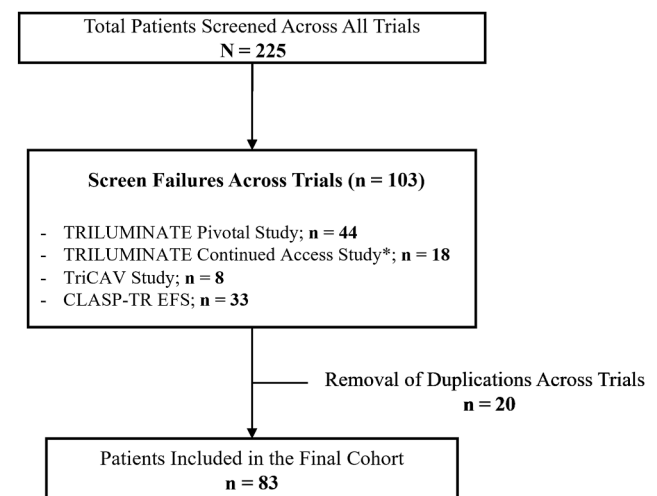


Figure 1. Patient selection flow diagram for transcatheter tricuspid valve intervention study. CLASP-TR EFS, Edwards **CLASP TR EFS**; TriCAV,.

Definition of screen failure

Patients were classified as screen failure if, after imaging evaluation, they were deemed anatomically or clinically unsuitable for the procedure, on the basis of predefined criteria and after providing informed consent. Clinical unsuitability could occur even if a patient initially appeared eligible, because screening committees apply strict criteria to optimize procedural safety and anticipated benefit. Reasons for screen failure were adjudicated from heart team documentation and included anatomical constraints, imaging limitations, comorbidities, frailty precluding intervention, or RV failure, defined according to the American College of Cardiology/American Heart Association guidelines.¹⁵

Data collection

Baseline demographic, clinical, and echocardiographic characteristics were extracted from electronic medical records. Transthoracic and/or transesophageal echocardiograms were reviewed to assess TR severity, RV size and function, leaflet morphology, annular dimensions, and coaptation gap measurements. TR and mitral regurgitation severity were assessed according to current guideline recommendations.¹⁶ Clinical outcomes, including all-cause mortality and HFH were recorded at the latest available follow-up. Follow-up was performed through review of electronic medical records.

Study end points

The primary end point of the study was all-cause mortality. Secondary end points included HFH and the composite end point of mortality and HFH at 1 year among patients who failed TTVI screening. Secondary analyses also were used to examine the stepwise treatment pathway from initial screen failure status through the chosen intervention to the final clinical outcome.

Statistical analysis

Continuous variables are presented as mean and standard deviation or median with interquartile range, depending on normality of distribution. Categorical variables are expressed as frequencies and percentages. Comparisons between groups were made using Student *t* test or Mann-Whitney *U* test for continuous variables and χ^2 or Fisher test for categorical variables. Time-to-event outcomes, including all-cause mortality and HFH and the composite of both were assessed using Kaplan-Meier survival analysis with log-rank testing for group comparisons. Patient pathways from initial screen failure status through management strategies to final outcomes were visualized using a Sankey diagram generated using [SankeyMATIC.com](https://sankeymatic.com). Predictors of all-cause mortality were evaluated using univariate Cox proportional hazards models, and variables with clinical relevance or *P* < 0.1 in univariate analysis were entered into a multivariate Cox model to identify independent predictors. A *P* value < 0.05 was considered statistically significant. All statistical analyses were performed using STATA Version 17.0 (StataCorp LLC, College Station, TX).

Results

Baseline and echocardiographic characteristics

Of the 205 patients referred for TTVR evaluation, 83 (40.5%) were screen failures. The mean age was 72.2 ± 14.4 years, and 57.3% were women. Most patients were White (74.7%). Cardiovascular comorbidities were highly prevalent, including hypertension (86.8%), hyperlipidemia (79.5%), coronary artery disease (78.3%), atrial fibrillation (68.7%), diabetes mellitus (31.3%), and chronic kidney disease (38.6%). Previous stroke occurred in 21.7%, and 31.3% had an existing pacemaker. Functional capacity was significantly limited, with 69.9% in New York Heart Association class III and 6.0% in class IV. Despite these burdens, most patients were treated with guideline-directed medical therapy, including diuretics (98.8%), β -blockers (80.8%), and angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (44.6%; [Table 1](#)).

Severe or torrential TR predominated—84.4% of patients—whereas 10.8% had moderate and 4.8% moderate-to-severe TR. Mitral regurgitation was absent or mild in 82.9%. Left ventricular ejection fraction was preserved ($57.5 \pm 9.3\%$), with mean end-systolic and end-diastolic diameters of 2.8 ± 0.9 cm and 4.4 ± 0.8 cm, respectively. The average left atrial volume was 98.2 ± 62.1 mL. Pulmonary artery systolic pressure averaged 46.0 ± 14.8 mm Hg and right atrial pressure (RAP) 15.8 ± 5.4 mm Hg. RV dysfunction was common: 36.1% moderate, 9.6% severe, and 95.2% had RV enlargement.

Screen failure etiologies

The mean interval from consent to screen failure determination was 6.5 ± 8.4 months. Anatomical exclusions predominated: excessive tricuspid annular dilation in 69.5%, coaptation gap ≥ 7 -10 mm in 59.8%, and leaflet tethering or abnormal coaptation in 48.8%. Device-related exclusions (intracardiac device presence) affected 31.3%, and severe pulmonary hypertension 51.8%. Less frequent reasons included advanced right heart failure (12.0%), high surgical risk (11.2%), short life expectancy (6.1%), and significant mitral valve disease (4.9%). Active endocarditis or sepsis and coagulopathy and/or bleeding each accounted for < 4% of exclusions ([Table 2](#)).

Right heart hemodynamics and mortality

[Figure 2](#) shows the Kaplan-Meier overall survival curves, with 77.5% of the cohort surviving at 1 year, 58.3% free from HFH, and 49% free from the composite outcome of mortality and HFH. Outcomes at 30 days, 1 year, and at final follow-up are summarized in [Table 2](#).

[Table 3](#) represents screen failure exclusion patterns and mortality rates at follow-up stratified according to tricuspid valve device type. Screen failure rates were highest in orthotopic trials, which occurred in 54.2% of patients in TRI-LUMINATE and 39.8% in Edwards CLASP-TR EFS (CLASP-TR), compared with only 6.0% in the heterotopic TRICAV-I cohort. Across all device types, anatomical factors were the predominant drivers of exclusion, particularly in orthotopic systems, where large coaptation gaps, severe annular dilation, and leaflet tethering were highly prevalent.

Table 1. Baseline clinical and echocardiographic characteristics of patients screen-failed for TTVI (N = 83)

Characteristic	Value
Baseline	
Mean age, years	72.2 ± 14.4
Race	
White	62 (74.7)
Black	10 (12.0)
Other	11 (13.3)
Female sex	47 (57.3)
Hypertension	72 (86.8)
Diabetes mellitus	26 (31.3)
Hyperlipidemia	66 (79.5)
Previous stroke	18 (21.7)
Previous myocardial infarction	23 (27.7)
Previous cardiac surgery	25 (30.1)
Coronary artery disease	65 (78.3)
Chronic kidney disease	32 (38.6)
Atrial fibrillation	57 (68.7)
Chronic obstructive pulmonary disease	8 (9.6)
Peripheral vascular disease	25 (30.1)
Previous pacemaker	26 (31.3)
NYHA classification	
III	58 (69.9)
IV	5 (6.0)
Medications prescribed	
β-Blockers	67 (80.8)
Diuretics	82 (98.8)
ACE inhibitors/ARB	37 (44.6)
Echocardiographic Characteristics	
TR severity	
Moderate	9 (10.8)
Moderate to severe	4 (4.8)
Severe	59 (71.1)
Torrential	11 (13.3)
MR severity	
None	32 (39.0)
Mild	36 (43.9)
Moderate	10 (12.2)
Severe	4 (4.9)
Ejection fraction, %	57.5 ± 9.3
LVIDs	2.8 ± 0.9
LVIDd	4.4 ± 0.8
LAV	98.2 ± 62.1
PASP	46.0 ± 14.8
RAP	15.8 ± 5.4
RV dysfunction	
None	22 (26.5)
Mild	20 (24.1)
Moderate	30 (36.1)
Moderate to severe	3 (3.6)
Severe	8 (9.6)
RV enlargement	79 (95.2)

Values are mean ± standard deviation or n (%).

ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; LAV, left atrial volume; LVIDd, left ventricular internal diameter in diastole; LVIDs, left ventricular internal diameter in systole; MR, mitral regurgitation; NYHA, New York Heart Association; PASP, pulmonary artery systolic pressure; RAP, right atrial pressure; RV, right ventricle; TR, tricuspid regurgitation; TTVI, transcatheter tricuspid valve intervention.

In contrast, clinical factors—including pulmonary hypertension, advanced right heart failure, and high procedural risk—were less frequent and contributed to a smaller proportion of exclusions. At follow-up, all-cause mortality was substantially higher among patients excluded from orthotopic trials (33.3% in TRILUMINATE and 18.2% in CLASP-TR), whereas no deaths were observed in the heterotopic group.

Table 2. Reasons for screen failure and subsequent clinical outcomes (N = 83 patients)

	Value
Reason for screen failure	
Time from consenting to screen failure, months	6.5 ± 8.4
Coaptation gap > 7-10 mm	49 (59.8)
Very large tricuspid annulus	57 (69.5)
Leaflet tethering/abnormal coaptation	40 (48.8)
Severely calcified, fibrotic, or retracted leaflets	5 (6.1)
Presence of intracardiac device	26 (31.3)
Severe pulmonary hypertension	43 (51.8)
Advanced right heart failure	10 (12.0)
Short life expectancy	5 (6.1)
High surgical risk	9 (11.2)
Active endocarditis or sepsis	2 (2.4)
Ongoing coagulopathy/bleeding	3 (3.7)
Significant MR or MS	4 (4.9)
Outcomes	
Median follow-up time, months	14.4 ± 14.7
In-hospital all-cause mortality	4 (4.9)
Outcomes at 30 days	
All-cause mortality	8 (9.6)
Heart failure hospitalization	6 (7.2)
Composite	14 (16.9)
Outcomes at 1 year	
All-cause mortality	17 (20.5)
Heart failure hospitalization	26 (31.3)
Composite	43 (51.8)
Outcomes at follow-up	
All-cause mortality	21 (25.6)
Heart failure hospitalization	51 (62.2)
Composite	72 (87.8)

Values are mean ± standard deviation, or n (%).

MR, mitral regurgitation; MS, mitral stenosis.

Right heart catheterization (Table 4) showed that patients who died by 1 year (n = 17) had higher baseline filling pressures than survivors (n = 66): RAP of 21.6 ± 2.9 vs 13.1 ± 0.7 mm Hg ($P < 0.001$), pulmonary artery diastolic pressure of 24.5 ± 3.0 vs 19.4 ± 1.0 mm Hg ($P = 0.05$), and pulmonary capillary wedge pressure of 22.0 ± 2.5 vs 17.1 ± 0.8 mm Hg ($P = 0.02$).

At the last follow-up, those who died (n = 21) had persistently higher right and left-sided filling pressures compared with survivors, including RAP of 19.3 ± 2.4 vs 13.1 ± 0.8 mm Hg ($P = 0.002$), pulmonary artery diastolic pressure of 24.5 ± 2.5 vs 19.0 ± 1.0 mm Hg ($P = 0.01$), mean pulmonary artery pressure of 33.3 ± 2.7 vs 27.1 ± 1.1 mm Hg ($P = 0.02$), and pulmonary capillary wedge pressure of 21.3 ± 2.0 vs 16.9 ± 0.9 mm Hg ($P = 0.02$). Other indices did not differ according to survival status.

Sequential management and outcomes of patients after failed TTVI screening

After failed TTVI screening, the stepwise management of patients over a mean follow-up of 14.4 months (standard deviation, 14.7 months) is shown in Figure 3. Among patients not initially eligible for T-TEER on the basis of trial-specific criteria, 5 patients who were not surgical candidates and received medical management only. Of the 49 patients initially deemed not candidates for TTVI on the basis of trial-specific criteria, 40 received medical management only. After reevaluation by the heart team or trial enrollment, 3

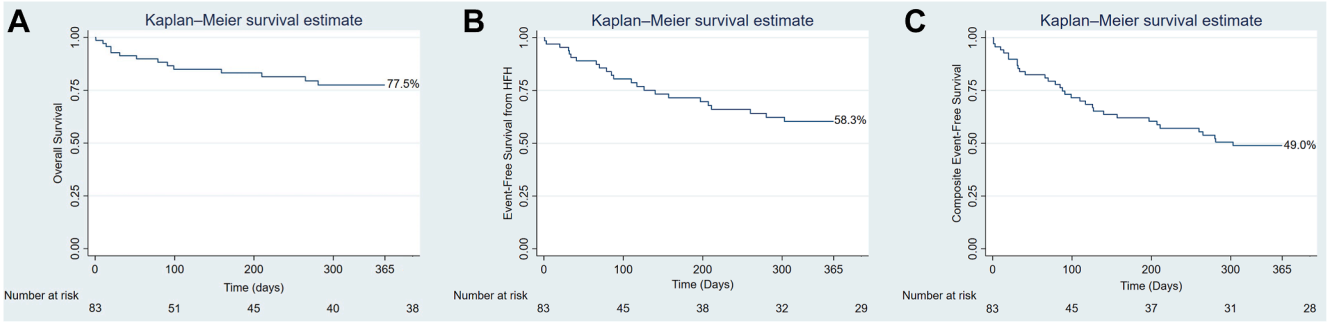


Figure 2. One-year event free survival from (A) all-cause mortality; (B) heart failure hospitalization HFH); and (C) composite of all-cause mortality and HFH in patients ineligible for transcatheter tricuspid valve intervention.

underwent surgery, 2 underwent TTVR, and 4 underwent T-TEER. An additional 29 patients were managed medically directly after failing T-TEER screening. Final outcomes differed according to management strategy: among patients who received medical management, 20 died, whereas 1 death occurred in the TTVR group. No deaths were reported in patients who underwent T-TEER or surgery (Central Illustration).

Univariate and multivariate predictors of all-cause mortality

In univariate analysis, age (hazard ratio [HR], 1.05; 95% confidence interval [CI], 1.00-1.10; $P = 0.04$), pulmonary artery systolic pressure (HR, 1.04; 95% CI, 1.00-1.08; $P = 0.03$), RAP (HR, 1.18; 95% CI, 1.00-1.09; $P = 0.05$), left

atrial volume (HR, 1.01; 95% CI, 1.00-1.01; $P = 0.02$), and short life expectancy (HR, 8.41; 95% CI, 2.28-30.98; $P = 0.001$) were prognostic factors. After adjustment, short life expectancy remained the only independent predictor of mortality (HR, 9.49; 95% CI, 1.50-60.01; $P = 0.02$; Table 5; Central Illustration).

Discussion

In the present study we examined the characteristics and clinical trajectory of patients deemed ineligible for TTVI at our institution, after evaluation for enrollment in TRILUMINATE, TRILUMINATE CAS, CLASP-TR, and TRICAV-I clinical trials. This work builds upon our previous experience focused specifically on patients evaluated for T-

Table 3. Exclusion patterns and mortality rates stratified according to tricuspid valve device type

	Orthotopic valve		Heterotopic valve*
	TRILUMINATE Pivotal and TRILUMINATE CAS	CLASP-TR EFS	TRICAV-I
Screen Failures	45/83 (54.2)	33/83 (39.8)	5/83 (6.0)
Exclusion criteria			
Anatomical reasons			
Coaptation gap > 7-10 mm	23 (51.1)	23 (69.7)	3 (60.0)
Very large tricuspid annulus	24 (53.3)	30 (90.9)	3 (60.0)
Leaflet tethering and/or malcoaptation	15 (33.3)	23 (69.7)	2 (40.0)
Severely calcified, fibrotic, or retracted leaflets	3 (6.7)	2 (6.1)	0 (0.0)
Presence of intracardiac devices	5 (11.1)	5 (15.2)	0 (0.0)
Unfavourable jugular access	0 (0.0)	0 (0.0)	0 (0.0)
Clinical status			
Severe pulmonary hypertension	2 (4.4)	1 (3.0)	1 (20.0)
Advanced right HF	1 (2.2)	0 (0.0)	1 (20.0)
Short life expectancy	5 (11.1)	0 (0.0)	0 (0.0)
Active endocarditis	2 (4.4)	0 (0.0)	0 (0.0)
Ongoing coagulopathy or bleeding	2 (4.4)	0 (0.0)	1 (20.0)
High surgical/anaesthetic risk	6 (13.3)	2 (6.1)	1 (20.0)
Significant MR or MS	1 (2.2)	0 (0.0)	0 (0.0)
Left-sided valvular disease	0 (0.0)	0 (0.0)	0 (0.0)
Mortality rates			
In-hospital mortality	3 (6.7)	1 (3.0)	0 (0.0)
Mortality at FU	15 (33.3)	6 (18.2)	0 (0.0)

Values are n (%).
CAS, Continued Access Study; FU, follow-up; CLASP TR EFS, Edwards CLASP TR EFS; HF, heart failure; MR, mitral regurgitation; MS, mitral stenosis; TRICAV-I, TRICAV biCAVal Valve System for Severe Tricuspid Regurgitation.
*Exclusion criteria were recorded on the basis of screening pathways and were not always device-specific. Anatomical features such as coaptation gap, annular dilation, and leaflet tethering primarily reflect exclusion from orthotopic therapies, even when reported within heterotopic trial cohorts. Heterotopic valve eligibility is predominantly determined by caval anatomy, which was not systematically captured in this data set.

Table 4. Right heart catheterization hemodynamic measurements in the overall cohort and stratified according to 1-year and follow-up all-cause mortality

Right heart catheterization	Overall (N = 83)	1-Year mortality			Mortality at FU		
		No (n = 66)	Yes (n = 17)	P	No (n = 62)	Yes (n = 21)	P
RAP, mm Hg	14.6 ± 7.2	13.1 ± 0.7	21.6 ± 2.9	< 0.001	13.1 ± 0.8	19.3 ± 2.4	0.002
PASP, mm Hg	45.2 ± 13.2	44.0 ± 1.7	50.5 ± 4.3	0.13	43.5 ± 1.7	50.8 ± 3.6	0.05
PADP, mm Hg	20.3 ± 8.1	19.4 ± 1.0	24.5 ± 3.0	0.05	19.0 ± 1.0	24.5 ± 2.5	0.01
mPAP, mm Hg	28.6 ± 9.1	27.6 ± 1.1	33.2 ± 3.2	0.06	27.1 ± 1.1	33.3 ± 2.7	0.02
PCWP, mm Hg	17.9 ± 6.8	17.1 ± 0.8	22.0 ± 2.5	0.02	16.9 ± 0.9	21.3 ± 2.0	0.02
TPG, mm Hg	10.7 ± 5.2	10.6 ± 0.7	11.2 ± 1.8	0.72	10.2 ± 0.6	12.0 ± 1.9	0.24
PAPi	2.2 ± 1.6	2.3 ± 0.2	1.5 ± 0.3	0.12	2.4 ± 0.2	1.7 ± 0.2	0.16
PVR, Wood units	2.9 ± 1.7	2.9 ± 0.2	2.6 ± 0.4	0.56	2.9 ± 0.2	3.0 ± 0.6	0.77
Elastance, mm Hg/mL	0.5 ± 0.2	0.5 ± 0.03	0.5 ± 0.07	0.99	0.5 ± 0.03	0.5 ± 0.05	0.88
PAC, mL/mmHg	2.7 ± 1.7	2.6 ± 0.2	2.9 ± 0.8	0.60	2.6 ± 0.2	2.8 ± 0.6	0.69
CI, L/min/m ²	2.1 ± 0.5	2.1 ± 0.1	2.1 ± 0.2	0.97	2.1 ± 0.07	2.2 ± 0.14	0.73

Values are mean ± standard deviation or n (%).

CI, cardiac index; FU, follow-up; mPAP, mean pulmonary artery pressure; PAC, pulmonary arterial compliance; PADP, pulmonary artery diastolic pressure; PAPi, pulmonary artery pulsatility index; PASP, pulmonary artery systolic pressure; PCWP, pulmonary capillary wedge pressure; PVR, pulmonary vascular resistance; RAP, right atrial pressure; TPG, transpulmonary gradient.

TEER,¹⁷ and expands our understanding of the broader population referred for transcatheter tricuspid therapies.

Our findings highlight that nearly half of the patients referred for TTVI were excluded, consistent with previous studies.^{12,18} As in those reports, the predominant exclusion criteria were structural barriers—severe annular dilation, large coaptation gaps, and significant leaflet tethering. Device-related limitations (eg, intracardiac leads) and advanced pulmonary hypertension further reduced procedural eligibility, reflecting the advanced stage of disease at referral.

Importantly, these screen failure patients represent a clinically unstable, high-risk cohort with poor prognosis despite guideline-directed medical therapy including diuretics, β-blockers, and renin-angiotensin system inhibitors. Unlike previous TTVI trials, which primarily reported procedural safety and short-term outcomes, our study provides critical insight into the postreferral trajectory of patients deemed ineligible for intervention. In this context, “screen failure” serves as a surrogate marker of advanced right heart disease, characterized by progressive volume overload and RV remodelling that medical therapy alone cannot reverse.¹⁹

Right heart catheterization revealed that patients with adverse outcomes exhibited markedly elevated right atrial,

pulmonary artery, and pulmonary capillary wedge pressures, indicative of biventricular pressure and volume overload. These elevated and fixed filling pressures suggest a transition from compensated to decompensated heart failure, a stage beyond which conservative management is unlikely to alter the clinical course.¹²

Reflecting this burden, fewer than half of screen failure patients were alive and free from HFH at 1 year. Kaplan-Meier analyses showed a steep and persistent decline in event-free survival, underscoring the inadequacy of medical therapy when severe TR and irreversible RV remodelling are present. This trajectory reinforces that late-stage referrals limit the therapeutic window; by the time severe annular dilation and RV dysfunction are established, procedural candidacy narrows, and mortality risk increases dramatically regardless of intervention.¹² Previous studies indicate that as TR severity progresses, the right ventricle’s ability to undergo reverse remodelling gradually diminishes.¹² Future randomized controlled trials are needed to evaluate whether earlier referral for transcatheter therapies—before advanced structural and functional deterioration—can improve outcomes. Even with successful TR correction, established RV failure often limits survival benefit because of irreversible myocardial damage. In parallel, optimized heart failure care—including

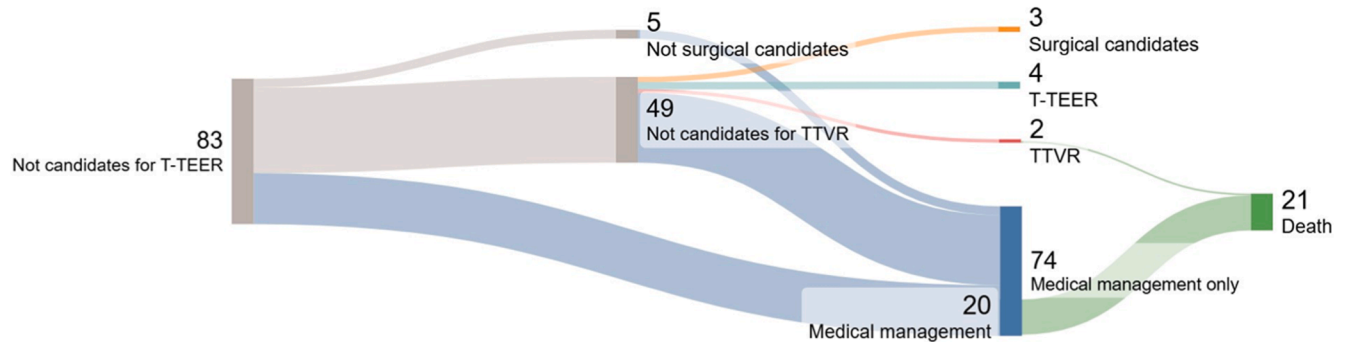


Figure 3. Stepwise flow of structural failure patients: initial status, management strategies, and clinical outcomes. T-TEER, transcatheter tricuspid edge-to-edge repair; TTVR, transcatheter tricuspid valve replacement.

Table 5. Univariate and multivariable analysis of predictors of all-cause mortality

	Univariate analysis			Multivariate analysis		
	HR	95% CI	P	HR	95% CI	P
Age (years)	1.05	1.00-1.10	0.04	1.00	0.95-1.06	0.85
CKD	1.81	0.69-4.70	0.23	-	-	-
Ejection fraction	0.99	0.94-1.04	0.60	-	-	-
NYHA III/IV	1.45	0.60-3.50	0.40	-	-	-
RV dysfunction	1.02	0.13-7.74	0.98	-	-	-
PASP	1.04	1.00-1.08	0.03	1.01	0.97-1.06	0.54
RAP	1.18	1.00-1.09	0.05	1.14	0.94-1.38	0.18
LA volume	1.01	1.00-1.01	0.02	1.00	1.00-1.01	0.06
Large coaptation gap	1.06	0.40-2.80	0.90	-	-	-
Short life expectancy	8.41	2.28-30.98	0.001	9.49	1.50-60.01	0.02

CI, confidence interval; CKD, chronic kidney disease; HR, hazard ratio; LA, left atrial; NYHA, New York Heart Association; PASP, pulmonary artery systolic pressure; RAP, right atrial pressure; RV, right ventricle.

The variables indicated with dashes (–) were not included in the multivariable analysis because they showed no significant association with the outcome on univariable analysis and therefore did not meet the criteria for inclusion in the multivariable model.

implantable hemodynamic monitors, advanced diuretic strategies, and selective pulmonary vasodilator use—might help alleviate symptoms and reduce hospitalization in patients who remain ineligible.^{20,21}

Continued device innovation is vital to overcome anatomical and clinical barriers to TTVI. Emerging transcatheter replacement systems such as EVOQUE TTVR (Edwards Lifesciences, Irvine, CA) are designed to address some of these challenges²²; however, severe annular dilation and prohibitive coaptation gaps continue to limit applicability. New heterotopic and hybrid device solutions—such as the TriFlo (TriFlo Cardiovascular, Newport Beach, CA) and CroiValve DUO (CroiValve, Dublin, Ireland)—are specifically engineered to expand treatment options for patients excluded from current platforms.²³ Emerging devices, such as Trilium²⁴ and UNICA²⁵ (Innoventric, Rehovot, Israel), are currently being evaluated in early feasibility studies. In addition, larger-size options for TricValve (P&F Products & Features GmbH, Vienna, Austria) are available through compassionate use programs. Including these developments helps to contextualize the evolving landscape of therapies for patients who are currently excluded from available devices and highlights ongoing efforts to expand procedural eligibility. Until such devices become broadly available, and their roles understood, enrolling screen failure patients into registries and feasibility studies will be key to refining patient selection, improving risk stratification, and broadening access to transcatheter tricuspid therapies.

Another important consideration is procedure selection and individualized care. Multidisciplinary heart team discussions, including interventional cardiology, cardiac surgery, imaging specialists, and heart failure experts, are essential to determine the most appropriate intervention. These meetings allow integration of anatomical data, hemodynamics, and comorbidities, and help to choose between T-TEER, TTVR, surgical options, or advanced medical therapy. A systematic, team-based approach is critical for optimizing outcomes and minimizing procedural futility.

Notably, when we compared our screen failure cohort with published outcomes of patients who passed screening

and underwent TTVI, mortality rates were substantially higher. Patients who failed screening were older, had more comorbidities, and exhibited more advanced right heart dysfunction, severe TR, and elevated filling pressures, whereas published registries and trials of TTVI recipients report lower early and midterm mortality. Data from contemporary T-TEER studies, including the Transcatheter Repair of Tricuspid Regurgitation With Edwards PASCAL Transcatheter Valve Repair System (TriCLASP) and PASCAL system (Edwards Lifesciences) cohorts, showed 30-day all-cause mortality in the range of 3%-5% and 1-year survival rates exceeding 85%-90%, with significant improvements in TR severity, functional class, and quality of life after successful repair.^{9,26} Similarly, early experiences with TTVR systems show 30-day mortality rates of 2%-3% and favourable hemodynamic and clinical outcomes at 1 year.^{27,28} These contrasts highlight that patients eligible for TTVI generally have more favourable clinical profiles and underscore the prognostic importance of earlier referral and careful anatomical and functional evaluation to maximize therapeutic benefit.

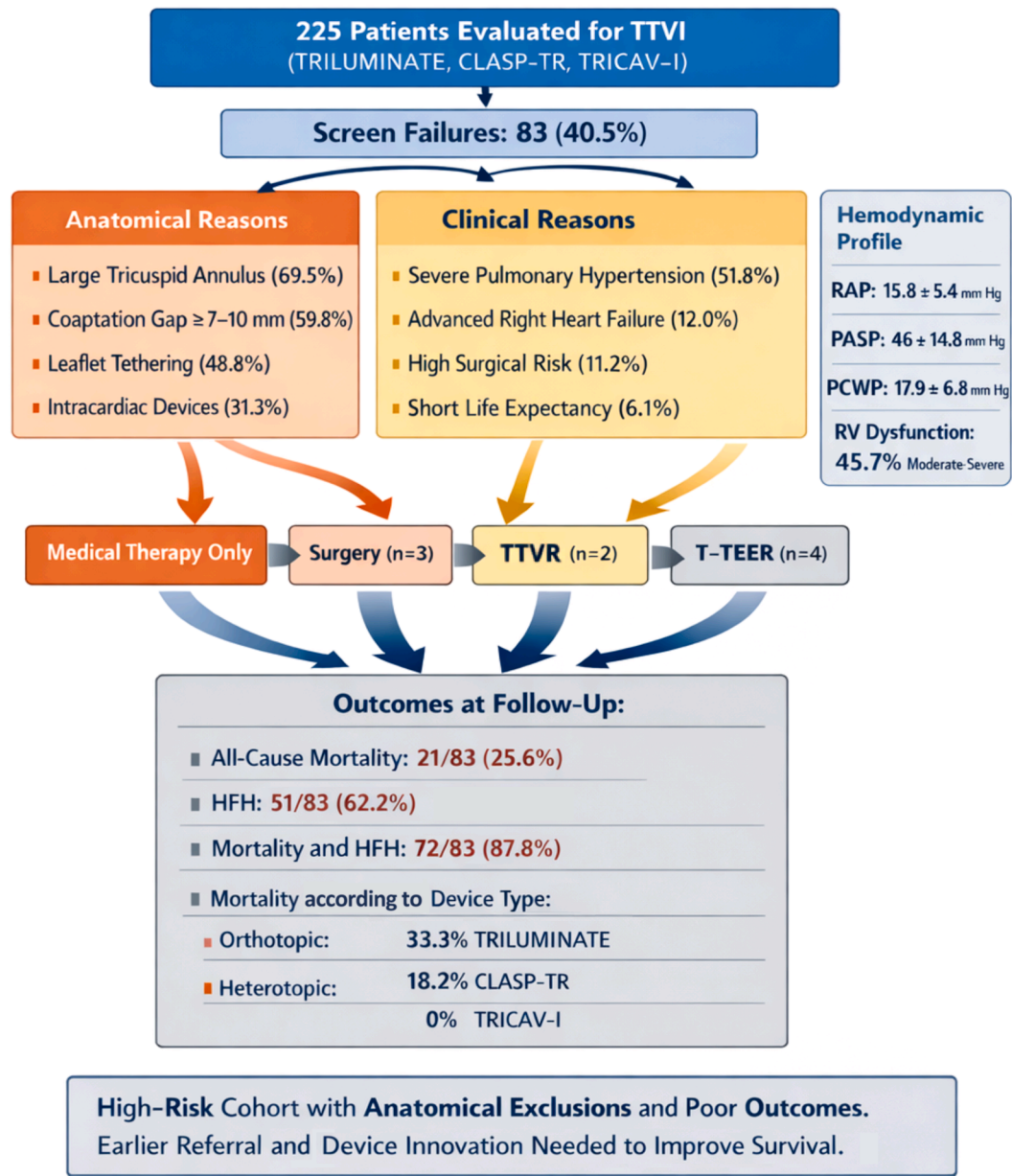
Finally, our study highlights several unmet research needs, including the identification of predictors of mortality and HFH in patients ineligible for TTVI, a deeper understanding of RV-pulmonary artery coupling and structural remodelling in patients with severe TR, determination of the optimal timing and selection of tricuspid valve intervention, and the development predictive risk models to guide clinical management. Addressing these gaps could enable better identification of high-risk patients, improve patient selection, and ultimately enhance survival and quality of life in individuals currently excluded from TTVI trials.

Limitations

This study is limited by its retrospective, single-centre design, modest sample size, and relatively short follow-up. Despite follow-up of a mean of 14.4 months, longer-term data are needed to fully characterize the clinical course and effect of evolving therapies in this vulnerable, high-risk population. In addition, data on patient-reported outcomes, including Kansas City Cardiomyopathy Questionnaire scores at 1 year were not consistently collected, which limited assessment of long-term functional status and quality of life. Furthermore, the analysis was restricted to patients screened within clinical trials and did not include those evaluated in the postapproval commercial setting. Although this approach ensured a standardized, protocol-driven assessment of eligibility, it might limit generalizability to contemporary real-world practice, in which patient selection is more heterogeneous and influenced by evolving indications and operator experience. Finally, device-specific exclusion data were not systematically captured, precluding a detailed assessment of eligibility according to individual therapies. As such, the reported reasons for exclusion should be interpreted at the cohort level, because some patients might have remained candidates for alternative device-based approaches.

Conclusion

Patients ineligible for TTVI represent a high-risk cohort with limited therapeutic options and poor prognosis.



Central Illustration. Transcatheter tricuspid valve intervention (TTVI) ineligibility: identifying gaps to expand treatment eligibility. CLASP-TR, Edwards **CLASP TR EFS**; HFH, heart failure hospitalization; PASP, pulmonary artery systolic pressure; PCWP, pulmonary capillary wedge pressure; RAP, right atrial pressure; RV, right ventricle; TRICAV-I, **TRIC**valve **biCAV**al Valve System for Severe Tricuspid Regurgitation; TRILUMINATE, TRILUMINATE Pivotal Trial; T-TEER, transcatheter tricuspid edge-to-edge repair; TTVR, transcatheter tricuspid valve replacement.

Channeling screen failure patients into dedicated registries and early-phase feasibility trials might enable refinement of selection criteria, promote innovation in device design, and ultimately broaden access to transcatheter therapies for this vulnerable population.

Ethics Statement

The study was conducted in accordance with institutional review board guidelines and adhered to the principles of the Declaration of Helsinki.

Patient Consent

The authors confirm that patient consent is not applicable to this article, because of the retrospective nature of the study.

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