Interventional procedure overview of caval valve implantation for tricuspid regurgitation

Contents

Table 1 Abbreviations

Abbreviation	Definition
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
CAVI	Caval valve implantation
Gamma-GT	Gamma-glutamyl transferase
GFR	Glomerular filtration rate
IQR	Interquartile range
IVC	Inferior vena cava
KCCQ	Kansas City Cardiomyopathy Questionnaire
MLHFQ	Minnesota Living with Heart Failure Questionnaire
6MWD	Six-minute walk distance
NYHA	New York Heart Association
OMT	Optimised medical therapy
RCT	Randomised controlled trial
RV	Right ventricular
SD	Standard deviation
STS score	The Society of Thoracic Surgeons' risk score
SVC	Superior vena cava
TAVR	Transcatheter aortic valve replacement
TR	Tricuspid regurgitation

Indications and current treatment

The tricuspid valve sits between the right atrium and right ventricle of the heart. TR occurs because the tricuspid valve does not close properly during systole. It can result in blood refluxing back into the right atrium (leading to haemodynamically significant TR) and the 2 main caval veins (the SVC and IVC). This makes the heart work harder and, if severe, can lead to heart failure. TR can mainly be because of a problem with the valve anatomy itself. But it is more commonly secondary to an underlying cardiac problem that causes tricuspid annular dilatation or leaflet tethering. The valve leaflets and chords may be normal but, because of the annulus dilatation, the valve leaflets fail to close properly and regurgitation of blood occurs.

People with mild TR do not usually have 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. There are no specific medicines for treating TR itself, but symptoms of heart failure are managed with medicines such as diuretics and angiotensin-converting enzyme inhibitors. Medicines to reduce pulmonary artery pressure, pulmonary vascular resistance or both, may be used when there is severe functional TR 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 because it is associated with high morbidity and mortality. More commonly, it is done at the same time as surgery to the valves on the left side of the heart (mitral and aortic). Transcatheter tricuspid valve interventions (tricuspid valve repair and replacement) are an alternative for managing TR.

Unmet need

TR is more common in older people and research suggests that about 4% of people aged 75 years or over may have significant TR. Many people with significant TR cannot tolerate open heart surgery due to their age or other comorbidities. As a result, many people with significant TR have limited treatment options. Caval valve implantation is less invasive and may be an option when surgery is contraindicated, and other transcatheter tricuspid valve interventions are not suitable. It also has the potential of reducing symptoms and improving quality of life whilst having fewer side effects.

What the procedure involves

CAVI is indicated for haemodynamically significant TR and caval reflux of tricuspid valve in people who have advanced disease (with severe leaflet tethering and a large coaptation gap) and are at extreme risk from surgery. The aim is to reduce caval reflux and stop venous congestion, so improving symptoms of heart failure and quality of life for people who cannot have open heart surgery.

The procedure is done under local or general anaesthesia, and with fluoroscopy guidance. Transoesophageal echocardiography may be used to monitor the position and function of the deployed bioprostheses. Depending on the anatomical suitability, CAVI can be single or bicaval. The bioprostheses can be dedicated self-expandable valves or balloon-expandable prostheses used for TAVR. They are implanted percutaneously through a delivery system using transfemoral access. The valves are implanted in the IVC, SVC or both, at the

level of the atriocaval junction. This is done without disturbing the native tricuspid valve in a cranial-caudal direction.

Outcome measures

The main outcomes include NYHA functional class, health and quality of life status using KCCQ, 6WMD, and maximal oxygen uptake. The measures used are detailed in the following paragraphs.

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.

Maximal oxygen uptake (VO_{2max})

The product of peak cardiac output and maximal arteriovenous oxygen difference is referred to as maximal oxygen uptake. This is the amount of oxygen used by a subject when exercising as hard as possible. The primary endpoint was determined by quantifying maximal oxygen uptake by treadmill spiro-ergometry.

Evidence summary

Population and studies description

This overview is based on 133 patients from 1 RCT, 2 registries, 2 non-randomised studies, 1 observational study and 1 case report. Of these 135

patients, 121 patients had the CAVI procedure and the remaining 14 patients had OMT. This is a rapid review of the literature, and a flow chart of the complete selection process is shown in figure 1. This overview presents 7 studies as the key evidence in table 2 and table 3, and lists 18 other relevant studies in table 5.

The countries where the procedures were carried out include Germany, Canada, Spain, Austria and the United States. The population is comprised of patients 18 years and over with severe TR. The study designs include RCTs, registries, and non-randomised studies. The follow-up periods ranged from 6 months to 12 months. Table 2 presents study details.

Figure 1 Flow chart of study selection

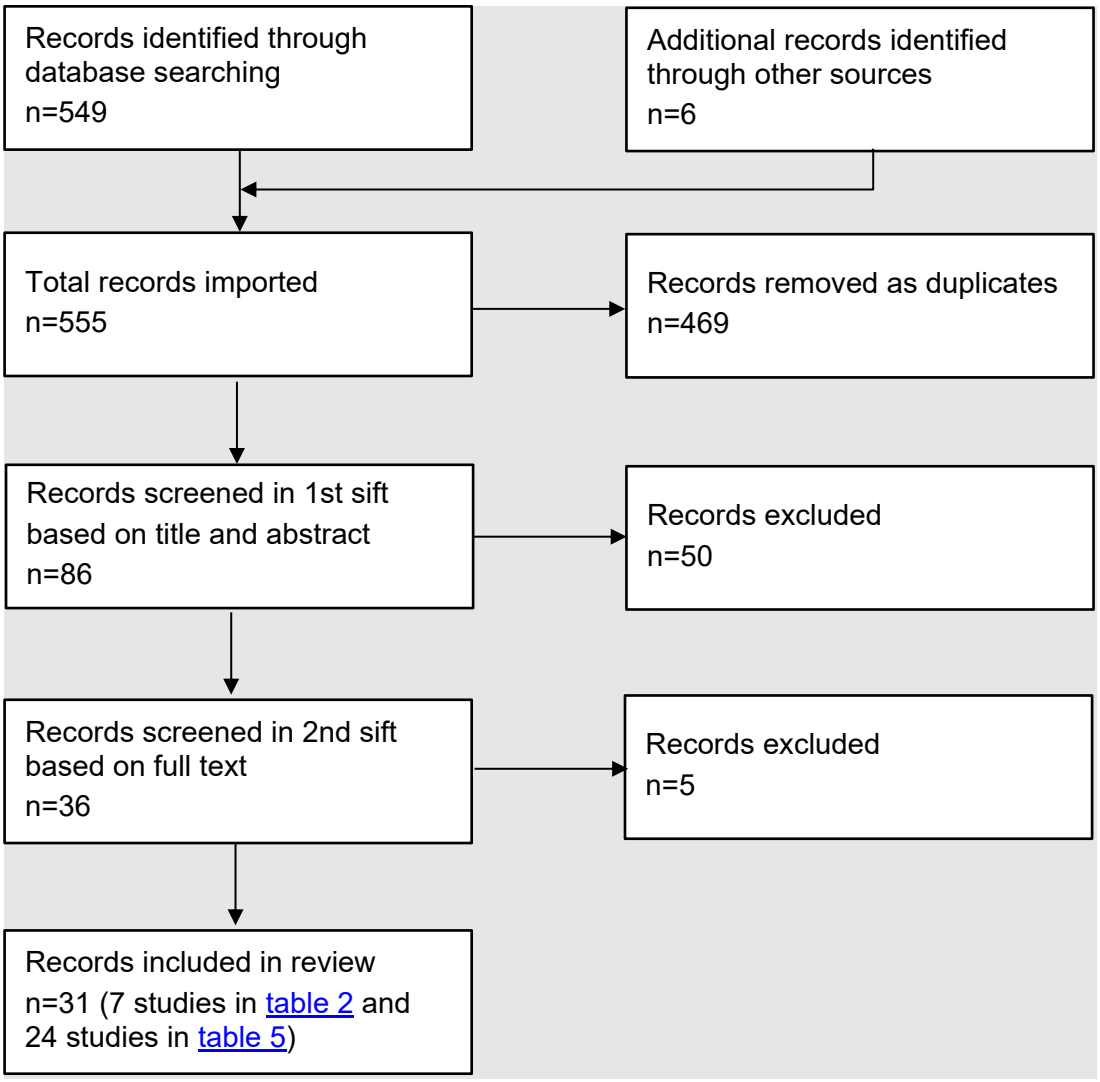

Table 2 Study details

Study no.	First author, date country	Patients (male: female)	Age	Study design	Inclusion criteria	Intervention	Follow up	Comments
1	Dreger H, 2022 Germany	N=28 patients with advanced heart failure CAVI group n=14 (2:12) OMT group n=14 (7:7)	CAVI mean age [IQR]: 77 [72.2-79.5] OMT mean age [IQR]: 77 [68.2-82.0] years	RCT TRICAVAL trial NCT02387697	NYHA Class ≥2 despite OMT, age ≥50 years, and high surgical risk (logistic EuroSCORE I ≥15% or other contraindications for conventional valve surgery according to the local heart team)	CAVI versus OMT Implantation of a balloon-expandable transcatheter valve (Edwards Sapien XT valve) into the IVC	12 months	The study was stopped early because of major complications related to valve dislocation and stent migration
2	Hewing B, 2021 Germany	N=18 patients with advanced heart failure CAVI group n=8 at completed 3-month follow up) (2:6)OMT	CAVI mean age [IQR]: 79 (68.3-82.6) years	Non-randomised study Subgroup analysis of RCT	Severe secondary TR, NYHA class ≥ 2, optimal medical treatment and high surgical risk	CAVI versus medical therapy Implantation of a balloon-expandable transcatheter valve	12 months	The study evaluated the effects of CAVI on clinical signs of congestion, renal and hepatic

Study no.	First author, date country	Patients (male: female)	Age	Study design	Inclusion criteria	Intervention	Follow up	Comments
		group n=10 at completed 3-month follow up) (5:5)	OMT mean age [IQR]: 78 (73.3-83.9) years	TRICAVAL trial NCT02387697		(Edwards Sapien XT Valve) into the IVC		function. Following major complications, the study was stopped prematurely resulting in a small study sample size for the present subanalysis
3	Lauten A, 2018 Germany and Canada (multicentre)	N=25 patients and 31 caval valves implanted (12:13)	Mean age: 73.9 years mean STS score of 14.0 ± 12.7	Multicentre observational study	Patients presenting with symptomatic severe TR despite OMT and considered unsuitable for surgery	Ballon-expandable (Sapien XT) or self-expanding valves (TricValve) (CAVI) Single valve implantation (76%, 19/25)	12 months	

Study no.	First author, date country	Patients (male: female)	Age	Study design	Inclusion criteria	Intervention	Follow up	Comments
						Bicaval valve implantation (24%, 6/25) Balloon-expandable valves (Sapien XT or Sapien 3: 78.3%,17/31) Self-expandable valves (TricValve: 21.7%, 7/31; Directflow valve: 4%, 1/31)		
4	Estévez-Loureiro R, 2022 Spain and Austria (12 centres)	N=35 patients with right heart failure had 70 valves implanted (6:29)	Mean age: 76 years	Non-randomised study (TRICUS EURO study)	Adult individuals with symptomatic severe TR (grade ≥3 in a 5-grade classification) despite OMT. Symptoms and signs of right heart failure and NYHA functional class 3 or 4 within	CAVI with TricValve (2 self-expand-ing valves specifically designed for the SVC and IVC)	6 months	

Study no.	First author, date country	Patients (male: female)	Age	Study design	Inclusion criteria	Intervention	Follow up	Comments
					8 weeks before implantation, with echocardiography showing backflow in the IVC and/or SVC and a tricuspid v- wave in the right heart catheterisation ≥ 25 mm Hg			
5	Wild MG, 2022 Switzerland	N=21 high-risk patients (7:14)	Mean age: 76 years	Multicentre registry	Patients with symptomatic severe TR and advanced right heart failure, ineligible for surgery or other transcatheter treatment systems	CAVI with TRICENTO implant that consists of a stent graft that extends from the IVC to the SVC	12 months	
6	O'Neill BP, 2020 United States	N=24 patients had 23 valves implanted (9:15)	Median age: 79.5 years (range, 49-91 years)	Multicentre registry	Patients with symptomatic TR and poor candidates for surgical tricuspid valve intervention as per local heart team discretion	CAVI with implant in IVC only using a single valve (Sapien 3 valve)	350 days	

Study no.	First author, date country	Patients (male: female)	Age	Study design	Inclusion criteria	Intervention	Follow up	Comments
7	Wilbring M, 2020 Germany	N=2 patients (2:0)	Ages 74 and 83 years	Case report	Patients with symptomatic severe TR	CAVI with Tricento transcatheter heart valve system	3 months	The radial force of the stent graft seemed to decrease and thus it is not sufficient after 3 months to keep the stent completely open during systole

Table 3 Study outcomes

First author, date	Efficacy outcomes	Safety outcomes
Dreger H, 2022	**Clinical outcomes** **NYHA functional class (12-month follow up)** NYHA class, ±SD: −0.6±0.5* (CAVI group, p=0.401) and −0.3±0.9 (OMT group, p=0.401) (p=0.025 versus baseline) Improved by 2 classes: 0 (CAVI group) and 0 (OMT group) Improved by 1 class: 5 (63%, CAVI group) and 5 (46%, OMT group)	**Periprocedural complications after CAVI** (resulting in open heart surgery): n=4 2 stent migration leading to cardiac tamponades 2 valve dislocations **Mortality** In-hospital mortality: CAVI group 21% (3/14) 12-month follow up: CAVI group 57% (n=8, including 4 after conversion to surgery) versus

First author, date	Efficacy outcomes	Safety outcomes
	Unchanged: 3 (38%, CAVI group) and 5 (46%, OMT group) Worsened by 1 class: 0 (CAVI group) and 0 (OMT group) Worsened by 2 classes: 0 (CAVI group) and 1 (9%, OMT group) **Exercise capacity** (measured by quantifying maximal oxygen uptake by treadmill spiroergometry at 3 months) primary outcome. VO_{2max}, ml·kg^{-1}·min^{-1}±SD: −1.0±1.6 (CAVI group, p=0.494) and −0.1±1.8 (OMT group, p=0.299) **SMWD** (mean±SD): 18.9±47.0 (CAVI group, p=0.494) and −2.8±71.3 (OMT group, p=0.299) **Quality of life** (assessed by the MLHFQ) MLHFQ, ±SD: CAVI group −19.9±13.1 versus OMT group −7.6±16.3 (p=0.098) and p=0.004 versus baseline **Dyspnoea** (Likert scale±SD) CAVI group 1.5±1.1 versus OMT group −0.2±1.3 (p=0.008)	OMT group 29% (n=4, from right heart failure, sepsis or haemorrhage) p=0.159 Right heart failure: CAVI group n=4 versus OMT group n=3 Sepsis: CAVI group n=3 versus OMT group n=1 Haemorrhage: CAVI group n=1 versus OMT group 0 Heart failure hospitalisations: CAVI group n=4 versus OMT group n=4 (p=1.00)
Hewing, 2021	**Clinical signs of venous congestion** **Bodyweight, kg±SD**	**Major complications** Valve dislocations: n=2 (CAVI group) Stent migrations: n=2 (CAVI group)

First author, date	Efficacy outcomes	Safety outcomes
	Baseline: CAVI group 74.6±12.1 versus OMT group 68.4±12.8 12 months: CAVI group 72.6±16.3 versus OMT group 70.7±13.0. **Abdominal circumference, cm±SD** Baseline: CAVI group 97.3±10.8 versus OMT group 97.3±10.3 12 months: CAVI group 96.2±13.2 versus OMT group 98.0±11.6 **Total lower leg circumference, cm (IQR)** Baseline: CAVI group 73.5 (61.3–76.3) versus OMT group 60.5 (54.8–66.6) 12 months: CAVI group 61.5 (48.5–76.5) versus OMT group 56.5 (49.0–66.8) **Renal and hepatic parameters** **Serum creatinine, mg/dl±SD** Baseline: CAVI group 1.6±0.6 versus OMT group 1.4±0.4 3 months: CAVI group 1.5±0.5 versus OMT group 1.7±0.7 **GFR (creatinine), ml/min (IQR)** Baseline: CAVI group 36.5 (24.5–62.8) versus OMT group 46.5 (30.0–56.0) 3 months: CAVI group 35.5 (28.0–60.8) versus OMT group 36.5 (23.5–58.8) **Urea, mg/dl (IQR)**	All occurred within 7 to 48 hours after implantation and needed open heart surgery to treat these major complications

First author, date	Efficacy outcomes	Safety outcomes
	Baseline: CAVI group 81.5 (40.8–144.8) versus OMT group 73.5 (47.8–150.8) 3 months: CAVI group 35.5 (28.0–60.8) versus OMT group 63.5 (46.8–124.8) **ALT, U/l (IQR)** Baseline: CAVI group 29.0 (15.0–31.3) versus OMT group 17.0 (13.8–34.3) 12 months: CAVI group 16.5 (11.5–22.8) versus OMT group 20.5 (17.0–27.8) **AST, U/l±SD** Baseline: CAVI group 30.0±6.6 versus OMT group 29.5±9.6 12 months: CAVI group 27.7±7.7 versus OMT group 31.7±8.0 **Gamma-GT, U/l (IQR)** Baseline: CAVI group 64.0 (51.0–116.0) versus OMT group 226.0 (86.0–872.0) (n=5) 12 months: CAVI group 65.0 (55.3–105.5) versus OMT group 166.0 (64.5–248.0) (n=5) **Bilirubin, mg/l (IQR)** Baseline: CAVI group 0.7 (0.4–0.9) versus OMT group 0.8 (0.7–1.0) 12 months: CAVI group 0.5 (0.4–0.7) versus OMT group 0.8 (0.6–1.3)	
Lauten A, 2018	Procedural success rate: n=23/25 (92%) **NYHA Functional Class (n)**	IVC prosthesis migration from the stent into the right atrium: n=1 Early and late valve migration needing surgical intervention occurred: n=1

First author, date	Efficacy outcomes	Safety outcomes
	class 4: 63.2 (12, baseline) and 10.5 (2, post-CAVI) Class 3: 36.8 (7, baseline) and 36.8 (7, post-CAVI) Class 2: 0 and 42.2 (8, post-CAVI) Class 1: 0 and 10.5 (2, post-CAVI) p<0.0001 NYHA improvement: 50% improving to NYHA class 1 or 2 <u>Right atrial pressure</u> Baseline: Mean 21.2±6.0 mm Hg and v-wave 29.5±7.1 mm Hg Post-CAVI: Mean 17.0±3.9 mm Hg (p=0.02) and v-wave 35.5±13.1 mm Hg (p=0.07). <u>IVC pressure</u> Baseline: Mean 21.7±4.3 mm Hg and v-wave 31.4±6.4 mm Hg Post-CAVI: Mean 17.6±3.3 mm Hg (p=0.01) and v-wave 21.1±4.5 mm Hg (p<0.0001)	Conversion to open heart surgery after migration of an SVC prosthesis: n=1 Device embolisation: 8% (2/25) Bleeding complications other than access site: 12% (3/25) In-hospital mortality: 24% (6/25) Thirty-day mortality: 12% (3/25)
Estévez-Loureiro R, 2022 TRICUS EURO study	Procedural success rate 94% **NYHA Functional Class (primary outcome)** Baseline (n=35): NYHA class 1-2: 0%, class 3: 82.9%, class 4: 17.1% 30-day (n=30):	**Overall major adverse cardiovascular events:** In-hospital mortality: 1 (2.8%) Procedural mortality 0 Mortality at 6 months: 8.5% Stroke: 5.7% Major bleeding: 17.1%

First author, date	Efficacy outcomes	Safety outcomes
	NYHA class 1-2: 50%, class 3: 50%, class 4: 0% (p=0.005) 3-month (n=31): NYHA class 1-2: 61.3%, class 3: 38.7%, class 4: 0% (p=0.005) 6-month (n=29): NYHA class 1-2: 79.4%, class 3: 20.6%, class 4: 0% (p=0.0006) **6MWD** **6MWD ±SD** Baseline (n=35): 244.96±85.96 30-days (n=23): 261.65±93.06 3-months (n=23): 262.48±114.09 6-months (n=27): 276.13±90 (p=0.462) Large improvements in 6MWD (>40 m) were evident in 24.1% of patients **Quality of life (primary outcome)** **KCCQ12±SD** Baseline (n=35): 42.01±22.3 30-days (n=29): 58.59±26.06 3-months (n=31): 56.5±23.59 6-months (n=30): 59.7±23.6 (p=0.0004) CT scan analyses at 3 months showed integrity of the leaflets and valve stents	Heart failure hospitalisation readmission rate was 20% (7/35) Transient shoulder pain（likely related to IVC prosthesis compression over the phrenic nerve): 28.5%

First author, date	Efficacy outcomes	Safety outcomes
	Echo analysis at 6 months showed absence of right chamber dilatation or significant RV function deterioration	
Wild MG, 2022	Procedural success rate 100% **NYHA functional class** **Baseline** NYHA class 1:4.8%, class 2: 85.7%, class 3: 9.5%; class 4: 0 **Follow up (median 61 days)** NYHA class 1: 30%, class 2: 35%, class 3: 30%, class 4: 5% (p<0.001)	Vascular complications, needing blood transfusion: 19% (n=4) Postprocedural acute kidney injury (stage 1 in 2, stage 2 and stage 3 in 1 case each): n=4 Temporary dialysis in a patient with previous impaired renal function: n=1 Systemic inflammatory syndrome of unclear origin with hypotension: n=1
O'Neill BP, 2020	**NYHA functional class** Baseline NYHA class 3 or 4: 95.9% 1 year follow up: Improvement in NYHA class: 78% Improvement in at least 1 NYHA class: 72.7% Worsened NYHA class: 9.1%	Procedural mortality rate: 0% In-hospital mortality rate: 20.8% 30-day mortality rate: 25% Overall mortality rate: 58% (14/24) at median follow up of 332 days (range, 2-1161 days) Vascular complication rate: 4.2% Acute renal failure rate: 20.8%
Wilbring M, 2020	None reported	Recurrent episodes of right heart failure: n=2 Systolic collapse: n=2

Procedure technique

All studies detailed their procedure technique with variations in the intervention implanted. One approach was CAVI with the balloon-expandable Edwards Sapien XT Valve (TRICAVAL) in patients with advanced heart failure (Dreger 2022). Another study used single and bicaval implantations with balloon-expandable (Sapien XT or Sapien 3) and self-expandable (TricValve) valves (Lauten, 2018). The TRICUS EURO study used only the TricValve transcatheter bicaval valves system (Estévez-Loureiro 2022). One study used the TRICENTO system (transcatheter bicaval valved stent graft) (Wild 2022). This device is no longer being manufactured.

Efficacy

NYHA functional class

In an RCT of 28 patients comparing CAVI with OMT in patients with severe TR, compared with baseline, CAVI improved NYHA class after 3 months. But there was no statistically significant difference in NYHA class between the CAVI and OMT groups (−0.3±0.9 compared with −0.6±0.5, p=0.401; Dreger 2022).

In an observational study of 25 patients who had CAVI (31 implanted valves, 13 out of 18 patients had NYHA improvement (p<0.0001). In patients discharged from hospital, CAVI was associated with a symptomatic improvement in 50.2% of patients improving to NYHA class 1 or 2 (Lauten 2018).

In a prospective non-randomised study of 35 patients, patients who had CAVI had statistically significant improvements in NYHA functional class at 6-month follow up compared with baseline (Class 3: 82.9% and class 4: 17.1% at baseline compared with class 1 to 2: 79.4% and class 3: 20.6% at 6-month, p=0.0006; Estévez-Loureiro 2022).

In a multicentre registry of 21 patients who had CAVI with the TRICENTO system, two-thirds of patients remained in NYHA class 1 or 2 at 12-month- follow up (65%, n=13; p<0.001; Wild 2022).

In a multicentre registry of 24 patients who had CAVI with a IVC implant using a single valve, 73% of patients had improvement in at least 1 NYHA class from baseline and 9% were considered worse at follow up compared with baseline (O'Neill 2020).

Quality of life

In the prospective non-randomised study of 35 patients, patients who had CAVI had statistically significant increases in quality of life (assessed using KCCQ12)

at 6-month follow up compared with baseline (42.01±22.3 at baseline compared with 59.7±23.6 at 6 month, p=0.0004; Estévez-Loureiro 2022).

In the RCT of 28 patients, compared with baseline, quality of life (assessed using MLHFQ) improved after 3 months in the CAVI group but not statistically significantly (MLHFQ: −19.9±13.1 compared with −7.6±16.3, p=0.098; Dreger 2022).

6MWD

In the RCT of 28 patients, there was no statistically significant difference in the secondary endpoint, the 6MWD, between CAVI and OMT groups (−2.8±71.3 compared with 18.9±47.0, p=0.494; Dreger 2022).

In the prospective non-randomised study of 35 patients, patients who had with CAVI had an increase in 6MWD at 6-month follow up compared with baseline but it was not statistically significant (244.96±85.96 at baseline compared with 276.13±90 at 6 months, p=0.462). But large improvements in 6MWD (>40 m) were evident in 24.1% of patients (Estévez-Loureiro 2022).

Maximal oxygen uptake

In the RCT of 28 patients, maximal oxygen uptake did not change statistically significantly in either group after 3 months, and there was no difference between the OMT and CAVI groups (−0.1±1.8 ml·kg^{-1} min−^{1} compared with −1.0±1.6 ml·kg^{-1} min−^{1}, p=0.4995; Dreger 2022).

Dyspnoea

In the RCT of 28 patients, compared with baseline, dyspnoea statistically significantly improved after 3 months in the CAVI group (1.5±1.1 compared with −0.2±1.3, p=0.008; Dreger 2022).

Clinical signs of venous congestion

In an RCT of 18 patients comparing CAVI (n=8) with OMT (n=10) in patients with severe TR, after 12 months, 6 patients in the CAVI group, who completed 12 months of follow up, showed a sustained trend to lower body weight as well as reduced abdominal and leg circumference. But, overall, no statistically significant intra- or intergroup difference about clinical signs of congestion were detected (Hewing 2021).

Renal and hepatic parameters

In a subgroup analysis of the RCT of 18 patients, there was no statistically significant change in levels of laboratory parameters including serum creatinine,

cystatin C, urea, serum protein, serum albumin as well as calculated GFR (based on creatinine and cystatin C) between baseline and 3-month follow up within each group. Also, there was no statistically significant difference in these parameters between the groups at 3-month follow up (Hewing 2021).

In the subgroup analysis of the RCT of 18 patients, in the CAVI group, liver function as measured by ALT, AST, gamma-GT and bilirubin remained stable after 3 and 12 months compared with baseline. Also, there was no statistically significant difference in these parameters between the groups at 3- and 12-month follow up (Hewing 2021).

Safety

Complications

Mortality

In the RCT of 28 patients, there was no statistically significant difference in mortality rate between the groups at 12-month follow up (CAVI 57%, n=8 [including 4 after conversion to surgery] compared with OMT 29%, n=4 [from right heart failure, sepsis or haemorrhage], p=0.159; Dreger 2022).

In the observational study of 25 patients,30-day mortality was 12% (3/25). The patients died from progressive multiorgan failure and septic complications (Lauten 2018).

In the multicentre registry of 24 patients, the in-hospital mortality rate (defined as death in the hospital after the procedure) was 21% and the 30-day mortality rate was 25%. Overall mortality occurred in 58% (14/24) patients during a median follow up of 332 days (range, 2-1161 days; O'Neill 2020).

Other major complications

In the RCT of 28 patients, there were2 major complications in the CAVI group within 7 to 48 hours after implantation. These included 2 valve dislocations and 2 stent migrations leading to cardiac tamponades. All patients needed open heart surgery for removal of dislocated valves and migrated stents (Dreger 2020, Hewing 2021). There were 4 heart failure hospitalisations in each of the groups (p=1.00). Sepsis (n=3) and haemorrhage (n=1) were also reported in the CAVI group (Dreger 2020).

In the prospective non-randomised study of 35 patients, major bleeding occurred in 17% of patients. The heart failure hospitalisation readmission rate was 20% (7/35), all of them mainly right heart failure, and mostly related to respiratory infections or renal function deterioration in a population with high comorbidity burden (Estévez-Loureiro 2022).

In the multicentre registry of 21 patients, vascular complications and postprocedural acute kidney injury occurred in 4 cases for each complication (Wild 2022).

In a case report of 2 patients using the TRICENTO transcatheter heart valve system, within the first 3 months, both patients developed recurrent signs of right heart failure despite sufficient function of the ectopic tricuspid valve system. Also, MRI scans of the heart revealed a nearly complete systolic compression of the stent graft at the level of the right atrium in both patients (Wilbring 2020).

Anecdotal and theoretical adverse events

Expert advice was sought from consultants who have been nominated or ratified by their professional society or royal college. They were asked if they knew of any other adverse events for this procedure that they had heard about (anecdotal), which were not reported in the literature. They were also asked if they thought there were other adverse events that might possibly occur, even if they had never happened (theoretical).

They suggested a theoretical adverse event of rhythm disturbance and conversion to open surgery (sternotomy and tricuspid valve repair).

Seven professional expert questionnaires for this procedure were submitted. Find full details of what the professional experts said about the procedure in the specialist advice questionnaires for this procedure.

Validity and generalisability

- One small RCT compared CAVI to optimal medical therapy.
- Follow up in studies ranged from 6 months to 12 months.
- Studies included patients with symptomatic severe TR that was ineligible for surgery.
- Studies on CAVI varied in terms of the approach (unicaval and bicaval), number of implants and the type of implant (self-expandable or balloon-expandable) being used.
- CAVI with balloon-expandable valves (Edwards Sapien XT or Sapien 3) has been done under compassionate clinical use.
- The company producing a dedicated CAVI device currently in clinical use (TRICENTO) are no longer manufacturing this device.

- A CE mark study (NCT04289870) is underway for another device (TILLIUM device).
- The title of this topic has been amended as ‘caval valve implantation for tricuspid regurgitation’ to cover both unicaval and bicaval valve implantations.

Related NICE guidance

Interventional procedures

- NICE interventional procedures guidance on Transcatheter tricuspid valve annuloplasty for tricuspid regurgitation IPG730 (Recommendation: special arrangements) Published date: July 2022.
- NICE interventional procedures guidance on Transcatheter tricuspid valve leaflet repair for tricuspid regurgitation IPG731 (Recommendation: special arrangements) Published date: July 2022.

NICE guidelines

- NICE guideline on Heart valve disease presenting in adults: investigation and management [NG208] Published date: November 2021
- NICE guideline on Chronic heart failure in adults: diagnosis and management. [NG106] Published date: September 2018

Professional societies

- Society of 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.

Company engagement

NICE asked 2 companies who manufacture a device potentially relevant to this procedure for information on it. NICE received 1 completed submission. This was considered by the interventional procedures team and any relevant points have been taken into consideration when preparing this overview.

References

1. Dreger H, Mattig I, Hewing B, Knebel F et al. (2020) Treatment of severe tricuspid regurgitation in patients with advanced heart failure with caval vein implantation of the Edwards Sapien XT VALve (TRICAVAL): a randomised controlled trial. EuroIntervention 15: 1506–13
2. Hewing B, Mattig I, Knebel F et al. (2021) Renal and hepatic function of patients with severe tricuspid regurgitation undergoing inferior caval valve implantation. Sci Rep 8;11(1): 21800
3. Lauten A, Figulla HR, Unbehaun A et al. (2018) Interventional treatment of severe tricuspid regurgitation: early clinical experience in a multicenter, observational, first-in-man study. Circ Cardiovasc Interv 11: e006061
4. Estévez-Loureiro R, Sanchez-Recalde A, Amat-Santos IJ et al. (2022) 6-month outcomes of the TricValve system in patients with tricuspid regurgitation: the TRICUS EURO study. J Am Coll Cardiol Int 15: 1366–77
5. Wild MG, Lubos E, Cruz-Gonzalez I et al. (2022) Early clinical experience with the TRICENTO bicaval valved stent for treatment of symptomatic severe tricuspid regurgitation: a multicenter registry. Circ Cardiovasc Interv 15: e011302
6. O'Neill B, Negrotto S, Yu D et al. (2020) Cava valve implantation for tricuspid regurgitation: insights from the United States caval valve registry. J Invasive Cardiol 32:470–5
7. Wilbring M, Tomala J, Ulbrich S et al. (2020) Recurrence of right heart failure after heterotopic tricuspid intervention: a conceptual misunderstanding? JACC Cardiovasc Interv 13: e95–6

Methods

NICE identified studies and reviews relevant to CAVI for TR from the medical literature. The following databases were searched between the date they started to 13.10.2023: MEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the internet were also searched (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 following inclusion criteria were applied to the abstracts identified by the literature search.

- Publication type: clinical studies were included with emphasis on identifying good quality studies. Abstracts were excluded if they did not report clinical outcomes. Reviews, editorials, and laboratory or animal studies, were also excluded and so were conference abstracts, because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
- Patients with CAVI.
- Intervention or test: TR.
- Outcome: articles were retrieved if the abstract contained information relevant to the safety, efficacy or both.

If selection criteria could not be determined from the abstracts the full paper was retrieved.

Potentially relevant studies not included in the main evidence summary are listed in the section on other relevant studies.

Find out more about how NICE selects the evidence for the committee.

Table 4 literature search strategy

Databases	Date searched	Version/files
MEDLINE ALL (Ovid)	13/10/2023	1946 to October 12, 2023
EMBASE (Ovid)	13/10/2023	1974 to 2023 October 13
EMBASE Conference (Ovid)	13/10/2023	1974 to 2023 October 13
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	13/10/2023	Issue 10 of 12, October 2023

Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	13/10/2023	Issue 10 of 12, October 2023
International HTA database (INAHTA)	13/10/2023	-

Trial sources searched 04/07/2023

- 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.

MEDLINE search strategy

Tricuspid Valve Insufficiency/
((Tricuspid or right atrioventricul*) adj4 (reflux or 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* or defect*)).tw.
(TR or FTR).tw.
(Caval adj4 (reflux* or insufficien* or incompeten* or regurgitat* or disease* or dysfunct* or malfunct* or degenerat* or fail* or leak* or backflow* or back-flow or defect*)).tw.
Right* side* heart* failur*.tw.
(Function* adj tricusp* adj regurgitat*).tw.
or/1-6
(Transcathet* adj4 tricuspid adj4 valve* adj4 (implant* or Intervent* or device* or intervene* or therap* or solut*)).tw.
((Heart* or Cardiac* or Caval* or Bivalve*) adj4 valve* adj4 Implant*).tw.

(CAVI or CAVR).tw.
transcathet* tricuspid valve intervent*.tw.
TTVIs.tw.
((Bicaval or tricaval) adj4 implant*).tw.

(((Percutan* adj4 tricuspid) or Bicuspid*) adj4 valve* adj4 (device* or interven* or therap* or implant* or solution*)).tw.
or/8-14
7 and 15
Tricvalve.tw.
TriCentro.tw.
17 or 18
16 or 19
Animals/ not Humans/
20 not 21
limit 22 to english language

Other relevant studies

Other potentially relevant studies to the interventional procedures overview that were not included in the main evidence summary (tables 2 and 3) are listed in table 5.

Table 5 additional studies identified

Article	Number of patients and follow up	Direction of conclusions	Reason study was not included in main evidence summary
Aalaei-Andabili SH, Bavry AA, Choi C et al. (2020) Percutaneous inferior vena cava valve implantation may improve tricuspid valve regurgitation and cardiac output: lessons learned. Innovations 15: 577–80	Case series N=6 patients who could not be operated on with severe TR who failed medical treatment had percutaneous CAVI with 9-mm SAPIEN 3 valve	The procedure was successfully performed in all 6 patients (100%). No procedural complication was detected. At 30 days, TR improved from severe to trace in 1 patient, to mild-moderate in 3 patients, and 2 patients remained with severe TR. Among patients with improved TR, left ventricular ejection fraction increased from 47.5%±18.5% to 55%±20.4% (p=0.014). No patient had readmission at 30 days. Four patients needed rehospitalisation within 6 months.	Large studies with longer follow up included in evidence summary
Abdul-Jawad Altisent O, and Estévez-Loureiro R (2022) Heterotopic transcatheter tricuspid valve implantation. a promising technology for patients with high-risk TR.	Review	Heterotopic CAVI is a promising technology for patients with high-risk TR and limited treatment options. There are several devices under study, the TricValve gained widespread adoption. The TRICUS EURO study showed a positive effect in clinical outcomes and quality of life.	Review

CARDIAC INTERVENTIONS TODAY 16 (5): 56–66			
Abdul-Jawad Altisent O, Benetis R, Rumbinaite E et al. (2021) Caval valve implantation (CAVI): an emerging therapy for treating severe tricuspid regurgitation. J Clin Med 10: 4601	Review on CAVI technique	In this review, the current evidence and ongoing uncertainties of CAVI, focusing on the novel CAVI-specific devices was discussed.	Review
Abdul-Jawad Altisent O, Codina P, Puri R et al. (2022) Transcatheter bi-caval valve implantation (CAVI) significantly improves cardiac output: mechanistic insights following CardioMEMS® and TricValve® implantation. Clin Res Cardiol 111: 966–8			No abstract provided
Aparisi Á, Amat-Santos IJ, Serrador A et al. (2020) Current clinical outcomes of tricuspid regurgitation and initial experience with	Case report N=2 patients had CAVI with Tricento and with TricValve	Assessment of potential prognostic benefit by bicavally implanted heterotopic prosthesis needs longer-term studies, but initial experience suggests safe and effective procedural and short-term outcomes.	Large studies with longer follow up included in evidence summary

the TricValve system in Spain. Rev Esp Cardiol 73: 853–4			
Asmarats L, Puri R, Latib A et al. (2018) Transcatheter tricuspid valve interventions: landscape, challenges, and future directions. Journal of the American College of Cardiology 71, 25: 2935–56	Review	The aim of this review is to provide an updated overview and a clinical perspective on novel transcatheter tricuspid valve therapies, highlighting potential challenges and future directions.	Review
Chandran K, Long A, Bishop J, Berman P et al. (2023) First in-man experience with TricValve transcatheter bicaval valve system in left ventricular assist device Heartmate II patient for high-risk tricuspid regurgitation. Circ Heart Fail 16(6): e010027	Case report An 80-year-old patient with severe TR and HeartMate had TricValve bicaval valve implantation	Patient reported a significant improvement in her symptoms to NYHA class I to II. She has felt an improvement in her quality of life with rare lower extremity oedema.	Large studies with longer follow up included in evidence summary
Datta R, Bharadwaj P, Keshavamurthy G et al. (2023) Caval valve implantation: First of its kind in a rare environment. Medical Journal	Case report N=1 76-year-old lady with severe TR and recurrent right heart failure had CAVI with TricValve in SVC and IVC	Significant haemodynamic and clinical improvement has been noted in this patient at 3-month follow up.	Large studies with longer follow up included in evidence summary

Armed Forces India. Online 8 February			
Dona C, Goliasch G, Schneider M et al. (2020) Transcatheter TricValve implantation for the treatment of severe tricuspid regurgitation. European Heart Journal - Cardiovascular Imaging online E92	Case report 78-year-old patient with heart failure and TR had transcatheter TricValve implantation	The valves were successfully deployed. The patient was discharged 3 days after the procedure. At 3 months, her symptoms and exercise capacity had significantly improved. On transthoracic echocardiogram, TR had decreased from torrential to mild-to-moderate.	Large studies with longer follow up included in evidence summary
Figulla HR, Kiss K, Lauten A (2016) Transcatheter interventions for tricuspid regurgitation - heterotopic technology: TricValve. EuroIntervention 18;12(Y): Y116–8	Review of concept	CAVI with the TricValve is a relatively simple procedure. However, valve design must cover a great range of caval vein anatomy. The haemodynamic concept is convincing and allows the RV to recover. Clinical experience is presently restricted to compassionate cases.	Review
Galasso M, Cartella I, Soriano F et al. (2023) Bi-caval valve implantation to palliate symptoms in a case of massive tricuspid regurgitation. Cardiovasc Revasc Med53S: S139–S143	Case report N=69-year-old man with significant TR and advanced heart failure without surgical options had heterotopic CAVI with TricValve	At 3-months follow up, the patient was alive and an improvement in functional status and heart failure symptoms (NYHA class II) noted. Renal and liver function did not worsen while a significant reduction of loop diuretic dosage was possible.	Large studies with longer follow up included in evidence summary
Cruz-González I, González-	Case series	Device was successfully deployed in all without any	Large studies with longer

Ferreiro R, Amat-Santos IJ et al. (2021) TRICENTO transcatheter heart valve for severe tricuspid regurgitation. Initial experience and mid-term follow-up. Rev Esp Cardiol 74: 351–4	N=6 patients with congestive heart failure had TRICENTO valve implantation for severe functional TR	major complications. During follow up (11±4.4 months), all patients showed NYHA functional class improvement (class I-II). No patients died. One patient was admitted with acute decompensation of heart failure (41 days after the procedure).	follow up included in evidence summary
Grazina A, Ferreira A, Ramos R et al. (2023) Heterotopic caval valve-in-valve procedure for prosthetic migration: two case reports. European Heart Journal - Case Reports, 7 (8), 1–7	Case report N=2 patients with severe TR and high surgical risk who had CAVI, and device migration to the right atrium (1 IVC and 1 SVC device) had treatment with a caval valve-in-valve procedure.	Both cases reported good technical and clinical results.	Caval valve-in-valve-study
Jin QW, Mohd Ghazi AB, Kolanthaivelu J et al. (2022) Novel treatment of atrial functional tricuspid regurgitation using transcatheter bicaval valve implantation (TricValve). Asia Intervention 6;8(2): 138–42	Case report N=67-year-old woman with underlying atrial fibrillation and severe TR had CAVI with TricValve	The procedure was uneventful and the patient was discharged. At 3-month follow up, there was marked improvement clinically and biochemically.	Large studies with longer follow up included in evidence summary
Kultursay B, Bingol G, Guven B et al. (2022)	Case report	At the time of deployment, the IVC valve migrated into the right atrium. There was	Large studies with longer follow up

TricValve pop-out: management of transcatheter caval valve migration. Anatol J Cardiol 26: 414–8		no hemodynamical worsening after migration of the valve. Deployment of another IVC valve protruding into the right atrium and overlapping the popped-out valve was done. After successful deployment of the second IVC valve, no paravalvular leak or caval backflow was seen. Significant improvement in functional capacity was seen at 3-months follow up.	included in evidence summary
Lauten A, Ferrari M, Hekmat K et al. (2011) Heterotopic transcatheter tricuspid valve implantation: first-in man application of a novel approach to tricuspid regurgitation. Eur Heart J 32: 1207–13	Case report N=1 patient with severe functional TR after multiple preceding open heart procedures, a self-expanding valve was implanted into the IVC at the cavoatrial junction to reduce regurgitant backflow	Excellent valve function was seen after deployment resulted in a marked reduction of caval pressure and an abolition of backflow to the IVC.	Large studies with longer follow up included in evidence summary
Lauten A, Hamadanchi A, Doenst T et al. (2014) Caval valve implantation for treatment of tricuspid regurgitation: post-mortem evaluation after mid-term follow-up. Eur Heart J 35: 1651	Case report N=1 patient with severe functional TR after multiple preceding open heart procedures, a self-expanding valve was implanted into the IVC at the cavoatrial junction to reduce regurgitant backflow	Successfully deployed and a marked reduction of caval pressure and an abolition of backflow to the IVC was noted. The patient was discharged home and had an improvement of physical capacity and symptoms of right heart failure within the 3-month follow-up period.	Large studies with longer follow up included in evidence summary
Lauten A, Dreger H, Laule M et al. (2022) Caval valve implantation.	Review on current evidence for CAVI and potential role for treatment of TR	CAVI was applied successfully for compassionate treatment in human patients. Haemodynamic	Review

Intervent Cardiol Clin 11: 95–102		improvement has been consistently seen; the clinical benefit of the procedure still needs further evaluation. It remains to be determined which patients benefit most from this approach and which outcome measures are most suitable.	
Laule M, Stangl V, Sanad W et al. (2013) Percutaneous transfemoral management of severe secondary tricuspid regurgitation with Edwards Sapien XT bioprosthesis: first-in-man experience. J Am Coll Cardiol 61: 1929–31	Case series N=3 patients with severe functional TR had treatment with IVC caval implantation (balloon-expandable valves Edwards Sapien XT valve)		Large studies with longer follow up included in evidence summary
O'Neill BP, Wheatley G, Bashir R et al. (2016) Study design and rationale of the heterotopic implantation of the Edwards Sapien XT transcatheter valve in the inferior vena cava for the treatment of severe tricuspid regurgitation (HOVER) Trial. Catheterization and Cardiovascular	Prospective non-randomised study. Heterotopic implantation of the Sapien XT valve in the IVC for the treatment of severe TR in patients who are at high risk or cannot be operated on	A total of 30 patients will be enrolled. The primary objective of the study will be to show procedural success at 30-days and patient success at 1-year.	Study design and rationale

Interventions 88: 287–93			
Romaguera R, Roura G, Ruiz-Majoral A et al. (2021) First bicaval valve implantation in a heart transplant patient to treat severe symptomatic tricuspid regurgitation. Circulation: Heart Failure 14,1278–9	Case report N=1 patient (67-year-old) with severe TR and RV dysfunction had a bicaval valve (TricValve) implantation	At 6-months follow up, functional status improved to NYHA class II, and the diuretic treatment was tapered without heart failure recurrence. Similar RV dysfunction and absence of systolic reverse flow to cava veins noted.	Large studies with longer follow up included in evidence summary
Sharkey A, Munoz Acuna R, Belani K et al. (2020) Heterotopic caval valve implantation for the management of severe tricuspid regurgitation: a case series. Eur Heart J Case Rep; 5: ytaa428	Case report N=2 patients with severe TR with symptoms of heart failure refractory to medical therapy had heterotopic CAVI with Edwards SAPIEN 3 valve	Valve was implanted in the IVC/right atrium junction. In both patients, there was improvement in the postoperative haemodynamics as measured by invasive and non-invasive methods. Successful discharge was achieved in both patients with improvement in their symptoms.	Large studies with longer follow up included in evidence summary
Sharma NK, Chouhan NS, Bansal M et al. (2021) Heterotopic caval valve implantation in severe tricuspid regurgitation. Ann Card Anaesth 2021 Jul-Sep;24(3):365–8	Case report N=1 patient with previous mitral valve surgery with chronic severe TR who had CAVI with self-expandable TricValve in SVC	The procedure was successful. The procedure resulted in significant haemodynamic and symptomatic improvement at 3-month follow up.	Large studies with longer follow up included in evidence summary
Toggweiler S, De Boeck B, Brinkert M et al.	Case report	Following successful implantation, caval vein regurgitant volume was	Large studies with longer follow up

(2018) First-in-man implantation of the Tricento transcatheter heart valve for the treatment of severe tricuspid regurgitation. EuroIntervention 2018; 14: 758–61	N=1 patient with severe TR and holosystolic hepatic vein backflow had Tricento transcatheter heart valve implantation via the transvenous transfemoral access	reduced leading to symptomatic and clinical improvement at 3-month follow up.	included in evidence summary