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STRUCTURAL

Functional and Echocardiographic Improvement After Transcatheter Repair for Tricuspid Regurgitation

A Systematic Review and Pooled Analysis

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ABSTRACT

OBJECTIVES The aim of this study was to assess the feasibility, efficacy, and clinical outcomes of transcatheter repair of tricuspid regurgitation (TR) in a pooled analysis of interventional studies.

BACKGROUND New percutaneous devices are available to treat severe TR, but the evidence is sparse and limited to smaller cohorts.

METHODS Several electronic databases were searched for interventional studies involving percutaneous repair of TR. Devices used were the Cardioband, FORMA, MitraClip, PASCAL, and Trialign. Outcomes included in the final analysis were successful implantation, residual severe TR, post-procedural New York Heart Association (NYHA) functional class III or IV, 6-min walk distance, and echocardiographic parameters. Subgroup and meta-regression analysis were performed to further explore residual heterogeneity.

RESULTS Seven studies and 454 patients undergoing transcatheter tricuspid valve repair were included in the pooled analysis; 95% of patients had at least severe TR, and 91% were in NYHA functional class III or IV. Successful implantation was achieved in 86% of patients. At the longest follow-up available (weighted mean 265 days), 9% had died. Compared with baseline, a significantly lower proportion of patients had at least severe TR (relative risk: 0.38; 95% confidence interval: 0.20 to 0.70; $p = 0.004$) and were in NYHA functional class III or IV (relative risk: 0.23; 95% confidence interval: 0.20 to 0.30; $p < 0.001$). Patients also experienced increases in 6-min walk distance (mean difference +64.6 m; $p < 0.001$) and significant reductions in tricuspid valve annular diameter (mean difference −3 mm; $p < 0.001$), while left and right ventricular function did not change significantly.

CONCLUSIONS A strategy of transcatheter repair for severe TR appears to be feasible, effective, and associated with improved clinical outcomes at mid-term follow-up. (J Am Coll Cardiol Intv 2020;13:2719–29) © 2020 by the American College of Cardiology Foundation.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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ABBREVIATIONS AND ACRONYMS

6MWT = 6-min walking distance

CI = confidence interval

EROA = effective regurgitant orifice area

EuroSCORE = European System for Cardiac Operative Risk Evaluation

LVEF = left ventricular ejection fraction

MD = mean difference

NYHA = New York Heart Association

RR = risk ratio

TAPSE = tricuspid annular plane systolic excursion

TR = tricuspid regurgitation

TTVr = transcatheter tricuspid valve repair

Tricuspid regurgitation (TR) is a prevalent valvular disease, associated with increased mortality and morbidity (1,2) and worsening of symptoms over time (3). In most cases, TR is secondary to left-sided heart disease (4) and is often left untreated at the time of surgical correction of the primary valve disease (5). At present, many patients with symptomatic severe TR are at high or prohibitive surgical risk (6,7), and pharmacological therapy, often ineffective, remains the only management option available (3).

Subsequently, transcatheter tricuspid valve repair (TTVr) technologies were developed to alleviate symptoms and improve quality of life. Although numerous devices have been tested, the first-in-human studies enrolled only small numbers of patients deemed at high surgical risk. In the present pooled analysis, we aimed to assess the feasibility, echocardiographic results, and functional improvements following TTVr according to current evidence.

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METHODS

SEARCH STRATEGY AND STUDY SELECTION. Two authors (C.M., A.S.) independently searched PubMed, Embase, BioMed Central, Google Scholar, and the Cochrane Central Register of Controlled Trials for papers published between January 1, 2000, and September 1, 2019, using the following combinations of search keywords: "tricuspid" and "percutaneous" or "transcatheter." An additional independent search was performed (G.C.) using a combination of the Medical Subject Headings category "tricuspid insufficiency" or search keywords "tricuspid regurgitation" and "transcatheter" or "percutaneous," and relevant results were double-checked. Papers were initially screened by title and abstract content. In addition, the reference lists of all eligible studies were screened to identify any additional citations. Hand searching of relevant congress presentations and abstracts was performed.

Papers that reported clinical and echocardiographic outcomes at follow-up of adult patients undergoing TTVr were included. In some cases in which the risk for overlap between cohorts was considered to be high, only the larger reported cohort was included in the analysis. All controversies were discussed and adjudicated by a senior author (A.M.). The present work was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses and Meta-Analysis of Observational Studies in Epidemiology guidelines (8,9). The study protocol was submitted to PROSPERO (10).

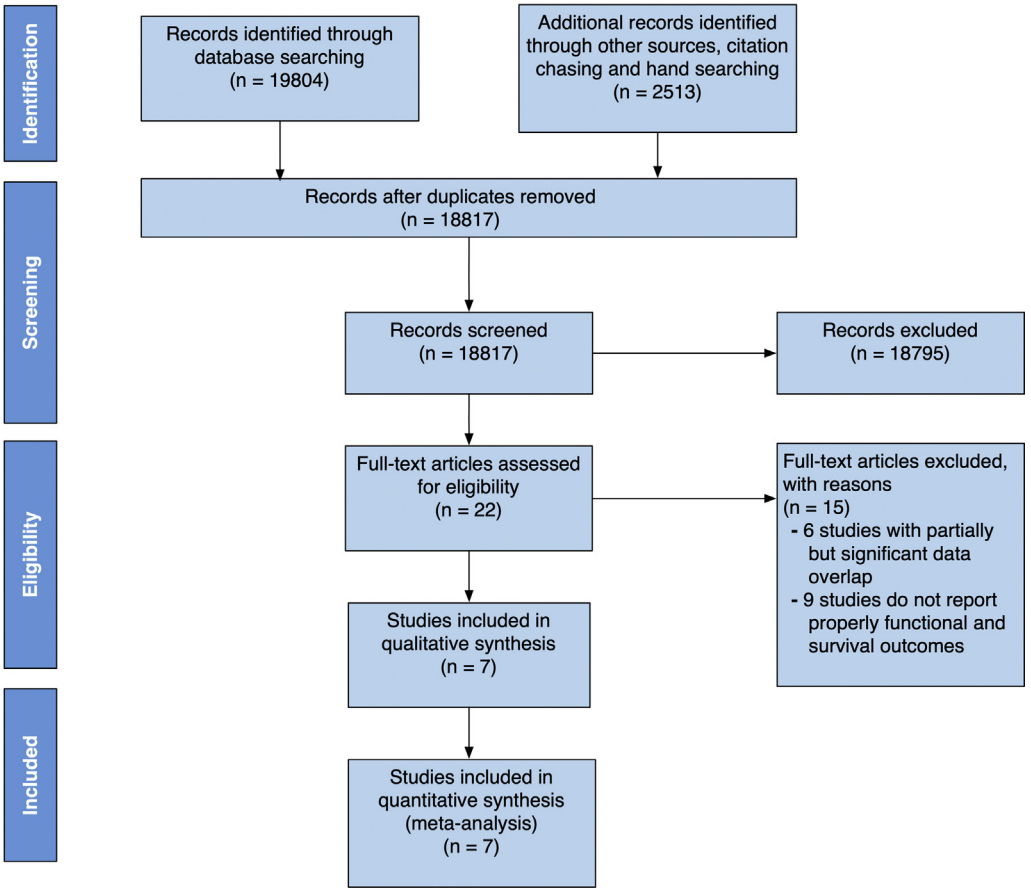
ELIGIBILITY CRITERIA. Studies were considered eligible if they fulfilled all the following criteria: 1) they included patients with at least moderate TR (adjudicated using a semiquantitative method) and treated with transcatheter repair devices; and 2) they reported at least 1 of the primary outcomes of interest at a minimum follow-up point of 30 days.

Case reports, letters and studies that failed to clearly report the numbers and rates of patients alive at follow-up were excluded from the analysis. Moreover, studies in which severe TR was treated using transcatheter implantation of prosthetic valves were excluded. Two authors (C.M., A.S.) independently assessed the quality of studies and risk for bias according to the ROBINS-I tool (11). All studies included had appropriate ethical oversight and approval.

STUDY OUTCOMES. The primary endpoints of this analysis were the rate reduction of: 1) severe TR; and 2) New York Heart Association (NYHA) functional class III or IV at longest follow-up available. Secondary endpoints were changes in functional and echocardiographic parameters, including 6-min walk distance (6MWT), left ventricular ejection fraction (LVEF), tricuspid annular plane systolic excursion (TAPSE), TR effective regurgitant orifice area (EROA), tricuspid valve annular diameter, and systolic pulmonary artery pressure. Vitality status at follow-up was also recorded. Procedural success definition included at least successful device implantation of device because of the varying definitions in all the studies.

STATISTICAL ANALYSIS. Pooled risk ratios (RR) and standardized mean differences (MDs) with 95% confidence intervals (CIs) were used as summary statistics for outcomes of interest and were calculated using a random-effects model according to DerSimonian and Laird (12); the outcomes of interest represent within-group changes. We also pooled the baseline characteristics individually and present them as pooled weighted means and 95% CIs. When data were available only as medians and interquartile ranges, mean ± SD were calculated according to Wan et al. (13). Statistical heterogeneity of exposure was assessed by calculating the I^2 index, which summarizes the amount of variance among studies beyond chance. Heterogeneity was considered to be low for I^2 <25%, moderate for I^2 <75%, and high for I^2 >75% (14,15). To account for heterogeneity in follow-up, we

FIGURE 1 Systematic Search: Strategy and Results



Flowchart demonstrating the search strategy and selection of eligible studies for the meta-analysis.

calculated linearized incidence rate using the person-year method and pooled outcomes on a logarithmic scale in a fixed-effect analysis using the inverse variance method. A weighted meta-regression with a random-effect model was performed to evaluate the effect of several baseline characteristics on functional outcomes of interest at follow-up (16). Residual heterogeneity of primary endpoints was further assessed in a random-effect subgroup analysis according to different device used. Statistical significance was set at a 2-sided p value <0.05. Finally, sensitivity analyses were performed for primary endpoints by assessing the effect of removing individual studies on the pooled RR. Publication bias was assessed for primary endpoints by visual inspection of funnel plots and using Egger and Begg tests. Data analysis was performed in the R environment (packages meta and metafor) (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

SYSTEMATIC REVIEW OF STUDIES. Our search identified a total of 22,317 studies; the process of study selection is summarized in **Figure 1**. In 1 case, a detailed report of outcomes was offered in an oral communication, and this was included. Seven studies were included in this systematic review with a total of 454 patients with at least moderate TR undergoing TTVr. All studies were interventional, single arm, and prospective and clearly reported follow-up times, ranging from 30 days to 1 year (**Table 1**), with an overall moderate risk for bias (Supplemental Table 1). Patients were treated with different devices, including the Cardioband (Edwards Lifesciences, Irvine, California; n = 30), FORMA (Edwards Lifesciences; n = 47), MitraClip (Abbott Vascular, Santa Clara, California; n = 334); PASCAL (Edwards Lifesciences; n = 28), and Trialign (Mitralign, Tewksbury,

TABLE 1 Details of Studies Included

First Author (Year) (Ref. #)	Device	Valve Repair Mechanism	Study Name	Study Notes
Nickenig et al. (2019) (23)	Cardioband	Annular reduction	TRI-REPAIR (NCT02981953)	International, multicenter, prospective, single arm, interventional
Kodali et al. (2017) (24)	FORMA	Increased leaflet coaptation surface	U.S. early feasibility	Multicenter, prospective, single arm, interventional
Perlman et al. (2017) (25)	FORMA	Increased leaflet coaptation surface	Compassionate use	International multicenter registry
Mehr et al. (2019) (26)	MitraClip	Edge-to-edge leaflet plasty	TriValve	International, multicenter registry
Nickenig et al. (2019) (23)	MitraClip	Edge-to-edge leaflet plasty	TRILUMINATE (NCT03227757)	Multicenter, prospective, single arm, interventional
Fam et al. (2019) (27)	PASCAL	Edge-to-edge leaflet plasty		Multicenter, prospective, single arm, interventional
Hahn et al. (2017) (28)	Trialign	Bicuspidalization via pledget-plication	SCOUT (NCT02574650)	Multicenter, prospective, single arm, interventional

TABLE 1 Continued

First Author (Year) (Ref. #)	n	Follow-Up (days)	Key Inclusion Criteria	Key Exclusion Criteria
Nickenig et al. (2019) (23)	30	180	TR grade: moderate to severe TR etiology: functional Symptomatic Annular diameter >40 mm High surgical risk	LVEF ≤30% sPAP >60 mm Hg Concomitant moderate to severe valvulopathy Previous TV intervention Transtricuspid pacing lead Life expectancy <12 months
Kodali et al. (2017) (24)	29	30	TR grade: severe TR etiology: functional Symptomatic (NYHA functional class ≥II) High surgical risk	LVEF ≤25% sPAP >70 mm Hg Concomitant valvulopathy requiring intervention Concomitant moderate to severe TV stenosis Life expectancy <12 months
Perlman et al. (2017) (25)	18	76	TR grade: severe TR etiology: functional Symptomatic High surgical risk	Severe LV dysfunction Primary etiology of TR Prior TV surgery Severe concomitant valvulopathies
Mehr et al. (2019) (26)	249	365	TR grade: moderate to severe TR etiology: predominantly functional Symptomatic (signs and symptoms of HF) High surgical risk	
Nickenig et al. (2019) (23)	85	180	TR grade: at least moderate Symptomatic (NYHA functional class ≥II) despite adequate therapy High surgical risk	LVEF ≤25% sPAP >60 mm Hg Previous TV intervention Transtricuspid pacing lead
Fam et al. (2019) (27)	28	30	TR grade: severe TR etiology: predominantly functional Symptomatic (NYHA functional class ≥III) despite medical treatment High surgical risk	Coaptation gap >15 mm Severe leaflet tethering Pacemaker lead–induced TR
Hahn et al. (2017) (28)	15	30	TR grade: at least moderate TR etiology: functional Symptomatic (NYHA functional class ≥III) No indication for left heart surgery	LVEF ≤35% sPAP >60 mm Hg

HF = heart failure; LV = left ventricular; NYHA = New York Heart Association; SCOUT = Early Feasibility of the Mitralign Percutaneous Tricuspid Valve Annuloplasty System (PTVAS) Also Known as TriAlign™; sPAP = systolic pulmonary artery pressure; TR = tricuspid regurgitation; TRILUMINATE = TRILUMINATE Study With Abbott Transcatheter Clip Repair System in Patients With Moderate or Greater TR; TRI-REPAIR = Tricuspid Regurgitation Repair With Cardioband Transcatheter System.

Massachusetts; n = 15). Additional information on individual studies appears in Table 1.

BASELINE CHARACTERISTICS AND PROCEDURAL SUCCESS. Patients had a mean age of 76.7 years (95% CI: 75.7 to 77.6 years) and were at high surgical risk, with a mean European System for Cardiac Operative Risk Evaluation [EuroSCORE] II score of 6.8 (95% CI: 5.4 to 8.1). TR etiology was predominantly functional (incidence 90%; 95% CI: 82% to 99%), and 90% (95% CI: 82% to 100%) of patients were in NYHA functional class III or IV. Other baseline characteristics are reported in Table 2. Procedural success of TTVr was achieved in 86% of patients (95% CI: 78% to 95%).

PRIMARY OUTCOMES. After a weighted mean follow-up period of 265 days, 393 patients were alive, and the

TABLE 2 Baseline Characteristics of Cohorts Included in the Pooled Analysis and Their Pooled Statistics

First Author (Year)	Device	n	Age (yrs)	Male	Diabetes	Lead Across TV	CKD	AF
Pooled estimates: mean/incidence (95% CI)			76.7 (75.7–77.6)	0.38 (0.30–0.48)	0.30 (0.20–0.44)	0.18 (0.11–0.30)	0.33 (0.15–0.75)	0.81 (0.73–0.89)
Nickenig et al. (2019)	Cardioband	30	75.2 ± 6.6	8	8	–	16	28
Kodali et al. (2017)	FORMA	29	76 ± 8	10	–	7	–	24
Perlman et al. (2017)	FORMA	18	76 ± 10	5	2	3	–	16
Mehr et al. (2019)	MitraClip	249	77 ± 9	121	73	74	17	184
Nickenig et al. (2019)	MitraClip	85	77.8 ± 9.0	29	19	12	39	78
Fam et al. (2019)	Pascal	28	78 ± 6	13	–	1	20	26
Hahn et al. (2017)	Trialign	15	73.6 ± 6.6	2	10	0	5	10

TABLE 2 Continued

First Author (Year)	CAD	NYHA Functional Class III or IV	EuroSCORE II (%)	Severe or Greater TR (%)	Functional TR	Procedural Success	Procedural Success Definition
Pooled estimates: mean/incidence (95% CI)	0.35 (0.21–0.59)	0.91 (0.82–1.00)	6.8 (5.4–8.1)	0.95 (0.87–1.00)	0.9 (0.82–0.99)	0.86 (0.78–0.95)	
Nickenig et al. (2019)	11	25	4.1 ± 2.8	24	30	30	Successful implantation and reduction of septolateral annular diameter
Kodali et al. (2017)	16	25	8.1 ± 5.3	29	29	27	Successful implantation
Perlman et al. (2017)	10	17	9 ± 5.7	18	–	16	Successful implantation
Mehr et al. (2019)	45	238	6.4 ± 2.8	249	223	192	Successful implantation, post-procedural TR ≤2 and no procedural death
Nickenig et al. (2019)	–	62	8.6 ± 10.9	84	71	85	Successful implantation
Fam et al. (2019)	13	28	6.2 ± 5.2	28	26	24	Successful implantation, post- procedural TR ≤2 and no procedural death or conversion to surgery
Hahn et al. (2017)	1	10	–	–	15	15	Successful implantation and annular plication

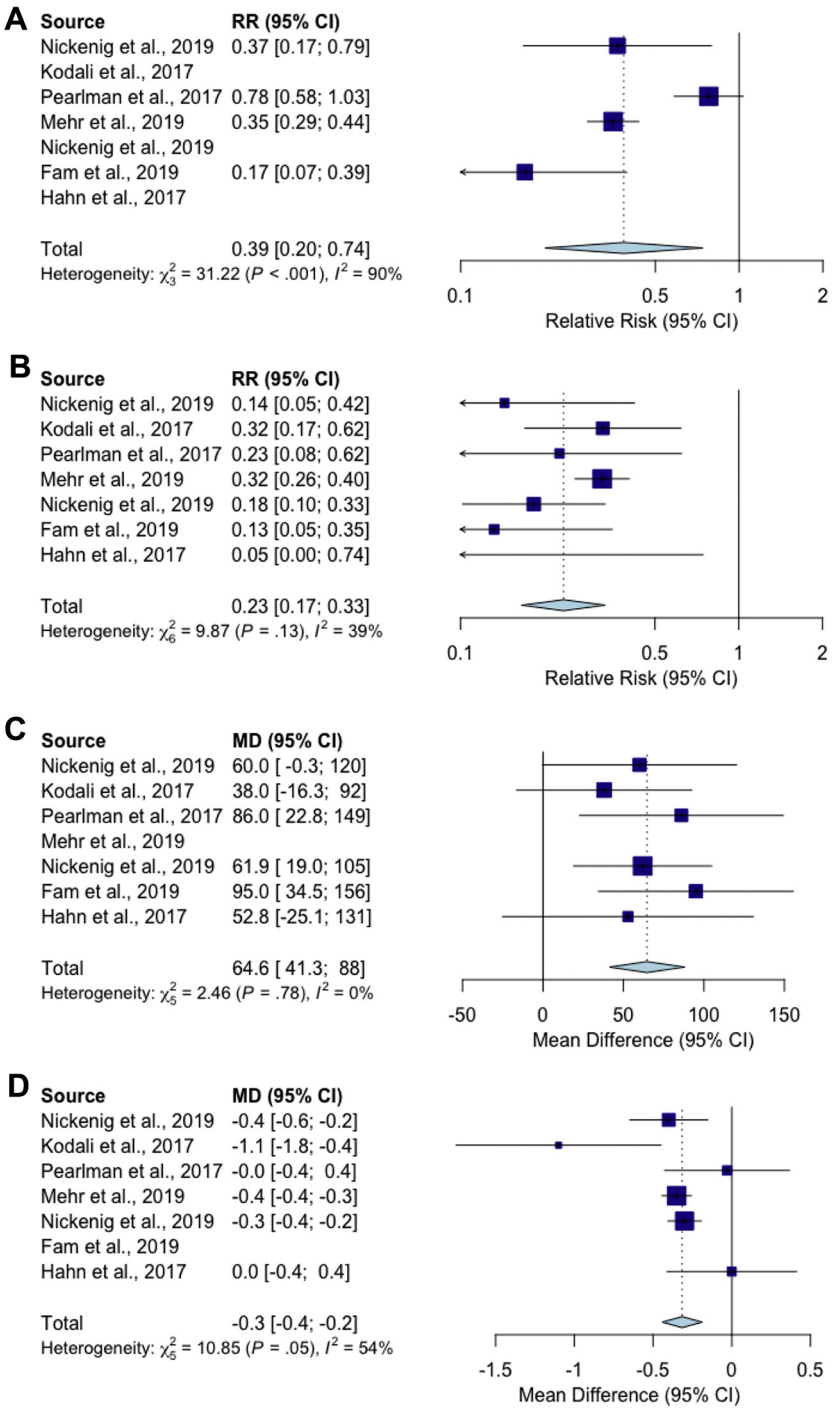
AF = atrial fibrillation; CAD = coronary artery disease; CI = confidence interval; CKD = chronic kidney disease; EuroSCORE = European System for Cardiac Operative Risk Evaluation; TV = tricuspid valve; other abbreviations as in Table 1.

all-cause mortality rate was 9% (95% CI: 5% to 16%). At follow-up, a significantly lower proportion of patients had at least severe TR (34%) and were in NYHA functional class III or IV (22%), with pooled RRs versus baseline of 0.38 (95% CI: 0.2 to 0.7; p = 0.004) and 0.23 (95% CI: 0.16 to 0.33; p < 0.001), respectively (**Figure 2, Table 3**). These results were confirmed in a secondary analysis using linearized incidence rates: mortality was 10% (95% CI: 8% to 14%), while the RRs of primary endpoints were significantly reduced at follow-up (p < 0.0001 for both) (Supplemental Table 2). Our sensitivity analysis revealed that no study significantly changed the relative risk of being in NYHA functional class III or IV at follow-up, as stepwise study omission did not result in a shift of the point estimate out of the 95% CI (Supplemental Table 3). Our random-effect subgroup analysis revealed that at follow-up, the proportions of patients in NYHA functional class III or IV and of patients with TR graded severe or worse were reduced regardless of the device used; a nonsignificant trend toward reduction of the latter endpoint was observed only for the FORMA device (Supplemental Figure 1).

SECONDARY OUTCOMES. Patients alive at follow-up experienced increases in 6MWD (MD +64.6 m; 95% CI: 41 to 88 m) (**Figure 3**). Significant reductions in tricuspid valve annular diameter (MD −3 mm; 95% CI: −4.7 to −1.4 mm) were observed, while LVEF, TAPSE, and systolic pulmonary artery pressure did not change significantly (**Table 3**). Finally, quantitative measurement of TR significantly decreased after TTVr, including TR EROA (MD −3.1 mm; 95% CI: −4.4 to −1.9 mm). All results were confirmed with the linearized incidence rates model.

META-REGRESSION AND PUBLICATION BIAS. Our meta-regression analysis revealed that neither follow-up length nor baseline parameters (including EuroSCORE II, age, LVEF, and TR EROA) significantly affected the observed improvements in 6MWD or

FIGURE 2 Forest Plots for Clinical Outcomes



Forest plot showing relative risk (RR) and mean differences (MD) for clinical outcomes at longest follow-up available: **(A)** tricuspid regurgitation (TR) severe or greater; **(B)** New York Heart Association functional class III or IV, **(C)** 6-min walk distance improvement, and **(D)** TR effective regurgitant orifice area reduction. All devices are included. CI = confidence interval.

TABLE 3 Functional and Echocardiographic Parameters at Baseline and After Transcatheter Tricuspid Valve Repair

		Baseline: Pooled Mean or Incidence (95% CI)	Number of Studies Included		Follow-Up: Mean Difference or Relative Risk (95% CI)	p Value	I^2 (%)	p for Heterogeneity
Functional status								
NYHA functional class III or IV	Incidence	90% (82% to 99%)	7	Relative risk	0.23 (0.16 to 0.33)	0.004	39	0.13
6MWD (m)	Mean	245.4 (215.8 to 275.0)	6	Mean difference	64.6 (41.3 to 87.9)	<0.0001	0	0.78
Echocardiographic data								
LVEF (%)	Mean	57 (52.9 to 61.0)	6	Mean difference	1.2 (−0.5 to 2.8)	0.16	0	0.99
TAPSE (mm)	Mean	15.1 (14.3 to 15.9)	6	Mean difference	−0.09 (−1.2 to 0.98)	0.85	64	0.02
TR severe or greater	Incidence	95% (87% to 100%)	4	Relative risk	0.38 (0.2 to 0.7)	0.004	90	0.0001
TR EROA (mm)	Mean	0.9 (0.7 to 1.0)	6	Mean difference	−3.1 (−4.4 to −1.9)	<0.0001	54	0.06
TV annular diameter (mm)	Mean	44.6 (42.5 to 46.7)	7	Mean difference	−3.0 (−4.7 to −1.4)	0.0004	63	0.01
sPAP (mm Hg)	Mean	41.7 (38.4 to 45.0)	4	Mean difference	−1.6 (−4.9 to 1.7)	0.33	53	0.09

6MWD = 6-min walk distance; EROA = effective regurgitant orifice area; LVEF = left ventricular ejection fraction; TAPSE = tricuspid annular plane systolic excursion; TV = tricuspid valve; other abbreviations as in Tables 1 and 3.

NYHA functional class (Supplemental Figure 2). No publication bias was identified by visually inspecting funnel plots and by mathematical testing (Supplemental Figure 3).

DISCUSSION

The main findings of this pooled analysis are as follows (**Central Illustration**): 1) at mid-term follow-up, TTVr is both feasible, with low mortality rates, and effective in reducing TR severity; 2) with regard to functional outcomes, TTVr is associated with alleviation of symptoms and with increased exercise capacity at follow-up; and 3) left and right ventricular function remained stable after TTVr, with sustained reductions in annular dimensions at follow-up.

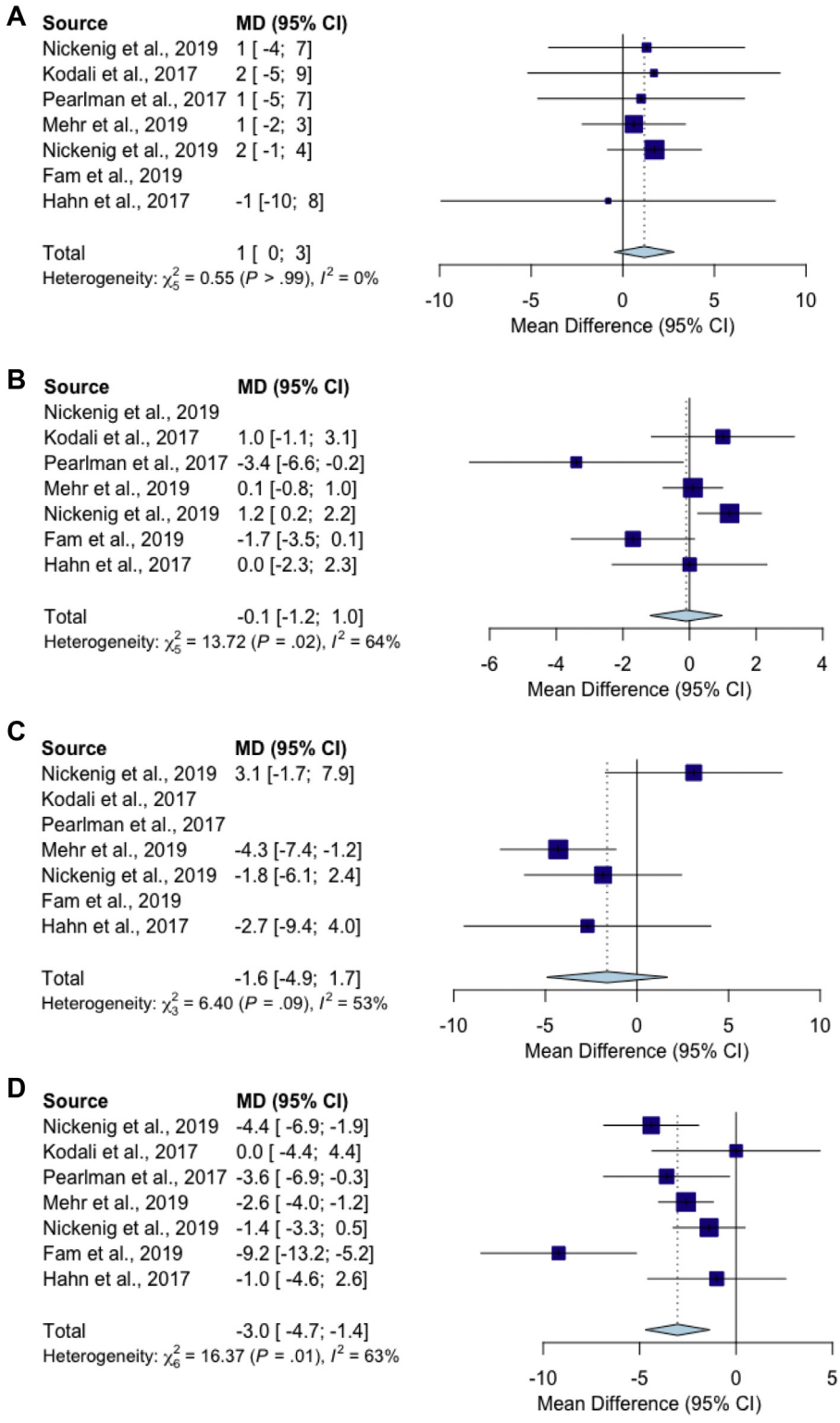
The tricuspid valve, previously the "forgotten valve," has recently gained increased clinical attention because of heightened awareness of the morbidity and mortality associated with severe TR coupled with an increase in the development of transcatheter devices to treat severe TR. In fact, the natural history of the disease is associated with progressive increase in symptoms (3,17) and in the need for loop diuretic agents for symptom reduction (3). Currently, robust data supporting the use of TTVr are limited, so current guidelines advocate only for surgical correction of TR (18,19). However, a significant proportion of patients with severe TR are at high or prohibitive risk for surgical intervention and thus remain untreated, patients who potentially stand to benefit the most from a relatively less invasive TTVr strategy.

An interventional strategy to treat severe TR has been shown to reduce mortality and rates of hospitalization in comparison with conventional pharmacological therapy. The reasons for these findings are not completely clear, but it has been suggested that TTVr could reduce right ventricular volume overload, alleviate peripheral venous congestion, and interrupt the vicious cycle of TR worsening and RV remodeling and dysfunction in synergy with medical therapy (20).

Our pooled analysis included 454 high-risk patients (pooled EuroSCORE II was 6.8%) with advanced signs and symptoms of heart failure (91% were in NYHA functional class III or IV) (**Table 2**). Irrespective of the advanced clinical condition, our pooled analysis confirmed the feasibility and the high successful implantation rates of TTVr (86%; 95% CI: 78% to 95%) with a low mortality rate (9%; 95% CI: 5% to 16%) at mid-term follow-up (weighted mean days 265). These findings compare favorably against prior cohorts consisting solely of medically managed patients (1,3), especially when considering that a learning-curve effect might have been observed in the earliest phase of patients treated with TTVr. Moreover, TTVr was effective, as patients experienced a significant reduction in TR, as assessed semiquantitatively (RR of having TR grade severe or greater: 0.38; 95% CI: 0.2 to 0.7) and quantitatively (mean reduction in TR EROA −3.1 mm; 95% CI: −4.4 to −1.9 mm) (**Figure 2**). These changes were also accompanied by clinical improvements, in terms of a lower proportion of patients in NYHA functional class III or IV (RR: 0.23; 95% CI: 0.16 to 0.33) and with an increase in 6MWD (mean increase +64.6 m; 95% CI: 41 to 88 m) (**Figure 3**).

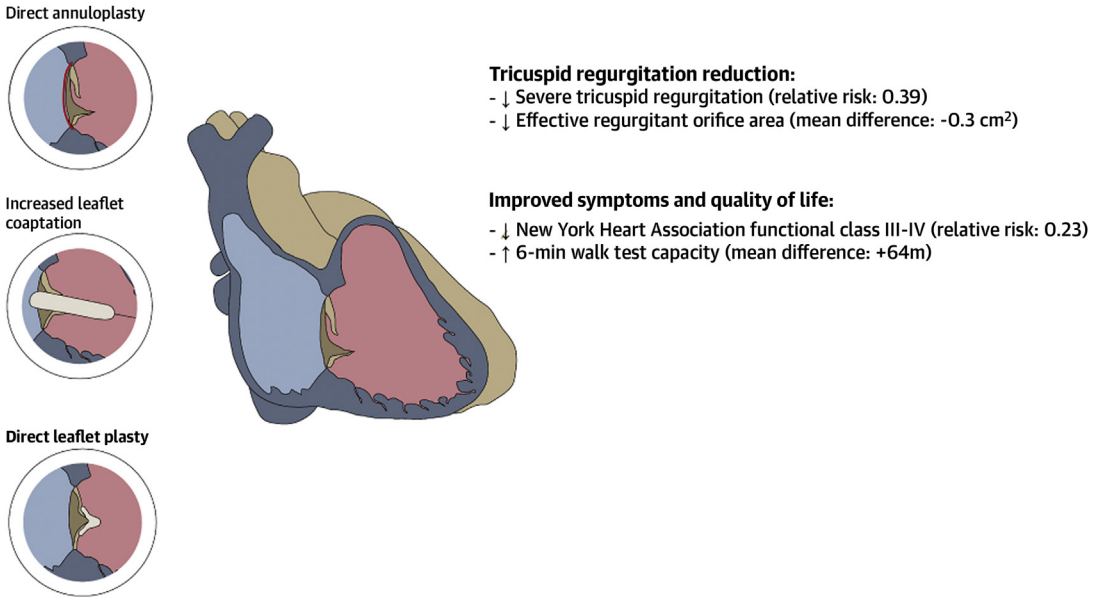
This pooled analysis included a range of devices that treat severe TR using different mechanisms: direct annular reduction (Cardioband and Trialign), increased coaptation surface (FORMA), and direct leaflet plasty (MitraClip and PASCAL). Although clinical and anatomic characteristics determine the most suitable device to treat TR in each patient, clinical improvement in terms of NYHA functional class was observed across all device subgroups (Supplemental Figure 1).

FIGURE 3 Forest Plots for Echocardiographic Outcomes



Forest plot showing MDs for clinical echocardiographic outcomes at longest follow-up available: **(A)** left ventricular ejection fraction, **(B)** tricuspid annular plane systolic excursion, **(C)** systolic pulmonary artery pressure, and **(D)** tricuspid valve diameter. All devices are included. Abbreviations as in Figure 2.

CENTRAL ILLUSTRATION **Transcatheter Tricuspid Valve Repair: Therapeutic Options and Outcomes**



Montalto, C. et al. J Am Coll Cardiol Intv. 2020;13(23):2719–29.

Several mechanisms of transcatheter tricuspid valve repair (TTVr) are available to treat severe tricuspid regurgitation (TR). In this pooled analysis of 454 patients, reductions in TR, alleviation of symptoms, and improvements in quality of life were observed after TTVr.

A significant reduction in tricuspid valve diameter was observed (mean reduction −3 mm; 95% CI: −4.7 to −1.4 mm), while pulmonary pressures, LVEF, and TAPSE remained unchanged (**Figure 3**). The reduction in tricuspid annular size was reported not only with annuloplasty TTVr devices but also acutely after MitraClip implantation (21). Leaflet plasty systems can reduce annular size with an acute, indirect effect through a global reshaping of the tricuspid valve apparatus. In the longer term, further reduction in annular size, associated with reversed right ventricular remodeling, has been observed following MitraClip implantation (22).

Further residual heterogeneity was explored with several additional analysis. First, a sensitivity analysis demonstrated the robustness of the findings, as individually omitting each study did not change the results significantly (Supplemental Table 3). Second, our meta-regression analysis revealed that neither follow-up time nor baseline characteristics (including age, surgical risk, symptoms, LVEF, and TR EROA) exerted an effect on NYHA functional class III or IV and on 6MWD at follow-up (Supplemental Figure 3). Third, our subgroup analysis revealed that the reduction in NYHA functional class III or IV was present irrespective of the device used (Supplemental Figure 2). As the majority of patients in this pooled analysis received edge-to-edge leaflet plasty (n = 362 [79.9%]), this is an important finding that supports the use of TTVr also in anatomic settings that are unsuitable for edge-to-edge plasty. Notably, all devices resulted in the reduction of severe or worse TR except for the FORMA device, for which our subgroup analysis included only 1 study (out of 2) that reported TR at follow-up in a semiquantitative fashion. Finally, also the Trialign study did not report TR grade in a semiquantitative fashion and was not included in the subgroup analysis. Of note, neither of these 2 devices is used in current clinical practice.

STUDY LIMITATIONS. First, our pooled analysis included only single-arm interventional studies, so no comparison arm was present.

Second, devices for TTVr feature different mechanisms, and the majority of subjects underwent edge-to-edge plasty, which might account for a large part of the observed positive effects of TTVr. Although their final effect is similar, as demonstrated in our per-device subgroup analysis, residual unexplained heterogeneity in their treatment effects cannot be excluded.

Third, as the population analyzed was advanced both clinically and in terms of echocardiographic

parameters, our results may not be applicable to a wider population with less severe clinical conditions.

Fourth, definitions of procedural success were different among the studies analyzed (**Table 2**); therefore, with regard to this endpoint, results should be interpreted with caution.

Finally, as the procedures included were performed at highly specialized centers and the use of an echocardiography core laboratory was inconstant the generalizability of our findings is limited. Although our results demonstrate favorable outcomes following TTVr, it must be recognized that for each specific device, there would have been a selection bias in terms of patient and anatomic characteristics.

CONCLUSIONS

Our pooled analysis revealed that TTVr with current devices is feasible and effective at reducing TR in high-risk patients with severe symptomatic TR. Moreover, patients treated with TTVr exhibit favorable outcomes with improved functional capacities. Further studies are required to confirm the positive effects of transcatheter therapies on patient prognosis and functional status at long term follow-up.

AUTHOR DISCLOSURES

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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PERSPECTIVES

WHAT IS KNOWN? TR is a prevalent disease associated with increased morbidity and mortality in patients with high or prohibitive surgical risk. Several percutaneous devices are designed to repair severe TR.

WHAT IS NEW? Transcatheter treatment of TR is associated with high survival rates and reduction of severe TR. Moreover, symptom relief, improved performance capacity, and good echocardiographic outcomes were observed.

WHAT IS NEXT? A larger randomized clinical trial should focus on each device for percutaneous repair of TR and highlight ideal characteristics for the selection of appropriate devices.

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KEY WORDS heart failure, transcatheter tricuspid valve repair, tricuspid regurgitation, tricuspid valve

APPENDIX For supplemental methods, tables, and figures, please see the online version of this paper.

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