NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of transcatheter tricuspid valve leaflet repair for tricuspid regurgitation

The tricuspid valve is a heart valve made up of 3 leaflets (flaps). Tricuspid regurgitation happens when the valve does not close properly, and blood flows the wrong way in the heart. This makes the heart work harder and, if severe, can lead to heart failure. In this procedure, a device is inserted into a vein in the groin or neck (transcatheter) and placed on the valve in the heart to bring the valve leaflets together. The aim is to reduce the severity of the leak and enable the heart to pump more efficiently, improving symptoms and quality of life.

Contents

Abbreviations

Word or phrase	Abbreviation
Confidence interval	CI
effective regurgitant orifice area	EROA
EuroQol 5-dimensions 5-level health questionnaire	EQ-5D-5L
European System for Cardiac Operative Risk Evaluation	EuroSCORE
Interquartile range	IQR
Kansas City Cardiomyopathy Questionnaire	KCCQ
Mean difference	MD
N-terminal pro-B type natriuretic peptide	NT-pro BNP
New York Heart Association	NYHA
proximal isovelocity surface area	PISA
Relative risk	RR
Standard deviation	SD
tricuspid annular plane systolic excursion	TAPSE
Transcatheter tricuspid valve intervention	TTVI

Introduction

The National Institute for Health and Care Excellence (NICE) prepared this interventional procedure overview to help members of the interventional procedures advisory committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and professional opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in October 2021.

Procedure name

- Transcatheter tricuspid valve leaflet repair for tricuspid regurgitation

Professional societies

- The Society for Cardiothoracic Surgery of Great Britain and Ireland
- British Cardiovascular Intervention Society
- Royal College of Physicians
- Royal College of Physicians of Edinburgh
- Royal College of Physicians and Surgeons of Glasgow.

Description of the procedure

Indications and current treatment

Tricuspid regurgitation occurs when the tricuspid valve does not close properly during systole, and blood flows backwards through the valve. It can be caused by a problem with the valve itself (primary), but it is more commonly secondary to an underlying cardiac problem that has caused the heart to become dilated. This has the effect of stretching the annulus that supports the valve leaflets to such an extent that the leaflets do not meet and regurgitation of blood occurs.

People with mild tricuspid regurgitation do not usually have any symptoms. If the regurgitation is severe, there may be fatigue and weakness, active pulsing in the neck veins, an enlarged liver, ascites, peripheral oedema and renal impairment. Pulmonary hypertension may develop.

Treatment may not be needed if there are no or mild symptoms. Symptoms of heart failure are managed with diuretics and other medications. Medication to reduce pulmonary artery pressure or pulmonary vascular resistance, or both, may be used when there is severe functional tricuspid regurgitation and severe pulmonary hypertension.

People with severe symptoms may have surgery to repair or replace the tricuspid valve. Isolated tricuspid valve surgery is rarely done. More commonly, it is done at the same time as left-sided valve surgery (mitral and aortic).

What the procedure involves

Transcatheter tricuspid valve leaflet repair for tricuspid regurgitation is designed to improve the function of the tricuspid valve with less morbidity and mortality than conventional surgical valve repair. It has been proposed as an option when conventional surgery poses a high risk. The procedure aims to reduce

regurgitation, improve quality of life and reduce hospital admissions related to heart failure.

The procedure is done under general anaesthesia using transoesophageal echocardiography and fluoroscopy guidance. Access is through the femoral or jugular vein.

Different systems have been used and exact details of the technique vary. A delivery system is used to introduce a device into the heart that can grip the leaflets of the tricuspid valve and bring them closer together. The device is then released from the delivery system. Adequate reduction of tricuspid regurgitation is assessed using echocardiography.

Outcome measures

NYHA functional class

The NYHA functional class is used to classify heart failure according to severity of symptoms and limitation of physical activity:

- Class 1 - no limitation of physical activity. Ordinary physical activity does not cause undue fatigue, breathlessness, or palpitations.
- Class 2 - slight limitation of physical activity. Comfortable at rest but ordinary physical activity results in undue breathlessness, fatigue, or palpitations.
- Class 3 - marked limitation of physical activity. Comfortable at rest but less than ordinary physical activity results in undue breathlessness, fatigue, or palpitations.
- Class 4 - unable to carry out any physical activity without discomfort. Symptoms at rest can be present. If any physical activity is done, discomfort is increased.

KCCQ

The KCCQ is a 23-item self-administered questionnaire that measures the patient's perception of their health status, including heart failure symptoms, effect on physical and social function and how their heart failure affects their quality of

life within a 2-week recall period. Scores are scaled from 0 to 100, where higher scores represent better health status.

Efficacy summary

Technical or procedural success

In a non-randomised comparative study of 213 matched pairs of patients who had TTVI or medical therapy alone, procedural success was 81%. Procedural success was defined as the device successfully implanted and the delivery system retrieved, with a residual tricuspid regurgitation of grade 2 or less (Schlotter, 2021).

In a non-randomised comparative study of 268 matched pairs of patients who had TTVI or medical therapy alone, procedural failure with residual tricuspid regurgitation of grade 3+ or above was 14% (38/268; Taramasso, 2019a).

In a registry of 312 patients, procedural success was 73% and there was no statistically significant difference between different devices. Procedural success was defined as the patient being alive at the end of the procedure, with the device successfully implanted and the delivery system retrieved, with a residual tricuspid regurgitation of grade 2 or less (Taramasso, 2019b).

In a registry of 249 patients, technical success was 96% and procedural success was 77%. Technical success was defined as placement of at least 1 clip in the tricuspid valve. Procedural success was defined as a successful implantation of the clip device and a post-procedural tricuspid regurgitation of grade 2+ or less (Mehr, 2019).

In a case series of 19 patients, procedural success was 90% (17/19). Procedural success was defined as successful device implantation in the absence of major device- or procedure-related serious adverse events (Asmarats, 2019).

Tricuspid septolateral annular diameter

In a systematic review of 454 patients (7 studies) who had transcatheter tricuspid valve leaflet repair or transcatheter tricuspid annuloplasty, the mean tricuspid valve annular diameter was statistically significantly reduced at follow up (MD -3.0 mm, 95% CI -4.7 to -1.4, p=0.0004, 7 studies, I^2=63%; Montalto, 2020).

In a single-arm study of 85 patients, the tricuspid annular diameter decreased from 4.34 cm at baseline to 4.03 cm at 1 year (p<0.0001; Lurz, 2021).

Tricuspid regurgitation severity

In the systematic review of 454 patients, the incidence of severe or greater tricuspid regurgitation was statistically significantly reduced at follow up (RR 0.38, 95% CI 0.2 to 0.7, p=0.004, 4 studies, I^2=90%; Montalto, 2020).

In the registry of 312 patients, 84% (235/280) of patients had a reduction of at least 1 degree of tricuspid regurgitation severity. The proportion of patients with tricuspid regurgitation severity 3 or 4 reduced from 98% at baseline to 38% at 30-day follow up (p<0.0001; Taramasso, 2019b).

In the registry of 249 patients, 89% (222/249) of patients had at least 1 grade reduction in tricuspid regurgitation after the procedure and 72% at least 1 grade reduction at last follow up (median 290 days). The proportion of patients with tricuspid regurgitation grade 3 or above reduced from 97% at baseline to 23% before discharge (p<0.001; Mehr, 2019).

In a non-randomised study of 124 patients who had TTVI or medical therapy alone, 77% (41/53) of patients who had TTVI had moderate or less tricuspid regurgitation and 23% (12/53) had severe or above tricuspid regurgitation after the procedure compared with 100% at baseline (53/53; p<0.001; Cai, 2020).

In the single-arm study of 85 patients, 87% (54/62) of patients had sustained tricuspid regurgitation reduction of at least 1 grade at 1-year follow up. Of the 63 patients with data at 1-year follow up, 44 (70%) had moderate or less tricuspid regurgitation compared with 8% at baseline (p<0.0001; Lurz, 2021).

In the case series of 19 patients, the rate of severe tricuspid regurgitation reduced from 95% at baseline to 33% at final follow up (median 32 months, p<0.001; Asmarats, 2019).

NYHA functional class

In the systematic review of 454 patients, the incidence of NYHA class 3 or 4 was statistically significantly reduced at follow up (RR 0.23, 95% CI 0.16 to 0.33, p=0.004, 7 studies, I^2=39%; Montalto, 2020).

In the non-randomised study of 124 patients who had TTVI or medical therapy alone, the proportion of patients in NYHA functional class 3 or 4 in the TTVI group reduced from 94% at baseline to 13% at follow up (median 14 months, p<0.001; Cai, 2020).

In the registry of 312 patients, the proportion of patients in NYHA functional class 3 or 4 reduced from 96% at baseline to 39% at 30-day follow up and 46% at 6-month follow up (p=0.04; Taramasso, 2019b).

In the registry of 249 patients, the proportion of patients in NYHA functional class 3 or 4 reduced from 96% at baseline to 31% at last follow up (median 290 days, p<0.001; Mehr, 2019).

In the single-arm study of 85 patients, the proportion of patients in NYHA functional class 3 or 4 reduced from 69% at baseline to 17% at last follow up (p<0.0001; Lurz, 2021).

In the case series of 19 patients, the proportion of patients in NYHA functional class 3 or 4 reduced from 93% at baseline to 34% at a median follow up of 32 months (n=15, p<0.001; Asmarats, 2019).

Quality of life

In the single-arm study of 85 patients, self-assessed heart failure symptoms measured by KCCQ showed an improvement of 20 points from baseline to 1 year (p <0.0001). There was an improvement of at least 10 points in 65% (43/66) of patients. The KCCQ score continued to improve from 30-day to 1-year follow up (6 point improvement, p=0.0290; Lurz, 2021).

In the case series of 19 patients, the KCCQ heart failure score improved by 16 points at a median follow up of 32 months (n=9, p=0.016; Asmarats, 2019).

6-minute walk test

In the systematic review of 454 patients, the mean 6-minute walk test distance statistically significantly increased at follow up (MD 64.6 m, 95% CI 41.3 to 87.9, p<0.0001, 6 studies, I^2=0%; Montalto, 2020).

In the non-randomised study of 124 patients, the mean 6-minute walk test distance statistically significantly increased in the TTVI group from 240.7 m at baseline to 334.4 m at follow up (median 14 months, p=0.01; Cai, 2020).

In the single-arm study of 85 patients, the 6-minute walk distance increased from 272 m at baseline to 303 m at 1 year (p=0.0023; Lurz, 2021).

Survival

In the non-randomised comparative study of 213 matched pairs of patients, estimated mortality at 1 year was 13% in the TTVI group and 25% in the medical therapy alone group (p=0.031; Schlotter, 2021).

In the non-randomised comparative study of 268 matched pairs of patients, mortality at 6 months was 14% in the TTVI group and 26% in the medical therapy

alone group, and at 1 year it was 23% compared with 36% (p=0.001;Taramasso, 2019a).

In the non-randomised study of 124 patients, overall survival was 75% in the TTVI group (median follow up 14 months) and 47% in the medical therapy alone group (p=0.047; Cai, 2020).

In the registry of 312 patients, overall actuarial survival at 1.5 years was 77%. Actuarial survival at follow up was statistically significantly better in patients who had a successful procedure (91% compared with 70% at 1 year, p=0.0002; Taramasso, 2019b).

In the registry of 249 patients, estimated mortality at 1 year was 20% (95% CI 15 to 26%). Procedural failure was a predictor of 1 year mortality (multivariate odds ratio 2.12, 95% CI 1.12 to 4.02, p=0.014; Mehr, 2019).

In the single-arm study of 85 patients, all-cause mortality was 7% (6/84) at 1 year (Lurz, 2021).

In the case series of 19 patients with a median follow up of 32 months, all-cause mortality was 24% (4/17) and cardiac mortality was 18% (3/17; Asmarats, 2019).

Rehospitalisation for heart failure

In the non-randomised comparative study of 268 matched pairs of patients, rehospitalisation for heart failure at 1 year was 26% in the TTVI group and 47% in the medical therapy alone group (p<0.0001; Taramasso, 2019).

In the non-randomised study of 124 patients, freedom from hospitalisation for heart failure was 62% in the TTVI group (median follow up 14 months) and 44% in the medical therapy alone group (p=0.074; Cai, 2020).

In the single-arm study of 85 patients, there was a 40% reduction in hospitalisation rate (from 1.30 events/patient-year 1 year before to 0.78 events/patient-year 1 year after the procedure, p=0.0030; Lurz, 2021).

In the case series of 19 patients with a median follow up of 32 months, the rate hospitalisation for heart failure was 18% (3/17) during follow up compared with 58% in the year before the procedure (Asmarats, 2019).

Safety summary

Overall

Mortality (within 30 days of initial hospitalisation)

Mortality at 30 days was 4% (10/280) in the registry of 312 patients. The causes of death were sepsis (n=2), respiratory insufficiency (n=2) and progressive right ventricular failure (n=6; Taramasso, 2019b).

Mortality during the initial hospitalisation was reported in 3% (7/249) of patients and cardiovascular mortality was 2% (6/249) in the registry of 249 patients (Mehr, 2019).

Conversions to surgery

Conversion to surgery was reported in 1% (4/280) of patients in the registry of 312 patients. Two patients had emergency surgery and the other 2 had elective tricuspid surgery because of procedural failure (Taramasso, 2019b).

Conversion to open heart surgery was reported in 1 patient in the registry of 249 patients (Mehr, 2019).

Myocardial infarction

Acute myocardial infarctions needing right coronary artery stenting was reported in 1% (2/280) of patients in the registry of 312 patients (Taramasso, 2019b).

Myocardial infarction within 1 year of the procedure was reported in 1 patient in the single-arm study of 85 patients (Lurz, 2021).

The incidence of myocardial infarction was 0 per 100 person-years in patients who had TTVI (n=53) and 1.0 per 100 person-years (95% CI 0 to 5.4) in patients who had medical therapy alone (n=71) in the non-randomised comparative study of 124 patients (p=1.00; Cai, 2020).

Stroke

Stroke was reported in 1% (3/280) of patients in the registry of 312 patients (Taramasso, 2019b).

Ischaemic stroke during the hospital stay was reported in 1% (2/249) of patients in the registry of 249 patients. Both patients had concomitant mitral valve intervention (Mehr, 2019).

Stroke within 1 year of the procedure was reported in 1 patient in the single-arm study of 85 patients (Lurz, 2021).

The incidence of stroke was 0 per 100 person-years in patients who had TTVI (n=53) and 2.9 per 100 person-years in patients who had medical therapy alone (n=71; 95% CI 0.6 to 8.5) in the non-randomised comparative study of 124 patients (p=0.41; Cai, 2020).

Pericardial effusion or cardiac tamponade

Pericardial effusion was reported in 1 patient in the registry of 249 patients (Mehr, 2019).

Cardiac tamponade was reported in 1 patient who had surgical conversion in the case series of 19 patients (Asmarats, 2019).

Arrhythmia and conduction disorders

Ventricular arrhythmia was reported in 1 patient in the registry of 312 patients (Taramasso, 2019b).

New onset atrial fibrillation was reported in 1 patient in the single-arm study of 85 patients (Lurz, 2021).

Renal complications

Acute kidney injury was reported in 4% (9/249) of patients in the registry of 249 patients (Mehr, 2019).

New onset renal failure within 1 year of the procedure was reported in 1 patient in the single-arm study of 85 patients (Lurz, 2021).

The incidence of acute kidney injury was 14.1 per 100 person-years (95% CI 6.8 to 26.0) in patients who had TTVI (n=53) and 37.0 per 100 person-years (95% CI 26.2 to 50.8) in patients who had medical therapy alone (n=71) in the non-randomised comparative study of 124 patients (p=0.006). The incidence of new initiation of renal replacement therapy was 4.2 per 100 person-years (95% CI 0.8 to 12.4) in patients who had TTVI (n=53) and 3.9 per 100 person-years (95% CI 1.1 to 10.0) in patients who had medical therapy alone (n=71, p=1.00; Cai, 2020).

Bleeding

Major bleeding was reported in 2% (5/280) of patients in the registry of 312 patients (Taramasso, 2019b).

Bleeding was reported in 6% (15/249) of patients in the registry of 249 patients (Mehr, 2019).

Major bleeding was reported in 12% (10/84) of patients in the single-arm study of 85 patients (Lurz, 2021).

Major or life-threatening bleeding was reported in 11% (2/19) of patients in the case series of 19 patients. One bleed was caused by cardiac tamponade in a patient who had surgical conversion (Asmarats, 2019).

The incidence of gastrointestinal bleed was 4.2 per 100 person-years (95% CI 0.8 to 12.4) in patients who had TTVI (n=53) and 15.6 per 100 person-years (95% CI 8.9 to 25.3) in patients who had medical therapy alone (n=71) in the non-randomised comparative study of 124 patients (p=0.04; Cai, 2020).

Infection

Infection was reported in 5% (12/249) of patients in the registry of 249 patients. Further details were not reported (Mehr, 2019).

Respiratory failure

Respiratory failure was reported in 1% (2/280) of patients in the registry of 312 patients (Taramasso, 2019b).

Device detachment

Device detachment was reported in 1 patient in the registry of 312 patients (Taramasso, 2019b).

Single leaflet device attachment was reported in 8% (5/65) of patients in the single-arm study of 85 patients. No additional intervention was needed and there was no worsening of clinical symptoms (Lurz, 2021).

Other

Aortic prosthetic valve thrombosis was reported in 1 patient in the registry of 312 patients (Taramasso, 2019b).

A mean tricuspid gradient 5 mmHg or above was reported in 6% (4/64) of patients in the single-arm study of 85 patients (Lurz, 2021).

Thrombus on the device and pulmonary embolism were reported as a late outcome in 1 patient each in the case series of 19 patients (Asmarats, 2019).

A case report described a clip device being stuck and knotted because of the Chiari network. Additional clips were implanted successfully and tricuspid regurgitation was reduced (Miura, 2019).

Anecdotal and theoretical adverse events

In addition to safety outcomes reported in the literature, professional experts are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never happened).

For this procedure, no responses were received.

The evidence assessed

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to transcatheter tricuspid valve annuloplasty for tricuspid regurgitation. The following databases were searched, covering the period from their start to 2 September 2021: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see the literature search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The inclusion criteria were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with tricuspid regurgitation.
Intervention/test	Transcatheter tricuspid valve leaflet repair
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on about 500 patients who had transcatheter tricuspid valve leaflet repair for tricuspid regurgitation from 1 systematic review (Montalto, 2020), 3 non-randomised comparative studies, 2 registry reports, 1 single-arm trial, 1 case series and 1 case report (Montalto 2020; Schlotter 2021; Taramasso 2019; Taramasso 2019b; Mehr 2019; Lurz 2021; Asmarats 2019; Cai 2020, Miura 2019). There is a lot of patient overlap because the systematic review and several of the studies include data from the TriValve registry.

Other studies that were considered to be relevant to the procedure but were not included in the main summary of the key evidence are listed in the appendix.

Summary of key evidence on transcatheter tricuspid valve leaflet repair for tricuspid regurgitation

Study 1 Montalto C (2020)

Study details

Study type	Systematic review and meta-analysis
Country	Not reported for individual studies (3 were described as international)
Recruitment period	Search date: September 2019
Study population and number	n=454 (7 studies); 362 edge-to-edge leaflet plasty, 47 increased leaflet coaptation surface, 30 annular reduction, 15 bicuspidalisation by pledget-plication
Age and sex	Mean 76.7 years; 41% (188/454) male
Patient selection criteria	Studies were eligible if they fulfilled all the following criteria: 1) they included patients with at least moderate tricuspid regurgitation (adjudicated using a semiquantitative method) and who had treatment with transcatheter repair devices; and 2) they reported at least 1 of the primary outcomes of interest at a minimum follow-up point of 30 days. Case reports, letters and studies that did not clearly report the numbers and rates of patients alive at follow up were excluded from the analysis. Studies in which severe tricuspid regurgitation was treated using transcatheter implantation of prosthetic valves were also excluded.
Technique	Transcatheter tricuspid valve repair. Devices included MitraClip (Abbott Vascular, US; n=334), PASCAL (Edwards Lifesciences; n=28), Cardioband (Edwards Lifesciences, US; n=30), FORMA (Edwards Lifesciences; n=47) and Trialign (Mitralign, US; n=15).
Follow up	range 30 days to 1 year
Conflict of interest/source of funding	None for authors of the review.

Analysis

Follow-up issues: Studies were only included if they had a minimum of 30 days follow up for at least 1 of the primary outcomes of interest.

Study design issues: The review was done in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses and Meta-Analysis of Observational Studies in Epidemiology guidelines. All included studies were interventional, multicentre, single arm, and prospective. The primary endpoints of the analysis were the rate reduction of severe tricuspid regurgitation and NYHA functional class 3 or 4 at longest follow up available. Procedural success definition included at least successful device implantation because of the varying definitions in the studies. Pooled risk ratios and standardised mean differences with 95% CIs were used as summary statistics for outcomes of interest and were calculated using a random-effects model.

Heterogeneity was considered to be low when I^2 was less than 25%, moderate when I^2 was less than 75%, and high when I^2 was more than 75%. No publication bias was identified by visually inspecting funnel plots and by mathematical testing.

Study population issues: Of the 454 patients, 45 had a transcatheter tricuspid valve annuloplasty, which is covered by a separate overview.

Patients were at high surgical risk, with a mean EuroSCORE 2 score of 6.8% (95% CI 5.4% to 8.1%). Tricuspid aetiology was mostly functional (90%; 95% CI 82% to 99%), and 90% (95% CI 82% to 100%) of patients were in NYHA functional class 3 or 4.

Studies included the following named trials: TRI-REPAIR, TriValve, TRILUMINATE and SCOUT.

Key efficacy findings

- Number of patients analysed: 454
- Procedural success: 86% of patients (95% CI 78% to 95%)
- All-cause mortality rate (weighted mean follow up 265 days): 9% (95% CI 5% to 16%)
- The sensitivity analysis revealed that no study statistically significantly changed the relative risk of being in NYHA functional class 3 or 4 at follow up, as stepwise study omission did not result in a shift of the point estimate out of the 95% CI.
- The random-effect subgroup analysis revealed that at follow up, the proportion of patients in NYHA functional class 3 or 4 and of patients with tricuspid regurgitation graded severe or worse were reduced regardless of the device used.

Functional and echocardiographic parameters at baseline and after transcatheter tricuspid valve repair

Parameter	Baseline value, incidence or pooled mean (95% CI)	No. of studies	RR or MD	Follow up: RR or MD (95% CI)	p value	I^2 (%)	p for hetero-geneity
Incidence of NYHA class 3 or 4	90% (82% to 99%)	7	RR	0.23 (0.16 to 0.33)	0.004	39	0.13
Mean 6-minute walk distance, metres	245.4 (215.8 to 275.0)	6	MD	64.6 (41.3 to 87.9)	<0.0001	0	0.78
Mean left ventricular ejection fraction, %	57 (52.9 to 61.0)	6	MD	1.2 (-0.5 to 2.8)	0.16	0	0.99
Mean TAPSE, mm	15.1 (14.3 to 15.9)	6	MD	-0.09 (-1.2 to 0.98)	0.85	64	0.02
Incidence of tricuspid regurgitation severe or greater	95% (87% to 100%)	4	RR	0.38 (0.2 to 0.7)	0.004	90	0.0001
Mean EROA, mm	0.9 (0.7 to 1.0)	6	MD	-3.1 (-4.4 to -1.9)	<0.0001	54	0.06
Mean tricuspid valve annular diameter, mm	44.6 (42.5 to 46.7)	7	MD	-3.0 (-4.7 to -1.4)	0.0004	63	0.01
Mean systolic pulmonary artery pressure, mmHg	41.7 (38.4 to 45.0)	4	MD	-1.6 (-4.9 to 1.7)	0.33	53	0.09

Key safety findings

No safety outcomes were reported.

Study 2 Schlotter F (2021)

Study details

Study type	Non-randomised comparative study (using data from the TriValve registry)
Country	Europe and North America
Recruitment period	2014 to 2020 (TTVI group); 2017 to 2017 (medical therapy group)
Study population and number	n=850 (288 TTVI, 562 medical therapy alone); 213 matched pairs Patients with severe or worse tricuspid regurgitation
Age and sex	In unmatched cohort, median age was 78 years in the TTVI group and 76 in the control group (p<0.001). In the matched cohort, median age was 78 years for both. The overall proportion of females was 54% (456/850) in the unmatched cohort and 53% (227/426) in the matched cohort.
Patient selection criteria	In the TTVI group, all patients were symptomatic with signs of heart failure. Tricuspid regurgitation therapy was indicated in accordance with international guidelines. Heart Team consensus rendered all patients at high or prohibitive surgical risk. Caval valve implantations were excluded from the study. In the medical therapy group, patients with at least severe tricuspid regurgitation (on a 4-grade scale) and with a functional tricuspid regurgitation aetiology were retrospectively identified. Patients were excluded if there was a lack of reported TAPSE, age, EuroSCORE 2, estimated glomerular filtration rate, left ventricular ejection fraction, left ventricular end-diastolic diameter, estimated systolic pulmonary artery pressure, haemodialysis, NYHA class, presence of atrial fibrillation or flutter, NT-proBNP, follow up below 31 days without an event, or non-functional aetiology.
Technique	Devices used in TTVI group: MitraClip (Abbott Vascular, US), Trialign (Mitralign Inc., US), Cardioband, FORMA, PASCAL (Edwards Lifesciences, US), TriCinch System (4Tech, Ireland), and GATE (NaviGate Cardiac Structures, US). Overall, 54 (32.9%) patients had concomitant mitral procedures for significant left-sided valve disease (MitraClip in all cases).
Follow up	1 year
Conflict of interest/source of funding	There is an extensive list of declared interests, including a number of authors reporting grants, personal fees, consultancy, honoraria or non-financial support from companies including Abbott, Amgen, BMS, Bayer, Boston Scientific, Biotronik, Cardinal Health, Cardiovalve, CardioGrad, 4Tech, CSL Behring, DaiichiSankyo, Edwards Lifesciences, Johnson&Johnson, Medtronic Guerbet, Polares, Sanofi, Terumo, Venus Medtech and NaviGate Cardiac Structures Inc. 1 is also Chief Scientific Officer for the Echocardiography Core Laboratory at the Cardiovascular Research Foundation for multiple industry-sponsored trials, for which she receives no direct industry compensation. 1 author has several patents issued. 1 author has a patent with and is a consultant for TricValve licensed to TricValve. 1 author is a consultant for Japan Lifeline.

Analysis

Follow up issues: In the TriValve registry, clinical and echocardiographic baseline and follow up data were prospectively collected. Clinical follow up was done by clinical visits or phone consultation at 30 days, 6 months, 1 year, and annually thereafter. Follow up in the medical therapy group was obtained by contacting the local registration offices.

Study design issues: Propensity-matched comparative study, using data on TTVI from a multicentre international registry (TriValve) and medical therapy data from 2 tertiary care centres. The primary endpoint was defined as the incidence of all-cause mortality within 1 year of follow up in the matched population. Patients in the TTVI cohort were matched with patients who had conservative management using propensity scores. The following variables were used for the calculation of propensity scores: TAPSE, age, EuroSCORE II, estimated glomerular filtration rate, left ventricular ejection fraction, left ventricular end-diastolic diameter, echocardiographically determined systolic pulmonary artery pressure, haemodialysis, NYHA class (binary class 1 and 2 compared with 3 and 4), presence of atrial fibrillation or flutter and NT-proBNP. Based on these propensity scores, patients who had TTVI were matched 1:1 with control patients randomly selected from the control pool of patients defined by the parameters using the nearest neighbour rule of ±0.2 standard deviations. The balance between the groups of patients with TTVI and controls was assessed by standardised differences (defined as the difference in means or proportions divided by the mutual standard deviation). Standardised differences below 0.1 were considered not statistically significant. Patients were stratified according to TAPSE (preserved [more than 17 mm], mid-range [13 to 17 mm] and reduced [less than 13 mm]) right ventricular function.

Study population issues: Patients in the unmatched TTVI cohort had statistically significantly higher age, EuroSCORE 2, higher rates of atrial fibrillation, higher left ventricular ejection fraction, larger left ventricular enddiastolic diameter and lower rates of haemodialysis, TAPSE, lower proportion of mitral regurgitation grade 3 or above and lower systolic pulmonary artery pressure compared with the unmatched conservatively treated cohort (all $p<0.05$).There were no statistically significant differences between unmatched and matched patients. Most patients (89%) were in NYHA functional classes 3 or 4. Overall, 166 patients had preserved, 179 mid-range reduced and 81 reduced right ventricular function, with no statistically significant difference between TTVI and medical therapy.

Key efficacy findings

- Number of patients analysed: 426 (213 TTVI, 213 medical therapy)

Procedural success (defined as a device successfully implanted and delivery system retrieved, with a residual tricuspid regurgitation grade 2 or less)

- In the matched TTVI cohort, procedural success was 80.7% (n=167).

Estimated mortality at 1 year in the matched cohort

- TTVI=13.1%
- Medical therapy=25.4%, p=0.031

- In isolated TTVI, the 1-year mortality rate was also statistically significantly lower in the matched TTVI cohort when compared to either conservative treatment or conservative treatment without mitral regurgitation grade 3 or higher (p=0.001 and p=0.006, respectively).

Relationship between outcome and right ventricular dysfunction

- In patients with mid-range RV function, TTVI was associated with a survival benefit when compared to medical therapy, but there was no survival benefit in patients with preserved or reduced right ventricular function.
- In patients who had TTVI or medical therapy, reduced right ventricular function was associated with impaired outcome (p log-rank 0.032 and 0.020, respectively).
- In patients who had TTVI, patients with mid-range right ventricular function improved to the level of patients with preserved RV function.
- In patients with mid-range right ventricular function, procedural success, EuroSCORE 2, left ventricular ejection fraction less than 40%, NT-proBNP and estimated glomerular filtration rate were associated with all-cause mortality. However, on multivariable analysis, only procedural success (HR 0.22, 95% CI 0.09 to 0.57) and EuroSCORE 2 (HR 1.10, 95% CI 1.01 to 1.20) remained independent predictors of an adverse outcome in this patient population.

Key safety findings

None reported

Study 3 Taramasso M (2019a)

Study details

Study type	Non-randomised comparative study (using data from the TriValve registry)
Country	Europe and North America
Recruitment period	2016 to 2018 (registry data)
Study population and number	n=1,651 (472 TTVI, 1,179 medical therapy); 268 matched pairs Patients with severe tricuspid regurgitation
Age and sex	In the unmatched cohort, mean age was 77 years in the TTVI group and 76 in the control group (p=0.07). In the matched cohort, mean ages were 77 and 76 years, respectively (p=0.2). In the unmatched cohort, the proportion of females was 55% in the TTVI group and 63% in the control group (p=0.007). In the matched cohort, the proportion of females was 56% and 59%, respectively (p=0.4).
Patient selection criteria	The TTVI cohort included patients with severe or greater symptomatic tricuspid regurgitation according to the European or American guidelines. The decision to do the procedure was taken by a local multidisciplinary team after clinical and anatomical assessment. Exclusion criteria in the control group were previous tricuspid valve surgery or intervention and iatrogenic (pacemaker lead-related) tricuspid regurgitation.
Technique	Devices used in TTVI cohort: MitraClip (Abbott Vascular, US), FORMA (Edwards Lifesciences, US), Cardioband (Edwards Lifesciences), Tri-Cinch (4TECH, Ireland), Trialign (Edwards Lifesciences), caval valve implantation devices), PASCAL (Edwards Lifesciences), and NaviGate (NaviGate Cardiac Structures, US). 63 (23%) patients in the TTVI group had concomitant mitral valve treatment (Mitraclip). All patients in both groups had medical treatment according to guideline-directed medical therapy.
Follow up	Median 11 months (IQR 4 to 28 months)
Conflict of interest/source of funding	There is an extensive list of declared interests, including a number of authors reporting grants, personal fees, consultancy, honoraria or non-financial support from companies including Abbott, Amgen, Boston Scientific, 4Tech, CoreMedic, St Jude Medical, Biotronik, Edwards Lifesciences, Medtronic, MitralTech, Neovasc, InnovHeart, Claret Medical, Meril Lifesciences, Admedus, Biosense Webster, Mitralign, Millipede, TricValve, Ablative Solutions, Ancora Heart, Bavaria Medizin Technologie GmbH, Bioventrix, Carag, Cardiac Dimensions, Celonova, Comed BV, Terumo and Vascular Dynamics. One is also Chief Scientific Officer for the Echocardiography Core Laboratory at the Cardiovascular Research Foundation for multiple industry-sponsored trials, for which she receives no direct industry compensation. One author has equity in Thubrikar Aortic Valve Inc, Dura Biotech, Biotrace Medical, and MID. One author is cofounder of Cardiac Implants and 1 is cofounder of 4Tech and founder of Occlufit, SwissVortex, transseptalsolutions, and Perifect.

Analysis

IP overview: transcatheter tricuspid valve leaflet repair for tricuspid regurgitation

Study design issues: Propensity matched retrospective case-control study, using data from the TriValve registry for the TTVI cohort and 2 large tertiary centres for the control cohort. The variables used to calculate propensity score were age, EuroSCORE 2, and pulmonary pressure level. For each case, a control patient was randomly selected from the potential pool of candidates defined by the parameters using the nearest neighbour rule of ±0.2 SD. The primary endpoint was mortality from any cause or rehospitalisation for heart failure. Survival was tested with Cox regression analysis. After TTVI, procedural success was defined as patient alive at the end of the procedure, with device successfully implanted, delivery system retrieved, and residual tricuspid regurgitation less than 3+. Medical regimens in the control cohort were not standardised. No central echocardiography core laboratory adjudication was available because of the type of the study.

Study population issues: Patients in the 2 groups had similar left ventricular ejection fraction and age. The cause of tricuspid regurgitation was mostly functional (91% in TTVI group, 96% in control subjects). The proportion of females was lower in the TTVI group (55% compared with 63% in the control group), and more patients had chronic atrial fibrillation (85% in the TTVI group compared with 57% in the control group). A total of 26% of TTVI compared with 5% of patients in the control group had a previously implanted pacemaker or defibrillator with a lead across the tricuspid valve. Most patients in the TTVI group were severely symptomatic at the time of the procedure (93% were in NYHA functional class 3 or 4). Patients in the TTVI group had lower EuroSCORE 2 (10.5 compared with 17.9), more prevalent right ventricular dysfunction (34% compared with 20%), and lower pulmonary pressure level (40 mmHg compared with 52 mm Hg). Baseline characteristics of the matched subgroup were more balanced between TTVI and control patients. Patients in the TTVI group still had higher NYHA functional class (93% had class 3 to 4 compared with 23% in the control group, p<0.0001) and higher prevalence of atrial fibrillation, right ventricular dysfunction, mitral regurgitation, and implanted pacemaker/defibrillator.

Key efficacy findings

- Number of patients analysed: 536 (268 TTVI, 268 medical therapy alone)
- Procedural failure with residual tricuspid regurgitation 3+ or above=14.2% (38/268)
- A higher proportion of patients with right ventricular dysfunction had a successful procedure (65% compared with 39%, p=0.002).

Mortality at 6 months

- TTVI=13.8%
- Medical therapy alone=26.1%

Mortality at 1 year

- TTVI=22.6%
- Medical therapy alone=36.2%, p=0.001

Rehospitalisation for heart failure at 1 year

- TTVI=26%
- Medical therapy alone=47%, p<0.0001

Composite endpoint

- TTVI=32%
- Medical therapy alone=49%, p=0.0003

Cox proportional hazard models testing the effect of TTVI in the propensity-matched cohort

Model for Control Group	Hazard ratio (95% CI) for death or heart failure hospitalisation (primary endpoint)	p value	Hazard ratio (95% CI) for mortality (secondary endpoint)	p value
Unadjusted	0.60 (0.46 to 0.79)	0.003	0.56 (0.39 to 0.79)	0.001
Adjusted for sex and NYHA functional class	0.46 (0.31 to 0.68)	0.0001	0.49 (0.31 to 0.79)	0.003
Adjusted for sex and NYHA functional class, atrial fibrillation, and right ventricular dysfunction	0.39 (0.26 to 0.59)	<0.0001	0.41 (0.26 to 0.67)	0.0004

The beneficial TTVI impact on survival persisted after a more extensive adjustment including mitral regurgitation and pacemaker/defibrillator, hazard ratio 0.35 (95% CI 0.23 to 0.54; p<0.0001).

In multivariable analysis, TTVI remained associated with greater survival free from heart failure rehospitalisation, when concomitant mitral regurgitation treatment (MitraClip), was added to the model (hazard ratio 0.28; 95% CI 0.11 to 0.79; p=0.02 after comprehensive adjustment).

Key safety findings

None reported

Study 4 Taramasso M (2019b)

Study details

Study type	Registry (TriValve)
Country	Switzerland, Germany, France, Italy, US, Canada (18 centres)
Recruitment period	2014 to 2018
Study population and number	n=312 Patients with severe or greater symptomatic tricuspid regurgitation
Age and sex	Mean 76 years; 56% female
Patient selection criteria	All patients included in the registry had severe or greater symptomatic tricuspid regurgitation according to the European or American guidelines for managing heart valve disease and had treatment according to local multidisciplinary team decision.
Technique	Devices: MitraClip (Abbott Vascular, US), FORMA (Edwards Lifesciences, US), Cardioband (Edwards Lifesciences), TriCinch (4tech, Ireland), Trialign (Mitralign, US), Caval valve implantation, PASCAL (Edwards Lifesciences), and NaviGate (NaviGate Cardiac Structures, US). Most procedures (n=210) used MitraClip. All but 1 procedures were done using general anaesthesia under fluoroscopic and echocardiographic guidance. One case of TriCinch was done under conscious sedation using intracardiac echocardiography. 64% of patients had isolated TTVI. In the remaining patients, TTVI was done concomitantly during transcatheter mitral repair (n=108), transcatheter aortic valve replacement (n=1) or paravalvular leak closure (n=1).
Follow up	Median 6.2 months (IQR 0.4 to 15.5 months)
Conflict of interest/source of funding	There is an extensive list of declared interests, including a number of authors reporting grants, fees, consultancy, honoraria or non-financial support from companies including Abbott, Amgen, Boston Scientific, 4Tech, CoreMedic, St Jude Medical, Biotronik, Edwards Lifesciences, Medtronic, MitralTech, Neovasc, InnovHeart, Biosense Webster, Mitralign, Millipede, TricValve, Ablative Solutions, Ancora Heart, Bavaria Medizin Technologie GmbH, Bioventrix, Carag, Cardiac Dimensions, Celonova, Comed BV, Terumo, Vascular Dynamics, NaviGate and GE Healthcare. One author is cofounder of Cardiac Implants and 1 is cofounder of 4Tech.

Analysis

Follow-up issues: Procedural and periprocedural outcomes were only available for 280 (89.7%) patients (the remaining 32 patients were included in ongoing unpublished trials, so only baseline characteristics were provided at this stage). Modalities of follow up differed between the different centres.

Study design issues: Prospective multicentre registry data. 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 tricuspid regurgitation 2 or less. There was no core lab adjudication.

Study population issues: At baseline, the mean EuroSCORE 2 was 9%. Aetiology of tricuspid regurgitation was functional in 92% (288/312) of patients and mean annular diameter was 46.9 mm; 71 patients (23%) had a previously implanted intracardiac device and presented with a transtricuspid right ventricular lead. Of the 312 patients, 35% had a history of previous left-side valve intervention (84 surgical, 24 percutaneous, 3 both). Prevalence of long-standing atrial fibrillation was 78%, and median NT-proBNP at baseline was 2,759 pg/ml (IQR 1,298 to 5,627 pg/ml). Most of the patients were severely symptomatic and 95% were in NYHA functional class 3 or 4.

Key efficacy findings

- Number of patients analysed: 280
- Procedural success=72.8% (there were no statistically significant differences between devices)
- Reduction of at least 1 degree of tricuspid regurgitation severity=83.9% (235/280)
- Overall actuarial survival at 1.5 years=77.2 ± 5.9%
- Actuarial survival at follow up was statistically significantly better in patients in whom acute procedural success was achieved (90.8% compared with 70.3% at 1 year, p=0.0002). Superior survival according to procedural success was also seen when only isolated TTVI were considered (69% compared with 89% at 1 year, p=0.0037)

Improvements in tricuspid regurgitation severity at 30 days follow up (p<0.0001)

Severity	Proportion of patients at baseline	Proportion of patients at 30 days
1+	0%	26%
2+	2%	36%
3+	35%	22%
4+	63%	16%

Improvements in NYHA functional class at 30 days and 6 months follow up (p=0.04)

NYHA functional class	Proportion of patients at baseline	Proportion of patients at 30 days	Proportion of patients at 6 months
1	0%	8%	7%
2	4%	53%	47%
3	65%	36%	37%
4	31%	3%	9%

Univariate and multivariate analysis of predictor of procedural failure

Variable	Univariate odds ratio (95% CI)	p value	Multivariate odds ratio (95% CI)	p value
Coaptation depth	31.8 (4.8 to 244)	0.0002	24.1 (3 to 231)	0.002
Annular diameter	8.07 (1.1 to 61.8)	0.03	7.2 (0.9 to 1.12)	0.06
Vena contracta	0.2 (0.1 to 37.9)	0.12	-	-
Presence of pacemaker lead	0.9 (0.5 to 4.5)	0.70	-	-
MitraClip versus other device	0.6 (0.5 to 5.8)	0.11	-	-
TAPSE <17 mm	1.02 (0.2 to 2.9)	0.90	-	-
Left ventricular ejection fraction, %	0.65 (0.12 to 2.7)	0.50	-	-
systolic pulmonary artery pressure	8.8 (1.8 to 77)	0.01	0.1 (0.06 to 1.5)	0.10

Key safety findings

- Intraprocedural deaths=0%

Major adverse events at 30 days

- Overall=10.4% (29/280)
- Mortality=3.6% (10 patients: 2 sepsis, 2 respiratory insufficiency, 6 progressive right ventricular failure). It was statistically significantly lower among patients with procedural success (1.9% compared with 6.9%, p=0.04).
- Major bleeding=1.7% (5/280)
- Stroke=1.1% (3/280)
- Acute myocardial infarctions needing right coronary artery stenting=0.7% (2/280)
- Conversions to surgery=1.4% (4/280) (in 2 patients, emergency surgery was needed and in the other 2 patients, tricuspid surgery was done electively because of procedural failure)
- Respiratory failure= 0.7% (2/280)
- Device detachment=0.4% (1/280)
- Ventricular arrhythmia=0.4% (1/280)
- Aortic prosthetic valve thrombosis=0.4% (1/280)

Study 5 Mehr M (2019)

Study details

Study type	Registry (TriValve)
Country	Europe and North America (14 centres)
Recruitment period	2015 to 2018
Study population and number	n=249 Patients with symptomatic tricuspid regurgitation
Age and sex	Mean 77 years; 51% (128/249) female
Patient selection criteria	All patients included were symptomatic, with signs of right-sided or global heart failure such as peripheral oedema, ascites, pleural effusion, and dyspnoea on exertion. Most patients were in NYHA functional class 3 or 4 and were deemed at high or prohibitive risk for surgery.
Technique	Devices: MitraClip (Abbott Structural Heart, US). Most procedures used MitraClip NT, but MitraClip XTR was introduced in 2018. The intervention was guided by 2-dimensional and 3-dimensional transthoracic and transoesophageal echocardiography as well as fluoroscopy. Concomitant edge-to-edge repair of the mitral valve was done when indicated (n=129, 52%).
Follow up	Median 290 days (IQR: 141 to 392 days)
Conflict of interest/source of funding	There is an extensive list of declared interests, including a number of authors reporting grants, fees, consultancy, honoraria or non-financial support from companies including Bristol-Myers Squibb, Abbott, Boston Scientific, 4tech, CoreMedic, Edwards Lifesciences, Neovasc, Amgen, Biotronik, Medtronic, St. Jude, Terumo, Biosense Webster, Mitralign, Ablative Solutions, Ancora Heart, Bavaria Medizin Technologie GmbH, Bioventrix, Carag, Cardiac Dimensions, Celonova, Comed B.V., Contego, CVRx, Endologix, Hemoteq, Lifetech, Maquet Getinge Group, Nuomao Medtech, Occlutech, pfm Medical, Recor, Renal Guard, Rox Medical, Vascular Dynamics, Vivasure Medical, InnovHeart, Millipede, Cardiovalve, and Valtech. One author is supported by a New Investigator award from the Canadian Institutes of Health Research and an Early Researcher award from the Ontario Ministry of Research. One author is cofounder of Cardiac Implants and 1 is cofounder of 4tech.

Analysis

Follow up issues: Data on clinical outcomes were available in 83% of eligible patients and echocardiographic follow up was available in 79% of eligible patients.

Study design issues: Prospective multicentre registry data. The main endpoints were all-cause mortality and a composite of all-cause mortality and unplanned rehospitalisation for heart failure within 12 months after the procedure. Technical success was defined as placement of at least 1 clip in the tricuspid valve. Procedural success was defined as a successful implantation of the clip device and a post-procedural tricuspid regurgitation of grade 2+ or less. Defined subgroups of the analysis were edge-to-edge repair in the tricuspid

valve only, compared with combined mitral and tricuspid repair as well as successful edge-to-edge repair, compared with procedural failure.

Study population issues: Most patients (94%) were in NYHA functional class 3 or 4 and severely symptomatic. 24% of patients had ascites, 84% peripheral oedema, and 74% had a history of hospital admission for heart failure. The mean EuroSCORE 2 was 6.4% (IQR 3.9% to 13.9%). The mean septolateral diameter of the tricuspid annulus was 47.0 mm, and tricuspid regurgitation was secondary in 90% of patients. The mean tricuspid coaptation gap was 5.3 mm.

This study is also included in the systematic review by Montalto et al. (2020).

Key efficacy findings

- Number of patients analysed: 249
- Technical success=96%
- Procedural success=77%
- Tricuspid regurgitation reduction of at least 1 grade after the procedure=89.2% (222/249)
- Tricuspid regurgitation reduction of at least 1 grade at last follow up=72%
- The proportion of patients with tricuspid regurgitation grade 3 or above reduced from 97% at baseline to 23% before discharge (p<0.001).
- Combined endpoint of death or unplanned hospitalisation for heart failure at follow up=31% (76/249)
- Estimated mortality at 1 year (Kaplan-Meier)=20.3% (95% CI 14.6% to 25.8%)
- Estimated rate of combined mortality and rehospitalisation for heart failure at 1 year (Kaplan-Meier)=34.7% (95% CI 27.7% to 41.0%)

Improvements in tricuspid regurgitation severity, n (%)

Severity	Proportion of patients at baseline, n=249	Proportion of patients before discharge, n=249	Proportion of patients at last follow up, n=167
1+, mild	0 (0)	95 (38.1)	61 (36.5)
2+, moderate	8 (3.2)	97 (39.0)	60 (35.9)
3+, severe	112 (45.0)	42 (16.9)	35 (21.0)
4+, massive	129 (51.8)	15 (6.0)	11 (6.6)

P<0.001 between baseline and discharge and p=0.89 between last follow up and discharge

Improvements in NYHA functional class, n (%), p<0.001

NYHA functional class	Proportion of patients at baseline, n=249	Proportion of patients at last follow up, n=175
1 or 2	11 (4.4)	121 (69.1)
3	170 (68.3)	52 (29.7)
4	68 (27.3)	2 (1.1)

Univariate and multivariate analysis of predictor of procedural failure

Variable	Univariate odds ratio (95% CI)	p value	Multivariate odds ratio (95% CI)	p value
Pacemaker or ICD lead	1.53 (0.81 to 2.84)	0.18	-	-
Left ventricular ejection fraction, %	1.00 (0.98 to 1.02)	0.95	-	-
TAPSE	1.02 (0.95 to 1.10)	0.55	-	-
Mitral regurgitation grade	1.10 (0.84 to 1.44)	0.48	-	-
Vena contracta	1.76 (0.87 to 3.53)	0.11	-	-
Coaptation gap >6.5 mm	6.16 (3.19 to 12.18)	<0.001	1.23 (1.10 to 1.38)	<0.001
EROA >0.695 cm^2	4.79 (2.52 to 9.33)	<0.001	1.21 (1.09 to 1.35)	<0.001
coaptation depth >9.75 mm	3.17 (1.71 to 6.04)	<0.001	1.01 (0.90 to 1.44)	0.83
tenting area >3.15 cm^2	4.78 (2.49 to 9.30)	<0.001	1.18 (1.01 to 1.37)	0.035
Noncentral or nonanteroseptal tricuspid regurgitation jet location	2.38 (0.98 to 5.52)	0.047	1.21 (1.04 to 1.41)	0.013
Annular diameter	1.03 (0.99 to 1.08)	0.098	1.00 (0.99 to 1.00)	0.60
Concomitant mitral valve edge-to-edge repair	0.66 (0.36 to 1.20)	0.17	-	-
Number of clips	0.81 (0.57 to 1.12)	0.20	-	-

Univariate and multivariate analysis of predictor of 1 year mortality

Variable	Univariate odds ratio (95% CI)	p value	Multivariate odds ratio (95% CI)	p value
Age (years)	1.02 (0.98 to 1.06)	0.31	-	-
EuroSCORE 2	0.99 (0.97 to 1.02)	0.57	-	-
Chronic obstructive pulmonary disease	0.49 (0.21 to 1.16)	0.103	-	-
Pacemaker/ICD	1.52 (0.83 to 2.79)	0.18	-	-
Absence of sinus rhythm	3.85 (1.19 to 12.43)	0.024	4.40 (1.34 to 14.49)	0.015
Decrease of 10 ml/min in estimated glomerular filtration rate	1.29 (1.07 to 1.55)	0.007	1.25 (1.02 to 1.51)	0.018
NYHA functional class	2.08 (1.20 to 3.62)	0.009	1.73 (0.96 to 3.13)	0.069
Decrease of 10% in left ventricular ejection fraction	1.25 (1.02 to 1.52)	0.028	1.20 (0.98 to 1.47)	0.084
TAPSE	0.97 (0.90 to 1.04)	0.42	-	-
Tricuspid regurgitation grade	1.16 (0.67 to 2.00)	0.59	-	-
Mitral regurgitation grade	1.13 (0.86 to 1.50)	0.39	-	-
Concomitant mitral valve edge-to-edge repair	1.07 (0.59 to 1.94)	0.83	-	-
Procedural failure	2.43 (1.33 to 4.46)	0.004	2.12 (1.12 to 4.02)	0.014

Key safety findings

- Procedural deaths=0%

Adverse events

- Mortality during initial hospitalisation=2.8% (7/249)
- Cardiovascular mortality=2.4% (6/249)
- Conversion to open heart surgery 3 days after procedure=0.4% (1/249)
- Ischaemic stroke during hospital stay=0.8% (2/249); both patients had concomitant mitral valve intervention
- Bleeding=6.0% (15/249)
- Acute kidney injury=3.6% (9/249)
- Infection=4.8% (12/249)
- Pericardial effusion=0.4% (1/249)

Study 6 Lurz P (2021)

Study details

Study type	Single arm study (TRILUMINATE)
Country	US, France, Germany, Italy, Spain, Switzerland (21 sites)
Recruitment period	Not reported
Study population and number	n=85 Patients with moderate or greater tricuspid regurgitation
Age and sex	Mean 77.8 years; 66% female
Patient selection criteria	Symptomatic patients at high surgical risk with moderate or greater tricuspid regurgitation (by transthoracic and transoesophageal echocardiography) and no indications for left-sided or pulmonary valve correction were included in this study. Exclusion criteria included: systolic pulmonary artery pressure greater than 60 mmHg, (estimated by echocardiography), previous tricuspid valve procedures or coaptation gaps bigger than 10 mm.
Technique	Device: TriClip (Abbott, US)
Follow up	Median 12 months
Conflict of interest/source of funding	The study was funded by Abbott. There is an extensive list of declared interests, including a number of authors reporting grants, fees, participation in trials, consultancy, honoraria or non-financial support from companies including Abbott, Amgen, Edwards Lifesciences, Medtronic, AGA Medical, AstraZeneca, Bayer, Baylis Medical, Berlin Chemie, Biosensus, Biotronic, Boston Scientific, Bristol Myers Squibb, Boehringer Ingelheim, Cardiovalve, Daiichi-Sankyo, Novartis, Navigate, Philips Healthcare, Siemens Healthcare, Pfizer, Resmed, Sanofi, and St. Jude Medical. Two authors have been employees of Abbott. One author has been Chief Scientific Officer for the Echocardiography Core Laboratory at the Cardiovascular Research Foundation for multiple industry-sponsored trials for which she has received no direct industry compensation.One author has been an unpaid member of the Corvia Medical Scientific Advisory Group. One author has received research funding from the Deutsche Forschungsgemeinschaft, the Federal Ministry of Education and Research and The European Union.

Analysis

Follow up issues: At 1 year, data to evaluate severity of tricuspid regurgitation was missing for 22 patients: 7 died, 5 withdrew, 4 missed visits and there was a lack of readable echocardiographic data to make an assessment for 6 patients. In addition, baseline imaging was missing for 1 patient, so there were 62 patients (73%) with paired tricuspid regurgitation severities at baseline and 1 year follow up. Data on major adverse events was not available for 1 patient who withdrew from the study.

Study design issues: Prospective, single-arm, multicentre study. The purpose of this report was to study the 1 year outcomes of the valve repair system, including repair durability, clinical benefit and safety.

Study population issues: the study population was the first 85 patients to have an attempted procedure upon femoral vein puncture. The mean EuroSCORE 2 was 8.7%. Tricuspid regurgitation aetiology included functional (84%), degenerative (12%), and mixed (4%). The most common comorbidities were atrial fibrillation (92%), hypertension (86%), renal disease (46%), diabetes (22%), and prior myocardial infarction (18%); 33% of patients had a prior mitral intervention and 75% were classified as NYHA functional class 3 or 4.

Other issues: data from this trial was included in the systematic review by Montalto et al. (2020).

Key efficacy findings

- Number of patients analysed: 85
- Sustained tricuspid regurgitation reduction of at least 1 grade at 1 year=87.1% (54/62)
- Patients with moderate or less tricuspid regurgitation at 1 year=69.8% (44/63)
- In multivariate logistic regression, patients with torrential (odds ratio 10.4, p=0.0007) or massive (odds ratio 4.3, p=0.03) tricuspid regurgitation at baseline were less likely to have moderate or less tricuspid regurgitation at follow up compared with patients who had severe tricuspid regurgitation at baseline.
- Among all patients with 1-year follow up (n=70), there was a 40% reduction in hospitalisation rate (from 1.30 to 0.78 events/patient-year 1 year before and 1 year after the procedure respectively; p=0.0030).
- Reduction to moderate or less tricuspid regurgitation was associated with reduced mortality and heart failure hospitalisations at 1 year (8.8% compared with 24.5%; hazard ratio 0.31, p=0.041).

Echocardiographic results, least-squares mean (standard error)

Variable	Baseline	30 days	1 year	p value (baseline versus 1 year)	p value (30 days versus 1 year)
EROA, cm^2	0.65 (0.03)	0.40 (0.03)	0.32 (0.05)	<0.0001	0.1053
Regurgitant volume, ml/beat	52.20 (2.35)	34.83 (2.92)	27.68 (3.08)	<0.0001	0.0607
Regurgitation jet area, cm^2	14.28 (0.69)	9.18 (0.64)	7.55 (0.56)	<0.0001	0.0007
Vena contracta width, cm	1.73 (0.07)	1.00 (0.06)	0.78 (0.05)	<0.0001	<0.0001
PISA radius, cm	0.91 (0.03)	0.68 (0.03)	0.63 (0.04)	<0.0001	0.2092
Inferior vena cava diameter, cm	2.29 (0.06)	2.20 (0.06)	2.06 (0.06)	0.0014	0.0216
Right ventricular end diastolic dimension, cm	5.28 (0.07)	4.93 (0.08)	4.79 (0.08)	<0.0001	0.0319
Tricuspid annular diameter S-L, cm	4.34 (0.06)	4.08 (0.06)	4.03 (0.07)	<0.0001	0.4640
Right atrial volume, ml	129 (5.84)	117 (6.03)	116 (6.55)	0.0166	0.8536
Right ventricular fractional area change, %	36.00 (0.85)	36.77 (0.74)	38.19 (0.57)	0.0057	0.0649
Right ventricular systolic pressure, mmHg	42.7 (1.08)	42.0 (1.49)	43.9 (2.30)	0.5727	0.4525
TAPSE, cm	1.44 (0.03)	1.49 (0.03)	1.59 (0.04)	0.0002	0.0069
Right ventricular global longitudinal strain, %	-14.1 (0.64)	-12.9 (0.86)	-14.6 (0.86)	0.5897	0.1083

Comparison of tricuspid regurgitation severity at baseline, 30 days, and 1 year

Severity	Proportion of patients at baseline, n=62	Proportion of patients at 1 year, n=62	Proportion of patients at 30 days, n=63	Proportion of patients at 1 year, n=63
None	0%	5%	5%	5%
Mild	0%	32%	30%	32%
Moderate	8%	34%	25%	33%
Severe	29%	19%	25%	21%
Massive	26%	6%	10%	6%
Torrential	37%	3%	5%	3%

p<0.0001 for comparison between baseline and 1 year; p=0.96 for comparison between 30 days and 1 year

Comparison of NYHA functional class at baseline, 30 days and 1 year

NYHA functional class	Proportion of patients at baseline, n=65	Proportion of patients at 1 year, n=65	Proportion of patients at 30 days, n=66	Proportion of patients at 1 year, n=66
1	0%	32%	20%	33%
2	31%	51%	62%	50%
3	64%	17%	18%	17%
4	5%	0%	0%	0%

p<0.0001 for comparison between baseline and 1 year; p=0.39 for comparison between 30 days and 1 year

- Self-assessed heart failure symptoms measured by KCCQ showed an improvement of 20 points from baseline to 1 year (p <0.0001); 65% (43/66) of patients had improvement of at least 10 points.
- KCCQ continued to increase from 30-day to 1-year follow up (6 point improvement; p=0.0290).
- The 6-minute walk distance increased from 272 m at baseline to 303 m at 1 year (p=0.0023).
- All-cause mortality at 1 year=7.1% (6/84)

Key safety findings

Major adverse events at 1 year

- Overall=7.1% (6/84)
- Cardiovascular mortality=4.8% (4/84)
- Myocardial infarction=1.2% (1/84)
- Stroke=1.2% (1/84)
- New onset renal failure=1.2% (1/84)
- Endocarditis needing surgery or nonelective cardiovascular surgery for a device-related adverse event=0%

Other clinical safety endpoints

- Major bleeding=11.9% (10/84)
- Pulmonary thromboembolism=0%
- New onset liver failure=0%
- New onset atrial fibrillation=1.2% (1/84)
- Single leaflet device attachment=7.7% (5/65); no additional intervention was needed and there was no worsening of clinical symptoms.
- Embolisation=0%
- Mean tricuspid gradient 5 mmHg or above=6.3% (4/64)

Study 7 Asmarats L (2019)

Study details

Study type	Case series
Country	Canada and Europe (4 centres)
Recruitment period	2015 to 2016
Study population and number	n=19 Patients with severely symptomatic functional tricuspid regurgitation
Age and sex	Mean 76 years; 74% female
Patient selection criteria	Patients had severely symptomatic functional tricuspid regurgitation and were deemed to be high or extreme risk for open-heart surgery based on local multidisciplinary heart team assessment. Patients with primary tricuspid regurgitation, prior tricuspid valve surgery, severe concomitant valve disease, or severe left ventricular dysfunction were excluded.
Technique	Device: FORMA Transcatheter Tricuspid Valve Repair system (Edwards Lifesciences, US); a coaptation transcatheter tricuspid valve repair device designed to increase the leaflet coaptation surface by occupying the regurgitant orifice area. Spacer size was either 15 mm (n=17) or 12 mm (n=1), determined by the largest vena contracta width.
Follow up	Median 32 months (IQR 24 to 36 months)
Conflict of interest/source of funding	There is an extensive list of declared interests, including a number of authors reporting grants, fees, participation in trials, consultancy, honoraria or non-financial support from companies including Edwards Lifesciences, Abbott, Amgen, Medtronic, Circle Cardiovascular Imaging, Neovasc, Gore,Tendyne Holdings, Bayer, Bristol-Myers Squibb, Boston Scientific, Biotronik, CSL Behring, Polares, Sinomed, and Heartflow. One author owns stock options in Circle Cardiovascular Imaging and Heartflow. The first author has been supported by a grant from the Fundación Alfonso Martin Escudero and another holds the Research Chair “Fondation Famille Jacques Larivière” for the Development of Structural Heart Disease Interventions.

Analysis

Follow up issues: Data were collected at baseline, 30 days, and 1 year, and yearly thereafter. Clinical follow up was available for all patients who had successful treatment.

Study design issues: The aim of the study was to evaluate long-term outcomes (2 years or more). Procedural success was defined as successful device implantation in the absence of major device- or procedure-related serious adverse events.

Study population issues: At baseline, the mean EuroSCORE 2 was 9.2%. Of the 19 patients, 18 were in NYHA functional class 3 or above.

Other issues: An earlier report from the same study is included in the systematic review by Montalto et al. (2020).

Key efficacy findings

- Number of patients analysed: 19
- Procedural success=89.5% (17/19); there was 1 right ventricular perforation needing conversion to open heart and 1 early device dislocation into the right atrium in a patient with severe right-sided chamber enlargement and trabeculation preventing proper anchoring, which was managed conservatively.
- All-cause mortality=23.5% (4/17)
- Cardiac mortality=17.6% (3/17)
- Rehospitalisation for heart failure=17.6% (3/17) during follow up, compared with 58% in the year before the procedure.
- The rate of severe tricuspid regurgitation reduced from 95% at baseline to 33% at final follow up ($p<0.001$).
- Mean vena contracta width reduced from 11.8 to 8.4 mm at final follow up ($p=0.005$).
- The proportion of patients in NYHA functional class 3 or 4 reduced from 93% at baseline to 34% at follow up ($n=15$, $p<0.001$).
- Mean increase in 6-minute walk test distance at follow up=54 m ($n=10$, $p=0.016$)
- Improvement in KCCQ heart failure score at follow up=16 points ($n=9$, $p=0.016$)
- There was a statistically significant reduction in peripheral edema ($p=0.002$), without statistically significant changes in N-terminal pro–B-type natriuretic peptide, renal function, or diuretic dose over time.

Key safety findings

- Procedural mortality=0%

Outcomes at 30 days

- All-cause mortality=0% (0/19)
- Stroke=0% (0/19)
- Transient ischaemic attack=5.3% (1/19)
- Myocardial infarction=0% (0/19)
- Major or life-threatening bleeding=10.5% (2/19); 1 cardiac tamponade in the patient who had surgical conversion and 1 pocket haematoma causing nerve compression.
- Acute kidney injury=0% (0/19)
- New pacemaker=0% (0/19)
- Rehospitalisation for heart failure=0% (0/19)

Late clinical outcomes

- Thrombus on device=5.9% (1/17)
- Endocarditis=0% (0/17)
- Pulmonary embolism=5.9% (1/17)
- Ventricular arrhythmia=0% (0/17)

Study 8 Cai S (2020)

Study details

Study type	Non-randomised comparative study
Country	Canada
Recruitment period	2015 to 2019
Study population and number	n=124 (53 TTVI, 71 medical therapy alone) Patients with severe symptomatic tricuspid regurgitation
Age and sex	TTVI: mean age 74.8 years; 59% female Medical therapy alone: mean age 77.2 years; 42% female
Patient selection criteria	Patients on maximally tolerated guideline directed medical therapy were referred for consideration of TTVI to treat symptomatic severe tricuspid regurgitation. Patients who had mild or moderate tricuspid regurgitation, needed open surgical intervention for tricuspid regurgitation, or died before initial consultation were excluded. Eligibility for TTVI was determined based on clinical and anatomical characteristics and by Heart team consensus. The main reason for ineligibility of TTVI was anatomical unsuitability such as a large coaptation gap (more than 10 mm), severe tethering of tricuspid valve leaflets, or lack of clear visualisation of the tricuspid valve on echocardiogram. 26% of patients in the medical therapy group improved with optimisation of medical therapy alone and did not need intervention.
Technique	Device: MitraClip NT system; median number of clips=2 All patients had guideline directed medical therapy.
Follow up	TTVI: median 14 months (IQR 7 to 25 months) Medical therapy alone: median 17 months (IQR 9.5 to 23 months), p=0.45
Conflict of interest/source of funding	The study was funded by the St Michael's Foundation. One of the authors received a Merit Award from the University of Toronto. Two authors received speaker honoraria from Abbott Vascular and 1 is also a consultant for Edward Lifesciences.

Analysis

Follow up issues: Follow up data regarding hospitalisation, adverse events, death, laboratory results and medication changes were obtained from patient records by 3 independent reviewers. Follow-up period started from time of initial consultation or time of TTVI and concluded with death or end of study. Patients who had medical therapy alone had routine follow up at time intervals determined by their treating cardiologists. Patients who had TTVI had follow up at 1 month after the procedure, then routine follow up.

Study design issues: Retrospective, single-centre non-randomised comparative study. The study was done in a centre with an experienced, high volume multi-disciplinary valve team specialising in advanced heart failure, cardiac imaging and interventions. The aim was to identify the clinical characteristics and examine outcomes in patients who had TTVI and medical therapy compared with medical therapy alone, using a real world, all-comers approach.

IP overview: transcatheter tricuspid valve leaflet repair for tricuspid regurgitation

Study population issues: The predominant aetiology of tricuspid regurgitation was functional in both groups, although the medical therapy alone group had a higher prevalence of rheumatic (12.7% compared with 1.9%, p=0.013) and device-lead induced tricuspid regurgitation (18.3% compared with 0%, p=0.013). At baseline, there were no statistically significant differences in age, sex and body mass index between the 2 groups. Compared with the TTVI group, the medical therapy alone group had a trend towards lower clinical risk score for mortality (5.0, IQR 4.0 to 6.0 compared with 6.0, IQR 5.0 to 7.0, p=0.08) and morbidity (5.0, IQR 4.0 to 6.5 compared with 6.0, IQR 5.0 to 7.0, p=0.02). Both groups had a median predicted perioperative mortality of 9% or higher and a median perioperative morbidity of 29% or higher, equating to high surgical risk and were not suitable for open tricuspid valve surgery. A higher proportion of patients in the medical therapy alone group were in NYHA class 1 or 2 compared to the TTVI group (32.4% compared with 6.2%, p=0.023). There was no statistically significant difference in the mean 6-minute walk test distances at baseline (240.7 m compared with 279.0 m, p=0.52). There was a statistically significantly lower prevalence of chronic kidney disease (19.7% compared with 37.8%, p=0.04), higher baseline eGFR (54.1 ml/min/1.73 m^2 compared with 44.5 ml/min/1.73m^2, p=0.02), and lower NT-proBNP levels (939.6 pg/litre compared with 3,598.0 pg/litre, p=0.006) in the medical therapy alone group compared with the TTVI group. There was a statistically significantly higher prevalence of concurrent moderate-severe or severe mitral regurgitation in the TTVI group compared with the medical therapy alone group (50.0% compared with 18.8%, p<0.01).

Key efficacy findings

- Number of patients analysed: 124
- Procedural success (tricuspid regurgitation moderate or less)=77.3%

Overall survival at follow up
- TTVI=75.1%
- Medical therapy alone=46.9%, p=0.047

Freedom from hospitalisation for heart failure
- TTVI=61.7%
- Medical therapy alone=43.6%, p=0.074

Freedom from hospitalisation for heart failure and all-cause mortality
- TTVI=62.7%%
- Medical therapy alone=33.2%, p=0.027

Tricuspid regurgitation severity, symptoms, and diuretics doses before and after TTVI

Outcome	Before TTVI, n=53	After TTVI, n=53	p value
Tricuspid regurgitation severity, n (%)			<0.001
severe and above	53 (100)	12 (22.6)	-
moderate	0 (0)	20 (37.7)	-
mild	0 (0)	21 (39.6)	-
trace	0 (0)	0 (0)	-
NYHA functional class, n (%)			<0.001
4	5 (10.9)	3 (5.7)	-
3	38 (82.6)	4 (7.5)	-
2	3 (6.5)	38 (71.7)	-
1	0 (0)	8 (15.1)	-
Mean 6-minute walk test distance, metres (SD)	240.7 (138.5)	334.4 (141.5)	0.01
Mean total daily loop diuretics dose, mg (SD)	100.8 (91.7)	107.7 (90.6)	0.60
Mean total daily mineralocorticoid receptor antagonist dose, mg (SD)	17.4 (21.7)	19.5 (18.8)	0.16

Key safety findings

- There were no periprocedural complications such as tamponade, stroke, death or myocardial infarction.
- There were no patients with worsening tricuspid regurgitation or clinically significant tricuspid stenosis after the procedure.
- Out of 96 clips deployed in 53 patients, there was 1 single leaflet device attachment which was treated with an additional clip.

Medical complications seen during follow up, incidence per 100 person-years (95% CI)

Complication	TTVI, n=53	Medical therapy alone, n=71	p value
Gastrointestinal bleed	4.2 (0.8 to 12.4)	15.6 (8.9 to 25.3)	0.04
Stroke	0	2.9 (0.6 to 8.5)	0.41
Myocardial infarction	0	1.0 (0 to 5.4)	1.00
Acute kidney injury	14.1 (6.8 to 26.0)	37.0 (26.2 to 50.8)	0.006
New initiation of renal replacement therapy	4.2 (0.8 to 12.4)	3.9 (1.1 to 10.0)	1.00

Study 9 Miura M (2019)

Study details

Study type	Case report
Country	Switzerland
Recruitment period	Not reported
Study population and number	n=1 Patient with severe tricuspid regurgitation
Age and sex	79 year old female
Patient selection criteria	Not applicable
Technique	Device: MitraClip XTR system (Abbott Vascular, US). A transfemoral approach was used.
Follow up	Not reported
Conflict of interest/source of funding	Not reported

Analysis

Case report of clip being stuck and knotted because of the Chiari network

At baseline, the patient was in NYHA class 3. She had severe tricuspid regurgitation with annular dilatation, coaptation loss, and pulmonary artery hypertension. A percutaneous edge-to-edge repair of the tricuspid valve was done. The trajectory of the clip was not adequate to grasp the anterior and septal leaflets, and it was pulled back to the right atrium. However, the clip was stuck and trapped by the Chiari network and it was impossible to control. An unsuccessful attempt was made to cross the wire in the gap between the clip's arms and to pull it back using a peripheral balloon. Finally, a clip was deployed and fixed in the inferior vena cava. Another clip was implanted in the anterior and septal leaflets, and 1 was implanted in the posterior and septal leaflets. After deploying the clips, tricuspid regurgitation was reduced.

Validity and generalisability of the studies

- No randomised controlled trials were identified.
- The evidence includes data from North America and Europe.
- Many of the studies report results from the first people to have the procedure.
- Results of the early feasibility study may not be applicable to the total population of patients with clinically significant tricuspid regurgitation (Lurz, 2021).
- There is more than 1 device available and different devices use different mechanisms.
- The study by Asmarats et al. (2019) used the FORMA device, which is no longer available. The study has been included because it reports longer term data (median follow up of 32 months), but the sample size is small.
- The definition of procedural success varied between studies.
- Two non-randomised comparative studies used data from the Tri-Valve registry but they compared it with different populations (Schlotter, 2021, Taramasso, 2019).
- There is some patient overlap between the studies.
- Most studies only reported outcomes up to 1 year. The longest median follow up was 32 months, in 1 small case series.

Existing assessments of this procedure

The Canadian Agency for Drugs and Technologies in Health (CADTH) published a rapid response report in 2020 on 'Transcatheter Mitral Valve Repair for Tricuspid Regurgitation with or without Mitral Regurgitation'. The report concluded:

'Overall, compared to pre-procedure, patients [who had] MitraClip for the treatment of tricuspid regurgitation or both tricuspid and mitral regurgitation had significantly improved tricuspid regurgitation grade, New York Heart Association functional class, edema, and ascites at follow-up. Across four studies that reported on procedural success, the percentage of patients with procedural success ranged from 92% to 97%. There was no statistically significant

difference in quality of life between baseline and follow-up in the three studies that measured this outcome. Four of the studies showed statistically significant improvement in the six-minute walking distance at one month or six months, in patients who received tricuspid valve (TV) repair or both TV and mitral valve (MV) repair. One study observed a numerical (but not significant) improvement in the six-minute walking distance from baseline to one-year follow up. For heart failure severity when comparing baseline and follow up, two studies found significant improvement; two studies found no statistically significant difference; and one study demonstrated a statistically significant improvement in patients who received TV-only repair but no significant difference in patients who received both TV and MV repair. The mortality incidence after the procedure was 4.7% to 7% across the included studies.

The findings summarized in this report have a high degree of uncertainty due to the limitations of the included studies (e.g., a total of 209 patients in single-arm studies, longest follow-up duration of one year).' (Li, 2020)

Related NICE guidance

Below is a list of NICE guidance related to this procedure.

Interventional procedures

- Percutaneous mitral valve leaflet repair for mitral regurgitation. NICE interventional procedures guidance 649 (2019). Available from http://www.nice.org.uk/guidance/IPG649
- Percutaneous mitral valve annuloplasty. NICE interventional procedures guidance 352 (2010). Available from http://www.nice.org.uk/guidance/IPG352

NICE guidelines

- Heart valve disease presenting in adults: investigation and management. NICE guideline 208 (2021). Available from http://www.nice.org.uk/guidance/NG208
- Chronic heart failure in adults: diagnosis and management. NICE guideline 106 (2018). Available from http://www.nice.org.uk/guidance/NG106

Additional information considered by IPAC

Professional experts' opinions

Expert advice was sought from consultants who have been nominated or ratified by their professional Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by professional experts, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate.

No professional expert questionnaires were submitted.

Patient commentators' opinions

NICE's Public Involvement Programme will send questionnaires to NHS trusts for distribution to patients who had the procedure (or their carers). When NICE has received the completed questionnaires, these will be discussed by the committee.

Company engagement

A structured information request was sent to 6 companies who manufacture a potentially relevant device for use in this procedure. NICE received 2 completed submissions. These were considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

Issues for consideration by IPAC

- This overview includes evidence on transcatheter leaflet modification devices. Evidence on transcatheter ring-based or suture-based annuloplasty devices has been excluded where possible because it is covered by a separate overview.
- Ongoing trials:
  - Berlin Registry of Right Heart Interventions (NCT04570163); registry; n=100; end date Dec 2023
  - International Multisite Transcatheter Tricuspid Valve Therapies Registry (NCT03416166); registry; n=269; end date Nov 2026

References

1. Montalto C, Sticchi A, Crimi G et al. (2020) Functional and echocardiographic improvement after transcatheter repair for tricuspid regurgitation: a systematic review and pooled analysis. JACC Cardiovascular Interventions 13: 2719–29
2. Schlotter F, Miura M, Kresoja K-P et al. (2021) Outcomes of transcatheter tricuspid valve intervention by right ventricular function: a multicentre propensity-matched analysis. EuroIntervention 17: e343–52
3. Taramasso M, Benfari G, van der Bijl P et al. (2019) Transcatheter versus medical treatment of patients with symptomatic severe tricuspid regurgitation. Journal of the American College of Cardiology 74: 2998–3008
4. Taramasso M, Alessandrini H, Latib A et al. (2019b) Outcomes after current transcatheter tricuspid valve intervention: mid-term results from the international TriValve registry. JACC. Cardiovascular interventions 12: 155–65
5. Mehr M, Taramasso M, Besler C et al. (2019) 1-year outcomes after edge-to-edge valve repair for symptomatic tricuspid regurgitation: results from the TriValve registry. JACC. Cardiovascular Interventions 12: 1451–61
6. Lurz P, Stephan von Bardeleben R, Weber M et al. (2021) Transcatheter edge-to-edge repair for treatment of tricuspid regurgitation. Journal of the American College of Cardiology 77: 229–39
7. Asmarats L, Perlman G, Praz F et al. (2019) Long-term outcomes of the FORMA transcatheter tricuspid valve repair system for the treatment of severe tricuspid regurgitation: insights from the first-in-human experience. JACC. Cardiovascular Interventions 12: 1438–47
8. Cai S, Bowers N, Dhoot A et al. (2020) Natural history of severe tricuspid regurgitation: Outcomes after transcatheter tricuspid valve intervention compared to medical therapy. International Journal of Cardiology 320: 49–54
9. Miura M, Zuber M, Taramasso M et al. (2019) An unusual complication during transcatheter tricuspid valve repair. European Heart Journal 40: 3209
10. Li K X, Wright MD (2020) Transcatheter Mitral Valve Repair for Tricuspid Regurgitation with or without Mitral Regurgitation: A Review of Clinical Effectiveness and Cost-Effectiveness. Ottawa: CADTH; 2020 Jun. (CADTH rapid response report: summary with critical appraisal).

Literature search strategy

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	02/09/2021	Issue 9 of 12, September 2021
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	02/09/2021	Issue 9 of 12, September 2021
International HTA database	02/09/2021	-
MEDLINE (Ovid)	02/09/2021	1946 to September 01, 2021
MEDLINE In-Process (Ovid) & MEDLINE ePubs ahead of print (Ovid)	02/09/2021	September 01, 2021
EMBASE (Ovid)	02/09/2021	1974 to 2021 September 01
Embase Conference (Ovid)	02/09/2021	1974 to 2021 September 01

Trial sources searched

- Clinicaltrials.gov
- ISRCTN
- WHO International Clinical Trials Registry

Websites searched

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

Literature search strategy

Number	Search term
1	Tricuspid Valve Insufficiency/
2	((Tricuspid or right atrioventricular) adj4 (insufficien* or incompeten* or regurgitat* or disease* or dysfunct* or malfunct* or degenerat* or fail* or leak* or backflow* or back-flow* or flow-back*)).tw.
3	(TR or FTR).tw.
4	or/1-3
5	Cardiac Valve Annuloplasty/
6	(Transcatheter* adj4 tricuspid adj4 valve* adj4 (annuloplast* or repair* or reconstruct* or re-construct* or clos* or device* or interven* or therap* or band* or clip*)).tw.
7	(Percutaneous* adj4 tricuspid adj4 valve* adj4 (annuloplast* or repair* or reconstruct* or re-construct* or clos* or device* or interven* or therap* or band* or clip*)).tw.
8	(direct* adj4 annuloplast*).tw.
9	(Annul* adj4 (repair* or reduc*)).tw.
10	or/5-9
11	4 and 10
12	Cardioband*.tw.
13	11 or 12
14	(Triclip* or MitraClip* or Tricinch* or Trialign* or Gate system* or PASCAL or FORMA).tw.
15	4 and 14
16	11 or 15
17	animals/ not humans/
18	16 not 17

Appendix

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the summary of the key evidence. It is by no means an exhaustive list of potentially relevant studies.

Case reports, case series with fewer than 10 patients and reviews that were published before 2020 have not been included.

Additional papers identified

Article	Number of patients/ follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Ali FM, Ong G, Edwards J et al. (2021) Comparison of transcatheter tricuspid valve repair using the MitraClip NTR and XTR systems. International Journal of Cardiology 327: 156–62	Non-randomised comparative study n=40 Follow up=30 days	Both systems were safe and effective. The XTR system allowed treatment of larger coaptation gaps, greater mean reduction in tricuspid regurgitation grade, with more effective reduction of torrential tricuspid regurgitation.	Small study, comparing 2 different systems.
Arora L, Krishnan S, Subramani S et al. (2021) Functional tricuspid regurgitation: analysis of percutaneous transcatheter techniques and current outcomes. Journal of Cardiothoracic and Vascular Anesthesia 35: 921–31	Review	Patients currently having transcatheter intervention are typically at high surgical risk and have severe functional tricuspid regurgitation in the absence of severely impaired right ventricular systolic function. Although there are limitations to the transcatheter options currently available for patients, the initial data show that these existing devices are relatively safe with good results and functional improvements. Further investigation is needed to optimise indications, patient	Review

		selection, anatomic eligibility, long-term outcome, and procedural timing for each device category.	
Aurich M, Volz MJ, Mereles D et al. (2021) Initial experience with the PASCAL Ace Implant System for treatment of severe tricuspid regurgitation. Circulation: Cardiovascular Interventions 14: e010770	Case series n=16 Follow up=4 weeks	Tricuspid valve leaflet repair using the transcatheter PASCAL Ace implant system has the potential to improve clinical status and right heart reverse remodelling in patients with severe tricuspid regurgitation.	Small case series with short follow up.
Ben Ali W, Ruf T, Perrin N et al. (2021) Indications, limitations and development of tricuspid valve interventions in adults. The Canadian Journal of Cardiology https://doi.org/10.1016/j.cjca.2021.08.013	Review	Procedures can be categorised into coaptation devices, annuloplasty devices, transcatheter tricuspid valve replacement, heterotopic caval valve implantation and tricuspid valve-in-valve. Despite the late referral and the patient's profile, there is good procedural device success, excellent safety profile and sustained reduction of regurgitation up to 1 year. As results are limited to the mid-term, TTVIs durability will need to be established before broader adoption of these technologies.	Review
Besler C, Unterhuber M, Rommel K-P et al. (2020) Nutritional status in tricuspid regurgitation: implications of transcatheter repair. European Journal of Heart Failure 22: 1826–36	Case series n=86 Follow up=median 6 months	Nutritional impairment is common and of prognostic importance in patients who have transcatheter repair. Hepatorenal function modestly improves after a successful procedure. Further study of extracardiac implications of tricuspid regurgitation-	Small case series, focusing on nutritional status.

		associated right heart failure is warranted to improve care in this vulnerable patient population.	
Besler C, Blazek S, Rommel K-P et al. (2018) Combined mitral and tricuspid versus isolated mitral valve transcatheter edge-to-edge repair in patients with symptomatic valve regurgitation at high surgical risk. JACC. Cardiovascular Interventions 11: 1142–51	Non-randomised comparative study n=61 Follow up=up to 18 months	Combined transcatheter mitral plus tricuspid valve edge-to-edge repair appears superior to transcatheter mitral valve edge-to-edge repair alone in terms of cardiac output and functional improvement early after the intervention and improves clinical outcome up to 18 months of follow up.	Small study, focusing on combination of mitral valve and tricuspid valve intervention.
Besler C, Orban M, Rommel K-P et al. (2018) Predictors of procedural and clinical outcomes in patients with symptomatic tricuspid regurgitation undergoing transcatheter edge-to-edge repair. JACC. Cardiovascular Interventions 11: 1119–28	Case series n=117 Follow up=median 184 days	Successful tricuspid regurgitation reduction by transcatheter tricuspid valve edge-to-edge repair serves as a predictor for reduced mortality and heart failure hospitalisation. Coaptation gap and jet location may assist in decision making whether a patient is anatomically suited for the procedure.	More recent studies are included.
Braun D, Nabauer M, Orban M et al. (2017) Transcatheter treatment of severe tricuspid regurgitation using the edge-to-edge repair technique. EuroIntervention 12: e1837-e1844	Case series n=18 Follow up=30 days	The short-term durability of tricuspid regurgitation reduction appeared promising, and most patients improved clinically. Further studies with larger patient populations and longer follow up have to define the role of this novel treatment option for patients with right-sided heart failure and severe tricuspid regurgitation.	Small case series with short follow up.
Chang CC, Veen KM Hahn RT et al. (2020)	Review	Although early safety and efficacy results are	Review

Uncertainties and challenges in surgical and transcatheter tricuspid valve therapy: a state-of-the-art expert review. European Heart Journal 41: 1932–40		encouraging, remaining uncertainties including grade of tricuspid regurgitation severity (quantitative and qualitative), patient selection, risk stratification, timing of intervention, and definition of successful repair warrant further investigations.	
Corpataux N, Winkel MG, Kassar M et al. (2020) The PASCAL device-early experience with a leaflet approximation device: what are the benefits/limitations compared with the MitraClip? Current Cardiology Reports 22: 74	Review	The PASCAL system is a valuable addition to the armamentarium of transcatheter mitral and tricuspid valve repair devices. Randomised head-to-head comparisons and long-term data are needed to confirm the promising results seen so far.	Review
Curio J, Abulgasim K, Kasner M et al. (2020) Intracardiac echocardiography to enable successful edge-to-edge transcatheter tricuspid valve repair in patients with insufficient TEE quality. Clinical Hemorheology and Microcirculation 76: 199–210	Case series n=11 Follow up=30 days	Intracardiac echocardiography guidance may offer an additional tool to guide edge-to-edge transcatheter tricuspid valve repair with the MitraClip device in patients with poor transoesophageal echocardiography quality.	Small case series, focusing on the use of intracardiac echo-cardiography.
Donatelle M, Ailawadi G (2020) Transcatheter tricuspid valve repair: Bringing the forgotten valve into the spotlight. The Journal of Thoracic and Cardiovascular Surgery 160: 1467–73	Review	It is evident that patients with significant tricuspid regurgitation must be identified earlier and referred to reference centres with expertise in the medical, surgical, as well as transcatheter approaches for treating the tricuspid valve	Review

		specifically before the onset of torrential tricuspid regurgitation or severe right-sided heart failure symptoms.	
Fam NP, Braun D, von Bardeleben RS et al. (2019) Compassionate use of the PASCAL transcatheter valve repair system for severe tricuspid regurgitation: a multicenter, observational, first-in-human experience. JACC. Cardiovascular Interventions 12: 2488–95	Case series n=28 Follow up=30 days	This first-in-human experience evaluating transcatheter tricuspid repair with the PASCAL system showed high procedural success, acceptable safety, and significant clinical improvement. Larger prospective studies with long-term follow up are needed.	Small case series with short follow up, included in the systematic review by Montalto et al. (2020).
Faries CM, Sengupta A, Alexis SL et al. (2020) Transcatheter tricuspid and pulmonary valve repair and replacement. Surgical Technology International 36: 217–23	Review	Challenges faced in TTVI device and trial designs include heterogeneous patient populations, the need for quality imaging, variations of imaging requirements and anatomic criteria by device, hard-to-define clinical endpoints, and the poor prognosis carried by significant residual tricuspid regurgitation.	Review
Gupta T, Wyler von Ballmoos MC, Goel SS (2021) Transcatheter treatment of severe tricuspid regurgitation. Current Opinion in Cardiology 36: 525–37	Review	Early results with both repair and replacement technologies have shown promising results. Ongoing pivotal studies will shed light on prognostic benefits compared with medical therapy and hopefully provide long-term data. Some important future perspectives in the field include improved preprocedural planning and intraprocedural imaging, standardisation	Review

		of echocardiographic measures and clinical endpoints for device trials; disease stage and anatomy tailored approach; and defining the optimal timing of treatment.	
Kaple RK, Agarwal V, Azarbal A et al. (2021) Tricuspid clip implantation using the MitraClip system-A step-by-step guide. Catheterization and Cardiovascular Interventions DOI: 10.1002/ccd.29796	Review	The use of the MitraClip system on the tricuspid valve has been shown to be a safe and effective treatment strategy in patients with symptomatic tricuspid regurgitation.	Review
Karam N, Mehr M, Taramasso M et al. (2020) Value of echocardiographic right ventricular and pulmonary pressure assessment in predicting transcatheter tricuspid repair outcome. JACC. Cardiovascular Interventions 13: 1251–61	Subanalysis of TriValve registry n=249 Follow up=1 year	Transcatheter tricuspid valve repair provided clinical improvement, with 1-year survival free from hospital readmission >75% in patients with severe tricuspid regurgitation. Conventional echocardiographic parameters used to assess right ventricular function and systolic pulmonary artery pressure did not predict clinical outcome.	Subanalysis of TriValve registry.
Karam N, Braun D, Mehr M et al. (2019) Impact of transcatheter tricuspid valve repair for severe tricuspid regurgitation on kidney and liver function. JACC. Cardiovascular Interventions 12: 1413–20	Case series n=126 Follow up=6 months	Tricuspid regurgitation reduction by transcatheter tricuspid valve repair is associated with an improvement in liver function, mainly among patients with abnormal liver function at baseline, whereas kidney function remained stable.	Studies with more patients or longer follow up are included.

Kavsur R, Hupp-Herschel HE, Sugiura A et al. (2021) Prognostic significance of the get with the guidelines-heart failure (GWTG-HF) risk score in patients undergoing trans-catheter tricuspid valve repair (TTVR). Heart Vessels https://doi.org/10.1007/s00380-021-01874-3	Case series n=181	The 'get with the guidelines-heart failure' score serves as a risk assessment tool in patients with heart failure and concomitant severe tricuspid regurgitation who have transcatheter tricuspid valve repair to predict 1 year mortality and hospitalisations for heart failure. The inclusion of NT-proBNP led to an improvement of the score's predictive power, emphasising its use in this patient population. Overall, in this present study, the procedure was feasible in most patients and led to a substantial improvement of tricuspid regurgitation and NYHA classes.	Study focuses on the Get-With-The-Guidelines-Heart-Failure (GWTG-HF) score as a risk assessment tool.
Kavsur R, Hupp H, Sugiura A et al. (2020) Pulmonary capillary wedge pressure (PCWP) as prognostic indicator in patients undergoing transcatheter valve repair (TTVR) of severe tricuspid regurgitation. International Journal of Cardiology 318: 32–8	Case series n=60 Follow up=6 months	PCWP is a predictive outcome parameter in TTVR patients. Patients with a PCWP ≤16 mmHg had a favourable outcome with lower mortality and morbidity gaining more benefit of TTVR.	Small case series.
Kitamura M, Thiele H, Lurz P et al. (2021) 12-Month outcomes of transcatheter tricuspid valve repair with the PASCAL system for severe tricuspid regurgitation. Catheterization and Cardiovascular Interventions 97: 1281–89	Case series n=30 Follow up=12 months	12-month outcomes showed high procedural success, acceptable safety, and significant clinical improvement.	Small case series

Kodali S, Hahn RT, Eleid MF et al. (2021) Feasibility study of the transcatheter valve repair system for severe tricuspid regurgitation. Journal of the American College of Cardiology 77: 345–56	Case series n=34 Follow up=30 days	The repair system performed as intended, with substantial tricuspid regurgitation reduction, favourable safety results with a low major adverse event rate, no mortality or reintervention, and statistically significant improvements in functional status, exercise capacity, and quality of life.	Small case series, included in the systematic review by Montalto et al. (2020).
Kolte D, Elmariah S (2020) Current state of transcatheter tricuspid valve repair. Cardiovascular Diagnosis and Therapy 10: 89–97	Review	The short- and mid-term data on the safety and efficacy of various transcatheter tricuspid valve therapies are encouraging. Procedural and clinical outcomes are expected to improve in the coming years with technological advancement, newer device iterations, and increased experience in this field. Appropriate patient selection, optimal timing of intervention, and evaluation of long-term outcomes and device durability will be key in ongoing and future studies.	Review
Kresoja K-P, Rommel K-P, Unterhuber M et al. (2021) Right ventricular contraction patterns in patients undergoing transcatheter tricuspid valve repair for severe tricuspid regurgitation. JACC: Cardiovascular Interventions 14: 1551–61	Cohort study n=79 Follow up=median 362 days	Global right ventricular dysfunction is a predictor of outcomes among patients who have transcatheter tricuspid valve repair. Tricuspid regurgitation patients can be stratified into 3 types of right ventricular contraction, in which a loss of longitudinal function can be compensated by increasing circumferential	Studies with more patients or longer follow up are included.

		function, preserving right ventricular ejection fraction and favourable outcomes.	
Kresoja K-P, Lauten A, Orban M et al. (2020) Transcatheter tricuspid valve repair in the setting of heart failure with preserved or reduced left ventricular ejection fraction. European Journal of Heart Failure 22: 1817–25	Cohort study n=111 and 94 pairs in propensity-matched cohort Follow up=median 238 days	Transcatheter tricuspid valve edge-to-edge repair might be a treatment option in patients with severe tricuspid regurgitation and left-sided heart failure with preserved (≥50%) ejection fraction compared to conservative therapy.	Studies with more patients or longer follow up are included.
Lurz P, Orban M, Besler C et al. (2020) Clinical characteristics, diagnosis, and risk stratification of pulmonary hypertension in severe tricuspid regurgitation and implications for transcatheter tricuspid valve repair. European Heart Journal 41: 2785–95	Case series n=243 Follow up=330 days	The discordant echocardiographic and invasive diagnosis of pulmonary hypertension in severe tricuspid regurgitation predicts outcomes after transcatheter tricuspid valve repair.	Studies with more patients or longer follow up are included.
Lurz P, Besler C, Noack T et al. (2018) Transcatheter treatment of tricuspid regurgitation using edge-to-edge repair: procedural results, clinical implications and predictors of success. EuroIntervention 14: e290-e297	Case series n=42 Follow up=30 days	Edge-to-edge repair of the tricuspid valve is feasible with a promising reduction in tricuspid regurgitation, which could result in clinical improvement.	Studies with more patients or longer follow up are included.
Mahowald MK, Pislaru SV, Reeder GS et al. (2020) Institutional learning experience for combined edge-to-edge tricuspid and mitral valve repair. Catheterization and Cardiovascular	Case series n=22 Follow up=30 days	Combined edge-to-edge tricuspid and mitral valve repair is safe and feasible. With experience, procedure duration and residual tricuspid regurgitation decreased.	Studies with more patients or longer follow up are included.

Interventions 96: 1323–30			
Mega S, Ussia GP, Grigioni F et al. (2021) Mitral and tricuspid valves percutaneous repair in patients with advanced heart failure: panacea, or Pandora's box? Heart Failure Clinics 17: 607–618	Review	In heart failure with reduced ejection fraction, the advent of transcatheter therapies to address secondary (functional) mitral and tricuspid regurgitation offers new therapeutic opportunities. Edge-to-edge tricuspid repair is the most developed transcatheter option currently available for functional tricuspid regurgitation.	Review
Mehr M, Karam N, Taramasso M et al. (2020) Combined tricuspid and mitral versus isolated mitral valve repair for severe mitral and tricuspid regurgitation: an analysis from the TriValve and TRAMI Registries. JACC. Cardiovascular Interventions 13:543–50	Analysis of registry data n=228 Follow up=1 year	Concurrent transcatheter mitral and tricuspid valve repair was associated with a higher 1-year survival rate compared with isolated transcatheter mitral valve repair in patients with both mitral and tricuspid regurgitation. Further randomised trials are needed to confirm these results.	Study focuses on patients with mitral valve repair with or without tricuspid valve repair.
Meijerink F, Koch KT, de Winter RJ et al. (2021) Transcatheter tricuspid valve repair: early experience in the Netherlands. Netherlands Heart Journal 29: 595–603	Case series n=21 Follow up=4 weeks	Transcatheter tricuspid valve repair seems a promising treatment option for patients with severe functional tricuspid regurgitation deemed high risk for surgery. Successful tricuspid regurgitation reduction is most likely in patients with limited coaptation gap size and strongly determines clinical benefit. Adequate patient selection and timing of treatment seem essential for an optimal patient outcome	Small case series

Miura M, Alessandrini H, Alkhodair A et al. (2020) Impact of massive or torrential tricuspid regurgitation in patients undergoing transcatheter tricuspid valve intervention. Cardiovascular Interventions 13: 1999–2009	Subanalysis of TriValve registry n=333 Follow up: median 237 days	Baseline massive or torrential tricuspid regurgitation is associated with an increased risk for all-cause mortality and rehospitalisation for heart failure 1 year after TTVI. Procedural success is related to better outcomes, even in the presence of baseline massive or torrential tricuspid regurgitation.	Subanalysis of TriValve registry, focusing on patients with massive or torrential tricuspid regurgitation.
Muntane-Carol G, Philippon F, Puri R et al. (2021) Transcatheter tricuspid valve intervention in patients with previous left valve surgery. Canadian Journal of Cardiology 37: 1094–1102	Subanalysis of TriValve registry n=82	In patients with previous left valve surgery, TTVI was associated with high rates of procedural success and low early mortality. However, about a third of patients needed rehospitalisation or died at midterm follow up.	Subanalysis of TriValve registry, focusing on patients with previous left valve surgery.
Muntane-Carol G, Philippon F, Puri R et al. (2021) Transcatheter tricuspid valve intervention in patients with right ventricular dysfunction or pulmonary hypertension: insights from the TriValve registry. Circulation: Cardiovascular Interventions 184–92	Subanalysis of TriValve registry n=300	The TTVI was associated with high procedural success and a relatively low in-hospital mortality, along with improvements in functional status. However, about 1 out of 5 patients died after a median follow up of 6 months, with hepatic congestion and renal dysfunction. The lack of procedural success determined an increased risk. These results may improve the clinical evaluation of TTVI candidates and would suggest a closer follow up in those at increased risk.	Subanalysis of TriValve registry, focusing on patients with right ventricular dysfunction or pulmonary hypertension.
Muntane-Carol G, Alperi A, Faroux L et al. (2021) Transcatheter interventions for	Review	The initial experience showed that most procedures were well tolerated, with high	Review

tricuspid valve disease: what to do and who to do It on. Canadian Journal of Cardiology 37: 953–67		procedural success and low in-hospital and early mortality. Also, most patients improved their functional status and recent data suggest improved outcomes compared with medical management. However, the rate of significant residual tricuspid regurgitation after transcatheter tricuspid valve repair remains high and very scarce data exist on longer term (beyond 6 to 12 months) outcomes.	
Muntane-Carol G, Del Val D, Bedard E et al. (2019) Transcatheter innovations in tricuspid regurgitation: FORMA device. Progress in Cardiovascular Diseases 62: 496–99	review of 2 cohort studies n=47 Follow up=1 and 12 months	Initial experience with the FORMA device in prohibitive surgical risk patients showed the feasibility of this procedure, albeit with a reasonable rate of device-related complications. The magnitude of tricuspid regurgitation reduction was moderate at long-term and there were improvements in heart failure symptoms and quality of life.	Studies with more patients or longer follow up are included.
Nagaraja V, Kapadia SR, Miyasaka R et al. (2020) Contemporary review of percutaneous therapy for tricuspid valve regurgitation. Expert Review of Cardiovascular Therapy 18: 209–18	Review	The early data available thus far on percutaneous tricuspid repair and replacement is promising and shows modest reductions in tricuspid regurgitation along with improvement in the quality of life. Different from transcatheter aortic valve intervention, percutaneous tricuspid repair and replacement does not have long-term data. The lack of standardised	Review

		protocols and definitions for enrolment and outcomes in these early tricuspid trials are a limitation.	
Nagaraja V, Mohananey D, Navia J et al. (2020) Functional tricuspid regurgitation: Feasibility of transcatheter interventions. Cleveland Clinic Journal of Medicine 87: 4–14	Review	The published data so far on percutaneous therapies show promising results in the form of a reasonable reduction in tricuspid regurgitation along with substantial improvement in the quality of life. The transcatheter device technology is currently evolving for the tricuspid valve. Patient selection based on anatomy for the appropriate device technology is imperative. Improved device technology best matched to patient factors is likely to increase the array of options available.	Review
Nickenig G, Weber M, Lurz P et al. (2019) Transcatheter edge-to-edge repair for reduction of tricuspid regurgitation: 6-month outcomes of the TRILUMINATE single-arm study. Lancet 394: 2002–11	Single arm trial n=85 Follow up=6 months	The TriClip system appears to be safe and effective at reducing tricuspid regurgitation by at least one grade. This reduction could translate to significant clinical improvement at 6 months post procedure.	A more recent report from the same trial is included (Lurz, 2021). Study is included in the systematic review by Montalto et al. (2020).
Nickenig G, Kowalski M, Hausleiter J et al. (2017) Transcatheter treatment of severe tricuspid regurgitation with the edge-to-edge MitraClip technique. Circulation 135: 1802–14	Case series n=64 Follow up=30 days	Transcatheter treatment of tricuspid regurgitation with the MitraClip system seems to be safe and feasible in this cohort of preselected patients. Initial efficacy analysis showed encouraging reduction of tricuspid regurgitation, which may potentially	Studies with more patients or longer follow up are included.

		result in improved clinical outcomes.	
Orban M, Rommel KP, Ho EC et al. (2020) Transcatheter edge-to-edge tricuspid repair for severe tricuspid regurgitation reduces hospitalizations for heart failure. JACC. Heart Failure 8: 265–76	Cohort study n=233 Follow up=median 360 days	Transcatheter edge-to-edge tricuspid repair for severe TR is associated with a reduction of hospitalisations for heart failure and improved clinical outcomes. Patients who had transcatheter mitral and tricuspid valve repair had comparable outcomes.	Studies with more patients or longer follow up are included.
Orban M, Orban MW Braun D et al. (2019) Clinical impact of elevated tricuspid valve inflow gradients after transcatheter edge-to-edge tricuspid valve repair. EuroIntervention 15: e1057-e1064	Cohort study n=145 Follow up=1 year	A small cohort of patients showed an elevated tricuspid valve gradient higher than 3 mmHg at discharge. This elevation had no impact on clinical improvement, mortality or hospitalisation for heart failure.	Studies with more patients or longer follow up are included.
Orban M, Besler C, Braun D et al. (2018) Six-month outcome after transcatheter edge-to-edge repair of severe tricuspid regurgitation in patients with heart failure. European Journal of Heart Failure 20: 1055–62	Case series n=50 Follow up=6 months	Transcatheter edge-to-edge tricuspid valve repair for severe TR is safe and effective in reducing TR. It appears to be associated with improved clinical outcome in most patients.	Studies with more patients or longer follow up are included.
Otto S, Velichkov M, Hamadanchi A et al. (2021) The impact of tricuspid annular geometry on outcome after percutaneous edge-to-edge repair for severe tricuspid regurgitation. Cardiology Journal 28: 579–88	Case series n=20 Follow up=30 days	No differences in conventional echocardiographic parameters for TR severity but more dilated tricuspid annulus geometry (tricuspid valve annulus, coaptation depth, tenting area) in the failed repair group were seen.	Small case series
Perlman G, Praz F, Puri R et al. (2017)	Case series n=18	Implantation of the FORMA system in high-	Small case series,

Transcatheter tricuspid valve repair with a new transcatheter coaptation system for the treatment of severe tricuspid regurgitation: 1-Year clinical and echocardiographic results. JACC. Cardiovascular Interventions 10: 1994–2003	Follow up=1 year	risk patients with severe TR shows feasibility with a good mid-term safety profile. At 1 year, despite variable success in reducing echocardiographic TR grade, there were significant clinical improvements and reductions in right ventricular dimensions.	included in the systematic review by Montalto et al. (2020).
Rahgozar K, Ho E, Goldberg Y et al. (2021) Transcatheter tricuspid valve repair and replacement: a landscape review of current techniques and devices for the treatment of tricuspid valve regurgitation. Expert Review of Cardiovascular Therapy 19: 399–411	Review	There is currently an unmet clinical need in the treatment of severe tricuspid regurgitation, but this paradigm is slowly shifting and the number of TTVIs is climbing each year. Promising early results with many of the devices and techniques available have shown the feasibility, safety, and short-term efficacy of transcatheter tricuspid valve repair.	review
Rommel K-P, Besler C, Noack T et al. (2019) Physiological and clinical consequences of right ventricular volume overload reduction after transcatheter treatment for tricuspid regurgitation. JACC. Cardiovascular Interventions 12: 1423–34	Case series n=29 Follow up=6 months	Transcatheter tricuspid valve repair reduces chronic right ventricular volume overload without increase in right ventricular afterload, improves right ventricular performance and left ventricular filling, and enhances cardiac output. These changes translate into symptomatic and functional improvement. These implications for biventricular physiology and clinical status are maintained at 6 months follow up.	Small case series
Ruf TF, Kreidel F, Hell M et al. (2021) Short-	Case series n=50	MitraClip XTR implantation is a safe, effective	Small case series

term clinical outcomes of transcatheter tricuspid valve repair with the third-generation MitraClip XTR system. JACC: Cardiovascular Interventions 14: 1231–40	Follow up=30 days	treatment for a wider range of coaptation gap sizes in patients with symptomatic, significant TR than prior device iterations. All patients showed improvement in NYHA functional class, and those with coaptation gap size less than 10 mm also had improved functional capacity.	
Santalo-Corcoy M, Asmarats L, Arzamendi D et al. (2020) Catheter-based treatment of tricuspid regurgitation: State of the art. Annals of Translational Medicine 8: 964	Review	Preliminary data has shown encouraging results, with significant functional and echocardiographic improvements. Further studies are greatly awaited to provide the necessary background to determine the optimal time and devices to intervene in this less symptomatic population, along with a deeper knowledge of the long-term performance of the variety of technologies currently used in different stages of the disease.	Review
Schlotter F, Rommel K-P, Besler C et al. (2019) Aetiology-based clinical scenarios predict outcomes of transcatheter edge-to-edge tricuspid valve repair of functional tricuspid regurgitation. European Journal of Heart Failure 21: 1117–25	Cohort study n=164 Follow up=median 248 days	Stratification of transcatheter tricuspid valve repair into aetiology-based clinical scenarios may open new paths to stratify for clinical risk and procedural benefit and may aid in the design of clinical trials in the heterogeneous patient population. Despite the observed clinical scenario outcome differences, it appears feasible and safe, and confers functional improvements in patients with TR and heart failure.	Studies with more patients or longer follow up are included.

Stocker TJ, Hertell H, Orban M et al. (2021) Cardiopulmonary hemodynamic profile predicts mortality after transcatheter tricuspid valve repair in chronic heart failure. JACC. Cardiovascular Interventions 14: 29–38	Single arm study n=236 Follow up=1 year	Invasive assessment of cardiopulmonary hemodynamic status predicts survival after transcatheter tricuspid valve repair. Invasive hemodynamic characterisation may help identify patients profiting most from the procedure.	The main aim of the study was to assess haemo-dynamic changes and identify haemo-dynamic predictors associated with mortality.
Sugiura A, Tanaka T, Kavsur R et al. (2021) Leaflet configuration and residual tricuspid regurgitation after transcatheter edge-to-edge tricuspid repair. JACC. Cardiovascular Interventions 14: 2260–70	Case series n=145 Follow up=30 days	A 4-leaflet configuration of the tricuspid valve was seen in about 33% of people having transcatheter edge-to-edge tricuspid repair, which is associated with an increased risk of residual TR after the procedure.	Study focuses on leaflet configuration.
Sugiura A, Vogelhuber J, Ozturk C et al. (2021) PASCAL versus MitraClip-XTR edge-to-edge device for the treatment of tricuspid regurgitation: a propensity-matched analysis. Clinical Research in Cardiology 110: 451–9	Non-randomised comparative study n=80 Follow up=3 months	Both devices, PASCAL and MitraClip-XTR, appeared feasible and comparable for an effective TR reduction.	Studies with more patients or longer follow up are included.
Tanaka T, Kavsur R, Sugiura A et al. (2021) Prognostic impact of hepatorenal function in patients undergoing transcatheter tricuspid valve repair. Scientific Reports 11: 14420	Case series n=172	The model for end-stage liver disease excluding international normalised ratio score was associated with the risk of 1-year composite outcome, consisting of mortality and heart failure hospitalisation, after the procedure and may help risk stratification.	The focus of the study was to assess the prognostic significance of hepatorenal dysfunction.

Taramasso M, Gavazzoni M, Pozzoli A et al. (2020) Outcomes of TTVI in patients with pacemaker or defibrillator leads: data From the TriValve registry. JACC. Cardiovascular Interventions 13: 554–64	Subanalysis of TriValve registry n=470 Follow up: median 7 months	TTVI is feasible in selected patients with cardiac implantable electronic device leads and acute procedural success and short-term clinical outcomes are comparable to those seen in patients without a transtricuspid lead.	Subanalysis of TriValve registry, focusing on patients with pacemaker or defibrillator leads.
Taramasso M, Hahn RT, Alessandrini H et al. (2017) The international multicenter TriValve registry: which patients are undergoing transcatheter tricuspid repair? JACC. Cardiovascular Interventions 10: 1982–90	TriValve registry n=106 Follow up: 30 days	Patients currently having transcatheter tricuspid valve therapy are mostly high risk, with a functional aetiology and very severe central regurgitation, and do not have severely impaired right ventricular function. Initial results suggest that transcatheter tricuspid valve therapy is feasible with different techniques, but clinical efficacy requires further investigation.	More recent publications with data from the TriValve registry are included.
Yandrapalli S, Kolte D (2021) Tricuspid regurgitation: when and how to treat. Current Treatment Options in Cardiovascular Medicine 23: 60	Review	Transcatheter tricuspid valve therapies may offer a less invasive and potentially safer alternative to surgery for managing severe symptomatic tricuspid regurgitation. Ongoing studies will shed light on long-term outcomes and device durability, and inform patient selection and optimal timing of intervention.	Review