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«ΚΑΡΔΙΑΚΗ ΑΝΕΠΑΡΚΕΙΑ - ΚΑΡΔΙΟ-ΟΓΚΟΛΟΓΙΑ - ΚΑΡΔΙΑΓΓΕΙΑΚΗ
ΑΠΟΚΑΤΑΣΤΑΣΗ»

(MSc in Heart Failure - Cardio-oncology - Cardiac Rehabilitation)



«Η θέση του TriClip σε ασθενείς με χρόνια καρδιακή ανεπάρκεια»

Λάρισα, Σεπτέμβριος 2025



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«The Role of TriClip in Patients with Chronic Heart Failure»

”

Λάρισα, Σεπτέμβριος 2025

«Βεβαιώνω ότι η παρούσα διπλωματική εργασία είναι αποτέλεσμα δικής μου δουλειάς και δεν αποτελεί προϊόν αντιγραφής. Στις δημοσιευμένες ή μη δημοσιευμένες πηγές έχω χρησιμοποιήσει εισαγωγικά και όπου απαιτείται έχω παραθέσει τις πηγές τους στο τμήμα της βιβλιογραφίας».

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Τσόκκου Κορνηλία

Περίληψη

Υπόβαθρο: Η χρόνια καρδιακή ανεπάρκεια (CHF) συχνά συνοδεύεται από λειτουργική ανεπάρκεια της τριγλώχινας βαλβίδας (TR), η οποία επιδεινώνει τη δυσλειτουργία της δεξιάς κοιλίας, εντείνει τα συμπτώματα και αυξάνει τις νοσηλείες. Οι χειρουργικές επιλογές είναι περιορισμένες λόγω του υψηλού εγχειρητικού κινδύνου, ιδιαίτερα σε ηλικιωμένους ή ευπαθείς ασθενείς. Η συσκευή TriClip, ένα διακαθετηριακό σύστημα επιδιόρθωσης με τεχνική συμπλησίας των γλωχίνων (TEER), προσφέρει μια ελάχιστα επεμβατική εναλλακτική λύση για τη θεραπεία της σοβαρής TR σε ασθενείς με CHF.

Σκοπός: Η παρούσα διατριβή αξιολογεί την κλινική χρησιμότητα του συστήματος TriClip σε ασθενείς με μέτρια έως σοβαρή δευτεροπαθή TR και CHF, με έμφαση στην ανατομική καταλληλότητα, τα αποτελέσματα της επέμβασης και τις στρατηγικές επιλογής ασθενών.

Μέθοδοι: Πραγματοποιήθηκε αφηγηματική ανασκόπηση της βιβλιογραφίας μέσω των βάσεων δεδομένων PubMed, Scopus και Web of Science, συμπεριλαμβάνοντας τυχαιοποιημένες μελέτες, μητρώα και παρατηρητικές μελέτες δημοσιευμένες την περίοδο 2018–2025. Τα δεδομένα αναλύθηκαν θεματικά με επίκεντρο την παθοφυσιολογία της TR, τον σχεδιασμό του συστήματος TriClip, την κλινική αποτελεσματικότητα και τους περιορισμούς της παρέμβασης.

Αποτελέσματα: Η θεραπεία TriClip επιτυγχάνει σημαντική μείωση της TR, βελτίωση της λειτουργικής κλάσης κατά NYHA και ενίσχυση της ποιότητας ζωής σε ασθενείς υψηλού κινδύνου με CHF. Το ποσοστό επιτυχίας υπερβαίνει το 85%, με ευνοϊκό προφίλ ασφάλειας και μειωμένα ποσοστά επανανοσηλείας. Οι ιδανικοί υποψήφιοι παρουσιάζουν διατηρημένη λειτουργία της δεξιάς κοιλίας, περιορισμένη διάταση του δακτυλίου και κατάλληλη μορφολογία γλωχίνων.

Συμπεράσματα: Το TriClip αποτελεί μια καινοτόμο επιλογή για τη διαχείριση της λειτουργικής TR σε ασθενείς με CHF. Παρότι απαιτείται περαιτέρω μελέτη για τη μακροχρόνια αποτελεσματικότητα και την οικονομική αποδοτικότητα της επέμβασης, τα υφιστάμενα δεδομένα υποστηρίζουν την ένταξή του στις σύγχρονες θεραπευτικές στρατηγικές για την καρδιακή ανεπάρκεια σε ασθενείς που δεν είναι κατάλληλοι για χειρουργική επέμβαση.

Λέξεις-κλειδιά: Ανεπάρκεια τριγλώχινας; Καρδιακή ανεπάρκεια; TriClip; Διακαθετηριακή επιδιόρθωση με την τεχνική συμπλησίας των γλωχίνων; Δυσλειτουργία δεξιάς κοιλίας

Abstract

Background: Chronic heart failure (CHF) is frequently complicated by functional tricuspid regurgitation (TR), which exacerbates right ventricular dysfunction, worsens symptoms, and increases hospitalizations. Surgical options are limited by high procedural risk, particularly in elderly or frail patients. The TriClip device, a transcatheter edge-to-edge repair (TEER) system, offers a minimally invasive alternative for treating severe TR in CHF populations.

Objective: This dissertation evaluates the clinical utility of the TriClip system in patients with moderate-to-severe secondary TR and CHF, focusing on anatomical suitability, procedural outcomes, and patient selection strategies.

Methods: A narrative literature review was conducted using PubMed, Scopus, and Web of Science, including randomized trials, registry data, and observational studies published between 2018 and 2024. Data were thematically analyzed to assess TR pathophysiology, TriClip device design, clinical efficacy, and procedural limitations.

Results: TriClip therapy achieves significant TR reduction, improved New York Heart Association (NYHA) functional class, and enhanced quality of life in high-risk CHF patients. Procedural success rates exceed 85%, with a favorable safety profile and reduced rehospitalization rates. Optimal candidates exhibit preserved right ventricular function, limited annular dilation, and suitable leaflet morphology.

Conclusion: TriClip represents a transformative option in the management of functional TR among CHF patients. While long-term durability and cost-effectiveness require further study, current evidence supports its integration into contemporary heart failure care pathways for patients ineligible for surgery.

Keywords: Tricuspid regurgitation; heart failure; TriClip; transcatheter edge-to-edge repair; right ventricular dysfunction

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1.Introduction

Chronic heart failure (CHF) remains a major contributor to global morbidity and mortality, characterized by progressive impairment of ventricular function, limited exercise capacity, frequent hospitalizations, and diminished quality of life [1]. Among its associated valvular complications, tricuspid regurgitation (TR), whether primary or secondary in origin has historically received limited clinical attention. Transcatheter therapies have transformed the management of aortic and mitral valve disease over the past two decades, while the tricuspid valve has long been considered “the forgotten valve,” often overlooked in diagnostic algorithms and therapeutic planning [2]. Although the clinical importance of TR is now increasingly recognized, definitive treatment remains elusive for many patients due to the high operative risk posed by advanced age, frailty, and multiple comorbidities. The current European Society of Cardiology (ESC) guidelines acknowledge transcatheter therapies for secondary TR, but assign them a weak recommendation (Class IIb, level C), due to limited supporting evidence and unclear candidate selection [3].

Secondary TR, also known as functional, is most often associated to left-sided heart disease, pulmonary hypertension (PHTN), or long-standing atrial fibrillation, all of which, over time, contribute to right ventricular dilation and annular enlargement. As our understanding of TR pathophysiology has advanced, so too has the awareness of its prognostic significance. Moderate to severe TR is now recognized as an independent predictor of adverse outcomes in patients with heart failure (HF) with reduced ejection fraction (HFrEF), as well as and in those with preserved ejection fraction (HFpEF), particularly in its atrial secondary form [4].

The emergence of transcatheter edge-to-edge repair (TEER) for TR reflects this shift in clinical priorities. Modeled after the MitraClip, the TriClip system enables leaflet approximation and regurgitation reduction without open-heart surgery, thus offering a valuable treatment option for patients with advanced CHF.

This dissertation focuses on evaluating the role of the TriClip transcatheter edge-to-edge repair system in the treatment of secondary tricuspid regurgitation among patients with chronic heart failure. It aims to review current evidence regarding anatomical considerations, patient selection, procedural strategies, and clinical outcomes associated with this evolving therapeutic approach.

2.Methodology

2.1 Narrative literature Review Strategy

This dissertation is designed as a narrative literature review aimed at evaluating the role of the TriClip transcatheter valve repair system in patients with chronic heart failure and tricuspid regurgitation. A focused literature search was primarily conducted through PubMed. Additional relevant studies were identified through manual reference screening and, where appropriate, from Google Scholar or Scopus. The search covered the period from 2018 to 2025 and used combinations of keywords including “TriClip”, “tricuspid valve anatomy and morphology”, “tricuspid regurgitation,” “chronic heart failure,” “transcatheter valve repair,” and “TEER”.

2.2 Inclusion and Exclusion Criteria

The selection of literature focused on peer-reviewed studies published in English that addressed adult populations diagnosed with moderate to severe secondary tricuspid regurgitation in the context of chronic heart failure. Eligible sources included randomized clinical trials, prospective and retrospective observational studies, registry data, expert consensus statements, and review articles. Studies were excluded if they consisted solely of

case reports, non-human or in vitro research, non-peer-reviewed content, abstract-only conference proceedings, or publications in languages other than English.

2.3 Thematic Analysis and Structuring

After the initial search and screening process, the selected studies were analyzed thematically. The material was organized into key domains that align with the scope of the dissertation: classification and pathophysiology of tricuspid regurgitation, anatomical substrates relevant to intervention, patient selection criteria, procedural aspects of TriClip implantation, clinical outcomes, and the current limitations and future directions of this therapeutic approach. Since no original patient data were collected or analyzed, and no statistical methods were employed, the methodology aligns with accepted practices for narrative clinical reviews.

3. Epidemiology, classification and Prognosis of Tricuspid Regurgitation

3.1 TR Epidemiology and Classification

Tricuspid regurgitation (TR) is increasingly recognized as an independent prognostic factor linked to substantial morbidity and mortality, with risk escalating in proportion to its severity, regardless of underlying etiology or comorbidities [5]. In current practice, TR is graded by severity as mild, moderate, severe, massive, or torrential, based on echocardiographic parameters [6]. Mild TR is estimated to be present in approximately 80% of the general population and is not associated with adverse outcomes [7]. In contrast, moderate to severe TR is known to affect 5–10% of adults in the United States and represents a clinically

significant burden [8]. These more advanced degrees are associated with significantly higher risk of right heart failure (HF), repeat hospitalizations, and reduced survival [8,9].

Heitzinger et al. (2023) conducted a large population-based study of over 13,000 HF patients, demonstrating that both moderate and severe secondary TR (STR) were independently associated with increased long-term mortality. Specifically, mortality risk was significantly elevated for moderate TR (HR 1.58; 95% CI, 1.48–1.69) and severe TR (HR 2.19; 95% CI, 2.01–2.38), even after multivariable adjustment. This association remained consistent across all HF subtypes and was most pronounced in patients younger than 70 years of age [9].

These findings are consistent with those reported in large-scale analyses. Messika-Zeitoun et al., demonstrated a robust, independent association between TR severity and reduced survival in HF patients [10]. Similarly, Rodríguez-Capitán et al. (2024) reported that nearly all etiological categories of significant TR (except atrial TR) were linked to markedly higher long-term mortality, underscoring the prognostic relevance of etiology alongside severity [11]. Furthermore, an observational analysis from the National Echocardiography Database of Australia (NEDA), which included more than 439,000 individuals, revealed that among patients with severe TR, escalating degrees of regurgitation were associated with significantly poorer outcomes, with 1-year mortality approaching 46% [7].

Within the broader spectrum of STR, a subset that has historically received limited clinical attention is isolated TR (iTR). iTR is defined as TR occurring in the absence of left-sided heart disease, PHTN, or significant right ventricular dysfunction. However, the terminology surrounding iTR has been inconsistent, and the construct is increasingly being supplanted by the more anatomically and pathophysiologically precise term of atrial secondary TR (A-STR) [12].

Epidemiological studies suggest that the incidence of TR is rising, with large registry data revealing that most cases previously labeled as iTR are in fact secondary in origin and independently associated with increased mortality. Despite this, iTR remains a commonly

used term in clinical practice, often without thorough etiological evaluation. Current guidelines provide limited recommendations for its management [5,13].

Beyond severity grading, TR is etiologically classified as either primary also known as organic or secondary (functional). Primary TR, comprising approximately 5–10% of cases, arises from intrinsic structural abnormalities of the tricuspid valve apparatus [14]. In contrast, secondary TR represents 90-95% of cases and typically results from annular dilation or right ventricular dysfunction, often with structurally normal leaflets [8].

3.2 Subtypes of Secondary TR

Secondary TR is further subclassified into ventricular and atrial types with a notably high incidence among older adults [15]. Ventricular secondary TR (V-STR), which accounts for approximately 80-85% of all secondary TR cases, is categorized according to underlying etiology into three main categories: left-sided heart disease, PHTN, and primary right ventricular (RV) dysfunction. These conditions contribute to annular dilatation and leaflet tethering through distinct pathophysiological mechanisms, central to the development of V-STR [16].

In contrast, A-STR represents about 10–15% of cases and is increasingly recognized as a distinct pathophysiological entity [17]. It is predominantly observed in elderly women with a history of HF with preserved ejection fraction (HFpEF) or persistent atrial fibrillation (AF) [18]. Unlike V-STR, A-STR is characterized by isolated dilation of the right atrium (RA) and tricuspid annulus without significant RV remodeling or leaflet tethering. [17]. If left untreated, this phenotype may progress to right-sided HF [19].

Notably, A-STR may developed in the absence of AF, particularly in the context of atrial myopathy and HFpEF-related factors such as advanced age, female sex, and left ventricular diastolic dysfunction. The emerging concept of right atrial myopathy may help explain

findings from the Heart Failure Long-Term Registry of the Heart Failure Association (HFA) of the European Society of Cardiology (ESC), which reported that up to 38% of patients previously classified as having isolated TR (iTR) had no history of AF [17,18].

Reflecting its distinct clinical and pathophysiological profile, A-STR appears to respond differently to intervention. Data from the EuroTR Registry underscore the clinical relevance of A-STR, which comprised 31% of TEER cases. These individuals were generally elderly, high-risk, and exhibited features of right-sided HF. Importantly, A-STR patients demonstrated more favorable outcomes after TEER, with higher freedom from HF hospitalization at 1 and 2 years compared to non-atrial TR (77.0% vs. 65.8% at 1 year; 66.3% vs. 47.5% at 2 years, $P < 0.001$). A-STR was identified as an independent predictor of 2-year survival free from HF hospitalization (HR 0.65, 95% CI: 0.45–0.95), supporting the role of TEER as a valuable therapeutic strategy in this patient subgroup [20].

An emerging form of TR is that associated with cardiac implantable devices (CIEDs), now increasingly recognized as a distinct clinical entity, separate from primary and secondary TR. CIED-induced TR accounts for approximately 5-10% of all TR cases and is typically attributed to mechanical interference from intracardiac leads, such as impingement or entanglement with tricuspid valve leaflets, as well as to pacing-induced RV remodeling. [21,22]. The diagnosis of CIED-induced TR carries significant prognostic weight, as it is strongly associated with HF hospitalization and cardiovascular mortality [22,23].

The reported incidence of CIED-related TR varies widely, ranging from 7% to 45%, with meta-analyses estimating a pooled rate of approximately 24% for ≥ 1 -grade TR worsening [21,23]. This heterogeneity largely reflects inconsistencies in TR definitions of severity and progression across studies, thus complicating direct comparison between them [21].

3.3 Overlapping Phenotypes and Clinical Complexity

In clinical practice, patients with CHF frequently present with overlapping forms of functional TR, including atrial, ventricular, and CIED-induced TR subtypes, rather than fitting neatly into a single etiological category. Utsunomiya et al. demonstrated that chronic AF-induced TR and V-STR frequently coexist; their real-time three dimensional (3D) echocardiographic study revealed that atrial enlargement and annular dilation are often accompanied by right ventricular remodeling, highlighting that these pathophysiological mechanisms are not mutually exclusive but may instead act synergistically in the progression of advanced HF [24]. Cammalleri et al. further supported this view, noting that shared mechanisms such as annular dilation and RV dysfunction contribute to the overlap between atrial and ventricular TR across the spectrum of HF phenotypes [25].

A large cluster analysis by Anand et al., involving over 13,000 patients with moderate or severe TR, identified multiple mixed TR phenotypes with distinct echocardiographic features and prognostic trajectories. The study advocates for a revised classification system, as existing etiological frameworks often fail to capture the full heterogeneity observed in clinical practice [26]. This phenotypic overlap complicates both diagnostic categorization and therapeutic decision-making, underscoring the need for comprehensive multimodal imaging to accurately delineate annular versus ventricular involvement and to guide individualized transcatheter intervention strategies [4,27]. As emphasized by Dreyfus et al. (2025) note, overlapping imaging features often blur the line between atrial and ventricular TR, and some patients may be misclassified entirely, particularly those with underlying organic valve pathology following left-sided valve interventions [28].

3.4 Clinical Implications for Transcatheter Therapy

Given the high burden of TR in patients with congestive HF, particularly in the setting of right-sided or biventricular dysfunction, there is a pressing need for effective treatment options. Many affected individuals are elderly, frail, or burdened with comorbidities that

preclude surgery, especially since isolated tricuspid valve surgery carries high perioperative mortality [29].

Observational evidence, including the large cohort by Wang et al. (2022), involving over 9,000 patients with moderate to severe iTR, revealed that 94.8% of cases were secondary in nature, with over half having a history of congestive HF. While secondary TR initially appeared to confer worse outcomes than primary TR, this difference lost significance after multivariable adjustment, highlighting RV dysfunction, rather than TR etiology, as the dominant prognostic factor. Notably, TR related to PHTN-related exhibited the poorest survival [13]. Conventional medical therapy, such as diuretics, offers only symptomatic relief without altering disease progression or long-term prognosis [7,8].

In this context, transcatheter tricuspid interventions have emerged as a promising therapeutic option. Devices such as the TriClip system provide a less invasive approach with encouraging safety and efficacy outcomes in high-risk populations [30]. The bRIGHT (An Observational Real-World Study Evaluating Severe Tricuspid Regurgitation Patients Treated With the Abbott TriClip Device) study, a prospective real-world registry evaluating TriClip-treated patients, demonstrated sustained improvements in TR severity, functional status, and quality of life (QoL) at one year [31].

Anatomical variation among TR subtypes may impact procedural success, with A-STR generally exhibiting more favorable annular geometry and leaflet coaptation compared to V-STR [28,32].

These observations reinforce the importance of accurate phenotyping, as RV dysfunction, rather than TR etiology alone, remains the principal determinant of prognosis [13]. Given this, TEER may address an important therapeutic gap for CHF patients with severe TR, offering a path toward more individualized and effective care [25].

4. Tricuspid Valve Anatomy and Relevance to Transcatheter Therapies

4.1 Leaflet Morphology and Anatomical Variants

The tricuspid valve (TV) is anatomically more variable and intricate than its left-sided counterparts [33]. It comprises three unequal leaflets (anterior, posterior, and septal) supported by the fibrous annulus, chordae tendineae, typically three papillary muscles, and the surrounding right atrial and ventricular myocardium [7,14]. The anterior leaflet is usually the largest, while the posterior is circumferentially the shortest and often scalloped. The septal leaflet, directly anchored to the annulus along the interventricular septum, is the least mobile and shortest in radial length [7,33].

Leaflet number and morphology varies considerably. Non-trileaflet morphologies, including bicuspid and quadricuspid configurations, are observed in up to 28% of patients undergoing TEER, with over 20% presenting with four or more leaflets segments. These anatomies are associated with increased procedural complexity, challenging leaflet coaptation, and a higher likelihood of residual regurgitation post-intervention [31,34]. To address this variability, a standardized nomenclature has been proposed to classify leaflet fusion patterns and morphological variants [4,34].

Functional TR is driven by progressive right atrial and annular dilation, which impairs leaflet coaptation and facilitates regurgitant jet formation [35]. These jets commonly originate in the central or antero-septal regions, between the anterior and septal leaflets, areas most frequently targeted for initial TriClip deployment [36].

Progressive right-sided remodeling exacerbates annular dilation, distorting tricuspid valve geometry and complicating device anchoring and leaflet capture. Consequently, detailed anatomical assessment is critical for procedural planning. Morphological factors such as

leaflet number and coaptation gap width, and commissural alignment significantly influence procedural success and post-intervention outcomes including HF hospitalization rates [37].

A comprehensive understanding of TV anatomy, including leaflet configuration, commissural orientation, and regurgitant jet direction is essential for tailoring transcatheter strategies such as TriClip and optimizing clinical results [33,37].

4.2 Tricuspid Annulus: Dilation and Remodeling Dynamics

The tricuspid annulus (TA) is an asymmetric, D-shaped, and highly dynamic structure that can undergo up to a 30% change in area during the cardiac cycle in response to fluctuating hemodynamic load [33,38]. Structurally, it comprises a larger, non-fibrous C-shaped segment along the right atrial and ventricular free wall, and a smaller, fibrous portion near the septal leaflet and ventricular septum, which provides greater resistance to dilation [33]. In the context of CHF, sustained volume and pressure overload promote RV enlargement and progressive annular dilation, contributing to the development of functional TR [39].

Remodeling patterns of the annulus vary depending on the underlying pathology. In A-STR, the annular dilation originates mainly from right atrial enlargement. This leads to a conical reshaping of the right ventricle, most evident at the basal segments, while the overall RV length remains unaffected. In contrast, V-STR is characterized by a more rounded right ventricular geometry, with milder annular dilation but increased leaflet tethering due to longitudinal remodeling [40].

Importantly, TR is highly sensitive to changes in annular dimensions. A 40% increase in annular area may be sufficient to induce regurgitation, whereas mitral regurgitation typically requires a 75% increase [14]. Under normal conditions, tricuspid leaflets coapt just below the annular plane, creating a “coaptation reserve” of approximately 5 to 10 mm [33]. This anatomical buffer allows modest dilation to occur without significant regurgitation.

However, once this reserve is exceeded, the septal leaflet becomes tethered and leaflet coaptation fails.

As annular dilation and RV remodeling progress in CHF, the orientation and mobility of valve leaflets are altered. These changes can complicate device delivery and leaflet capture during tricuspid valve TEER (T-TEER). While common in CHF, annular dilation also occurs in AF and other conditions associated with right atrial or ventricular enlargement [41].

Quantitative data from multicenter registries reinforce the procedural implications of these anatomical variations. In the Transcatheter Tricuspid Valve Therapies (TriValve) registry, the mean tricuspid annular diameter was 46.7 ± 6.3 mm, with a post-procedural reduction to 44.4 ± 7.1 mm following T-TEER, supporting the technique's role in reducing annular dimensions [42].

An observational anatomical sub-analysis of the bRIGHT by Donal et al. reported considerable variability in coaptation gaps, with central gaps exceeding 10 mm in some patients, underscoring the technical challenges of achieving effective leaflet coaptation. This postmarket analysis highlighted the diversity of valve anatomies encountered in clinical practice, emphasizing the need for individualized procedural planning. Detailed anatomical evaluation, including annular dimensions and coaptation gaps is crucial for optimizing clip sizing, delivery trajectory, and procedural strategy during T-TEER, especially in patients with complex tricuspid valve morphology [31].

Recent evidence also suggests that successful T-TEER may induce right ventricular reverse remodeling (RVRR). A study by Stolz et al. (2024) demonstrated a biphasic response: early RV volume unloading, followed by later structural remodeling and functional improvement over two years. This remodeling, marked by progressive reductions in RV end-diastolic volume (RVEDV) and RV end-systolic volume (RVESV), supports the therapeutic potential of annular correction even in patients with advanced disease [43].

4.3 Mechanisms and Pathophysiology of TR

The pathological progress of TR results from a disruption in the coordinated function of the TV and surrounding right heart structures. While primary TR arises from structural valve lesions, secondary (functional) TR is typically the consequence of chamber remodeling. Understanding the distinct mechanisms of each form is essential to guide appropriate clinical management.

4.3.1 Primary (Organic) TR

Primary TR arises from intrinsic structural abnormalities of the tricuspid valve apparatus, including leaflet prolapse or flail (often due to chordal rupture), infective endocarditis rheumatic disease, leaflet perforation, commissural fusion, iatrogenic valvular trauma and congenital malformations such as Ebstein's anomaly or atrioventricular septal defects [44]. Additionally, papillary muscle displacement or chordal elongation may compromise leaflet support and coaptation [45]. These structural lesions impair the normal sealing of the valve leaflets during systole, allowing regurgitant flow from the right ventricle into the right atrium.

Over time, chronic TR, if uncorrected, may lead to progressive annular dilation, right-sided volume overload, and eventually right HF [46]. Although less common, primary TR can be found in patients with chronic heart failure (CHF), particularly in those with previous cardiac surgery, trauma, infective endocarditis, or congenital anomalies, where structural valve damage is present [40]. Recognizing primary TR in this population is crucial as it may warrant a different therapeutic approach than functional forms. [46].

4.3.2 Ventricular Secondary TR

Ventricular secondary tricuspid regurgitation (V-STR) occurs in the presence of anatomically intact valve leaflets and is typically driven by structural and functional alternations of the RV. It is commonly associated with CHF, left-sided heart disease, PHTN, or AF [7,9]. Recent studies have delineated V-STR from A-STR, emphasizing the dominant role of RV dysfunction and geometric distortion in V-STR, in contrast to atrial dilation in A-STR [9,47].

In case of chronic PHTN, the RV initially compensates via concentric hypertrophy but eventually undergoes maladaptive eccentric remodeling as filling pressures rise. This process results in tricuspid annular dilation, papillary muscle displacement, and leaflet tethering, hallmarks features of V-STR [39]. As regurgitation worsens, exacerbation of RV volume overload increases wall stress and accelerates ventricular dysfunction. Interventricular septal shift may impair left ventricular (LV) filling, contributing to biventricular failure [48]. Elevated right atrial and venous pressures lead to systemic congestion, manifesting as hepatic dysfunction, renal impairment, intestinal edema, and diuretic resistance [49].

Notably, TR may persist or progress even after correction of left-sided lesions, particularly in patients with advanced RV or annular remodeling. In such cases, isolated surgical annuloplasty may be inadequate. Residual TR strongly correlates with leaflet tethering height and tenting area [39]. Therefore, therapeutic strategy should reflect the patient's specific anatomical and hemodynamic profile.

4.3.3 Atrial Secondary TR

Atrial secondary tricuspid regurgitation (A-STR) represents a distinct phenotype defined by tricuspid annular dilation without significant leaflet tethering. It is commonly linked to chronic AF and HFpEF, conditions that typically present with preserved RV geometry and normal pulmonary pressures [47]. Right atrial (RA) enlargement drives posterior annular remodeling, resulting in a disproportion between leaflet size and annular dimension. This geometric mismatch is further compounded by limited leaflet adaptation. Histopathological

suggests atrial myocardium extension into the leaflet base, compromising effective coaptation, while 3D echocardiographic studies confirm right atrial volume as a key determinant of annular enlargement in functional TR [35].

In patients with A-STR, the loss of atrial contraction disrupts presystolic annular shortening and desynchronizes valve dynamic from RV systole, promoting regurgitation. Early stages may be clinically silent, but disease progression can lead to symptomatic TR, reduced exercise tolerance, and signs of right HF. Standard echocardiographic parameters may underestimate severity due to non-central jets and annular deformation. Restoration of sinus rhythm has been associated with regression of annular dilation and improvement in TR, highlighting the role of the atrial contraction in maintaining valve competence [50].

From a therapeutic standpoint, early rhythm control and intervention appear to offer benefits. Patients with A-STR tend to exhibit more favorable anatomy for transcatheter tricuspid valve interventions (TTVIs), particularly edge-to-edge repair and annuloplasty, with improved procedural outcomes compared to V-STR, especially when performed prior to irreversible RV remodeling [17]. Data from the EuroTR Registry further underscore the prognostic value of this phenotype: A-STR was associated with lower residual TR, better symptom relief, and higher freedom from heart failure hospitalization at 1 and 2 years. Moreover, A-STR independently predicted long-term survival without HF admissions, supporting its role as a meaningful therapeutic target [20]. Although current guidelines remain imprecise, dedicated phenotyping and early referral to specialist heart valve centers are strongly encouraged to improve prognosis in this underrecognized subgroup [17].

4.3.4 TR Secondary to Left-Sided Valve Disease

Frequently, TR is encountered in patients with severe aortic stenosis (AS) and other left-sided valvular pathologies. Registry data indicate that 11–27% of patients undergoing transcatheter aortic valve replacement (TAVR) present with at least moderate TR [51]. In

such cases, TR is predominantly functional and reflects the downstream effects of chronic left-sided pressure overload, including PHTN, right ventricular remodeling, and annular dilation [51]. Persistent TR further impairs right-sided hemodynamics and contributes to recurrent decompensation and hospitalizations [52].

Although TAVR may reduce TR severity in 30–60% of cases, persistent TR seen in approximately half of patients is strongly linked with worse outcomes, including higher rates of HF readmissions and all-cause mortality. AF and tricuspid annular diameter ≥ 37 mm have been identified as predictors of persistent TR post-TAVR [53]. In these high-risk populations, T-TEER with the TriClip system has emerged as a promising adjunctive strategy. Recent evidence have shown that TriClip therapy significantly reduces TR severity and improves QoL, particularly among those with NYHA Class III–IV symptoms [54]. By targeting residual or worsening TR after left-sided interventions, TriClip provides a new therapeutic option for CHF patients.

Longitudinal studies indicate that nearly one-third of HFrEF patients with initially mild TR progress to more severe stages, underscoring the need for early identification and continuous monitoring. Prognosis is further influenced by comorbidities such as systemic hypertension, ischemic heart disease, and increased LV end-diastolic dimensions [55].

In a subanalysis of the Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation (COAPT) trial showed that patients with secondary mitral regurgitation (MR) and coexisting moderate or greater TR exhibited worse baseline profiles and outcomes. Nevertheless, MitraClip plus guideline-directed medical therapy (GDMT) significantly improved survival and reduced HF hospitalizations compared to GDMT alone. These findings support the clinical value of MitraClip in patients with combined mitral and tricuspid valve disease, although they also highlight the persistent burden of TR on overall prognosis [56].

5. Patient Selection for TriClip TEER Procedure

5.1 Hemodynamic Assessment and Patient Stratification

Accurate hemodynamic profiling is essential for selecting appropriate candidates for TriClip therapy in patients with TR. While anatomical feasibility is a prerequisite, favorable clinical outcomes also depend heavily on right heart function, pulmonary vascular load, and overall systemic condition. A comprehensive evaluation combining transthoracic echocardiography (TTE), transesophageal echocardiography (TEE), and right heart catheterization (RHC) is the cornerstone of appropriate candidate identification [57].

One of the most significant predictors of poor procedural outcomes is severe RV dysfunction [40]. Specifically, patients with tricuspid annular plane systolic excursion (TAPSE) <13 mm are often excluded from TriClip therapy due to low therapeutic benefit. Modern approaches to RV function assessment incorporate multiparametric indices such as 3D RV ejection fraction (RVEF), RV longitudinal strain, and RV–pulmonary artery (RV–PA) coupling [57].

The TAPSE to pulmonary artery systolic pressure (TAPSE/PASP) ratio is a well-established, noninvasive echocardiographic surrogate for RV-PA coupling. A threshold value of <0.406 mm/mmHg has been strongly associated with RV–PA uncoupling and correlates with higher procedural failure rates and increased mortality following T-TEER, as demonstrated in a multicenter analysis by Brener et al. from the TriValve registry [58]. This index has demonstrated independent prognostic value in patients undergoing transcatheter TV replacement (TTVR), supporting its role in both patient selection and risk stratification. Moreover, improvements in the TAPSE/PASP ratio following successful TR reduction emphasize its responsiveness to therapeutic intervention and its utility in ongoing functional monitoring [59].

PHTN is another critical factor influencing patient selection. Differentiation between pre-capillary and post-capillary PHTN using RHC is essential. Pre-capillary PHTN is defined as mean pulmonary artery pressure (mPAP) >30 mmHg, pulmonary vascular resistance (PVR) ≥ 3 Wood units (WU), or transpulmonary gradient (TPG) >17 mmHg and is associated with unfavorable outcomes and typically warrants medical optimization prior to any intervention. In contrast, patients with isolated post-capillary PH, often due to left-sided heart disease, may still be considered for TriClip, particularly if mPAP remains <30 mmHg and PVR is <3 WU. A pulmonary Capillary Wedge Pressure (PCWP) >15 mmHg alongside a low PVR confirms post-capillary PH, whereas a PCWP ≤ 15 mmHg with elevated PVR suggests a pre-capillary phenotype [48,60].

Volume overload from TR also influences hemodynamic interpretation. Elevated right atrial pressure (RAP) and RV end-diastolic pressure (RVEDP >8 mmHg) indicate impaired RV compliance and poorer prognosis. Impaired RA compliance and large v-waves, as emphasized by Hahn et al., reflect volume overload and venous congestion, contributing to right heart dysfunction. Hemodynamic waveforms from RHC, including prominent v-waves, absent a-waves in AF, and steep y-descents can further support the diagnosis of severe TR and right-sided congestion [48]. In addition to diagnosis, Hahn et al. highlight the role of RHC in procedural timing and risk stratification, particularly in borderline or high-risk patients, where static echocardiographic parameters may underestimate severity [61].

Finally, systemic and extracardiac conditions must be considered. Patients on chronic dialysis, having advanced malignancy, cardiac cachexia, or hemoglobin ≤ 9 g/dL are frequently excluded due to high procedural risk and limited recovery potential. Likewise, recent coronary revascularization (<30 days), intracardiac thrombus, and access-limiting deep vein thrombosis represent procedural contraindications [62].

5.2 Integrating Hemodynamics with Clinical and Anatomical Eligibility

Optimal patient selection for TriClip therapy requires an integrated assessment of hemodynamic, anatomical, and clinical parameters. While hemodynamic thresholds offer some guidance, echocardiographic imaging remains the cornerstone of evaluation play a pivotal role throughout the patient's journey: from diagnosis and procedural planning to intraprocedural guidance and follow-up.

Key anatomical factors include valve morphology, annular dimensions, coaptation gap, leaflet mobility, and jet location. Features such as excessive leaflet tethering, severe annular dilation, or coaptation gaps exceeding 7.2 mm may limit the feasibility of TEER [63,64]. Ideal candidates demonstrate tricuspid leaflet lengths greater than 7 mm, preserved leaflet mobility, and a coaptation reserve of at least 5 mm. Central or anteroseptal regurgitant jets and coaptation gaps between 3 and 7 mm are associated with higher procedural success [64]. Conversely, coaptation defects exceeding 8.5 mm or a leaflet-to-annular ratio ≥ 1.06 are linked with markedly reduced procedural success [61,65].

Imaging clarity is critical. Clearly visualized leaflets and favorable jet direction support optimal clip alignment, whereas bicuspid or quadricuspid valves or eccentric jets may complicate grasping and reduce procedural efficacy [61]. Detailed preprocedural imaging, primarily TTE and TEE, supplemented with 3D intracardiac echocardiography (ICE) when necessary, is essential for assessing leaflet number, mobility and jet direction. However, poor acoustic windows remain a limitation in some patients [66].

RV function is a central prognostic factor. In an observational study by Vogelhuber et al. (2024), procedural success was achieved in 88.6% of patients with RV dysfunction. However, impaired global RV dysfunction was predictive of increased mortality and rehospitalization at two years. Longitudinal dysfunction alone was not prognostic, emphasizing the need for comprehensive RV evaluation [67].

Echocardiographic substudies have shown that successful TriClip treatment can lead to reductions in right atrial pressure and RVEDV, reflecting favorable RVRR. These structural

changes are particularly relevant in CHF patients with chronic volume overload and chamber dilation [68].

Comorbidities such as AF and PHTN (especially in A-SVR) necessitate individualized assessment. In patients with preserved RV function and moderate volume overload, where TR is primarily annular in origin without significant tethering TriClip therapy may still provide benefit [17]. The presence of pacemaker or defibrillator leads is not an absolute contraindication unless leaflet coaptation is impaired, particularly with centrally located leads. Commissural leads may be manageable, but recently implanted ones may require delayed intervention [69].

Ultimately, integrating clinical, anatomical, and hemodynamic data allows for precise risk stratification. This comprehensive approach identifies patients most likely to benefit from TriClip, while avoiding futile procedures in those with advanced, irreversible pathology or high procedural risk. Thus, maximizing procedural success and improving short-term long-term outcomes [61,62,66].

6. TriClip and other Transcatheter Devices

A thorough understanding of transcatheter device classification is essential for selecting the appropriate intervention in patients with TR. Based on their mechanism of action, these therapies can be broadly categorized into four groups: annuloplasty systems, caval valve implantation (CAVI) devices, orthotopic valve replacement devices, and coaptation devices [8].

Annuloplasty systems aim to restore leaflet coaptation by reducing the diameter of the tricuspid annulus. These include suture-based technologies like Trialign and TriCinch, as well as implantable ring-based systems like Cardioband. They are typically most effective in patients with annular dilation and preserved leaflet motion; however, their efficacy decreases

in the presence of significant leaflet tethering or anatomical distortion, which are common in CHF patients [70,71,72]. Although annuloplasty may be more successful in selected cases of isolated annular dilation, TriClip G4 shows broader utility in complex, high-risk populations. Both strategies can reduce TR by approximately two grades and improve symptoms, but further randomized trials are needed to clarify comparative long-term outcomes [73].

Caval valve implantation (CAVI) represents a different approach, wherein valves are placed within the superior and/or inferior vena cava. These devices do not directly correct regurgitation but aim to reduce systemic venous congestion, which can be particularly symptomatic in right-sided heart failure. The TricValve system is a key example under evaluation in this category, although long-term efficacy data remain limited. CAVI offers symptomatic relief but does not treat the regurgitation itself. It may represent a better-tolerated alternative to orthotopic valve replacement in with severe RV dysfunction [74].

6.1 TriClip versus Valve Replacement Systems

Orthotopic tricuspid valve replacement devices, such as the EVOQUE system, deliver a prosthetic valve directly into the tricuspid position with the goal of complete elimination of regurgitant flow. The EVOQUE system consists of a self-expanding nitinol frame with bovine pericardial leaflets, an intra-annular fabric sealing skirt, and ventricular anchors. It is delivered via transfemoral access using a 28 Fr delivery system and is available in 44 mm and 48 mm sizes [75, 76].

Clinical trials and compassionate use studies have demonstrated high procedural success with EVOQUE, with sustained TR reduction and improved symptoms. In the TRISCEND study, 98% of patients had mild or less TR at one year, with improvements in NYHA class, cardiac output, and quality-of-life scores. The TRISCEND II randomized trial confirmed EVOQUE's superiority of over medical therapy, achieving its primary composite endpoint, although no significant differences in mortality or heart failure hospitalization were observed.

Bleeding and pacemaker requirements were more frequent in the EVOQUE arm. While the device is particularly useful in patients with large coaptation gaps or severely dilated annuli, its large-caliber delivery system and higher procedural risk may limit its use in advanced heart failure patients. In February 2024, EVOQUE became the first dedicated tricuspid valve replacement system to receive FDA approval, expanding access beyond clinical trials [75]

Other orthotopic systems, such as the NaviGate valve, have shown early feasibility in small compassionate-use series, but challenges such as significant bleeding rates and the need for a transatrial approach have limited their broader adoption [76]

These procedural and anatomical limitations, along with increased perioperative risk, make patient selection critical when considering orthotopic replacement over edge-to-edge repair [8,74,75]. Although EVOQUE may offer higher TR reduction rates, TriClip is associated with a lower risk profile and reduced one-year mortality, supporting its use in high-risk patients who may not tolerate valve replacement [73].

6.2 TriClip versus Edge-to-Edge Devices

In contrast to annuloplasty, valve replacement, and caval valve implantation techniques, leaflet approximation (edge-to-edge repair) devices are currently the most widely adopted transcatheter strategy for treating severe TR. Coaptation devices, such as TriClip and PASCAL, reduce regurgitant flow by grasping the tricuspid leaflets to improve coaptation and create a double orifice [77]. Delivered via a transfemoral approach under real-time imaging, they have become the most widely used transcatheter therapies for tricuspid regurgitation due to their procedural simplicity, anatomical adaptability, and favorable outcomes [71]. By combining anatomical efficacy with procedural safety, coaptation systems are especially valuable in high-risk CHF populations [78]

Among these, TriClip G4 System, designed specifically for the tricuspid valve, has emerged as a leading option and has evolved into its current form with four available clip sizes (NT, XT, NTW, and XTW) [77]. The TriClip system holds CE Mark approval in Europe and remains the only FDA-approved device for T-TEER in the United States. Its device architecture is equipped with wider clip arms, Controlled Gripper Actuation (CGA), and enhanced steerability enabling more precise leaflet capture. These features provide strong coaptation and facilitate independent grasping and optimization of the grippers which is particularly advantageous in patients with complex tricuspid valve anatomy [79].

The PASCAL system, holds CE Mark in Europe since 2020, integrates a central spacer and an independent clasping mechanism. It has shown comparable safety and efficacy comparable to TriClip in early studies [80]. Unlike TriClip, PASCAL employs a spacer-based coaptation mechanism and offers a wider profile, which may be advantageous in patients with large coaptation gaps [81].

Meta-analyses suggest that TriClip achieves significantly greater reductions in vena contracta width while maintaining equivalent procedural safety and success [82]. Both systems improve clinical status and RV function, including NYHA class and 6-minute walk distance. However, TriClip's tailored design may offer incremental benefit in CHF patients with severe annular dilation or leaflet tethering [83]. In addition, TriClip is currently supported by a more robust body of clinical evidence, including results from the TRILUMINATE pivotal trial and large post-approval registries, reinforcing its role as the preferred edge-to-edge option for high-risk CHF populations [84]. This preference is further supported by broader clinical adoption, greater operator familiarity, and the current lack of head-to-head randomized trials directly comparing the two systems.

Emerging evidence increasingly supports the clinical advantage of the TriClip system over other TEER devices such as MitraClip and PASCAL in managing TR. A 2024 meta-analysis by Balata et al. demonstrated that while all devices reduced regurgitant volume and effective regurgitant orifice area, TriClip achieved the most significant reduction in vena contracta width: a critical marker of TR severity [82]. These findings are corroborated by 1-year

outcomes from the TRILUMINATE trial, in which TriClip achieved sustained TR reduction in 71% of patients and led to marked improvements in functional capacity and quality of life [85].

However, both studies had limitations. The meta-analysis relied on heterogeneous datasets, and although TRILUMINATE was randomized, it lacked blinding and had a relatively short follow-up. These methodological constraints underscore the need for larger trials to confirm benefits and guide device selection. Still, current data suggest TriClip may be preferred in patients with severe symptomatic TR [86].

6.3 TriClip Alignment and Biomechanical Impact

Beyond TR reduction, TriClip may exert biomechanical benefits by promoting reverse annular and RV remodeling, making it more than a purely symptom-relief intervention. Once deployed, the device approximates valve leaflets, reducing the effective regurgitant orifice area and improving coaptation. This restores valve competence and decreases right atrial volume overload, alleviating symptoms such as fatigue, edema, and hepatorenal congestion [40].

In V-STR, characterized by leaflet tethering and reduced coaptation reserve, the first clip should be placed across the septal–lateral axis. An anterior-first approach may hinder access to posterior planes, whereas placing the first clip posteriorly may provide better alignment, even if it introduces acoustic shadowing. In A-STR, where RV function is preserved but annular dilation and leaflet flattening predominate, careful perpendicular alignment to the coaptation plane is essential. Clip placement near commissures (typically anterior-septal leaflets) may be required to restore valve function [87].

Mechanically, clip placement may counteract outward annular forces. In functional TR, progressive dilation of the RV free wall and atrium distorts the annulus, worsening leaflet

tethering. Targeted clip positioning along the anteroseptal and posteroseptal lines can draw annular segments inward, enhance coaptation and may even promote septal realignment toward the RV. Dual clip strategies maximize this remodeling potential while preserving multiple valve orifices. By contrast, anteroposterior placement offers less remodeling potential and may tension the anterior leaflet, impairing coaptation [88,89].

In a study by Stocker et al. (2021), TTVR using an average of two clips reduced severe TR ($\geq 3+$) from 100% at baseline to 16% at discharge. Hemodynamic improvements included a 13% drop in RAP, a 19% reduction in the v wave, and a cardiac output increase from 3.5 to 4.5 L/min. These changes persisted at follow-up and were linked to improved 1-year survival [60].

7. Clinical Evidence and Outcomes

7.1 Clinical Trials and Registries

The clinical evaluation of the TriClip system for treating TR in CHF patients has progressed from early feasibility studies to large-scale randomized trials. The TRILUMINATE Early Feasibility Study, published in 2019, was the first major investigation of TriClip, enrolling 85 patients. This single-arm study demonstrated high device success and showed that 86% of patients achieved TR reduction to moderate or less at 30 days [90].

Real-world registry data has supported these outcomes. The TriValve Registry, published in 2019, compiled data from 249 patients with severe symptomatic tricuspid regurgitation treated with edge-to-edge repair systems, including off-label MitraClip use. Procedural success defined as TR reduction to grade $\leq 2+$ was achieved in 77% of patients, with 72% maintaining that reduction at 1 year [91].

This was followed by the TRILUMINATE Pivotal Randomized Controlled Trial, reported by Sorajja et al. (2023), which enrolled 350 patients (175 in the device group). In this trial, 87% of TriClip-treated patients achieved moderate or less TR at 30 days, and most patients remained stable in terms of residual TR severity at 1 year follow up [78]. A subsequent 1-year outcomes analysis from an expanded randomized cohort (n = 392), published by Tang et al. (2024), confirmed similar durability of TR reduction [92].

At 2 years, among the same cohort, 76% maintained TR reduction to $\leq$ moderate [93]. Most recently, the 3-year follow-up of the original TRILUMINATE Feasibility cohort (n = 98) confirmed durable anatomical success, with 79% of patients maintaining moderate or less TR, and 92% achieving at least a one-grade reduction from baseline [94].

The bRIGHT Study, published in 2024, enrolled 511 patients—many of whom were elderly and had CHF, including individuals with CIEDs. This multicenter post-approval registry demonstrated excellent device safety—with no lead-device interactions—and showed that 81% achieved TR reduction to moderate or less at 1 year [95].

The transcatheter edge-to-edge repair for severe isolated TR (TRI-FR) Trial, published in 2025, further confirmed these findings in a European randomized controlled setting. This multicenter trial enrolled 300 patients with symptomatic severe secondary TR and CHF who were not surgical candidates. Participants were randomized to TriClip plus GDMT (n=152) or GDMT alone (n=148). At 1-year follow-up, 78% of TriClip patients achieved TR less than grade 4+, versus 46.5% in the control group, demonstrating a statistically significant improvement [96].

7.2 Procedural Safety and Efficacy

Transcatheter edge-to-edge repair (TEER) with the TriClip system has demonstrated consistent safety and efficacy across all major trials and registries. The 2019

TRILUMINATE Early Feasibility Study (EFS) was the first to establish the technical feasibility and safety of TriClip in high-risk patients with symptomatic severe TR. Device success exceeded 90%, and freedom from major adverse events (MAEs) at 30 days was 98%, with no procedural mortality [90].

This was followed by the TRILUMINATE Pivotal Trial (2023), which confirmed a strong safety profile. In this study, 98.3% of patients were free from MAEs at 30 days, where MAEs included cardiovascular death, new-onset kidney failure, endocarditis requiring surgery, or nonelective cardiovascular surgery for a TriClip-related adverse event. Serious complications such as major bleeding, stroke, or device embolization were rare [78].

Importantly, TriClip avoids the need for cardiopulmonary bypass, a significant advantage for patients with CHF, frailty, renal dysfunction, or PHTN. Procedural guidance using TEE and fluoroscopy allows accurate leaflet alignment and grasping, ensuring efficacy even in anatomically challenging cases, thus contributing to safety [97].

Further safety confirmation comes from both the TRI-FR trial and the bRIGHT study. TRI-FR reported no periprocedural deaths, one in-hospital death (0.6%), and low complication rates (8.0% overall; single leaflet device attachment (SLDA) 5.2%) [96]. Similarly, a dedicated subanalysis of the 2025 TRILUMINATE Pivotal Trial evaluating patients with transvalvular CIED leads found no evidence of lead-device interactions or device malfunction. Patients with CIEDs achieved comparable rates of TR reduction and improvements in functional and quality-of-life outcomes, reinforcing the safety and efficacy of TriClip therapy in this subgroup [98].

The incidence of serious complications, such as major bleeding, stroke, or device embolization, is very low according to all the major studies. These findings align with earlier data demonstrating that freedom from MAEs consistently exceeds 95%, reinforcing the safety of TriClip in high-risk TR patients unsuitable for surgery [78,96,97,98].

7.3 Symptom Relief, Quality of Life, and Clinical Outcomes After TEER

In the TRILUMINATE Pivotal Trial, TriClip therapy led to rapid and sustained improvements in symptoms, QoL, and clinical status among patients with severe TR and CHF). At 1 year, 80.6% of TriClip patients were in NYHA class I or II, compared to 59.5% in the control group. The mean Kansas City Cardiomyopathy Questionnaire (KCCQ) score improvement was 12.3 points versus 0.6 points, respectively ($P < 0.001$) and 49.7% of TriClip patients achieved a ≥ 15 -point gain in KCCQ score, compared to 26.4% in the control group. These benefits were consistent across all subgroups regardless of demographic or clinical profile [78].

According to Prandi et al residual TR $\geq 3+$ on echocardiography is independently associated with higher risk of heart failure (HF) rehospitalization within 1 year, highlighting the prognostic importance of achieving durable TR reduction [97].

At 2 years, early TriClip intervention continued to show sustained symptomatic improvement and fewer recurrent HF hospitalizations, while delayed crossover treatment was linked to greater interim symptom burden and more frequent hospitalizations [93]. By 3 years, the TRILUMINATE study confirmed durability, with 79% maintaining TR of moderate or less and 92% achieving ≥ 1 -grade TR reduction, underscoring the long-term anatomical and clinical benefits of T-TEER with TriClip [94].

The TRI-FR Trial (2025) further supported TriClip's clinical utility in symptomatic secondary TR. A composite endpoint (NYHA class, patient global assessment [PGA], and CV hospitalization or death) favored TEER, with 75% of TEER patients improving vs. 40% of controls. PGA improved in 74.6% of treated patients vs. 39.5% of controls ($P < 0.0001$), and mean KCCQ score at one year was higher in the TEER group (69.9 vs. 55.4, $P < 0.001$). TEER patients also had significantly fewer readmissions (35 among 121 previously hospitalized) [96].

Sustained KCCQ improvements were observed across all domains at 6 weeks (+17.0), 6 months (+15.9), and 1 year (+18.7), with a between-group difference of +10.3 points favoring TriClip (95% CI, 5.6–15.0) [99].

Real-world bRIGHT study data support these findings. At 1 year, NYHA class I/II rose from 21% to 75% ($P < 0.0001$), and mean KCCQ score improved by 19 ± 26 points ($P < 0.0001$); 56.2% experienced a ≥ 15 -point gain. Outcomes were consistent across sites, regardless of procedural volume, supporting generalizability in broader HF populations [95].

Altogether, these findings underscore TriClip's consistent ability to improve quality of life, symptom burden, and hospitalization outcomes—especially when used early in disease progression.

7.4 Comparative Efficacy with Alternative Interventions

TriClip and other TTVI offer a less invasive alternative to surgery for patients with severe TR [100]. While surgical repair remains the definitive option in anatomically suitable patients, its applicability is limited by high perioperative mortality, especially in older adults with comorbidities or biventricular dysfunction. A pivotal retrospective study by Axtell et al. (2019) evaluated 3,276 patients with severe iTR and found no significant advantage in long-term survival between those who underwent surgery and those treated medically, even after adjusting for immortal time bias. These findings question the survival benefit of surgical intervention in isolated TR and support the growing interest in less invasive transcatheter approaches for high-risk populations [101].

Real-world registries such as TriValve and TRIGISTRY have confirmed the feasibility and safety of TEER in high-risk patients with symptomatic TR, laying the foundation for more targeted technologies like TriClip (Mehr et al., 2024; Dreyfus et al., 2024). Many treated

patients are elderly, frail, or have CIEDs, necessitating individualizing therapeutic approaches [102,103].

Among current TTVI options, TriClip and EVOQUE have emerged as leading systems with complementary roles. EVOQUE, a transcatheter valve replacement device, achieves more complete TR elimination (TR $\leq 2+$ in up to 86% at 30 days) but is associated with higher procedural complexity and MAEs (26.8%), including a 9.1% 1-year mortality and a risk of device embolization [104]. In contrast, TriClip offers a safer procedural profile, with no observed device embolization, a lower 1-year mortality (7.1%), and greater suitability for frail patients or those with CIEDs. As a result, TriClip is increasingly favored for patients ineligible for surgery or valve replacement [105].

Comparative analyses further support TriClip's clinical value. A 2024 meta-analysis by Balata et al. found that TriClip had the highest procedural success rate (92%) and the lowest incidence of SLDA among devices like PASCAL and MitraClip [82]. Additionally, Ebsen et al. reported that while both TriClip and PASCAL offered comparable safety and outcomes, TriClip showed a trend toward better TR reduction and technical success, without affecting the composite endpoint of mortality, HF hospitalization, or reintervention [80]. A recent observational study by Fernandes et al. compared TriClip and Pascal in patients undergoing TEER for severe TR. Both devices improved TR severity and NYHA class at three months, but TriClip led to significantly greater RVRR ($p = 0.02$) at 3 months post-procedure, suggesting a true clinical effect rather than chance. NYHA class improvement was also slightly more pronounced in the TriClip group [106]. These findings indicate a potential advantage of TriClip in supporting RV recovery in CHF patients, warranting further investigation in larger cohorts.

Finally, while annuloplasty and transcatheter valve replacement technologies continue to evolve, they remain investigational and are not yet widely adopted. TriClip's procedural simplicity, strong safety profile, and proven symptom relief position it as the current first-line transcatheter therapy for patients with symptomatic secondary TR, especially those with CHF and elevated surgical risk [8].

8. Limitations and Challenges

8.1 Durability, Long-term outcomes and Evidence Gaps

While TriClip has shown encouraging short- and mid-term outcomes, its long-term durability remains uncertain. Most studies report follow-up of up to three years, with limited data on mechanical fatigue, leaflet detachment, or recurrent regurgitation. Given the distinct biomechanics of the right heart, continued echocardiographic surveillance and long-term randomized data are essential to establish durability benchmarks [94].

A recent systematic review and meta-analysis by Suc et al. (2025) highlighted the significant long-term mortality associated with isolated severe TR, regardless of treatment strategy. Five-year mortality reached 46% with medical therapy and 30% even after surgery or percutaneous intervention. The authors concluded that, despite potential selection bias, percutaneous and surgical approaches did not significantly reduce mortality beyond two years, underscoring the urgent need for more effective therapies and earlier intervention in this high-risk population [107].

Although long-term mortality data are still emerging, early real-world outcomes suggest a trend toward reduced cardiovascular mortality in patients with sustained TR reduction, particularly those with preserved or moderately impaired RV function. The durability of symptom relief and functional improvement has been supported by registry cohort follow-up data extending to three years, with ongoing studies expected to provide critical five-year outcome data to further define long-term durability and benefit.

While TriClip has consistently demonstrated improvements in TR severity, symptom burden, QoL, and HF-related hospitalizations, survival benefits remain less certain. As highlighted

by Suc et al. (2025), overall mortality in patients with severe iTR remains high across treatment groups, suggesting that symptomatic improvement alone may not yet translate into significant long-term survival gains, particularly in patients with advanced or unselected disease [94,107].

8.2 Economic Considerations

A recent cost-effectiveness study evaluated TriClip in NYHA III–IV patients with severe TR. The 5-year survival rate was higher with TriClip (57.6%) compared to medical therapy (49.9%), with an average gain of 1.64 life years. Total 60-month costs were €25,661.15 for TriClip versus €3,879.72 for medication alone [108]. Separately, a Polish analysis estimated the cost per quality-adjusted life years (QALY) at polish złoty (PLN) 85,000–100,000, below the national reimbursement threshold. Together, these findings support TriClip as a cost-effective option and underscore the need for structured reimbursement pathways and early access in advanced CHF care. [109].

9. Future perspectives

9.1 Ongoing Clinical Trials and Registries

The next phase of TriClip evaluation will focus on long-term and comparative outcomes. Continued follow-up from trials like TRILUMINATE is expected to provide insight into device durability, survival, and late complications [78]. Although post-market surveillance and registry efforts may yield valuable real-world data, their current status is not consistently available in the public domain.

To support long-term safety assessment, the TriClip Post-Approval Study (PAS) is an ongoing observational study designed to systematically collect real-world data on patients treated with the TriClip G4 system. While no formal results are available yet, the PAS will be instrumental in informing future evaluations of device performance, safety, and clinical outcomes across diverse patient populations [110].

9.2 Expanding Indications and Guideline Integration

TriClip has primarily been used in patients with secondary TR and advanced HF who are not surgical candidates. However, its potential application is broadening. Emerging evidence suggests benefit in patients with isolated atrial TR, often related to long-standing AF and preserved RV function, where early intervention may prevent irreversible remodeling [17].

Additional populations under investigation include those with CIED-induced TR, congenital anomalies, and post-heart transplant cases, provided anatomical suitability is confirmed [111]. There is also growing interest in TriClip as a bridge-to-decision therapy—temporarily stabilizing patients with severe TR to reassess surgical candidacy [8].

As evidence matures, broader guideline recommendations may follow. Current ESC (2021) guidelines offer limited endorsement for transcatheter tricuspid repair in high-risk patients [3]. Future integration into heart failure pathways and value-based care models will depend on long-term outcome data and robust cost-effectiveness analyses.

9.3 Technological Innovation and Personalization

Emerging technologies such as artificial intelligence (AI) and 3D printing are poised to enhance patient selection and procedural planning in transcatheter tricuspid interventions.

AI-driven cardiac computed tomography (CT) analysis has demonstrated excellent correlation with core-lab assessments in TTVR, enabling fast and accurate RV quantification [112]. Meanwhile, 3D-printed valve models have been successfully used to simulate device deployment, optimize clip positioning, and even explore patient-specific valve designs [113]. As these technologies evolve, their integration with imaging and procedural platforms may support more personalized, precise, and reproducible outcomes in TR management, particularly for anatomically complex or high-risk CHF patients.

10. Conclusion

Tricuspid regurgitation (TR) is a significant driver of morbidity, mortality, and hospitalizations in CHF, particularly when left untreated. The TriClip TEER system provides a safe and effective treatment for patients with symptomatic, secondary TR who are not surgical candidates. Clinical trials and real-world data have shown that TriClip reduces TR severity, improves NYHA class, exercise capacity, and QoL, and is associated with fewer HF-related hospitalizations.

Benefits are most evident in patients with preserved RV function and earlier-stage disease. As long-term data accumulate, TriClip is expected to play an increasingly central role in CHF management. Health economic analyses show it is cost-effective, and increasing evidence may soon lead to stronger guideline support for proactive treatment of tricuspid valve disease.

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List of Abbreviations

Abbreviations	Definitions
3D	Three Dimensional
AS	Aortic Stenosis
A-STR	Atrial Secondary Tricuspid Regurgitation
AF	Atrial Fibrillation
AI	Artificial Intelligence
bRIGHT	An Observational Real-World Study Evaluating Severe Tricuspid Regurgitation Patients Treated With the Abbott TriClip™ device
CAVI	Caval Valve Implantation
CHF	Chronic Heart Failure
CGA	Controlled Gripper Actuation
CIEDs	Cardiac Implantable Electronic Devices
COAPT	Cardiovascular Outcomes Assessment of the MitraClip Therapy for Heart Failure Patients with Functional Mitral Regurgitation
CT	Computed Tomography
EFS	Early Feasibility Study
ESC	European Society of Cardiology
EuroTR	European Registry of Tricuspid Regurgitation
GDMT	Guidelines Directed Medical Therapy
HFA	Heart Failure Association
HF	Heart Failure
HFpEF	Heart Failure with preserved Ejection Fraction
HFrEF	Heart Failure with reduced Ejection Fraction
ICE	Intracardiac Echocardiography
iTR	Isolated Tricuspid Regurgitation
KCCQ	Kansas City Cardiomyopathy Questionnaire
LV	Left Ventricle
MAEs	Major Adverse Events
MR	Mitral Regurgitation
mPAP	Mean Pulmonary Artery Pressure
NYHA	New York Heart Association
NEDA	National Echocardiography Database of Australia
PAS	Post Approval Study
PASP	Pulmonary Artery Systolic Pressure
PCWP	Pulmonary Capillary Wedge Pressure
PGA	Patient Global Assessment
PHTN	Pulmonary Hypertension
PLN	Polish zloty
PVR	Pulmonary Vascular Resistance
QALY	Quality Adjusted Life Years
QoL	Quality of Life
RA	Right Atrium
RAP	Right Atrial Pressure
RHC	Right Heart Catheterization

RV	Right Ventricle
RV-PA	Right Ventricular- Pulmonary Artery
RVEDP	Right Ventricular End Diastolic Pressure
RVEDV	Right Ventricular End Diastolic Volume
RVEF	Right Ventricular Ejection Fraction
RVESV	Right Ventricular End Systolic Volume
RVRR	Right Ventricular Reverse Remodeling
SLDA	Single Leaflet Device Attachment
STR	Secondary Tricuspid Regurgitation
TA	Tricuspid Annulus
T-TEER	Tricuspid valve – Transcatheter edge-to-edge repair
TAPSE	Tricuspid Annular Plane Systolic Excursion
TAPSE/PASP	Tricuspid Annular Plane Systolic Excursion / Pulmonary Artery Systolic Pressure
TAVR	Transcatheter Aortic Valve Replacement
TEE	Transesophageal Echocardiography
TEER	Transcatheter Edge-to-Edge Repair
TPG	Transpulmonary Gradient
TRI.fr	Transcatheter Edge-to-Edge Repair for Severe Isolated Tricuspid Regurgitation The Tri.Fr Randomized Clinical Trial (France)
TR	Tricuspid Regurgitation
TRISCEND	Edwards EVOQUE Transcatheter Tricuspid Valve Replacement: Pivotal Clinical Investigation of Safety and Clinical Efficacy Using a Novel Device
TRILUMINATE	Trial to Evaluate Cardiovascular Outcomes In Patients Treated with the Tricuspid Valve Repair System Pivotal
TriValve	Transcatheter Tricuspid Valve Therapies
TTE	Transthoracic Echocardiography
TTVIs	Transcatheter Tricuspid Valve Interventions
TTVR	Transcatheter Tricuspid Valve Replacement
TV	Tricuspid valve
V-STR	Ventricular Functional Secondary Tricuspid Regurgitation
WU	Woods Units

Τελευταία σελίδα

ΤΜΗΜΑ ΙΑΤΡΙΚΗΣ

**ΣΧΟΛΗ ΕΠΙΣΤΗΜΩΝ ΥΓΕΙΑΣ
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