



## Monaldi Archives for Chest Disease

eISSN 2532-5264

<https://www.monaldi-archives.org/>

**Publisher's Disclaimer.** E-publishing ahead of print is increasingly important for the rapid dissemination of science. The **Early Access** service lets users access peer-reviewed articles well before print / regular issue publication, significantly reducing the time it takes for critical findings to reach the research community. These articles are searchable and citable by their DOI (Digital Object Identifier).

The **Monaldi Archives for Chest Disease** is, therefore, e-publishing PDF files of an early version of manuscripts that have undergone a regular peer review and have been accepted for publication, but have not been through the typesetting, pagination and proofreading processes, which may lead to differences between this version and the final one.

The final version of the manuscript will then appear in a regular issue of the journal.

E-publishing of this PDF file has been approved by the authors.

*All legal disclaimers applicable to the journal apply to this production process as well.*

Monaldi Arch Chest Dis 2024 [Online ahead of print]

*To cite this Article:*

Bashir A, Tahir Z, Ahmad M, et al. **A decade's summary of transcatheter tricuspid valve repair.** *Monaldi Arch Chest Dis* doi: 10.4081/monaldi.2024.3029

 ©The Author(s), 2024  
Licensee [PAGEPress](#), Italy

Note: The publisher is not responsible for the content or functionality of any supporting information supplied by the authors. Any queries should be directed to the corresponding author for the article.

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article or claim that may be made by its manufacturer is not guaranteed or endorsed by the publisher.



## **A decade's summary of transcatheter tricuspid valve repair**

Aladdin Bashir,<sup>1</sup> Zaheer Tahir,<sup>2</sup> Mahmood Ahmad,<sup>3</sup> Kyriacos Mouyis,<sup>4</sup> Ali Zuhair Kirresh,<sup>5</sup>  
Sameh Atta,<sup>1</sup> Clinton Lloyd,<sup>1</sup> Malcolm Dalrymple-Hay<sup>1</sup>

<sup>1</sup>University Hospitals Plymouth NHS Trust; <sup>2</sup>Bristol Heart Institute; <sup>3</sup>Royal Free London NHS Foundation Trust; <sup>4</sup>Barts Health NHS Trust, London; <sup>5</sup>Imperial College Healthcare NHS Trust, London, United Kingdom

**Correspondence:** Aladdin Bashir, University Hospitals Plymouth NHS Trust, Plymouth, United Kingdom.

E-mail: aladdin.bashir@outlook.com

**Contributions:** all authors have contributed significantly and all authors agree with the content of the manuscript. All the authors have read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

**Conflict of interest:** the authors declare no conflict of interest

**Ethics approval and consent to participate:** the study protocol was approved by the Audit, Assurance & Effectiveness Team of the University Hospitals of Plymouth. (protocol no. CA\_2021-22-120 dated 17/09/2021)

**Patient consent for publication:** not applicable.

**Funding:** none.

**Availability of data and materials:** the data used to support the findings of this study are available from the corresponding author upon request.

## **Abstract**

Tricuspid regurgitation (TR) is the most common pathology for the tricuspid valve. Moderate to severe TR is associated with morbidity and adverse outcomes. The concept that TR resolves on its own if the underlying disease is successfully treated has proven to be false. Only a few patients with significant TR are deemed suitable for surgery. Given the late presentation of patients with high perioperative risks and substantial perioperative mortality, the development of transcatheter therapies and the experience gained with transcatheter aortic valve implantation operations have turned attention towards treating this challenging group of patients. In this article, we review the treatment options and highlight the role of transcatheter valve therapies in patients with severe TR.

**Key words:** tricuspid regurgitation, valvular heart disease, transcatheter therapy.

## **Introduction**

Tricuspid regurgitation (TR) is the most common form of tricuspid valve (TV) disease. Mild TR is usually benign but moderate to severe TR is associated with significant morbidity and adverse outcomes. The aetiology of TR is subdivided into primary, secondary and isolated TV pathology. The primary TR can be inherited or acquired and accounts for 10% of TR in adults [1]. Secondary TR accounts for approximately 90% of TR and is due to a heterogeneous group of aetiologies that result in right atrial (RA) or right ventricular (RV) dilatation. This leads to annular dilatation and tethering of TV leaflets [2]. Isolated TR can occur in atrial fibrillation (AF) in the absence of left or right-sided heart disease (Figure 1) [3].

The most common presentation of TR is secondary to cardiac valvular pathology, commonly mitral valve (MV) disease. Despite Braunwald and others [4], in an earlier era recommended against concomitant MV and TV surgery, the importance of late TR has become clear. The associated pulmonary hypertension (PH) leads to RV dilatation, and consequently TV annular dilatation resulting in significant functional tricuspid regurgitation (fTR).

Echocardiographic studies have suggested the incidence of at least moderate TR in patients with rheumatic MV disease to exceed 60%. Clinically severe TR is present in 25-33% of patients undergoing surgery for rheumatic MV disease [5,6]. Moderate to severe TR is reported in more than 70% of patients 3 years following surgical repair of ischemic mitral regurgitation (MR) [7].

However, the prevalence of late severe TR of less than 20% in those with concomitant tricuspid annuloplasty at the time of MV surgery [8]. Late severe TR is less common after surgery for degenerative MV disease, with a prevalence of less than 20% at 4 years [9].

There is significant morbidity and mortality as well as financial implications in symptomatic patients with severe TR. Nath et al. found that TR severity is associated with worse survival in men regardless of LVEF or pulmonary artery (PA) pressure [10]. Severe TR is associated with a poor prognosis, independent of age, biventricular systolic function, RV size, and dilation of the inferior vena cava. In a recent large retrospective study, Chorin et al. concluded that even moderate TR is independently associated with increased mortality [11]. One-year mortality rates were 7.7%, 16.8%, 29.5%, and 45.6% for patients with no, mild, moderate, and severe TR respectively. Additionally, the rate of heart failure hospitalization (HFH) is also positively correlated with TR severity [11,12].

Isolated severe TR is often undertreated surgically, given the late presentation of patients at high perioperative risks and substantial perioperative mortality. The development of transcatheter therapies and the experience gained with TAVI operations turned our attention to the TV aiming to help this challenging group of patients. In this article, we review the treatment options and highlight the role of transcatheter valve therapies in patients with severe TR.

## **Methodology**

A search was done in Medline from 2000 to January 2023 using the PubMed interface (((("Tricuspid Valve Prolapse"[Mesh]) OR "Tricuspid Valve Insufficiency"[Mesh])) AND "Heart Valve Prosthesis Implantation"[Mesh]). A total of 1352 papers were found using the reported search. From these, 45 papers provided the best evidence to review topic. Papers were analysed and summarized in the review below.

## **Anatomy**

The TV is the largest of the 4 cardiac valves and can be subdivided into 4 components: the leaflets, papillary muscles, chordal attachments and the annulus. It consists of three leaflets (anterior, septal and posterior) of unequal size and shape. The anterior leaflet is the largest and the septal leaflet is the smallest. The anterior leaflet is predominantly attached to the right ventricular outflow tract, the posterior leaflet to the muscular wall of the right ventricle and the septal leaflet to the septum. During diastole, the anterior and posterior cusps meet to join the smaller septal leaflet. Thus, functionally, the TV acts more like a bicuspid valve.

The TV is one part of a functional system that includes the RA, RV and pulmonary circulation. The sequential contraction and relaxation of these components in conjunction with the flow pattern also serve a major role in valve function. The subvalvular apparatus functions to restrict the limit of upward displacement of the leaflets during systole as well as facilitate the opening of leaflets during diastole. The fibrous structure, called the annulus, provides the support structure for the TV (Figure 2). It separates the RA from the RV. The annulus is less fibrous than other annuli and its shape changes throughout the cardiac cycle. The septal portion of the annulus is fixed and thus dilatation of the annulus occurs primarily at the free wall (Figure 3). There are three groups of papillary muscles that are inserted on the ventricular wall. The chordae tendinae arise from the papillary muscles to fuse with the leaflets.

### **Treatment options**

All symptomatic individuals diagnosed with severe TR should undergo optimal medical therapy, which typically involves diuretic therapy and addressing any underlying heart failure (HF) and PH [13]. The addition of tricuspid repair in the presence of annular dilatation, during left-sided surgery does not increase operative risk and has (potential) benefits of reverse remodeling of the RV and improvement of functional status [14-16].

Reoperation on the TV in cases of persistent TR after MV surgery carries a high risk, mostly due to the late referral and the consequent poor clinical condition of patients. To improve the prognosis of patients with severe TR, earlier intervention should be considered even in asymptomatic patients with features of progressive RV dilatation or decline in RV function. Percutaneous and surgical intervention is contraindicated in patients with severe RV or LV dysfunction and severe PH [17]. Transcatheter tricuspid valve repair (TTVR) is an evolving field aimed at providing treatment options for patients ineligible for surgery.

### **Initial interventions**

The first transcatheter caval valve implantation (CAVI) in humans occurred in 2010 [18] (Figure 4). In 2015, Latib demonstrated the feasibility of performing TTVR under conscious sedation without TEE monitoring using the TriCinch system from 4Tech Cardio Ltd., Galway, Ireland [19]. In 2016, Schueler reported the first direct annuloplasty using the Cardioband device to address severe TR in a high-risk patient. The procedure, guided by fluoroscopy and 3-dimensional transoesophageal echocardiography (TEE), resulted in an improvement in the patient's NYHA functional class [19]. Transthoracic echocardiography conducted before discharge revealed mild-

to-moderate TR and a reduction in inferior vena cava diameters. Additionally, Hahn et al. conducted one of the initial single-center studies [20], reporting outcomes of GATE System implantation (NaviGate Cardiac Structures, Inc., Lake Forest, California) via minimally invasive right thoracotomy under TEE guidance. Despite the small sample size (5 patients) and short-term follow-up, TV replacement led to RV remodeling, increased cardiac output, and improvement in NYHA functional class for most patients.

### **TriValve registry**

The TriValve registry, an international collaboration across multiple centers, was established to explore the utilization of therapies for TV issues and to define treatment criteria. Between January 2014 and December 2016, 106 patients with severe symptomatic TR underwent TTVR in 11 centers spanning Europe, the United States, and Canada. These patients, included in the TriValve registry, were predominantly high-risk individuals with functional aetiology and notably severe central regurgitation, yet without severely impaired RV function.

A considerable portion of the patients in the registry presented with AF and had markedly enlarged tricuspid annuli (anteroseptal diameter  $45.4 \pm 11$  mm) [21]. Moreover, severe leaflet tethering (coaptation depth  $11.9 \pm 5$  mm) was observed among the registry participants. Initial findings indicated that only 62% of patients achieved the desired outcome of successful device implantation with residual TR grade 2+. Nevertheless, patients consistently reported enhanced quality-of-life measures despite achieving only modest reductions in TR. Over time, procedural success rates improved, reaching 80.0% of patients, likely attributable to the learning curve associated with these interventions.

Mid-term data from the TriValve registry affirms that transcatheter interventions for TV are linked to low mortality rates and significant clinical enhancements. Notably, mid-term survival rates were excellent in this cohort of high-risk patients. It was found that greater coaptation depth (>1 cm), indicative of valve tethering, independently correlated with reduced success rates, serving as a robust predictor of mortality during follow-up, even in cases of isolated tricuspid procedures. This underscores the importance of timely intervention to address patients before advanced RV remodeling occurs [22].

## **Device selection**

Many of devices have been developed recently to facilitate TTVR (Table 1). These devices can be divided into 3 main groups: coaptation enhancement devices, annuloplasty devices, valve implantation devices (caval and tricuspid valves). The selection of the appropriate device depends on the severity and the underlying mechanism of TR, severity of PH and RV dysfunction.

### ***Coaptation enhancement devices***

Coaptation enhancement devices are typically advised for treating TR in cases where moderate leaflet tethering and a commissural jet are present, preferably when the coaptation depth measures less than 1 cm. However, a greater coaptation depth (>1 cm) is independently linked to a lower success rate and serves as a strong predictor of mortality during follow-up, even in procedures focusing solely on the TV. These devices fall into two main categories: edge-to-edge devices (such as MitraClip, Pascal) and leaflet coaptation devices (such as TriCinch, FORMA).

Among these, the MitraClip device is the most commonly used and well-known, originally designed for treating MR. Data from the TriValve registry indicate that the MitraClip was employed in 66% of cases. Its popularity stems mainly from prior experience with mitral applications. It functions as a double-armed mechanical clip, grasping and bringing together the leaflets to achieve coaptation. The TriClip, developed as a sibling device of the MitraClip specifically for TTVR, operates similarly, although it requires simultaneous capture of both leaflets, which can be challenging and time-consuming.

A study by Besler et al. shared results of edge-to-edge repair using the TriClip device in 117 patients, with procedural success defined as TR reduction  $\geq 1$  achieved in 81% of cases [23]. The observation that a non-central or non-anteroseptal TR jet is associated with procedural challenges is insightful. It highlights the technical difficulties and less favorable anatomical conditions encountered during clip placements in these positions, particularly posteroseptal and anteroposterior. The correlation between these challenging positions and poorer outcomes underscores the need for careful consideration and perhaps alternative approaches when dealing with non-central/non-anteroseptal TR jets. Clinical outcomes did not significantly differ between patients undergoing combined mitral and tricuspid valve edge-to-edge repair and those undergoing isolated tricuspid repair. Effective TR reduction emerged as the primary predictor for survival and freedom from HFH.

The efficacy of the TriClip device at 6 months was evaluated in the TRILUMINATE trial [24], involving 85 patients. The trial demonstrated significant improvements in clinical parameters, although some adverse events were noted, including single-leaflet device attachment and tricuspid stenosis. Similarly, Mehr et al. reported 1-year outcomes after MitraClip device implantation [25]. Data from the TriValve registry of 249 patients were analysed. Successful procedure with TR reduction to grade 2 was achieved in 77% by the placement of  $2 \pm 1$  tricuspid clips. At 1-year follow-up, significant and durable improvements in TR severity (TR 2 in 72% of patients) and NYHA functional class (II in 69% of patients) were observed. Unfortunately, echocardiographic follow-up was available for 79% of patients only.

Recently, PASCAL repair system has been used for leaflet repair in patients with severe MR [26,27]. The PASCAL implant consists of a central spacer with 2 adjacent and contoured wide paddles. The clasps can be operated either simultaneously or independently for leaflet grasping. The PASCAL system can also be elongated to achieve a narrow profile that allows the option for subvalvular maneuvering with low risk for entanglement. Fam et al. demonstrated the usage of PASCAL repair system for treatment of severe TR on a small group (28 patients) [28], even in patients with large coaptation gaps (maximum 12mm). Procedural success was 86% with  $1.4 \pm 0.6$  devices implanted per patient. Two patients experienced single-leaflet device attachment (SLDA) during the hospital stay. The thirty-day mortality was 7.1% (2 of 28 patients). Most of the patients (23 of 26 patients) were in NYHA functional class III which was reduced from 100% (28 of 28 patients) at baseline to 12% (3 of 26 patients) at 30 days.

A most recent multicenter study evaluated the safety and efficacy of the PASCAL and PASCAL Ace transcatheter leaflet repair systems for treating symptomatic TR in a high-risk patient cohort [29]. Data from 235 patients across eight centers showed that TR was functionally severe in 91% of cases. The procedure successfully reduced TR to moderate or less in 78% of patients, with procedural success being 78%. At a median follow-up of 173 days, TR reduction was sustained, and right ventricular remodeling was observed. Patients experienced significant symptomatic improvement, with 63% in NYHA class I or II. No significant difference was found between the PASCAL and PASCAL Ace systems in terms of TR reduction. The study concluded that the PASCAL systems offer a high rate of technical and procedural success, efficient TR reduction, and significant clinical and echocardiographic improvements at follow-up, making them promising options for high-risk patients with severe TR.



The leaflet coaptation devices, such as FORMA, aim to increase leaflet coaptation surface by occupying the regurgitant orifice area. Despite satisfactory midterm results with FORMA [30,31], some concerns regarding anchoring system have been raised [32].

### ***Annuloplasty devices***

Annuloplasty devices are typically employed in patients exhibiting annular dilatation (>40 mm) with little or no leaflet tethering and a predominant central jet in TR. Recent data from the TriValve registry indicate that only 14% of patients undergoing TTVR between 2014 and 2018 received treatment with these devices [22]. This limited use may be attributed to the technical complexities and the intricate anatomy of the TV. These devices fall into two categories: ring annuloplasty (such as Cardioband, Millipede, DaVigni) and suture annuloplasty (such as Trialign, TriCinch, MIA, PASTA).

The Cardioband system, the first commercially available system, comprises a corkscrew anchor connected to a Dacron band and a self-expandable stent. It is implanted under fluoroscopic and echocardiographic guidance, with the anchor positioned at the tricuspid annulus supporting the anterior leaflet. Tension applied to the system reshapes the tricuspid annulus, enhancing leaflet coaptation and reducing TR severity [33].

The Trialign device, a transjugular suture-based TV annuloplasty system, reduces tricuspid annular diameter through tissue plication, resembling the suture bicuspidization technique originally described by Kay et al. [34]. As a result, the tricuspid annular circumference is reduced and the TV is converted into a smaller but competent mitral-like valve [35].

The TriCinch device consists of a corkscrew anchor, a self-expandable stent, and a Dacron band. It is inserted through the femoral vein, with the anchor placed inside the anteroposterior portion of the annulus. Subsequently, the self-expandable stent is implanted into the inferior vena cava, cinching the annulus to reduce septolateral diameter through the Dacron band [36].

The limited use of these devices may stem from anatomical challenges, such as their targeting of the anterolateral part of the tricuspid annulus, close to the right coronary artery (RCA), posing a risk of injury. Additionally, angulation between the TV, inferior vena cava (IVC), and superior vena cava (SVC), along with a prominent Eustachian valve, can complicate the transfemoral approach. Although access from the internal jugular vein or superior vena cava offers a more favorable approach angle, performing transjugular procedures can be ergonomically challenging with greater radiation exposure. The frailty of the targeted tissue may also contribute to device detachments and tissue dehiscence [37].

Studies suggest that recurrence of TR following valve repair can be anticipated by leaflet tethering, potentially limiting the efficacy of tricuspid annular devices. Therefore, the implantation of two repair devices (annuloplasty and edge-to-edge devices) may be necessary to achieve efficient TR reduction [38].

### ***Valve implantation devices***

Valve implantation devices are primarily indicated for severe TR accompanied by severe leaflet tethering and significant RV dilatation. These devices can be categorized into caval valve and tricuspid valve implantation devices based on their implantation position. The first transcatheter caval valve implantation (CAVI) in humans occurred in 2010 [18]. However, despite being one of the initial transcatheter therapies, the first multicenter observational study on CAVI was published eight years later, involving only 25 patients [39]. This delay in research progress was due to the limited availability of certain devices over the six-year treatment period. The Edwards Sapien XT and Sapien 3 valves have been utilized for treating severe TR due to their commercial availability. Data from the TriValve registry indicates that CAVI was performed in only 3% of patients. Implanting these valves necessitates pre-stenting with self-expandable stents in the superior vena cava (SVC) and inferior vena cava (IVC) to create a suitable landing zone. This approach primarily targets the resolution of backflow into the caval veins and the alleviation of associated HF symptoms. These devices are typically reserved for the most severely ill subset of patients. An advantage of these devices is their suitability for patients with preexisting permanent pacemakers, which may be contraindications for other TR-specific devices [39]. Recently, the LuX-Valve Plus has introduced a unique approach to transjugular delivery [40]. Unlike traditional methods, it achieves stability through septal insertion and leaflet engagement, rather than relying on radial force. In a single-center observational study [41] spanning from September 2020 to May 2021, 15 patients with severe or extremely severe TR, who were considered high-risk candidates for traditional surgery, underwent TTVR using the LuX-Valve. The primary objective was to assess safety and efficacy at the 1-year follow-up. The LuX-Valve was successfully implanted in all patients, resulting in a significant reduction in TR severity. One patient died unrelated to the procedure, while the remaining 14 reached the primary endpoint. NYHA functional class and symptoms improved, and there was a decrease in peripheral edema and ascites. One patient was rehospitalized due to device thrombosis. Follow-up echocardiographic measurements showed sustained improvement in TR severity, right ventricular remodeling, and functional capacity.

Overall, TTVR with the LuX-Valve demonstrated feasibility, safety, and promising clinical outcomes, although further research is warranted for long-term assessment and comparison with traditional surgery.

The TRISCEND study evaluated the safety and efficacy of transfemoral tricuspid valve replacement in 176 patients with moderate or severe TR unresponsive to medical therapy [42]. The results showed significant and sustained reductions in TR, improved stroke volume, cardiac output, and quality of life over one year. Key findings included a reduction in TR to mild or less in 97.6% of patients, increased NYHA class I or II status in 93.3%, and a notable decrease in HFH by 74.9%. Despite a high comorbidity rate in the elderly cohort, the procedure was associated with low mortality (9.1%) and HFH (10.2%) at one year. These promising outcomes underscore the potential of TTVR as a viable treatment for severe TR, offering marked clinical and functional benefits.

Transcatheter tricuspid valve-in-ring (TVIR) implantation has also been reported using either Melody or Sapien family valves [43]. Although the implantation procedure was deemed technically straightforward, three-quarters of the patients experienced paravalvular leaks (PVL), with one-third necessitating treatment with occlusion devices.

### **Combined tricuspid and mitral valve repair**

Given the prevalence of moderate to severe TR in patients undergoing surgery for left-sided valvular issues, Mehr et al. investigated whether simultaneous intervention would impact outcomes [25]. They conducted a retrospective analysis of data from 228 patients drawn from two registries: the international multicentre TriValve registry and the German multicentre TRAMI registry. These patients presented with concomitant severe MR and TR. Among them, 106 patients from the TRAMI registry underwent isolated transcatheter mitral valve repair (TMVR), while 122 patients from the TriValve registry underwent concurrent transcatheter repair of the mitral and tricuspid valves (TMTVR). Patients treated with TMTVR exhibited higher 1-year survival rates compared to those who underwent isolated TMVR. Notably, there was no significant difference in NYHA functional class during follow-up between the two groups. However, this study is limited by the varying characteristics of the patient populations. Further randomized controlled trials are necessary to validate these findings.

### **Pacemaker related TR**

Cardiac implantable electronic devices (CIEDs), such as permanent pacemakers and implantable cardioverter-defibrillators, have significantly enhanced and prolonged the quality of life for millions of patients globally. The presence of an endocardial lead traversing the TV may contribute to or be the sole cause of TR. The existence of a CIED transvalvular lead has been correlated with the progression of TR and poorer outcomes. Insights from the TriValve registry [2] have indicated the feasibility of TTVR in carefully selected patients. It's noteworthy that nearly all of these patients have TR unrelated to CIED leads. Although patients with CIEDs exhibited more symptoms, larger left ventricular dimensions, lower left ventricular ejection fraction, and slightly worse right ventricular dysfunction, the short- and mid-term outcomes were similar. Therefore, the presence of a trans-tricuspid CIED lead was not linked to adverse outcomes [44].

### **Tricuspid valve repair for HF patients**

Severe TR poses a significant threat to the prognosis of patients with HF, regardless of their LV function. Topilsky et al. have demonstrated that even moderate TR correlates with a more severe presentation of HF. Their quantitative analysis indicates that a threshold of effective regurgitant orifice (ERO) area 0.4 cm<sup>2</sup> is linked to diminished survival and increased cardiac events [45]. Orban et al. found that TTVR for severe TR leads to a notable reduction (22%,  $p = 0.02$ ) in the estimated annual rate of HFH post-procedure, accompanied by enhanced clinical outcomes [46]. Patients undergoing TMTVR exhibited an even greater reduction in estimated HFH per patient-year (66%,  $p < 0.001$ ). It's important to note a recent escalation in pre-interventional diuretic dosage, which may have influenced the outcomes. With a median follow-up of 360 days, procedural success was linked to improved 1-year survival compared to those experiencing procedural failure (79% vs. 60%;  $p = 0.04$ ). However, this study is limited by its observational, nonrandomized, and noncontrolled nature, as well as its inclusion of a small patient cohort (119 patients in TTVR and 114 patients in the TMTVR group). In another study, Kresoja et al. observed that successful TTVR in highly selective patients with severe TR was associated with improved outcomes in individuals with HF with preserved ejection fraction (HFpEF) but not in those with HF with reduced ejection fraction (HFrEF) [47].

### **Physiological effects after intervention**

Rommel et al.'s analysis utilizing cardiac magnetic resonance (CMR) imaging before and after TTVR indicates favorable biventricular physiology associated with this procedure [48]. Their

findings suggest that effective stroke volumes and, consequently, cardiac output can be improved by addressing isolated TR percutaneously. TTVR resulted in a reduction in right ventricular end-diastolic volume (RVEDV), while right ventricular end-systolic volume (RVESV) remained unchanged. These observations may be attributed to decreased right ventricular volume overload alongside unchanged right ventricular afterload. These changes help elucidate the clinical and functional enhancements observed in patients undergoing TTVR [49]. Dershowitz et al. investigated the impact of residual TR on RV remodeling and clinical outcomes after TTVR in a single-center retrospective analysis of 61 patients [50]. They compared the outcomes of TTV repair and TTV replacement regarding RV function, hemodynamics, and clinical results. The study found that TTV replacement achieved a greater reduction in TR than TTV repair, with a median TR reduction of 4 grades for TTV replacement versus 1 grade for TTV repair. Greater TR reduction was associated with RV reverse remodeling, indicated by decreased RV dimensions. Additionally, TTV replacement was specifically linked to declines in tricuspid annular plane systolic excursion (TAPSE) and pulmonary artery systolic pressure (PASP). Larger RV dimensions were associated with higher risks of adverse clinical outcomes, such as death, HFH, or the need for re-do TV intervention. This study underscores the importance of TR reduction in achieving RV reverse remodeling and improving clinical outcomes, with TTV replacement showing superior efficacy in TR reduction compared to TTV repair. Brener et al.'s study [51], using data from 444 patients, aimed to link RV-PA coupling with clinical outcomes. They found that a low TAPSE/PASP ratio, indicating poor RV-PA coupling, was associated with higher mortality. Despite the promise of this measure, the study faced limitations such as variability in echocardiogram measurements and potential oversimplification of RV-PA physiology.

## **Conclusions**

The field of transcatheter therapies has seen significant advancement in recent years. While transcatheter aortic valve implantation (TAVI) has rapidly evolved and become widely established across many medical centers, TTVR has not progressed as much and remains limited in certain centers, typically for carefully selected patients. This limitation is likely due to the intricate anatomy of the TV. Various approaches for transcatheter treatment of severe TR are still being explored, yet there remains a dearth of data regarding the feasibility, safety, and effectiveness of these treatment modalities. Moreover, the delayed presentation of many patients with TR poses an additional challenge, often excluding them from such interventions. The prognostic benefit of TTVR remains unclear, and any symptomatic improvements observed post-intervention may be

attributed to enhanced patient follow-up rather than the intervention itself. A recent meta-analysis evaluated clinical outcomes and safety of TTVR in patients with severe TR, encompassing 21 studies with 896 patients [52]. The majority of patients (81.4%) underwent TEER, and procedural success rates were high at 93.9%, with low perioperative and short-term all-cause mortality rates at 1.0% and 3.3%, respectively. However, long-term all-cause mortality and HFH rates were higher at 14.1% and 21.5%. Major complications included significant bleeding (14.3%) and SLDA (6.4%). Compared to previous studies, this analysis highlighted lower mortality rates but underscored the high complication rates associated with annuloplasty devices. Despite the limitations of small sample sizes and lack of control groups, TTVR shows promise with high procedural success, although long-term outcomes need further evaluation through randomized clinical trials. Rigorous clinical trials are imperative to ascertain the superiority of TTVR over medical therapy.

## References

1. Fender EA, Zack CJ, Nishimura RA. Isolated tricuspid regurgitation: outcomes and therapeutic interventions. *Heart* 2018;104:798-806.
2. Taramasso M, Gavazzoni M, Pozzoli A, et al. Outcomes of TTVI in patients with pacemaker or defibrillator leads: data from the trivalve registry. *JACC* 2020;13:554-64.
3. Prihadi EA. Tricuspid valve regurgitation: no longer the 'forgotten valve'. *J Cardiol Pract* 2018;16.
4. Kirklin JK, Blackstone EH. *Kirklin/Barratt-Boyes Cardiac Surgery*. Amsterdam: Elsevier Health Sciences; 2012.
5. Izumi C, Miyake M, Takahashi S, et al. Progression of isolated tricuspid regurgitation late after mitral valve surgery for rheumatic mitral valve disease. *J Heart Valve Dis* 2022;11:353-6.
6. Porter A, Shapira Y, Wurzel M, et al. Tricuspid regurgitation late after mitral valve replacement: clinical and echocardiographic evaluation. *J Heart Valve Dis* 1999;8:57-62.
7. Matsunaga A, Duran CMG. Progression of tricuspid regurgitation after repaired functional ischemic mitral regurgitation. *Circulation* 2005;112:1453-7.
8. De Bonis M, Lapenna E, Sorrentino F, et al. Evolution of tricuspid regurgitation after mitral valve repair for functional mitral regurgitation in dilated cardiomyopathy. *Eur J Cardiothorac Surg* 2008;33:600-6.

9. Alfieri O, Maisano F. An effective technique to correct anterior mitral leaflet prolapse. *J Card Surg* 1999;14:468-70.
10. Nath J, Foster E, Heidenreich PA. Impact of tricuspid regurgitation on long-term survival. *J Am Coll Cardiol* 2004;43:405-9.
11. Chorin E, Rozenbaum Z, Topilsky Y, et al. Tricuspid regurgitation and long-term clinical outcomes. *Eur Heart J Cardiovasc Imaging* 2020;21:157-65.
12. De la Espriella R, Santas E, Chorro FJ, et al. Functional tricuspid regurgitation and recurrent admissions in patients with acute heart failure. *Int J Cardiol* 2019;291:83-8.
13. Besler C, Seeburger J, Thiele H, Lurz P. Treatment options for severe functional tricuspid regurgitation: indications, techniques and current challenges. *ESC Eur J Cardiol Pract* 2018;16.
14. Dreyfus GD, Corbi PJ, Chan KMJ, Bahrami T. Secondary tricuspid regurgitation or dilatation: which should be the criteria for surgical repair?. *Ann Thorac Surg* 2005;79:127-32.
15. Van de Veire NR, Braun J, Delgado V, et al. Tricuspid annuloplasty prevents right ventricular dilatation and progression of tricuspid regurgitation in patients with tricuspid annular dilatation undergoing mitral valve repair. *J Thorac Cardiovasc Surg* 2011;141:1431-9.
16. Chikwe J, Itagaki S, Anyanwu A, Adams DH. Impact of concomitant tricuspid annuloplasty on tricuspid regurgitation, right ventricular function, and pulmonary artery hypertension after repair of mitral valve prolapse. *J Am Coll Cardiol* 2015;65:1931-8.
17. Vahanian A, Beyersdorf F, Praz F, et al. 2021 ESC/EACTS guidelines for the management of valvular heart disease: developed by the task force for the management of valvular heart disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2022;43:561-632.
18. Lauten A, Ferrari M, Hekmat K, et al. Heterotopic transcatheter tricuspid valve implantation: first-in-man application of a novel approach to tricuspid regurgitation. *Eur Heart J* 2011;32:1207-13.
19. Schueler R, Hammerstingl C, Werner N, Nickenig G. Interventional direct annuloplasty for functional tricuspid regurgitation. *JACC Cardiovasc Interv* 2017;10:415-6.
20. Hahn RT, George I, Kodali SK, et al. Early single-site experience with transcatheter tricuspid valve replacement. *JACC Cardiovasc Imaging* 2019;12:416-29.
21. Taramasso M, Hahn RT, Alessandrini H, et al. The international multicenter TriValve registry: which patients are undergoing transcatheter tricuspid repair?. *JACC Cardiovasc Interv* 2017;10:1982-990.

22. Taramasso M, Alessandrini H, Latib A, et al. Outcomes after current transcatheter tricuspid valve intervention: mid-term results from the international TriValve registry. *JACC Cardiovasc Interv* 2019;12:155-65.
23. Besler C, Orban M, Rommel KR, et al. Predictors of procedural and clinical outcomes in patients with symptomatic tricuspid regurgitation undergoing transcatheter edge-to-edge repair. *JACC Cardiovasc Interv* 2018;11:1119-28.
24. Nickenig G, Weber M, Lurz P, et al. Transcatheter edge-to-edge repair for reduction of tricuspid regurgitation: 6-month outcomes of the TRILUMINATE single-arm study. *Lancet* 2019;394:2002-11.
25. Mehr M, Taramasso M, Besler C, et al. 1-Year outcomes after edge-to-edge valve repair for symptomatic tricuspid regurgitation: results from the TriValve registry. *JACC Cardiovasc Interv* 2019;12:1451-61.
26. Praz F, Spargias K, Chrissoheris M, et al. Compassionate use of the PASCAL transcatheter mitral valve repair system for patients with severe mitral regurgitation: a multicentre, prospective, observational, first-in-man study. *Lancet* 2017;390:773-80.
27. Scott Lim D, Kar S, Spargias K, et al. Transcatheter valve repair for patients with mitral regurgitation: 30-day results of the CLASP study. *JACC Cardiovasc Interv* 2019;12:1369-78.
28. Fam NP, Braun D, von Bardeleben RS, et al. Compassionate use of the PASCAL transcatheter valve repair system for severe tricuspid regurgitation: a multicenter, observational, first-in-human experience. *JACC Cardiovasc Interv* 2019;12:2488-95.
29. Wild MG, Löw K, Rosch S, et al. Multicenter experience with the transcatheter leaflet repair system for symptomatic tricuspid regurgitation. *JACC Cardiovasc Interv* 2022;15:1352-63.
30. Puri R, Rodés-Cabau J. Transcatheter interventions for tricuspid regurgitation: the FORMA repair system. *Interv Cardiol Clin* 2018;7:47-55.
31. Perlman G, Praz F, Puri R, et al. Transcatheter tricuspid valve repair with a new transcatheter coaptation system for the treatment of severe tricuspid regurgitation: 1-year clinical and echocardiographic results. *JACC Cardiovasc Interv* 2017;10:1994-2003.
32. Asmarats L, Perlman G, Praz F, et al. 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 Cardiovasc Interv* 2019;12:1438-47.
33. van Rosendael PJ, Delgado V, Bax JJ. The tricuspid valve and the right heart: anatomical, pathological and imaging specifications. *EuroIntervention* 2015;11:W123-7.



34. Siminiak T, Dankowski R, Baszko A, et al. Percutaneous direct mitral annuloplasty using the Mitralign Bident™ system: description of the method and a case report. *Kardiol Pol* 2013;71:1287-92.
35. Besler C, Meduri CU, Lurz P. Transcatheter treatment of functional tricuspid regurgitation using the trialign device. *Interv Cardiol* 2018;13:8-13.
36. Latib A, Agricola E, Pozzoli A, et al. First-in-man implantation of a tricuspid annular remodeling device for functional tricuspid regurgitation. *JACC Cardiovasc Interv* 2015;8:e211-4.
37. Mangieri A, Latib A. Transcatheter innovations in tricuspid regurgitation: cardioband. *Prog Cardiovasc Dis* 2019;62:482-5.
38. von Bardeleben RS, Ruf T, Schulz E, et al. First percutaneous COMBO therapy of tricuspid regurgitation using direct annuloplasty and staged edge-to-edge repair in a surgical-like Clover technique. *Eur Heart J* 2018;39:3621-2.
39. Lauten A, Figulla HR, Unbehaun A, et al. Interventional treatment of severe tricuspid regurgitation: early clinical experience in a multicenter, observational, first-in-man study. *Circ Cardiovasc Interv* 2018;11:e006061.
40. Liu Y, Li W, Zhou D, et al. Step-by-step transesophageal echocardiographic guidance for transjugular transcatheter tricuspid valve replacement with a radial force-independent bioprosthesis. *Quant Imaging Med Surg* 2024;14:1061-9.
41. Mao Y, Li L, Liu Y, et al. Safety, efficacy, and clinical outcomes of transcatheter tricuspid valve replacement: one-year follow-up. *Front Cardiovasc Med* 2022;9:1019813.
42. S. Kodali et al., "Transfemoral tricuspid valve replacement and one-year outcomes: the TRISCEND study," *Eur Heart J*, vol. 44, no. 46, pp. 4862–4873, 2023.
43. Aboulhosn J, Cabalka AK, Levi DS, et al. Transcatheter valve-in-ring implantation for the treatment of residual or recurrent tricuspid valve dysfunction after prior surgical repair. *JACC Cardiovasc Interv* 2017;10:53-63.
44. Mao Y, Liu Y, Meng X, et al. Treatment of severe tricuspid regurgitation induced by permanent pacemaker lead: transcatheter tricuspid valve replacement with the guidance of 3-dimensional printing. *Front Cardiovasc Med* 2023;10:1030997.
45. Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J, et al. 2018 ESC guidelines for the management of cardiovascular diseases during pregnancy. *Eur Heart J* 2018;39:3165-241.

46. Orban M, Rommel KP, Ho EC, et al. Transcatheter edge-to-edge tricuspid repair for severe tricuspid regurgitation reduces hospitalizations for heart failure. *JACC Heart Fail* 2020;8:265-76.
47. Kresoja KP, Lauten A, Orban M, et al. Transcatheter tricuspid valve repair in the setting of heart failure with preserved or reduced left ventricular ejection fraction. *Eur J Heart Fail* 2020;22:1817-25.
48. Rommel KP, Besler C, Noack T, et al. Physiological and clinical consequences of right ventricular volume overload reduction after transcatheter treatment for tricuspid regurgitation. *JACC Cardiovasc Interv* 2019;12:1423-34.
49. Lurz P, Giardini A, Taylor AM, et al. Effect of altering pathologic right ventricular loading conditions by percutaneous pulmonary valve implantation on exercise capacity. *Am J Cardiol* 2010;105:721-6.
50. Lyle Dershowitz 1, Lawlor MK, Hamid N, et al. Right ventricular remodeling and clinical outcomes following transcatheter tricuspid valve intervention. *Catheter Cardiovasc Interv* 2024;103:367-75.
51. Rudski LG, Afilalo J. Right ventricle-pulmonary artery coupling in percutaneous tricuspid valve repair: is simple sufficient?. *J Am Coll Cardiol* 2022;79:462-4.
52. Wu Z, Zhu W, Kaisaier W, et al. Periprocedural, short-term, and long-term outcomes following transcatheter tricuspid valve repair: a systemic review and meta-analysis. *Ther Adv Chronic Dis* 2023;20406223231158610.

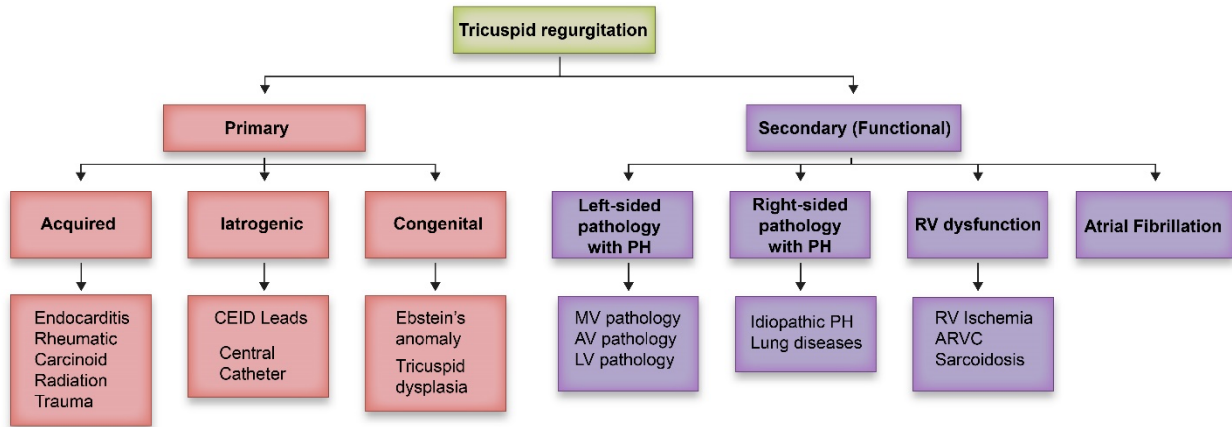


Figure 1. ARVC, arrhythmogenic right ventricular cardiomyopathy; CEID, cardiovascular implantable electronic device; LV, left ventricle; PH, pulmonary hypertension; RA, right atrium; RV, right ventricle; TR, tricuspid regurgitation; TV, tricuspid valve. Modified from: Modified from: Prihadi (2018) with permission of the author.

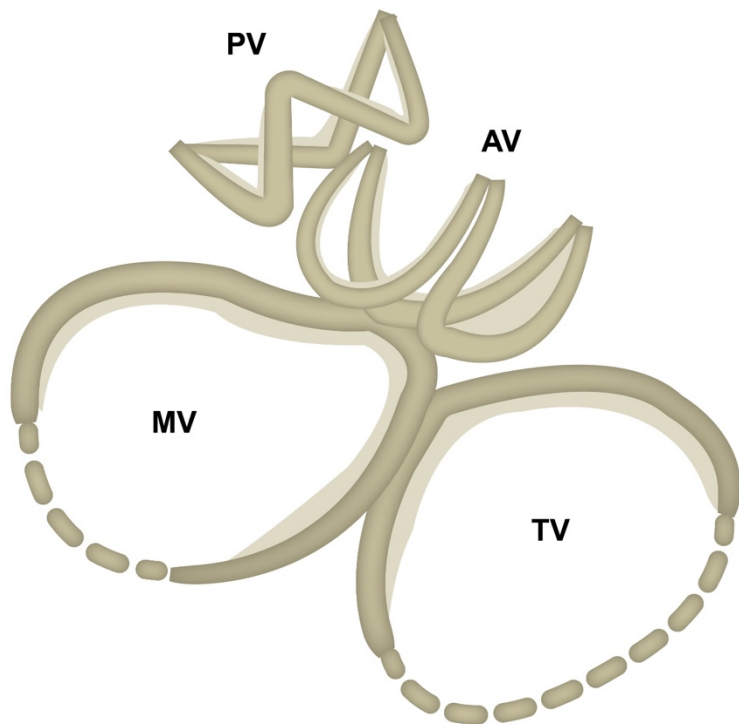
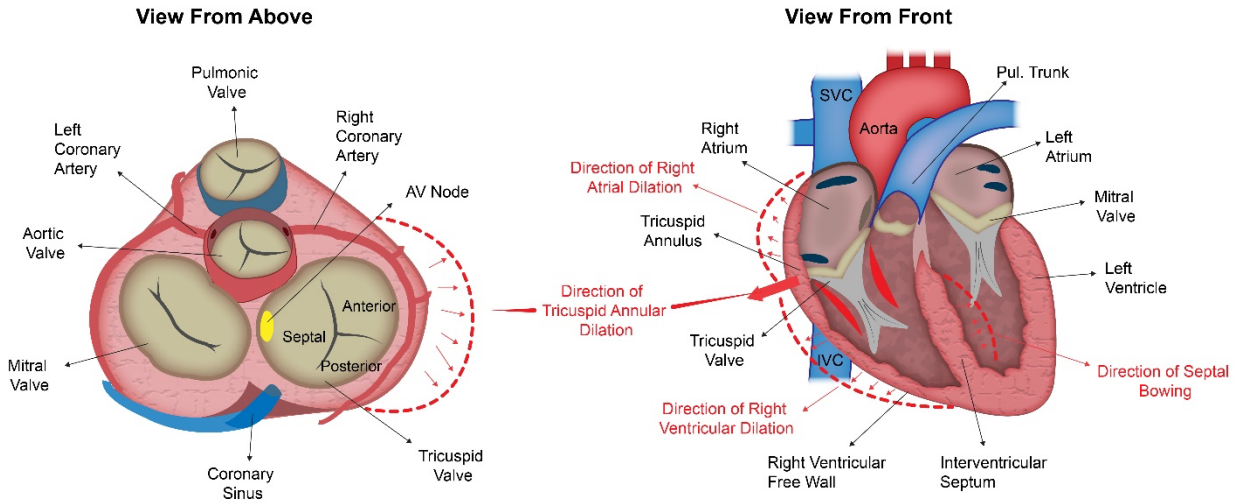
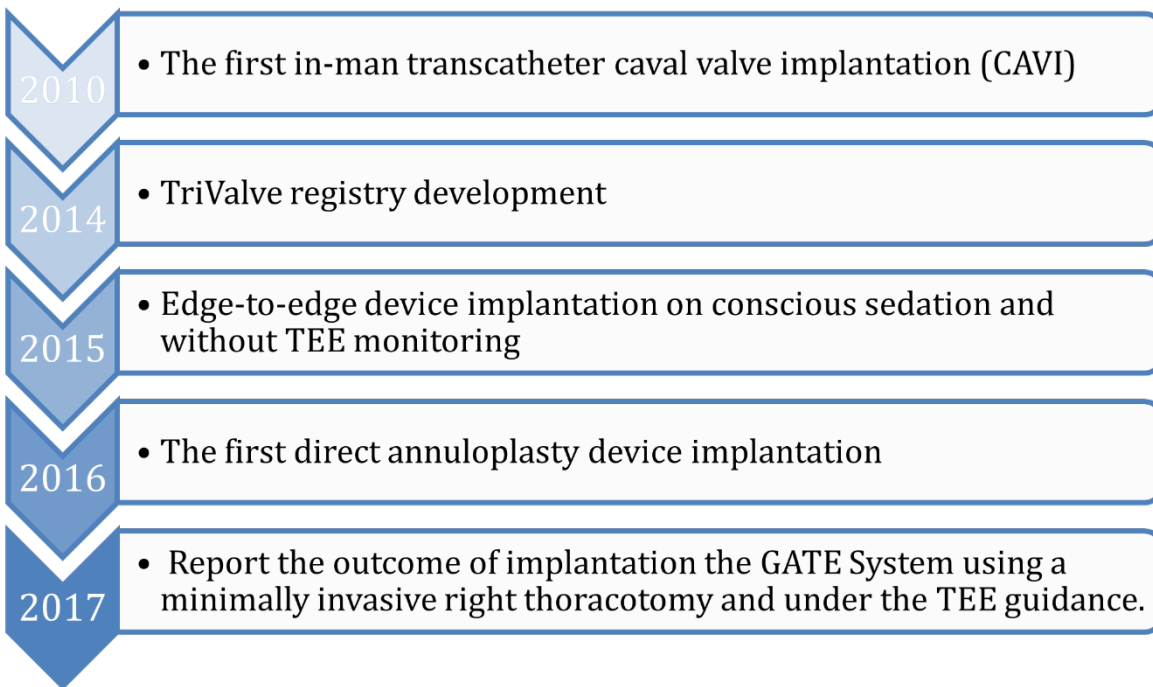


Figure 2. The fibrous skeleton of the heart.



**Figure 3. Tricuspid valve anatomy.**



**Figure 4. Timeline of interventions and data collection.**

**Table 1. Transcatheter tricuspid valve repair (TTVR) devices.**

<b>Annuloplasty Devices</b>	TriCinch	Trialign	Cardioband	Millepede	MIA-T	PASTA	Davingi
<b>Coaptation Enhancement Devices</b>	Mitraclip	Triclip	Forma	Pascal			
<b>Tricuspid Valves</b>	NaviGate	Trisol	Lux	Evoque			
<b>Caval Valves</b>	TriCalve	TriCentro	Caval S3				