Aus der Zentrum für Kardiologie

der Universitätsmedizin der Johannes Gutenberg-Universität Mainz

Right Heart Remodeling and Outcomes in Patients with Tricuspid Regurgitation: A Literature Review and Meta-Analysis

Remodellierung des rechten Herzens und klinische Ergebnisse bei Patienten mit Trikuspidalinsuffizienz: Eine Literaturübersicht und Metaanalyse

Inauguraldissertation

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1 Einleitung

1.1 Einleitung

Die Trikuspidalklappeninsuffizienz (TI) ist eine häufige Herzklappenerkrankung, welche besonders häufig bei älteren Patienten und Frauen auftritt. Überdies ist die TI ist mit einer schlechten Prognose assoziiert. Traditionell war die chirurgische Reparatur oder der Klappenersatz die Standardbehandlung bei schwerer TI, wird jedoch oft nicht durchgeführt aufgrund der hohen perioperativen Mortalität. Daher wurden diese Patienten in der Regel nur medikamentös behandelt. Um diesen unbehandelten Patienten eine Therapieoption zu bieten, wurden mehrere transkatheterbasierte Behandlungsoptionen entwickelt. Insbesondere die TRILUMINATE-Pivotal Studie zeigte, dass transkatheterbasierte Reparaturen der Trikuspidalklappe die Lebensqualität verbessern, jedoch keine Verbesserung der Überlebensraten nach einem Jahr erzielen konnten. Neue Studien haben gezeigt, dass die Anatomie der Trikuspidalklappe und die Ursache der Insuffizienz den Erfolg von Therapien und die klinischen Ergebnisse entscheidend beeinflussen. Im Rahmen der TRILUMINATE-Studie wurden die Patienten nicht nach den verschiedenen Phänotypen der sekundären TI unterteilt. Daher war die Hypothese, dass das Ausbleiben einer Verbesserung der Überlebensraten in der TRILUMINATE-Pivotal-Studie auf die Heterogenität der Studienpopulation zurückzuführen sein könnte und dass die rechtskardialen Remodeling-Parameter einen Einfluss auf die Mortalität haben könnten.

1.2 Ziel der Dissertation

Diese Meta-Analyse untersuchte die Ergebnisse verschiedener Behandlungsstrategien, einschließlich medikamentöser Behandlung, transkatheterbasierter Interventionen und chirurgischer Verfahren, sowie den Einfluss rechtskardialer Remodeling-Parameter (verschiedene TI-Phänotypen) auf die Langzeitsterblichkeit.

2 Literaturdiskussion

Die am häufigsten verwendete Klassifikation der TI unterteilt die Insuffizienz in primäre TI und funktionelle TI. Funktionelle (oder sekundäre) TI bezieht sich auf eine Regurgitation, die in Abwesenheit einer signifikanten strukturellen Erkrankung der Trikuspidalklappe und/oder des Apparats auftritt. Eine funktionelle TI kann entweder durch ein rechtsventrikuläres (RV) Remodeling (ventrikuläre funktionelle TI) und/oder durch eine rechtsatriale (RA) Dilatation (atriale funktionelle TI) entstehen. Bei einer ventrikulären TI wird der rechte Ventrikel ellipsoid verformt, was eine Verlagerung der Papillarmuskeln verursacht und zu einem Tethering der Segel führt. Bei einer atrialer funktioneller TI hingegen führen die Dilatation des RA und die Erweiterung des Trikuspidalringes zu einem Mangel an Segelkoaptation ohne Tethering und einer vorwiegenden basalen RV-Dilatation.

3 Material und Methoden

Eine systematische Suche wurde in MEDLINE, ISI Web of Science und SCOPUS durchgeführt, um Studien bis Juli 2022 zu finden. Eingeschlossen wurden Studien mit Langzeitverläufen (>1 Jahr) von Patienten mit signifikanter TR und mindestens einem Parameter zur Beurteilung der rechtskardialen Funktion. Der primäre Endpunkt dieser Studie war die Gesamtmortalität über den Langzeitnachbeobachtungszeitraum. Untergruppenanalysen nach Behandlungsstrategie (medikamentös, chirurgisch oder gemischt) wurden durchgeführt. Die Studie wurde gemäß den Anforderungen der Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) konzipiert.

4 Ergebnisse

4.1 Studienauswahl

14 Studien mit 4394 Patienten wurden eingeschlossen, davon waren 7 medikamentöse, 4 chirurgische und 3 gemischte Behandlungsgruppen. Die Nachbeobachtungsdauer lag zwischen 15,5 und 73,2 Monaten.

4.2 Ergebnisse

Die Gesamtmortalität betrug 31%, wobei Unterschiede zwischen medikamentöser Behandlung (43%) und chirurgischer Behandlung (11%) beobachtet wurden. Eine reduzierte Trikuspidalannulärsystolenexkursion (TAPSE) und reduzierte fraktionelle Flächenänderung (FAC) waren mit einer erhöhten Mortalität assoziiert. Größere Werte der rechten Vorhofgröße und des Trikuspidalannulus waren hingegen mit einer niedrigeren Mortalität verbunden. Darüber hinaus waren traditionelle kardiovaskuläre Risikofaktoren, einschließlich Alter, Diabetes mellitus, systemischer arterieller Hypertonie und Dyslipidämie, signifikant mit einem erhöhten Mortalitätsrisiko assoziiert. Auch die chronisch obstruktive Lungenerkrankung und die linksventrikuläre Ejektionsfraktion wurden mit dem Mortalitätsrisiko in Verbindung gebracht.

5 Diskussion

Diese Meta-Analyse hebt die hohe Langzeitsterblichkeit bei Patienten mit signifikanter TI hervor, insbesondere bei medikamentöser Behandlung. Eine höhere Mortalität wurde mit einer RV-Dysfunktion in Verbindung gebracht, während eine reduzierte Mortalität mit zunehmender Dilatation des RA assoziiert war. Darüber hinaus zeigte die Studie, dass traditionelle kardiovaskuläre Risikofaktoren (einschließlich Alter, Diabetes mellitus, arterieller Hypertonie und Dyslipidämie) signifikant mit einem erhöhten Mortalitätsrisiko verbunden waren.

6 Zusammenfassung

Die Langzeitmortalität bei signifikanter TI bleibt hoch, insbesondere bei medikamentöser Behandlung. Rechtskardiale Parameter sind wichtige Prädiktoren für die Prognose. Die Unterscheidung zwischen atrial und ventrikulär funktioneller TI ist essenziell, da sie unterschiedliche pathophysiologische Mechanismen und Prognosen aufweisen können. Zukünftige Studien sind erforderlich, um optimale Behandlungsstrategien für verschiedene TI-Phänotypen zu identifizieren.

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ORIGINAL RESEARCH

Right Heart Remodeling and Outcomes in Patients With Tricuspid Regurgitation

A Literature Review and Meta-Analysis

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ABSTRACT

BACKGROUND Functional tricuspid regurgitation (TR) can develop either because of right ventricular (RV) remodeling (ventricular functional TR) and/or right atrial dilation (atrial functional TR).

OBJECTIVES This meta-analysis aimed to investigate the association between right heart remodeling and long-term (>1 year) all-cause mortality in patients with significant TR (at least moderate, ≥2+).

METHODS MEDLINE, ISI Web of Science, and SCOPUS databases were searched. Studies reporting data on at least 1 RV functional parameter and long-term all-cause mortality in patients with significant TR were included. This study was designed according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) requirements.

RESULTS Out of 8,902 studies, a total of 14 were included, enrolling 4,394 subjects. The duration of follow-up across the studies varied, ranging from a minimum of 15.5 months to a maximum of 73.2 months. Overall, long-term all-cause mortality was 31% (95% CI: 20%-41%; $P \leq 0.001$). By means of meta-regression analyses, an inverse relation was found between tricuspid annular plane systolic excursion (11 studies enrolling 3,551 subjects, −6.3% [95% CI: −11.1% to −1.4%]; $P = 0.011$), RV fractional area change (9 studies, 2,975 subjects, −4.4% [95% CI: −5.9% to −2.9%]; $P < 0.001$), tricuspid annular dimension (7 studies, 2,986 subjects, −4.1% [95% CI: −7.6% to −0.5%]; $P = 0.026$), right atrial area (6 studies, 1,920 subjects, −1.9% [95% CI: −2.5% to −1.3%]; $P < 0.001$) and mortality.

CONCLUSIONS RV dysfunction parameters are associated to worse clinical outcomes in patients with TR, whereas right atrial dilatation is linked to a better prognostic outcome. Further studies are needed to unravel the pathophysiological differences within the functional TR spectrum. (Right heart remodeling and outcomes in patients with tricuspid regurgitation; CRD42023418667) (J Am Coll Cardiol Img 2024;17:595-606) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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ABBREVIATIONS AND ACRONYMS

FAC = fractional area change

LVEF = left ventricular ejection fraction

RV = right ventricular

T-TEER = transcatheter tricuspid edge-to-edge repair

TAPSE = tricuspid annular plane systolic excursion

TR = tricuspid regurgitation

Tricuspid regurgitation (TR) of at least moderate severity (ie, ≥2+) is not uncommon, with a higher prevalence among women and the elderly, and is associated with dismal prognosis.[1-5] Due to the historically suboptimal results of surgery in a population by definition at high risk, several transcatheter options have been developed for patients with significant TR.[6-14] The Triluminate trial has recently shown that in patients with at least severe TR, transcatheter tricuspid edge-to-edge repair (T-TEER) was superior to medical therapy in improving quality-of-life metrics, though not in ameliorating survival at 1-year follow-up.[15] Other randomized trials with T-TEER, annular reduction, transcatheter tricuspid valve replacement, and other novel approaches are undergoing and will probably provide more evidence to answer the question of whether transcatheter treatment of TR will reduce mortality in this population. Importantly, novel evidence and consensus documents have shed light on the multiple phenotypical expressions of functional TR, whose relevance is not merely qualitative. In fact, tricuspid valve anatomy and TR etiology can be important determinants of device success and, in general, clinical outcomes.[16] Atrial functional TR, formerly known as isolated TR, has been shown to have a better natural history when compared with the classic ventricular functional phenotype.[17-19] However, the lack of a consistently accepted definition for atrial functional TR, until very recently, has generated disparate interpretations on the topic. Based on these premises, this meta-analysis was designed: 1) to investigate TR outcomes according to different treatment options, including medical management, transcatheter interventions, and surgical procedures; and 2) to analyze the impact of right heart remodeling (ie, different TR phenotypes) on long-term mortality in this heterogeneous population.

METHODS

LITERATURE SEARCH AND STUDY SELECTION. MEDLINE, ISI Web of Science, and SCOPUS databases were searched for studies published up to July 2022. Studies were identified using the major medical subject heading "tricuspid regurgitation AND (survival OR mortality OR outcome OR prognosis)." English was set as a language restriction. Two authors (S.B. and G.V.) independently examined the titles and abstracts and excluded irrelevant studies. The full texts of potentially eligible studies were obtained, and disagreement was resolved by discussion. To look for additional relevant studies, the full texts and references of all potential articles were also retrieved. Abstracts, meeting proceedings, and personal communications were not used for the purpose of this study.

ELIGIBILITY CRITERIA. Included studies had to report data on long-term outcomes of patients with significant TR and at least 1 parameter of right heart function/remodeling. Long-term outcome data were defined in this study as a follow-up period exceeding 1 year. Both randomized controlled trials and observational studies were considered for inclusion.

Studies were excluded if they met any of the following criteria: 1) duplicate or overlapping publication data; 2) lack of long-term outcome data; 3) the outcome of interest was not clearly reported or was impossible to extract or calculate from the published results; 4) nonisolated tricuspid valve intervention; 5) previous tricuspid valve intervention; 6) sample size <25 patients; and 7) inclusion of patients with tricuspid valve stenosis or mild TR.

DATA EXTRACTION. Baseline characteristics, clinical outcomes, and data from echocardiography and cardiac magnetic resonance were systematically extracted in a prespecified database independently by 2 investigators (S.B. and G.V.). Discrepancies were resolved by discussion and consensus.

ENDPOINTS AND DEFINITIONS. The primary endpoint of this study was all-cause mortality over the long-term follow-up period. This endpoint was initially evaluated across all included studies. Subsequently, subgroup analyses were conducted based on the distinct treatment strategies employed in these studies. In addition, the impact of the following right heart imaging parameters on long-term outcomes was investigated: tricuspid annular plane systolic excursion (TAPSE), fractional area change (FAC), tricuspid annular tissue Doppler imaging systolic velocity, right ventricular (RV) basal diameter, tricuspid annulus diameter, right atrial area, pulmonary artery systolic pressure, and TR vena contracta. Data extracted for

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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these parameters were continuous variables and were reported at the study level.

QUALITY ASSESSMENT. Risk of bias for each included study was assessed using the Newcastle-Ottawa quality assessment scale, as previously described.[20] This scale allows for the evaluation of the internal validity of cohort studies included in meta-analysis based on 3 main criteria: 1) selection (adequate selection and definition of groups); 2) comparability (comparability of 2 groups for a selected variable and comparability for other variables); and 3) outcome (modality of assessment, sufficient length of follow-up and adequacy of follow-up). Based on the previous criteria, studies with 4 stars for selection, 2 for comparability, and 3 for outcome were defined at low risk of bias. Studies with 2 or 3 stars for selection, 1 for comparability, and 2 for outcome were defined at medium risk. Studies with a score of 1 for selection or outcome ascertainment, or 0 for any of the 3 domains, were classified as having a high risk of bias.

STATISTICAL ANALYSIS. An inverse variance-weighted study-level meta-analysis with a random effect model was used to estimate the mean all-cause mortality rate during the longest follow-up reported in each study. The results were presented as forest plots of all-cause mortality rate and 95% CIs. A random effect model was chosen because this analysis compared heterogeneous studies with different treatments and population baseline characteristics.[21] The percentage of total variance due to between-study variance was expressed by means of I^2.[22] I^2 values of 25%, 50%, and 75%, indicated small, moderate, and large amounts of heterogeneity, respectively. The source of heterogeneity was explored by performing subgroup analyses. A subgroup analysis to evaluate the consistency of the results according to the type of TR treatment (medical therapy vs surgery vs miscellaneous) was performed. Univariable meta-regression analyses were performed to analyze the association between right heart imaging parameters and long-term all-cause mortality. Considering the heterogeneous follow-up length across the studies, multiple sensitivity analyses using a patient-year approach were performed in order to verify the consistency of the results, In addition, for descriptive purposes, an inverse variance-weighted study-level meta-analysis with a random effect model was also performed to estimate the mean values of right heart imaging parameters with their 95% CI. Statistical significance was set at a 2-sided value of $P = 0.05$. The analyses were performed with Review Manager version 5.3 (Nordic Cochrane Centre, Cochrane Collaboration) and OpenMeta-Analyst version beta 1.0 (Brown University), and in R environment 4.0.3 (R Foundation for Statistical Computing). Publication bias was assessed using funnel plots, and when a significant publication bias was found, it was further explored by Egger's test, consisting of a linear regression of the intervention effect estimates on their SEs, weighting by 1/(variance of the intervention effect estimate). Reporting of this meta-analysis follows the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) requirements.

RESULTS

IDENTIFICATION OF STUDIES. The database search identified a total of 8,902 studies, of which 173 were selected for further evaluation. Finally, after rigorous assessment, 14 studies met the inclusion criteria with a total of 4,394 patients with significant TR (Supplemental Figure 1).[23-36] All the included studies were nonrandomized and retrospective, except for 1 prospective study. The duration of follow-up in the study varied, ranging from a minimum of 15.5 months to a maximum of 73.2 months. Among the 14 included studies, 7 examined exclusively patients who underwent medical therapy, while 4 examined exclusively patients who underwent surgical therapy. The remaining 3 studies investigated a combination of medical, surgical, or percutaneous interventions, which were collectively categorized as a miscellaneous intervention group in this analysis.

BASELINE CHARACTERISTICS. Mean age varied across the studies, ranging from 46 to 82 years, with most of the patients being female (59.2%) and a high prevalence of atrial fibrillation (63.2%). Notably, a significant proportion of the patients (85.7%) had functional etiology of TR (including both atrial and ventricular functional subtypes). Echocardiographic baseline characteristics were extracted, with a focus on RV function and right heart size. The mean TAPSE was 17.2 mm (95% CI: 15.9-18.5 mm; $I^2 = 98\%$; $P < 0.001$), while the mean FAC was 37.4% (95% CI: 35.6%-39.3%; $I^2 = 95.2\%$; $P < 0.001$). In terms of right heart size, the mean tricuspid annulus diameter was 41.2 mm (95% CI: 38.6-43.9 mm; $I^2 = 99\%$; $P < 0.001$), the mean RV basal diameter was 46.7 mm (95% CI: 44.9-48.5 mm; $I^2 = 97.4\%$; $P < 0.001$), and the mean right atrial area was 32.3 cm^2 (95% CI: 29.5-35.1 cm^2; $I^2 = 95.8\%$; $P < 0.001$). Additional pertinent baseline characteristics are provided in **Tables 1 and 2**, while comprehensive information can be found in Supplemental Tables 1 and 2.

TABLE 1 Baseline Characteristics of the Included Studies

First Author, Year	N	Follow-Up (mo)	MT (%)	Long-Term Mortality (%)	Age (y)	BMI (kg/m²)	Male (%)	DM (%)	HTN (%)	HLD (%)	AF (%)	COPD (%)	PM/ICD (%)	Functional TR (%)	CKD (%)	NYHA Functional Class III-IV (%)
Ancona et al,[23] 2021	171	30	44	21	74.3 ± 10.2	NA	36.8	16.3	68.4	35.7	71.9	13.5	32.2	83	31.6	56.1
Bar et al,[24] 2018	178	22 ± 16	100	59.0	81.5 ± 11	NA	35	30	NA	NA	68	21	18	100	35.5	54
Dreyfus et al,[25] 2020	466	31 (10-59)	0	8.6	60 ± 16	25 ± 5	51	13	41	NA	39	11	22	49	33	47
Fortuni et al,[26] 2021	1,149	51 (17-86)	100	51	72 (63-79)	26 ± 4	51	20	81	48	50	15	37	100	NA	44
Kim et al,[27] 2013	61	55 (37-72)	0	9.8	57.9 ± 8	NA	11.5	NA	NA	NA	85.2	NA	NA	82.1	NA	NA
Park et al,[28] 2021	238	49	0	22.3	59.6 ± 12.4	NA	40.3	14.3	30.7	NA	61.8	8.8	NA	78.2	NA	39.9
Romano et al,[29] 2021	544	73 (41-118)	100	23.5	60.6 ± 18.6	27.3 ± 5.9	41	16.5	53.7	35.6	NA	NA	NA	100	NA	NA
Saeed et al,[30] 2020	209	70 ± 33	100	59	72 ± 14	26.0 ± 5.4	44	31	84	69	78	14	26	94	NA	NA
Schneider et al,[31] 2021	220	35 (19-53)	100	29	69 (52-79)	NA	40	20	59	NA	49	NA	NA	100	NA	19
Cai et al,[32] 2020	124	16 (8-24)	57	0	76.2 ± 10.2	25.5 ± 5.6	50.8	29.8	65.3	53.2	89.5	12.9	33	91.1	NA	73.4
Peugnet et al,[33] 2020	259	24 (7-47)	91	36	75 ± 13	27.2 ± 5.4	45.9	26.2	73.4	47.5	72.2	NA	NA	50.6	NA	28.1
Utsunomiya et al,[34] 2022	64	19 (9-29)	100	31	74 ± 11	NA	48	NA	NA	NA	67	NA	23	100	19	NA
Liang et al,[35] 2019	76	43 ± 22	0	4	45.7 ± 13.1	NA	32.9	NA	9.2	NA	39.5	NA	NA	60.5	NA	25
Ng et al,[36] 2022	635	26 (5-52)	100	45	68.6 ± 15.4	23.8 ± 5	41.6	27.4	57.8	NA	53.1	NA	NA	100	NA	NA

AF = atrial fibrillation; BMI = body mass index; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; HLD = hyperlipidemia; HTN = hypertension; ICD = implantable cardioverter-defibrillator; MT = medical therapy; NA = not applicable; PM = pacemaker; TR = tricuspid regurgitation.

CLINICAL OUTCOMES. The overall incidence of long-term all-cause mortality was 31% (14 studies; 95% CI: 20%-41%; $P < 0.001$, $I^2 = 98.55\%$) (**Figure 1**). Despite the absence of direct comparison in the original studies, and thus no possible direct comparison in this present analysis, different mortality rates were observed in association with surgical intervention and medical treatment, with rates reported at 11% (95% CI: 20%-41%) and 43% (95% CI: 32%-53%), respectively. These results were consistent in a sensitivity analysis performed with patient-year approach (Supplemental Figure 2).

META-REGRESSION ANALYSIS AND PUBLICATION BIAS. In the meta-regression analysis, a significant and inverse relation was found between TAPSE, FAC, and mortality (11 studies enrolling 3,551 subjects, beta coefficient −6.3% [95% CI: −11.1% to −1.4%]; $P = 0.011$; and 9 studies, 2,975 subjects, beta coefficient −4.4% [95% CI: −5.9% to −2.9%]; $P < 0.001$, respectively) (**Figures 2A and 2B**). Similarly, larger values of tricuspid annulus diameter and right atrial area were associated with reduced mortality (7 studies, 2,986 subjects, beta coefficient −4.1% [95% CI: −7.6% to −0.5%]; $P = 0.026$; and 6 studies, 1,920 subjects, beta coefficient −1.9% [95% CI: −2.5% to −1.3%]; $P < 0.001$, respectively) (**Figures 2C and 2D**, **Central Illustration**). Furthermore, all of the main traditional cardiovascular risk factors, including age, diabetes mellitus, systemic arterial hypertension, and dyslipidemia, were significantly associated with an increased risk of mortality (age, 14 studies, 4,394 subjects, beta coefficient 1.4% [95% CI: 0.7%-2.1%]; $P < 0.001$; diabetes mellitus, 11 studies, 4,193 subjects, beta coefficient 2.1% [95% CI: 1.2%-3.0%]; $P < 0.001$; arterial hypertension, 11 studies, 4,091 subjects, beta coefficient 0.6% [95% CI: 0.3%-0.9%]; $P < 0.001$; dyslipidemia, 6 studies, 2,456 subjects, beta coefficient 1.1% [95% CI: 0.5%-1.8%]; $P < 0.001$) (Supplemental Figures 3A-3D). Chronic obstructive pulmonary disease and left ventricular ejection fraction (LVEF) were also found to be associated with mortality risk (7 studies, 2,535 subjects, beta coefficient 3.8% [95% CI: 0.4%-7.1%]; $P = 0.027$; 12 studies, 3,630 subjects, beta coefficient −2.4% [95% CI: −4.1% to −0.8%]; $P = 0.003$, respectively) (Supplemental Figures 3E and 3F). **Table 3** presents the remaining

TABLE 2 Imaging Characteristics of the Included Studies

First Author, Year	LVEF (%)	TAPSE (mm)	TA (mm)	RV EDD Basal (mm)	RA Area (cm^2)	PASP (mm Hg)	S′ TDI RV (cm/s)	FAC (%)	Vena Contracta (mm)	EROA (cm^2)	CMR-RVEF (%)
Ancona et al,[23] 2021	52.2 ± 12.7	18.6 ± 4.7	NA	46.6 ± 9.1	NA	50 ± 14.5	10.3 ± 3.1	40.1 ± 9.4	9.5 ± 3.1	NA	NA
Bar et al,[24] 2018	57.7 ± 3.5	16.9 ± 5.5	38 ± 7	NA	27.2 ± 8.1	66.2 ± 12.6	NA	32.2 ± 9.9	7.7 ± 2.9	NA	NA
Dreyfus et al[25] 2020	58 ± 9	20 ± 7	44 ± 9	48 ± 11	NA	40 ± 11	11.9 ± 4.1	NA	NA	NA	NA
Fortuni et al,[26] 2021	44 ± 16	15 ± 5	42 ± 8	45 ± 8	28 ± 11	44 ± 16	NA	34 ± 13	11 ± 4	0.68 ± 0.46	NA
Kim et al,[27] 2013	58.1 ± 8.1	NA	43.7 ± 6.9	NA	51.8 ± 19.2	40.4 ± 8.6	9.2 ± 2.5	42.1 ± 8.0	NA	NA	NA
Park et al,[28] 2021	58.3 ± 8.0	NA	40.9 ± 7.4	NA	NA	29.2 ± 12.1	NA	38.1 ± 7.7	NA	NA	NA
Romano et al,[29] 2021	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	37.2 ± 14.2
Saeed et al,[30] 2020	49 ± 14	18.3 ± 5.5	NA	42 ± 6	28 ± 9	47 ± 16	11.3 ± 3.4	NA	NA	NA	NA
Schneider et al,[31] 2021	NA	19 (15-22)	NA	45 ± 9.4	NA	70 (53-96)	11 (8.5-12)	42 (30-52)	10 ± 3	0.4 ± 0.21	NA
Cai et al,[32] 2020	50.7 ± 14.6	16.0 ± 4.0	NA	50.4 ± 7.6	NA	44.7 ± 15.0	NA	NA	NA	NA	NA
Peugnet et al,[33] 2020	53.2 ± 13	17 ± 6	44 ± 5.4	50.3 ± 7	30.6 ± 9.5	NA	10.5 ± 3.4	36.4 ± 10	NA	NA	NA
Utsunomiya et al,[34] 2022	57 (46-63)	16 ± 4	NA	NA	35 (29-41)	36 (30-42)	NA	37 ± 9	10 ± 3	NA	NA
Liang et al,[35] 2019	61.8 ± 7.5	18.8 ± 4.9	NA	NA	NA	NA	NA	NA	NA	NA	NA
Ng et al,[36] 2022	48.4 ± 17.2	14.0 ± 4.9	36.0 ± 6.3	46.5 ± 8.2	NA	53.8 ± 20.0	9.45 ± 3.29	35.9 ± 11.2	NA	NA	NA

Values are mean ± SD, or median (Q1-Q3).

CMR = cardiac magnetic resonance; EROA = effective regurgitation orifice area; FAC = fractional area change; LVEF = left ventricular ejection fraction; PASP = pulmonary artery systolic pressure; RA = right atrial; RV EDD = right ventricular end-diastolic diameter; RVEF = right ventricular ejection fraction; S′ TDI = tricuspid annular tissue Doppler imaging systolic velocity; TA = tricuspid annulus; TAPSE = tricuspid annular plane systolic excursion; other abbreviation as in Table 1.

results of the meta-regression analysis. The main findings were consistent in the meta-regression analyses performed with a patient-year approach (Supplemental Table 3).

The funnel plot did not show any significant publication bias for all the performed analyses (Supplemental Figure 4).

HETEROGENEITY AND STUDY QUALITY ASSESSMENT. Heterogeneity assesses whether observed differences in results arise by chance alone. To assess the impact of study quality (bias) on heterogeneity, we applied the Newcastle-Ottawa quality assessment scale to the primary studies included in the meta-analysis. All the studies included in this meta-analysis were assessed as either low or medium risk of bias (Supplemental Table 4).

DISCUSSION

This study represents the first comprehensive meta-analysis to assess the prognostic value of right heart imaging parameters in patients with significant TR. The main findings of the present study can be summarized as follows: 1) the overall long-term mortality rate of patients with significant TR remains high at 31% at a mean follow-up of 39 months; 2) differences in mortality rates were observed based on the treatment strategy, with the medical treatment subgroup showing a rate of 43%, while the surgery subgroup had a rate of 11%; and 3) a higher mortality was associated with RV dysfunction, whereas a reduced mortality was associated with increasing right atrial dilatation. In addition, the study found that all traditional cardiovascular risk factors (including age, diabetes mellitus, arterial hypertension, and dyslipidemia) were significantly associated with an increased risk of mortality.

In recent years, the perception of TR has undergone a significant paradigm shift. Severe TR can have a detrimental effect on the quality of life of patients and is associated with high mortality rates ranging from 30% to 50%.[1-5] The current meta-analysis confirms these findings by indicating a high long-term mortality rate, thus highlighting the significant impact that severe TR can have on patient outcomes and the need for timely and appropriate management.

Surgical intervention has traditionally been the primary treatment option for patients with severe TR. However, the decision to undergo surgery for TR has been a matter of debate over the years due to the high perioperative mortality rates associated with the

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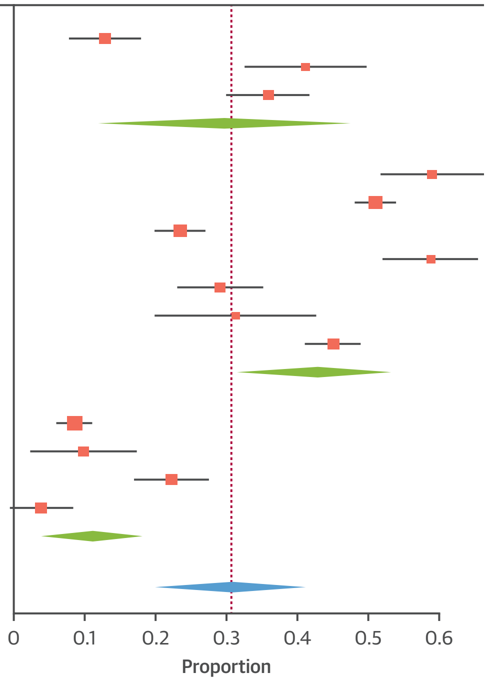
FIGURE 1 Forest Plot for the Incidence of Long-Term All-Cause Mortality of Patients With Significant Tricuspid Regurgitation

Studies	Estimate (95% C.I.)	All-Cause Death / N. of Patients
Ancona F	0.129 (0.078, 0.179)	22/171
Cai S	0.411 (0.325, 0.498)	51/124
Peugnet F	0.359 (0. 301, 0.417)	93/259
Subgroup Miscellaneous (I^2 = 95.92 %, *P* < 0.0001)	**0.298 (0.117, 0.478)**	**166/554**
Bar N	0.590 (0.518, 0.662)	105/178
Fortuni F	0.510 (0.481, 0.539)	586/ 1,149
Romano R	0.235 (0.200, 0.271)	128/544
Saeed S	0.589 (0.522, 0.655)	123/209
Schneider M	0.291 (0.231, 0.351)	64/220
Utsunomiya H	0.312 (0.199, 0.426)	20/64
Ng p	0.450 (0.412, 0.489)	286/635
Subgroup Medical Therapy (I^2 = 97.14 %, *P* < 0.0001)	**0.426 (0.318, 0.534)**	**1,312/2,999**
Dreyfus J	0.086 (0.060, 0.111)	40/466
Kim J	0.098 (0.024, 0.173)	6/61
Park S	0.223 (0.170, 0.276)	53/238
Liang W	0.039 (−0.004, 0.083)	3/76
Subgroup Surgery (I^2 = 89.69 %, *P* < 0.0001)	**0.110 (0.040, 0.181)**	**102/841**
Overall (I^2 = 98.55%, *P* < 0.0001)	**0.308 (0.204, 0.412)**	**1,580/4,394**

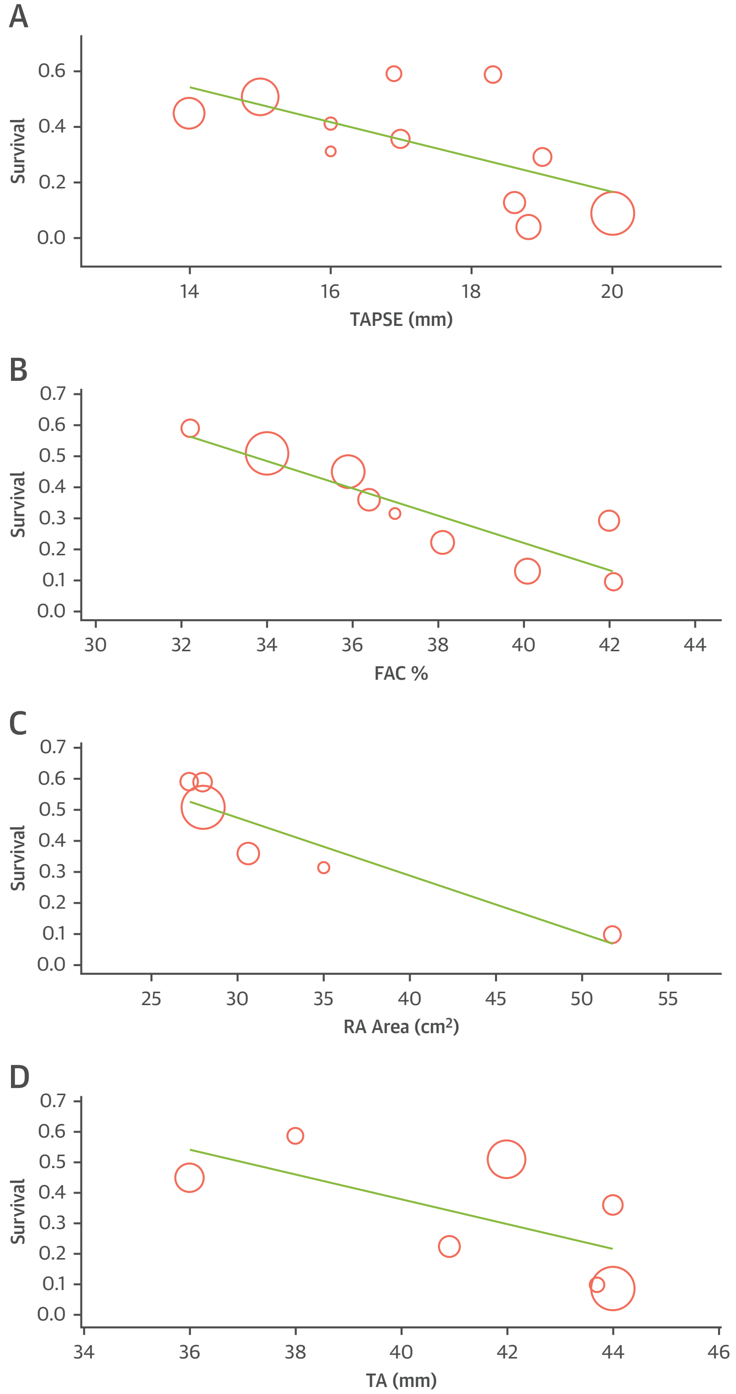


The overall incidence of long-term all-cause mortality was 31% (14 studies; 95% CI: 20%-41%; $P < 0.001$; $I^2 = 98.55\%$). Different mortality rates were observed in association with surgical intervention and medical treatment, with rates reported at 11% (95% CI: 20%-41%) and 43% (95% CI: 32%-53%), respectively.

procedure. Moreover, the effectiveness of surgery for isolated secondary TR compared with medical treatment is not established.[37] Despite not being the result of a direct comparison, the current meta-analysis suggests a higher long-term mortality rate in the medical subgroup (43%) compared with the surgery subgroup (11%), leading to the speculative hypothesis that surgery could be more effective in reducing mortality rates compared with medical management alone. It is essential to note that the disparity in mortality rates between the 2 subgroups may have been influenced by multiple factors, especially a survivorship bias in surgically treated patients, and therefore, firm conclusions cannot be definitively drawn. The 2 subgroups exhibited significant heterogeneity in their characteristics and only a randomized clinical trial can direct compare them. In fact, it must be noted that patients treated conservatively are usually older and with more comorbidities compared with those who undergo surgery, and this play a clear role in the observed outcomes. Moreover, in the current meta-analysis, functional TR was more frequently observed in the medical subgroup (99% ± 2% vs 68% ± 15%). Despite these limitations, our findings underscore the unmet need for effective treatment options for patients with significant TR. Transcatheter procedures offer a promising perspective for these patients and long-term data on this treatment modality are eagerly awaited to validate their impact on long-term prognosis.

The development of interventional treatment options for TR has increased the recognition of atrial functional TR as a distinct pathophysiological entity and generated enthusiasm for its better classification and prognostic implications. By using 3-dimensional echocardiography, recent studies have shown that atrial TR is characterized by marked right atrial dilation and tricuspid annulus enlargement, which cause lack of leaflet coaptation without leaflet tethering and a conical deformation of the RV caused by RV basal enlargement. Conversely, ventricular functional TR is commonly characterized by an ellipsoidal-shaped RV remodeling caused by RV mid enlargement, which causes displacement of the papillary muscles and leaflet tethering and tenting.[38-42] The abnormal tension and displacement of the valve leaflets caused by

FIGURE 2 **Plots Showing the Result of the Meta-Regression Analyses to Investigate the Association Between the Variables of Interest and All-Cause Mortality**



(A) Tricuspid annular plane systolic excursion (TAPSE); (B) fractional area change (FAC); (C) right atrial (RA) area; (D) tricuspid annulus (TA). An inverse relation was found between TAPSE (11 studies enrolling 3,551 subjects, −6.3% [95% CI: −11.1% to −1.4%]; $P = 0.011$), FAC (9 studies, n = 2,975, −4.4% [95% CI: −5.9% to −2.9%]; $P < 0.001$), RA area (6 studies, n = 1,920, −1.9% [95% CI: −2.5% to −1.3%]; $P < 0.001$), TA dimension (7 studies, n = 2,986, −4.1% [95% CI: −7.6% to −0.5%]; $P = 0.026$), and mortality.

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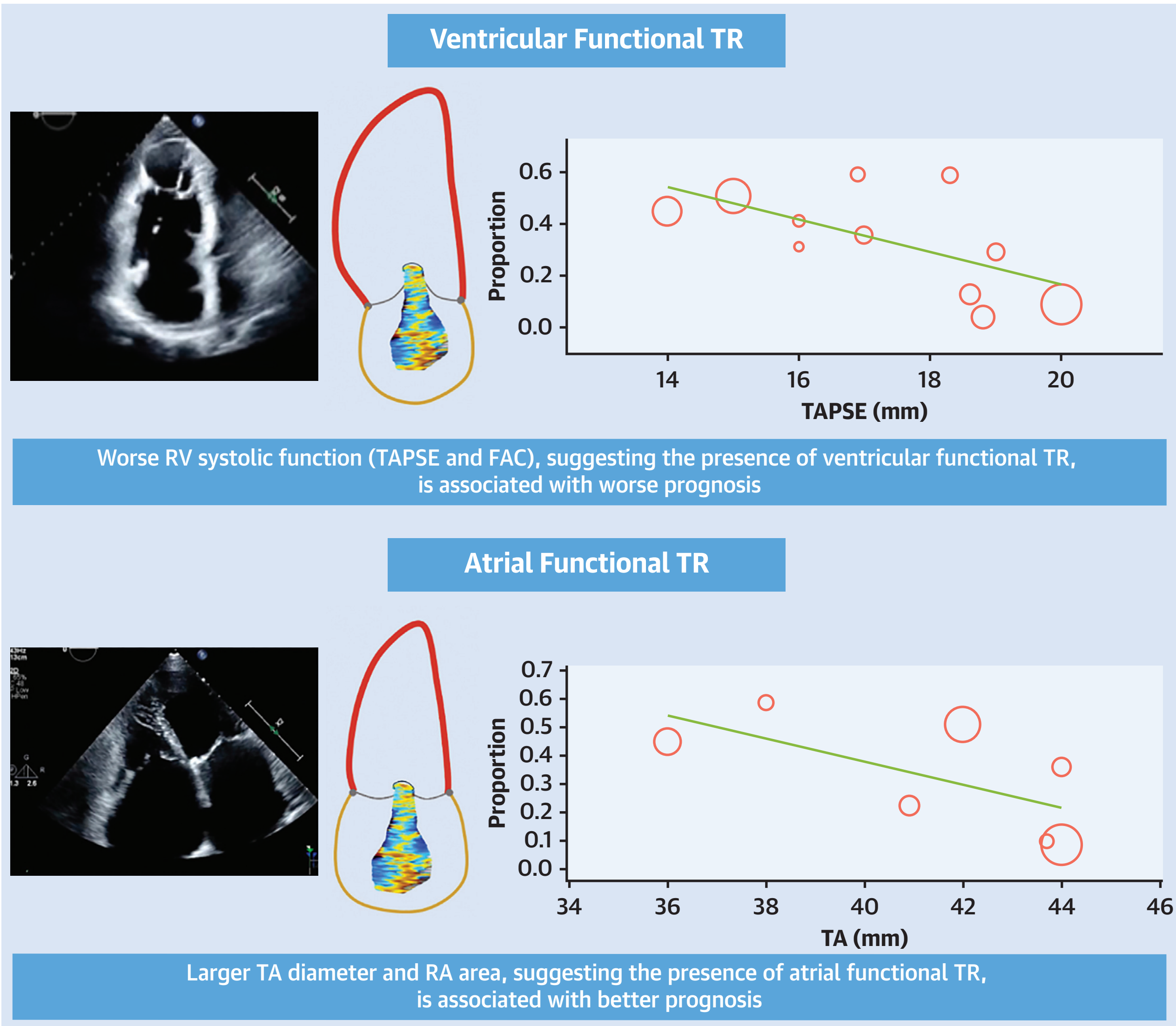
CENTRAL ILLUSTRATION Differential Prognostic Impact: Atrial and Ventricular Functional TR



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FAC = fractional area change; RA = right atrium; RV = right ventricular; TA = tricuspid annulus; TAPSE = tricuspid annular plane systolic excursion; TR = tricuspid regurgitation.

tenting can complicate surgical or transcatheter interventions, making the procedures more challenging and potentially leading to suboptimal outcomes, characterized by a high early residual rate of TR.[18,43,44] Distinguishing between these 2 phenotypes of functional TR can be challenging, particularly in advanced stages in which the 2 conditions may overlap. Longitudinal studies are needed to achieve a better understanding of TR pathophysiology and will thus help in identifying the original causative etiology of functional TR.[45] Nonetheless, despite the lack of unifying definition up until very recently, preliminary evidence points to a better survival of the atrial functional phenotype when compared with ventricular functional. Gavazzoni et al[17] demonstrated that patients with atrial functional TR, defined using the criteria proposed in the last American College of Cardiology/American

Heart Association guidelines (LVEF >60%, pulmonary artery systolic pressure <50 mm Hg, absence of left-sided valve disease, and normal appearance of tricuspid valve leaflets),[46] had a significantly lower incidence of the combined endpoint of all-cause death and heart failure hospitalizations at the 1-year follow-up. Galloo et al[19] proposed a stepwise approach to classify functional TR into 4 etiologies based on clinical and echocardiographic characteristics: left-sided cardiac disease, pulmonary hypertension, RV dysfunction, and atrial functional TR. Etiologies 1 to 3 were grouped as ventricular functional TR, whereas atrial functional TR remained an independent group. Noteworthy, patients with functional TR in the presence of atrial fibrillation were excluded from the final analysis (to reduce ambiguity in the true etiology of ventricular functional TR). Their findings indicated that patients with atrial functional TR had a significantly better long-term survival rate compared with those with ventricular functional TR. On the other hand, Schlotter et al[18] used a different approach to define atrial functional TR, focusing on the presence of tenting height ≤10 mm, midventricular RV diameter ≤38 mm, and LVEF ≥50%. Their results showed that atrial functional TR had a lower incidence rate of the combined endpoint in both the conservative and T-TEER cohort when compared with ventricular functional TR. Overall, despite variations in definitions, these studies consistently showed a better prognosis for patients with atrial functional TR. The current meta-analysis showed that in patients with significant TR undergoing different treatment options, RV dysfunction (identified by reduction of TAPSE and FAC) was associated with a higher mortality rate, whereas increasing right atrial and tricuspid annulus dilation were associated with a reduced mortality rate. These findings provide further support for the hypothesis that atrial functional TR may have a more favorable prognostic outcome compared with ventricular functional TR. A careful assessment of right heart anatomy and function is warranted, as it may facilitate the identification of distinct subtypes of functional TR with different clinical and echocardiographic characteristics, as well as with different prognosis. Distinguishing between ventricular and atrial functional TR may have practical implications for patient care in terms of need for close monitoring and patient selection for tricuspid valve interventions. Gavazzoni et al[17] found that the severity of functional TR was the only independent factor affecting the prognosis of atrial functional TR patients, while RV function was also associated with outcomes in ventricular functional TR patients. These findings highlight the need to reduce the severity of TR as the main goal of treatment in atrial functional TR patients, while in ventricular functional TR patients, both TR severity and RV function need to be addressed to disrupt the vicious cycle between the two. Future research is necessary to determine the optimal therapeutic strategy according to the TR functional phenotype.

In addition, the observed association between traditional cardiovascular risk factors and increased mortality highlights the importance of comprehensive management of these patients, with a focus on optimizing therapy to control hypertension, hyperlipidemia, and diabetes.

STUDY LIMITATIONS. This study has intrinsic limitations common to all meta-analyses, which should be considered when interpreting the findings. First, the inclusion of a relatively small number of studies, particularly in the surgery group, may limit the generalizability of our results. However, this was necessary to ensure a more homogeneous study population through strict exclusion criteria. Additionally, the nonrandomized and retrospective nature of the included studies introduces the potential for selection bias.

Second, utilizing all-cause mortality as the primary endpoint raises questions regarding the specific causes of death. However, the absence of consistent and

TABLE 3 Meta-Regression Analysis for the Outcomes of Interest

	Beta Coefficient (%)	95% CI (%)	*P* Value
Sex	0.7	−0.2 to 1.6	0.105
BMI	−1.1	−11.2 to 8.9	0.826
Age	1.4	0.7 to 2.1	<0.001
DM	2.1	1.2 to 3.0	<0.001
Hypertension	0.6	0.3 to 0.9	<0.001
Hyperlipidemia	1.1	0.5 to 1.8	<0.001
COPD	3.8	0.4 to 7.1	0.027
LVEF	−2.4	−4.1 to −0.8	0.003
AF	0.3	−0.3 to 0.9	0.328
PM/ICD	−0.2	−2.5 to 2.2	0.896
CKD	0.1	−2.7 to 3.0	0.932
NYHA functional class III-IV	0.3	−0.4 to 1.0	0.402
TAPSE	−6.3	−11.1 to −1.4	0.011
FAC	−4.4	−5.9 to −2.9	<0.001
S′ TDI	0.9	−13.8 to 15.6	0.903
RV basal diameter	−2.5	−6.5 to 1.5	0.223
TA diameter	−4.1	−7.6 to −0.5	0.026
RA area	−1.9	−2.5 to −1.3	<0.001
PASP	0.6	−0.3 to 1.4	0.168
Vena contracta	0.3	−0.9 to 1.5	0.660
Follow-up	−0.1	−0.6 to 0.5	0.786

Abbreviations as in Tables 1 and 2.

systematically recorded data hinders a comprehensive understanding of contributing factors.

Third, the results mainly derive from standard 2-dimensional transthoracic echocardiography measurements, which exhibit limited accuracy because of the complex RV geometry. Due to the limited echocardiographic data and to the absence of a standardized definition, the study had to rely on the available data to differentiate between atrial and ventricular TR, predominantly focusing on the unique functional and morphological characteristics of the right heart in these 2 scenarios.[38-42] Furthermore, in the included studies with a multicenter design, the echocardiographic assessment relied on evaluations conducted by individual centers, rather than by a centralized laboratory.

Last, the analysis may be susceptible to ecological bias, as the data were aggregated at the study level rather than at the individual level.

Overall, the findings of this meta-analysis emphasize the need for continued research to better understand the prognostic implications of TR and to identify different subtypes of TR, which may require different management strategies.

CONCLUSIONS

Functional TR is a complex, highly prevalent disease, with serious effects on survival. Multiple phenotypes can be recognized in the functional TR spectrum. Patients with functional TR and signs RV systolic dysfunction are likely expected to experience dismal prognosis, whereas the presence of right atrial dilatation suggest a better prognostic outcome. However, these results should be considered as hypothesis-generating. Prospective, multicenter studies based on a shared definition of the atrial and ventricular STR phenotypes with appropriate evaluation of RV anatomy and function are warranted to achieve definitive conclusions.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: In a meta-analysis of 4,394 subjects with significant TR undergoing different treatment options, we showed that RV dysfunction, identified by reduction of TAPSE and FAC, was significantly associated with increased incidence of all-cause mortality, whereas right atrial and tricuspid annulus dilation were associated with a reduced mortality rate. These findings further support the more favorable prognostic outcome for atrial functional TR compared with ventricular functional TR.

TRANSLATIONAL OUTLOOK: The findings of this meta-analysis provide a strong rationale for distinguishing between ventricular and atrial functional TR in clinical practice. Future research should aim to determine the optimal therapeutic management strategies based on the underlying etiology of TR.

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KEY WORDS echocardiography, functional tricuspid regurgitation, right ventricle, survival, tricuspid valve

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

8 Tabellarischer Lebenslauf

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  Prof. Dr. Dr. Med. Philipp Lurz

- 02/2023 – 30/10/2023 Leipzig, Deutschland
  Studienärztin - Herzzentrum Leipzig
  Prof. Dr. Med. Holger Thiele, Prof. Dr. Dr. Med. Philipp Lurz

- 04/2022 – 01/2023 Leipzig, Deutschland
  Fellowship Kardiovaskuläre Bildgebung - Herzzentrum Leipzig
  Prof. Dr. Med. Holger Thiele, Prof. Dr. Dr. Med. Philipp Lurz

- 11/2018 – 10/2022 Mailand, Italien
  Assistenzärztin - Istituto Clinico Humanitas
  Prof. Dr. Gianluigi Condorelli

- 09/2015 – 07/2017 Neapel, Italien
  Praktikum in der Kardiologie - Azienda Ospedaliera Universitaria - Federico II
  Prof. Dr. Bruno Trimarco

ALLGEMEINE UND BERUFLICHE BILDUNG

- 07/2023 Dresden, Deutschland
  Anerkennung Innere Medizin und Kardiologie
  Sächsische Landesärztekammer

- 03/2023 Dresden, Deutschland
  Approbation Als Arzt
  Landesdirektion Sachsen

- 11/2018 – 10/2022 Rozzano, Italien
  Facharztausbildung für Kardiologie
  Humanitas University

- 02/2018 Neapel, Italien
  Staatsexamen und Approbation als Arzt
  Università Federico II

- 10/2011 – 07/2017 Neapel, Italien
  Studium der Humanmedizin
  Università Federico II
  Abschlussnote 110/110 cum laude

- 09/2006 – 07/2011 Giugliano in Campania, Italien
  Abitur “Maturità Scientifica" Liceo Scientifico De Carlo
  Abschlussnote 100/100 cum laude

SPRACHKENNTNISSE

- Muttersprache(n): Italienisch
- Weitere Sprache(n): Englisch, Deutsch

DIGITALE KOMPETENZEN

- MS-Office (Word Excel Power-Point Outlook)
- Graphpad Prism
- Prometa3
- STATA

BESCHEINIGUNGEN

- 2024 EACVI Certification in Adult Transoesophageal Echocardiography
- 2023 Goethe-Zertifikat C1
- 2022 EACVI Certification in adult transthoracic echocardiography

MITGLIEDSHAFTEN

- Deutsche Gesellschaft für Kardiologie – Herz- und Kreislaufforschung e.V.
- ESC Professional Member
- Silver member of the European Association of Cardiovascular Imaging

PUBLIKATIONEN

1. Duerr GD, Zancanaro E, Bombace S, Stephan von Bardeleben R. Right Sinus Valsalva Aneurysm Ruptured Into the Right Ventricular Outflow Tract. JACC Case Rep. 2025
2. De Luca VM, Censi S, Conti R, Nerla R, Bombace S, Ruf TF, von Bardeleben RS, Lurz P, Castriota F, Squeri A. Tricuspid Regurgitation in the Era of Transcatheter Interventions: The Pivotal Role of Multimodality Imaging. J Clin Med. 2025
3. Sugiura A, Dreyfus J, Bombace S, Ivannikova M, Bartkowiak J, Haussig S, Schneider LM, Kassar M, Horn P, Taramasso M, Iliadis C, Osawa I, Goto T, Weber M, Tanaka T, Zimmer S, Obadia JF, Habib G, Bazire B, Iung B, Bohbot Y, Tribouilloy C, Donal E, Nejjari M, Riant E, Le Tourneau T, Lavie-Badie Y, Coisne A, Modine T, Lim P, Doguet F, Selton-Suty C, Baldus S, Kelm M, Praz F, Rottbauer W, Hans-Peter Linke A, Hahn R, Volker R, Messika-Zeitoun D, Lurz P, Nickenig G. Transcatheter Edge-to-Edge Repair in Patients With Primary Tricuspid Regurgitation. JACC Cardiovasc Interv. 2025
4. Stefanini G, Carlo-Stella C, Cannata F, Chiarito M, Figliozzi S, Novelli L, Lisi C, Bombace S, Catapano F, Indolfi E, Panico C, Corrado F, Masci G, Mazza R, Ricci F, Monti L, Ferrante G, Reimers B, Santoro A, Francone M, da Costa BR, Jüni P, Condorelli G. Cardioprotection with nebivolol in patients undergoing anthracyclines: a randomized placebo-controlled trial. Cardiovasc Res. 2025
5. Weckbach LT, Stolz L, Doldi PM, Glaser H, Ennin C, Kothieringer M, Stocker TJ, Näbauer M, Kassar M, Bombace S, Kresoja KP, Lurz P, Praz F, Thiele H, Rudolph V, Massberg S, Hausleiter J. Relevance of residual tricuspid regurgitation for right ventricular reverse remodelling after tricuspid valve intervention in patients with severe tricuspid regurgitation and right-sided heart failure. Eur J Heart Fail. 2024
6. De Luca VM, Cammalleri V, Antonelli G, Bombace S, Ruf TF, Gößler TAM, Lurz P, von Bardeleben RS, Grigioni F, Ussia GP. The Other Side of the Coin: Transesophageal Echocardiography Complications following Cardiac Surgery and Transcatheter Structural Heart Interventions. J Clin Med. 2024
7. Figliozzi S, Stankowski K, Tondi L, Catapano F, Gitto M, Lisi C, Bombace S, Olivieri M, Cannata F, Fazzari F, Bragato RM, Georgiopoulos G, Masci PG, Monti L, Condorelli G, Francone M. Mitral annulus disjunction in consecutive patients undergoing cardiovascular magnetic resonance: Where is the boundary between normality and disease? J Cardiovasc Magn Reson. 2024

8. Kresoja KP, Rosch S, Schöber AR, Fengler K, Schlotter F, Bombace S, Sagmeister P, von Roeder M, Kister T, Gutberlet M, Thiele H, Rommel KP, Lurz P. Implications of tricuspid regurgitation and right ventricular volume overload in patients with heart failure with preserved ejection fraction. Eur J Heart Fail. 2024
9. Bombace S, Fortuni F, Viggiani G, Meucci MC, Condorelli G, Carluccio E, von Roeder M, Jobs A, Thiele H, Esposito G, Lurz P, Grayburn PA, Sannino A. Right Heart Remodeling and Outcomes in Patients With Tricuspid Regurgitation: A Literature Review and Meta-Analysis. JACC Cardiovasc Imaging. 2024
10. Stolz L, Doldi PM, Kresoja KP, Bombace S, Koell B, Kassar M, Kirchner J, Weckbach LT, Ludwig S, Stocker TJ, Glaser H, Schöber AR, Massberg S, Näbauer M, Rudolph V, Kalbacher D, Praz F, Lurz P, Hausleiter J. Applying the TRILUMINATE Eligibility Criteria to Real-World Patients Receiving Tricuspid Valve Transcatheter Edge-to-Edge Repair. JACC Cardiovasc Interv. 2024
11. Cremonesi M, Felicetta A, Cannata F, Serio S, van Beek J, Bombace S, My I, Zanon V, Catalano C, Papadopoulou V, Monti L, Chiarito M, Stefanini G, Panico C, Francone M, Lugli E, Kallikourdis M, and Condorelli G. Long COVID-19 cardiac complications are associated with autoimmunity to cardiac self-antigens sufficient to cause cardiac dysfunction. Circulation 2023
12. Bombace S, Meucci MC, Fortuni F, Ilardi F, Manzo R, Canciello G, Esposito G, Grayburn PA, Losi MA, Sannino A. Beyond Aortic Stenosis: Addressing the Challenges of Multivalvular Disease Assessment. Diagnostics (Basel). 2023
13. Cannata F, Stefanini G, Carlo-Stella C, Chiarito M, Figliozzi S, Novelli L, Lisi C, Bombace S, Panico C, Cosco F, Corrado F, Masci G, Mazza R, Ricci F, Monti L, Ferrante G, Santoro A, Francone M, da Costa BR, Jüni P, Condorelli G. Nebivolol versus placebo in patients undergoing anthracyclines (CONTROL Trial): rationale and study design. J Cardiovasc Med (Hagerstown) 2023
14. Mushtaq S, Monti L, Rossi A, Pontone G, Conte E, Nicoli F, di Odoardo L, Guglielmo M, Indolfi E, Bombace S, Baggiano A, Gripari P, Pepi M, Bartorelli A, Oliveira M, Santos A, Francone M, Andreini D. The prognostic role of right ventricular dysfunction in patients with hypertrophic cardiomyopathy. Int J Cardiovasc Imaging 2023
15. Cannata F, Pinto G, Chiarito M, Maurina M, Condello F, Bombace S, Villaschi A, Novelli L, Stankowski K, Liccardo G, Gasparini G, Donia D, Celata A, My I, Kallikourdis M, Figliozzi S, Mantovani R, Fazzari F, Bragato RM, Condorelli G, Stefanini GG. Long-term prognostic impact of subclinical myocardial dysfunction in patients recovered from COVID-19. Echocardiography 2023
16. Consonni FM, Durante B, Manfredi M, Bleve A, Pandolfo C, Garlatti V, Vanella VV, Marengo E, Barberis E, Bottazzi B, Bombace S, My I, Condorelli G, Torri V, Sica A. Immunometabolic interference between cancer and COVID-19. Front Immunol. 2023
17. Ranucci M, Parati G, Di Dedda U, Bussotti M, Agricola E, Menicanti L, Bombace S, De Martino F, Giovinazzo S, Zambon A, Menè R, La Rovere MT. When Outcomes Diverge: Age and Cardiovascular Risk as Determinants of Mortality and ICU Admission in COVID-19. J Clin Med. 2022
18. De Luca G, Bombace S, Monti L. Heart Involvement in Systemic Sclerosis: the Role of Magnetic Resonance Imaging. Clin Rev Allergy Immunol. 2022
19. Bombace, S, My, I, Francone, M. Monti, L. Tumoral Phenocopies of Hypertrophic Cardiomyopathy: The Role of Cardiac Magnetic Resonance. J. Clin. Med. 2022
20. Cannata F, Bombace S, Stefanini GG. [Cardiac biomarkers in patients with COVID-19: pragmatic tools in hard times]. Revista Espanola de Cardiologia. 2021