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ORIGINAL RESEARCH

Prospective Quantification of Tricuspid Regurgitation With Echocardiography vs 4D Flow Cardiac Magnetic Resonance

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ABSTRACT

BACKGROUND Cardiac magnetic resonance (CMR) is a valuable tool in the assessment of valvular disease. However, its utilization in tricuspid regurgitation (TR) evaluation has been limited.

OBJECTIVES The authors sought to compare TR grading with 4D-CMR and transthoracic echocardiography (TTE).

METHODS We prospectively recruited patients with ≥ moderate TR on TTE to undergo multiparametric CMR with integrated cardiac function and 4D flow assessments using a 1.5-T scanner (Siemens Somatom Aera). Patients with other severe valvulopathy, end-stage renal disease, or pacemakers were excluded. TR was graded severe on CMR when TR volume ≥45 mL and/or TR fraction ≥50%. The weighted kappa test was used to assess the agreement in overall TR grading on TTE and CMR.

RESULTS Fifty-two patients were enrolled (mean age 78.5 ± 7.6 years, 53.8% men). The median interval between CMR and TTE was 2 days (Q1-Q3: 1-37 days). The agreement between TTE and CMR-derived TR volume was fair (kappa = 0.28, 95% CI: 0.13-0.45), with only 10 of 31 patients (32%) with ≥ severe TR on TTE meeting severe TR volume criterion on CMR (TR volume ≥45 mL). There was no agreement between TTE and CMR-derived TR fraction (kappa = 0.04, 95% CI: 0.13-0.46), with only 3 of 31 patients (13%) with ≥ severe TR on TTE meeting severe TR criterion on CMR (TR fraction ≥50%).

CONCLUSIONS Grading of TR was frequently discordant between TTE and 4D magnetic resonance imaging. Further studies are needed to elucidate the clinical impact of concordant/discordant TR grading on multimodality imaging. (JACC Adv. 2025;4:101759) © 2025 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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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

2D = 2-dimensional

4D = 4-dimensional

CMR = cardiac magnetic resonance

RV = right ventricle

RVEDV = right ventricular end-diastolic volume

SAX = short-axis imaging

TR = tricuspid regurgitation

TTE = transthoracic echocardiography

Tricuspid regurgitation (TR) is common and associated with right ventricular (RV) dysfunction and all-cause mortality.[1] Tricuspid valve surgery is typically reserved for symptomatic patients or those with progressive RV failure and is associated with high perioperative morbidity and mortality.[2,3] However, surgical outcomes have been attributed to inadequate understanding of the natural progression of TR, its classification, and the optimal timing of intervention.[4-8] The advent of transcatheter interventions for TR has recently fueled a growing interest in bridging these knowledge gaps. In this context, many recent studies explored various methods for grading TR on echocardiography.[5,9-11] These studies emphasized the challenges in accurate quantification of TR, suggesting the need to explore the role of other imaging modalities in grading TR.

Cardiac magnetic resonance (CMR) is increasingly recognized as a useful tool for the assessment of valvular heart disease.[12-15] Nevertheless, the accuracy of CMR in estimating TR can be affected by the exaggerated motion of the tricuspid annulus,[12] difficulty with breath-holding, and arrhythmia. Newer volumetric techniques such as 4-dimensional (4D) flow CMR can more accurately assess flow across the valve and track the position of the tricuspid annulus over time.[16] In addition, 4D flow CMR enables single-volume acquisition of the entire heart and does not require specialized knowledge of cardiac anatomy and imaging planes. This allows TR jets to be directly quantified with a single measurement, eliminating the need for ventricular endocardial contouring and increasing reporting efficiency.[16,17] Few studies assessed the agreement between the transthoracic echocardiography (TTE) and CMR in quantifying TR,[16,18,19] similar to what has been reported on the quantification of mitral and aortic regurgitation.[20-24] However, except for in the context of congenital heart disease, these comparative studies did not include 4D flow CMR assessment. We compared TR grading by TTE vs multiparametric CMR with integrated 4D flow analysis in patients with ≥moderate regurgitation at TTE. Additionally, we investigated the correlation between CMR-derived TR metrics and RV volumes.

METHODS

STUDY POPULATION. We prospectively enrolled patients referred to the structural heart disease clinic at Mayo Clinic, Minnesota, USA, between January 2022 and December 2023. Patients with moderate or greater TR on the most recent TTE were included (within 45 days without apparent change in volume status). We excluded patients with other significant valvulopathy (>moderate regurgitation, and/or stenosis), end-stage renal disease, permanent pacemakers, claustrophobia, and pregnant women. All patients provided written consent. This prospective study was registered on ClinicalTrials.gov (NCT05006443).

CMR ACQUISITION. Comprehensive CMR scans were acquired on a 1.5-T magnetic resonance imaging scanner (MAGNETOM Aera, Siemens Healthineers). Two cine sequences were acquired for each subject: the standard breath-hold segmented cine (Seg Cine) and the free-breathing compressed-sensing sequence with motion correction (Supplemental Table 1). A 2-dimensional (2D) phase contrast imaging (2D flow) was obtained through the main pulmonary artery, aortic root at the sinotubular junction, through the open leaflets of the mitral valve in diastole, and through the tricuspid annulus in diastole. A 4D flow magnetic resonance imaging was performed post-contrast with whole heart coverage. Acquisition parameters are presented in the Supplemental Material.

CMR ANALYSIS. We used Circle Cvi42 version 5.13.5 (Circle Cardiovascular Imaging Inc), an artificial intelligence-assisted segmentation software, for augmented manual postprocessing. A doctor of medicine researcher with 2 years of postprocessing training performed all aspects of CMR analysis, including the short-axis imaging (SAX) cine stack biventricular, 2D flow, and 4D flow analysis (Supplemental Figures 1 to 7). A cardiovascular radiologist with 13 years of experience validated all measurements. We assessed biventricular size and systolic function using Simpson method on the SAX cine imaging. Segmented cine images were used for biventricular systolic analysis if of diagnostic quality; otherwise biventricular systolic function was derived from free-breathing compressed-sensing sequence with motion correction cine images. Valvular function was assessed on 2D and 4D flow contrast phases. Regurgitant volume and fraction were estimated using total forward and backward volumes (2D and 4D flow contrast phase only). We then graded TR severity according to thresholds described elsewhere:[25]

1. Based on TR volume: mild <30 mL; moderate = 30 to 44 mL; severe ³45 mL by CMR.
2. Based on TR fraction: mild <30%; moderate = 30% to 49%; severe ³50%.[25]

In a separate analysis, we graded TR according to TR volume indexed by body surface area (BSA).

ECHOCARDIOGRAPHY. All patients underwent standard-of-care TTE with commercially available systems. Standard views were acquired. At our institution, TR is graded as trivial, mild, mild-moderate, moderate, moderate-severe, severe, massive, and torrential based on the integration of several parameters according to the American Society of Echocardiography guidelines.[26] Those parameters include valve morphology, color Doppler TR jet, continuous-wave Doppler signal of the regurgitant jet, vena contracta width, proximal flow convergence zone, systolic hepatic vein flow reversal, inferior vena cava maximal diameter, and tricuspid inflow velocities. The specific parameters used to grade TR were left to the discretion of the operator, and additional images were obtained as needed. All echos were subsequently reviewed and adjudicated by a dedicated independent core laboratory.

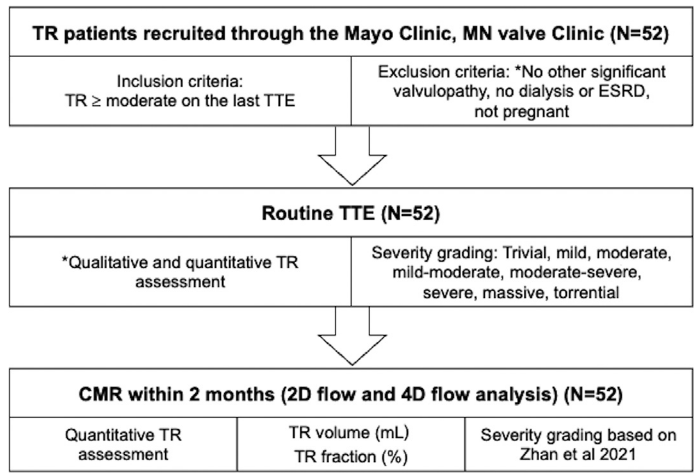
STATISTICAL ANALYSIS. Continuous data are expressed as means $\pm$ SD. Categorical data are presented as counts and frequencies (%). We assessed agreement in nonsevere vs severe TR classification between the 2 imaging modalities using the weighted kappa test with quadratic weight. The calculated kappa coefficients were interpreted as 0 to 0.20 low, 0.20 to 0.40 fair, 0.40 to 0.60 moderate, 0.60 to 0.80 good, and >0.80 excellent. Additionally, we performed the McNemar test to assess for significant differences in the proportion of observations classified as severe vs nonsevere TR. We used the Kruskal-Wallis test to compare TTE-based TR grades in terms of TR volume, TR fraction, and RV end-diastolic volume (RVEDV) indexed by BSA (details in the Supplemental Table 2). For pairwise comparisons, we used the Dunn test with Bonferroni correction. Finally, we used the Spearman correlation coefficient (rho) to assess the correlation between TR volume and TR fraction, indexed TR volume and TR fraction, TR volume and indexed RVEDV, indexed TR volume and indexed RVEDV, and TR fraction and indexed RVEDV. P value <0.05 was considered statistically significant. All statistical analyses were performed using the R Studio software (version 2023.09.1+494, Posit Software, PBC).

RESULTS

PATIENT SELECTION AND BASELINE CHARACTERISTICS. Fifty-two patients were enrolled (Figure 1). The 2D flow and 4D flow CMR data were interpretable in 46 of 52 (88%) patients and 49 of 52 (94%) patients, respectively. Mean age was 78.5 $\pm$ 7.6, and 28 of 52 (53.8%) were men (Table 1). The median interval between CMR and TTE was 2 days (Q1-Q3: 1-37 days). Seven patients had primary TR; the remainder (45/52) had nonpacemaker-related secondary TR. RV dilatation and impaired RV systolic function were present in 45 of 52 (87%) patients and 29 of 52 (56%) patients (Table 1, Supplemental Table 4). Figure 2 illustrates the distribution of TR grading by TTE, CMR-derived TR volume, and TR fraction. One patient was initially graded as moderate TR but later reclassified as mild-to-moderate TR after core lab review of the baseline TTE. They were still included in the final analysis because eligibility was determined based on the initial screening TTE acquired at the time of recruitment. Table 1 and Supplemental Tables 5 to 7 summarize the CMR results.

COMPARISON OF TR SEVERITY BETWEEN TTE AND CMR-DERIVED TR VOLUME. The agreement between TTE and CMR-derived TR volume in severe or higher vs nonsevere TR classification was fair (kappa = 0.28, 95% CI: 0.13-0.45). There was complete agreement in 31 (60%) cases (Table 2). Only 10 of 31 patients (32%) with severe or higher TR on TTE had severe TR on CMR (TR volume $\geq$45 mL). The McNemar test result was consistent and indicated a statistically significant difference in classification performance between the 2 modalities ($P < 0.001$).

FIGURE 1 Study Flow Chart



2D = two-dimensional; 4D = four-dimensional; CMR = cardiac magnetic resonance; ESRD = end-stage renal disease; TR = tricuspid regurgitation; TTE = transthoracic echocardiography.

TABLE 1 Baseline Characteristics, Laboratory, and Imaging Results (N = 52)

Age, y	78.4 ± 7.6
Male	28 (53.8)
White ethnicity	52 (100)
BMI (kg/m^2)	28.7 ± 6.3
NYHA functional class	
I	18 (34.6)
II	18 (34.6)
III	10 (19.2)
IV	1 (1.9)
Prior sternotomy	28 (53.8)
Prior CABG	14 (26.9)
Prior PCI	11 (21.2)
Prior aortic valve intervention	14 (26.9)
Prior mitral valve intervention	11 (21.2)
Prior myocardial infarction	4 (7.7)
Chronic lung disease	8 (15.4)
Coronary artery disease	21 (40.4)
Atrial fibrillation/atrial flutter	
Paroxysmal	13 (25)
Persistent	8 (15.4)
Permanent	14 (26.9)
Baseline lab values	
Hemoglobin (g/dL)	13.3 ± 1.7
BUN (mg/dL)	22.1 ± 8.8
Creatinine (mg/dL)	1.1 ± 0.2
GFR (mL/min)	61.5 ± 15.0
NT-pro BNP (pg/mL)	1,220.5 ± 1,894.7
Transthoracic echocardiography	
LVEF (%)	60 ± 7
TR severity	
Mild-moderate	1 (1.9)
Moderate	9 (17.3)
Moderate-severe	11 (21.2)
Severe	22 (42.3)
Massive	6 (11.5)
Torrential	3 (5.8)
PISA TR Grade	
2	4 (7.7)
3-4	32 (61.5)
Inferior vena cava collapsibility	
>50%	34 (65.4)
<50%	16 (30.8)
Indeterminate	1 (1.9)
Unavailable	1 (1.9)
Hepatic venous flow	
Systolic reversals	26 (50.0)
Systolic blunting	9 (17.3)
Systolic predominant	4 (7.7)
Codominant	2 (3.9)
Intermediate	1 (1.9)
Unavailable	10 (19.2)
RV dilation	
None	4 (7.7)
Mild	20 (38.5)
Moderate	16 (30.8)
Severe	9 (17.3)
Indeterminate	3 (5.8)
RV systolic dysfunction	
None	32 (61.5)
Mild	17 (32.7)
Moderate	3 (5.8)
Cardiac magnetic resonance	
LVSV (mL)	77.8 ± 21.5
RVSV (mL)	102.0 ± 32.4
RVEDV (mL)	220.2 ± 73.3
TR fraction (%)	30.4 ± 14.5
PR fraction (%)	6.8 ± 10.4
TR volume (mL)	31.4 ± 22.1

Values are mean ± SD or n (%).

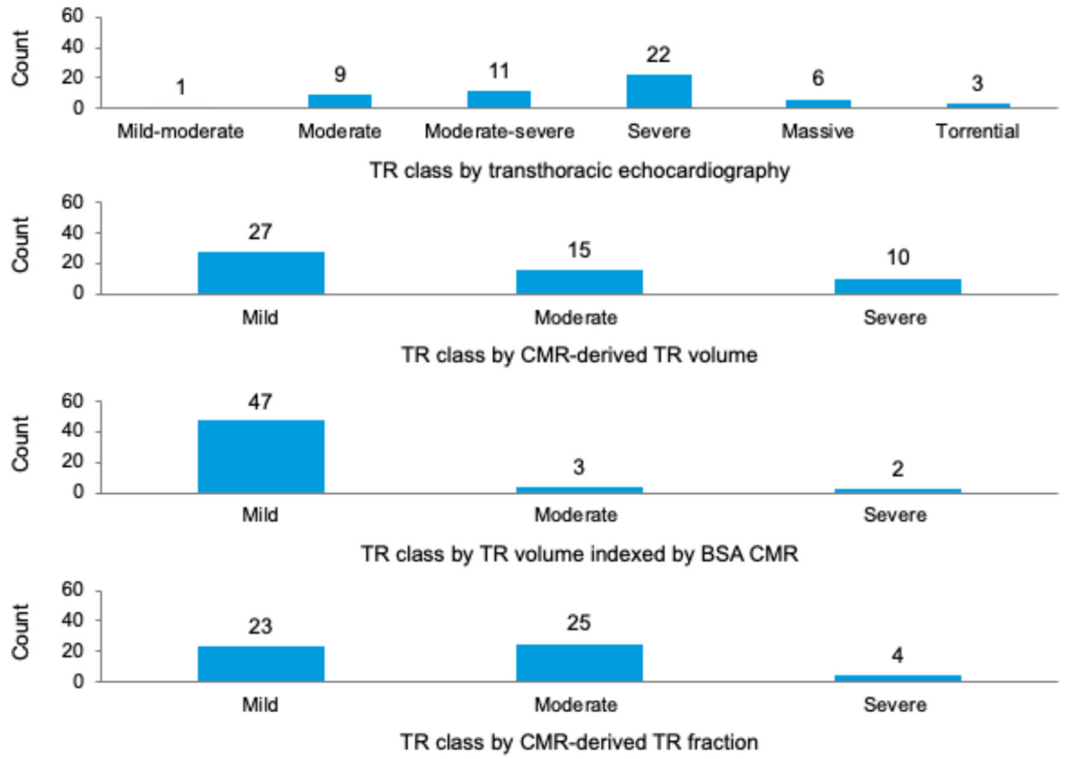
BMI = body mass index; BUN = blood urea nitrogen; CABG = coronary artery bypass graft; GFR = glomerular filtration rate; LVEF = left ventricular ejection fraction; LVSV = left ventricular systolic volume; NT-pro BNP = N-terminal pro B-type natriuretic peptide; PCI = percutaneous coronary intervention; PISA = proximal isovelocity surface area; PR = pulmonary regurgitation; RV = right ventricle; RVEDV = right ventricular end-diastolic volume; RVSV = right ventricular stroke volume; TR = tricuspid regurgitation.

COMPARISON OF TR SEVERITY BETWEEN TTE AND CMR-DERIVED TR VOLUME INDEXED BY BSA. The agreement between severe vs nonsevere TR classification by TTE and CMR (TR volume indexed by BSA mL/m^2) was low (kappa: 0.096; 95% CI: 0.0-0.25). Only 2 of 23 patients (9%) with severe TR on TTE had severe TR on CMR (indexed TR volume ≥45 mL/m^2) (Table 2). The McNemar test result was consistent and indicated a statistically significant difference in classification performance between the 2 modalities ($P < 0.001$).

COMPARISON OF TR SEVERITY BETWEEN TTE AND CMR-DERIVED TR FRACTION. The agreement between TTE and CMR-derived TR fraction was low (kappa: 0.040; 95% CI: 0.13-0.46). Only 3 of 31 patients (9.6%) with severe or greater TR on TTE had severe TR on CMR (TR fraction ≥50%) (Table 2). The McNemar test result was consistent and indicated a statistically significant difference in classification performance between the 2 modalities ($P < 0.001$).

COMPARISON OF CMR-DERIVED TR VOLUME, FRACTION, AND INDEXED RVEDV WITH TTE GRADE. TTE-based TR grades were significantly different in terms of CMR-derived TR volume ($P < 0.001$) (Figure 3). In pairwise comparisons, the severe or greater vs moderate and severe or greater vs

FIGURE 2 The Distribution of Tricuspid Regurgitation Grading by Transthoracic Echocardiography, Cardiac Magnetic Resonance-Derived TR Volume, and TR Fraction



BSA = body surface areax; CMR = cardiac magnetic resonance; TR = tricuspid regurgitation.

moderate or less TR groups were significantly different ($P = 0.021$, $P < 0.001$). TR volume indexed by BSA (mL/m^2) was significantly different between TTE-based grades ($P < 0.001$). In pairwise comparisons, moderate vs severe and moderate-severe vs severe grades were significantly different ($P < 0.001$ and $P = 0.007$, respectively). TR fraction was also significantly different between groups ($P < 0.001$). In pairwise comparisons, only the moderate vs severe or greater TR grades were significantly different ($P < 0.001$). TTE grades were also significantly different in indexed RVEDV (mL/m^2) ($P = 0.040$). In pairwise comparisons, none of the groups were significantly different from each other ($P > 0.050$).

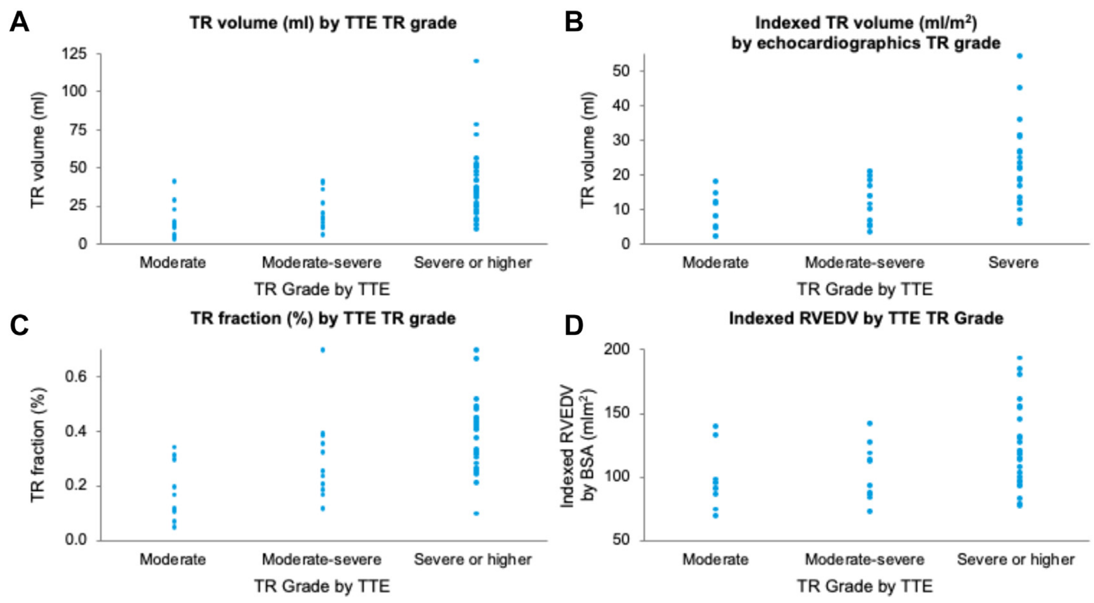
COMPARISON OF TR VOLUME AND TR FRACTION IN THE ASSESSMENT OF TR SEVERITY. There was a strong correlation between TR volume and TR fraction (rho = 0.805; 95% CI: 0.372-0.923; $P < 0.001$) (Figure 4). The correlation between TR volume and indexed RVEDV was moderate to strong (rho = 0.60; 95% CI: 0.38-0.74; $P < 0.001$). The correlation between TR volume indexed by BSA (mL/m^2) and indexed RVEDV was also moderate to strong (rho = 0.58; 95% CI: 0.37-0.73; $P < 0.001$). The correlation between TR fraction and indexed RVEDV was only moderate (rho = 0.37; 95% CI: 0.09-0.59; $P = 0.008$).

TABLE 2 TR Grade by TTE vs CMR-Derived Severity Grading

	CMR by TR Volume (Severe ≥45 mL)		CMR-Derived TR Volume Indexed by BSA (mL/m^2) (Severe >45 mL/m^2)		CMR Grade by TR Fraction (%) (Severe >50%)	
TTE	Nonsevere	Severe	Nonsevere	Severe	Nonsevere	Severe
Nonsevere	21	0	29	0	20	1
Severe	21	10	21	2	28	3

All observations are presented as counts.
BSA = body surface area; CMR = cardiac magnetic resonance; TR = tricuspid regurgitation; TTE = transthoracic echocardiography.

FIGURE 3 The Distribution of Tricuspid Regurgitation Grading by Transthoracic Echocardiography and Cardiac Magnetic Resonance-Derived TR Volume, TR Fraction, and TR Volume Indexed by BSA



The distribution of (A) TR volume; (B) TR volume indexed by BSA; (C) TR fraction; and (D) indexed RVEDV BSA in patients with moderate or less, moderate-severe, and severe or higher TR grades according to TTE. BSA = body surface area; RVEDV = right ventricular end-diastolic volume; TR = tricuspid regurgitation; TTE = transthoracic echocardiography.

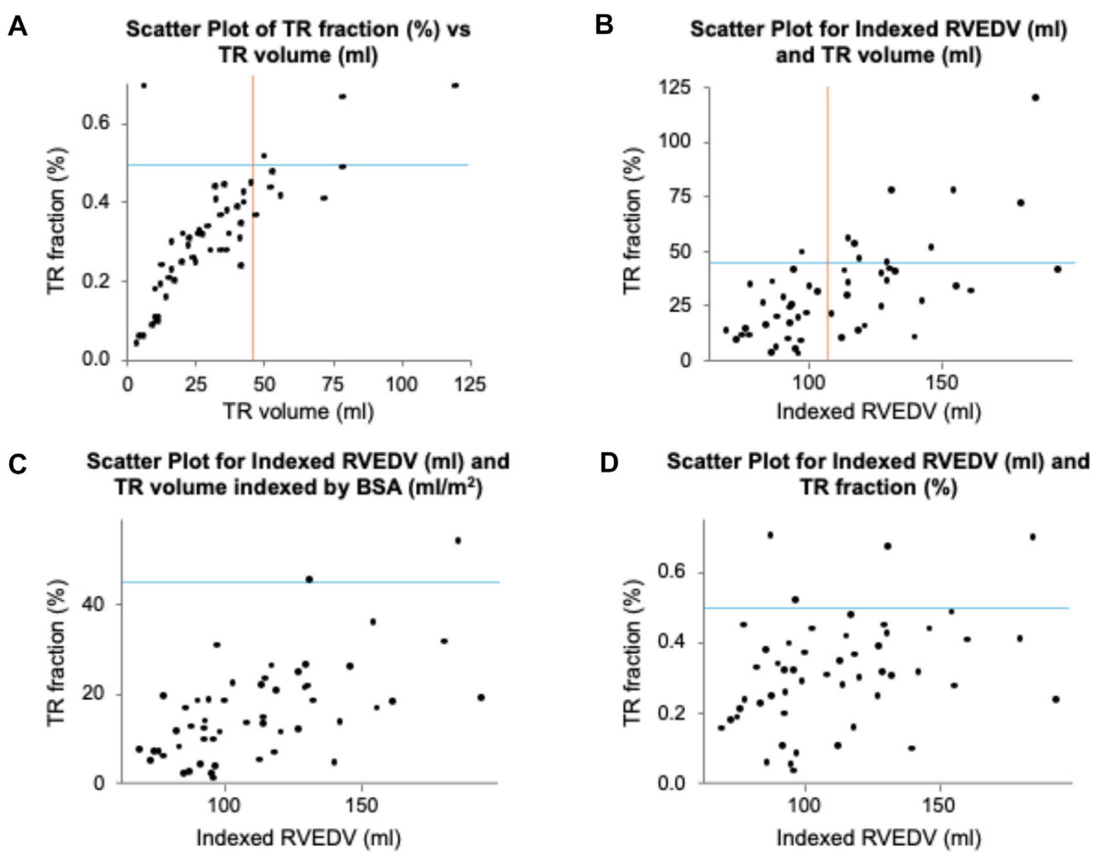
DISCUSSION

This is the first analysis of TR classification by TTE vs multiparametric CMR using integrated 4D flow analysis in patients with moderate or greater degrees of TR on TTE. We assessed agreement between modalities using established CMR thresholds.[25] We showed that there was limited agreement between the modalities (**Central Illustration**). For instance, 61% of patients with severe TR on TTE were classified as nonsevere on CMR (as defined by TR volume <45 mL). When TR fraction was used to grade TR on CMR, 87% of patients with severe TR on TTE were classified as nonsevere TR on CMR (TR fraction <50%).

Assessment of TR with 4D flow CMR has been shown to be more accurate than traditional CMR.[17] The increased accuracy stems from the ability of 4D flow to capture complex blood flow patterns in 3 dimensions over time. This enables a more comprehensive analysis of flow dynamics, especially in the presence of multiple TR jets. Moreover, the imaging for 4D flow analysis can be obtained in a single volume acquisition, which shortens scanning times and reduces the need for breath-holding and image postprocessing.[17] The 4D flow parameters have been validated against 2D flow parameters, and 4D flow imaging has been previously used to assess TR in patients with complex congenital heart disease.[27]

Few studies have directly compared TR grading between TTE and CMR, and those leveraging 4D CMR included only patients with congenital heart disease. Driessen et al measured 4D flow CMR-derived TR volume and fraction in 21 patients with congenital heart disease and pulmonary hypertension, 12 of whom had moderate or higher TR. Similar to our results, 75% of their patients were classified differently by at least 1 grade.[16] In a larger study, Zhan et al compared TR grading by TTE and SAX CMR in 337 patients with functional TR. They assessed the diagnostic performance of several TTE parameters against CMR-derived TR volume to design a new hierarchical TTE algorithm based on the best-performing parameters. They then compared TR severity grading by the American Society of Echocardiography-directed[26] and hierarchical echocardiographic algorithms vs CMR. The hierarchical approach performed marginally better than the American Society of Echocardiography-directed approach (65% vs 69% agreement with CMR-based TR grade). In most discordant cases, CMR

FIGURE 4 The Correlation Analysis of Tricuspid Regurgitant Volume, Tricuspid Regurgitant Fraction, and Indexed Right Ventricular End-Diastolic Volume Across Transthoracic Echocardiography-Based Tricuspid Regurgitant Severity Grades



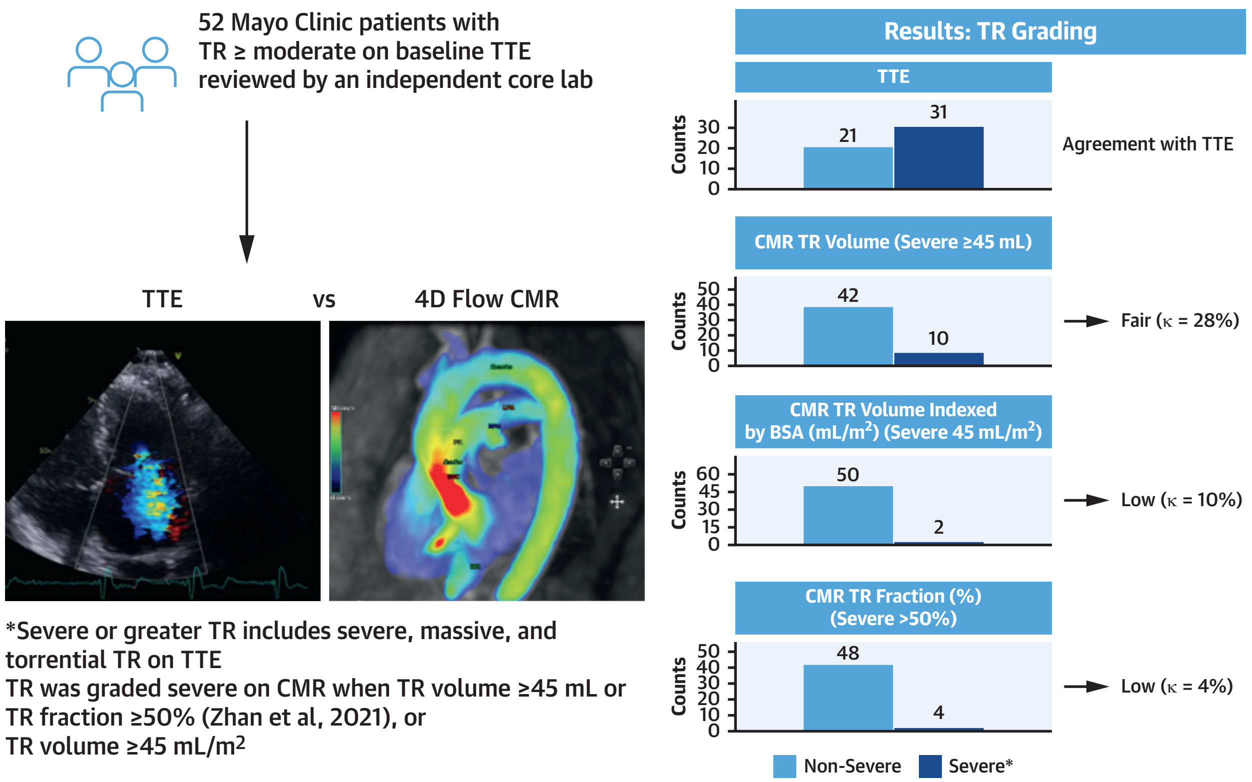
Correlation between (A) TR volume (mL) and TR fraction (%); (B) RVEDV indexed by BSA (mL/m^2) and TR volume; (C) indexed RVEDV and TR volume; (D) indexed RVEDV and TR fraction in patients with moderate or less, moderate-severe, and severe or higher TR grades according to TTE. BSA = body surface area; RVEDV = right ventricular end-diastolic volume; TR = tricuspid regurgitation; TTE = transthoracic echocardiography.

suggested a less severe TR grade than TTE.[18] A similar trend was found by Medvedofsky et al[19] in a study of 61 patients with isolated TR. Our results are consistent with these reports; regardless of the parameter used to grade TR (volume or fraction), CMR-based grades were on average lower than TTE-based grades.

Unlike with TTE, there are no universal thresholds for TR grading in CMR; nevertheless, several grading systems have been proposed. Few studies used echocardiographic TR volume thresholds,[19,26,28] or leveraged similar CMR-derived thresholds that are used in the assessment of pulmonic[16,29] or mitral valve regurgitation.[30] Recently, CMR-specific thresholds for TR volume and fraction have been derived from all-cause mortality outcome data in prospective cohort studies of patients with isolated severe TR,[28,31] functional TR,[14,25] and heart failure with reduced ejection fraction.[32] In our study, we used thresholds proposed by Zhan et al, the largest TR cohort studied thus far. After adjusting for clinical and imaging variables, including RV function, both TR fraction and TR volume were associated with increased mortality. Patients in the highest-risk group of TR volume ≥45 mL or TR fraction ≥50% had the worst prognosis. A summary of CMR thresholds for TR grading proposed in selected prospective studies of TR patients can be found in Table 3.

Although TR volume and TR fraction correlate strongly, they are distinct parameters that may result in differences in TR grading depending on the method selected (Figure 2). Both parameters are a measure of the regurgitant volume, but only the

CENTRAL ILLUSTRATION Prospective Quantification of Tricuspid Regurgitation With Echocardiography vs 4D Flow Cardiac Magnetic Resonance



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4D = four-dimensional; CMR = cardiac magnetic resonance; TR = tricuspid regurgitation; TTE = transthoracic echocardiography.

regurgitant fraction takes into account the total volume of blood ejected by the ventricle, adjusting for systemic flow. In functional TR, which frequently occurs in a low-flow state, a relatively small TR volume can yield a large TR fraction. In a population with varying flow states, TR volume may not be as useful as TR fraction in accounting for a dilated RV. As an alternative, we decided to index TR volume by BSA. This allows normalization of TR volume, adjusting for larger regurgitant volumes in larger individuals. As shown in **Figure 2**, the distributions of TR grades by TR fraction vs indexed TR volume are strikingly similar.

Current guidelines recommend using CMR in the evaluation of right heart size and function in patients with severe TR and the assessment of reverse RV remodeling (both atrial and ventricular).[33] An accurate TR classification is important because functional TR subtypes follow different clinical courses. Gavazzoni et al[34] showed a 2.15-fold higher risk of a 1-year composite of death and hospitalization in patients with secondary ventricular TR compared to secondary atrial TR, emphasizing the importance of early diagnosis of RV dysfunction. Several studies correlated different 2D flow CMR parameters of RV volume and function with increased all-cause mortality in TR patients; this includes RVEDV, RV end-systolic volume, RV ejection fraction, and RV strain (**Table 4**).[13-15] A 4D flow RV assessment can be useful in patients with pulmonary hypertension and RV diastolic dysfunction, which frequently coexist.[35,36] In our study, different echocardiographic grades were not fully distinguishable by RVEDV indexed by BSA. We also found a moderate correlation between indexed RVEDV and TR volume as well as indexed RVEDV and TR fraction. This highlights the need for more routine

TABLE 3 CMR Thresholds for TR Grading Proposed in Selected Prospective Studies of TR Patients

First Author	Year	Study Type	Patient Population	Primary Endpoint	N	Follow-Up	CMR Criteria for TR Volume (mL) (With aHR)	CMR Criteria for TR Fraction (%) (With aHR)	CMR Details
Zhan et al	2020	Prospective cohort	Functional TR	5-y all-cause mortality	547	Median 2.6 y	Low: <30 (reference) Intermediate: 30-44 (1.46) High: ^{3}45 (2.26)	Low: <30 (reference) Intermediate: 30-49 (1.21) High: ^{3}50 (2.60)	Steady-state free-precession
Wang et al	2021	Prospective cohort	Isolated severe TR	10-y all-cause mortality	262	Mean 2.5 y	Low: <30 High: ^{3}30 HR per 5 mL increase 1.05 (95% CI: 1.02-1.08)	Minimal: <25 Low: 26-36 Intermediate: 37-49 High: ^{3}50 HR per 5% increase 1.13 (95% CI: 1.06-1.21)	Steady-state free-precession
Seo et al	2023	Prospective cohort	Patients with HFrEF	3-y: A composite of all-cause death and hospitalization for HF	262	Median 921 d	Low: 10 (reference) Intermediate: 10-30 (2.11 [95% CI: 1.15-3.89]) High: >30 (7.16 [95% CI: 3.33-15.41])	Low: ≤15 (reference) Intermediate: 16-30 (2.26 [95% CI: 1.14-4.51]) High: >30 (4.23 [95% CI: 2.22-8.04])	Steady-state free-precession
Hinojar et al	2021	Prospective cohort	Patients with significant TR	5-y: A composite of hospital admission due to right heart failure and cardiovascular mortality	75	Median 3 y	Low: <42 (reference) High: >42 (HR 2.89) TR volume per 1 mL aHR: 1.06 (95% CI: 1.03-1.08)	Low: <40 (reference) High: >40 (HR 4.04) TR fraction per 1% aHR: 1.02 (95% CI: 1.01-1.03)	Steady-state free-precession

aHR = adjusted HR; CMR = cardiac magnetic resonance; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; TR = tricuspid regurgitation.

TABLE 4 CMR Thresholds for RV Indices Proposed in Selected Prospective Studies of TR Patients

First Author	Year	Study Type	Patient Population	Primary Endpoint	N	Follow-Up	RV Parameters Associated With the Primary Outcome	HR	CMR Details
Park et al	2016	Prospective cohort	Patients undergoing surgery for severe functional TR	5.8 y: Cardiac death	75	Median 57 mo	RV EF (%):≥46 vs <46 RV ESVI (mL/m^2): ≥76 vs <76	RV EF aHR: 0.714 (95% CI: 0.528-0.966) RV ESVI aHR: 1.183 (95% CI: 1.025-1.365)	Steady-state free-precession
Hinojar et al	2021	Prospective cohort	Patients with significant TR	5-y: A composite of hospital admission due to right heart failure and cardiovascular mortality	75	Median 3 y	eRVEF (%) ≥24 vs <24 RV strain (%) −14 (HR: 4.76)	eRVEF: HR per 1% aHR: 0.91 (0.87-0.95) RV strain per 1% aHR: 1.24 (95% CI: 1.11-1.39)	Steady-state free-precession
Ahn et al	2021	Prospective cohort	Patients who underwent TV surgery for functional TR were comprehensively reviewed	10 y: MACE and all-cause mortality	78	Median 5.4 y	Systolic RVMI <22 vs ≥22.0	RVMI: HR per increase of 5 mL/m^2 = 1.75	Steady-state free-precession

aHR = adjusted HR; CMR = cardiac magnetic resonance; EF = ejection fraction; eRVEF = effective right ventricular ejection fraction; MACE = major adverse cardiovascular events; RV = right ventricular; RV ESVI = right ventricular end-systolic volume index; RVMI = right ventricular motion index; TR = tricuspid regurgitation; TV = tricuspid valve.

CMR evaluation of the RV in TR patients, as TR severity may not always indicate the extent of RV dilation.

The results of our study raise several important questions: What is the "gold standard" for grading TR? Is it TTE, CMR, or other modalities? Which parameter is most accurate (TR volume, TR fraction, or others)? What is the impact of the dynamic nature of TR? Should we consider stress testing or incorporating invasive hemodynamic assessment in the evaluation of these patients? What is the impact of extra-valve cardiac abnormalities (RV size and function, pulmonary artery pressures, RV-pulmonary artery coupling) on the grading of TR? Should multimodality imaging be considered in patients referred for the newly commercially available tricuspid valve repair and replacement technologies?[37] Will patients who have concordantly severe TR on TTE and CMR derive the most benefit from TR interventions? These questions require further collaborative investigations and will inform the quickly growing field of transcatheter tricuspid valve interventions.

STUDY LIMITATIONS. Our pilot study has several limitations: First, TR severity is preload-dependent and therefore affected by volume status and diuretics. As such, the discrepancies observed in some patients might be explained by the time interval between the TTE and CMR imaging. This was unfortunately unavoidable considering the logistics of securing a research 4D-CMR for patients who are largely traveling to our tertiary center. However, we observed no significant changes in body weight or diuretic dose between the 2 scans, suggesting that this difference is not predominantly related to difference in loading conditions. Second, some patients had atrial fibrillation, which may have introduced beat-to-beat variability and can impact our assessment. Third, patients with pacemakers or ICDs were excluded to minimize imaging artifacts. Therefore, our findings may not be fully generalizable to this cohort. Fourth, determining the ideal imaging modality to assess TR requires benchmarking TR grades between modalities against long-term clinical outcomes. This necessitates a larger study, which was beyond the scope of this exploratory study. Finally, the modest sample size limited our ability to assess the between-group differences in CMR-based TR metrics in patients with differing stages of RV dilation and function.

CONCLUSIONS

Grading of TR is frequently discordant between TTE and CMR. Further studies are needed to elucidate the clinical impact of concordant/discordant TR grading on multimodality imaging.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Discrepancies between TTE and CMR imaging with integrated 4D flow analysis in TR severity assessment highlight the need for a standardized multimodal approach. The most relevant TR parameter remains unclear, but 4D flow CMR offers advantages with 3-dimensional flow visualization, single-volume acquisition, and streamlined processing.

TRANSLATIONAL OUTLOOK: Standardized CMR thresholds for TR grading are lacking. Future research should validate these thresholds, assess TR dynamics through stress imaging or invasive hemodynamics, and integrate CMR-derived metrics to refine risk stratification and treatment.

REFERENCES

1. Hahn RT. Tricuspid regurgitation. *N Engl J Med*. 2023;388:1876–1891. https://doi.org/10.1056/NEJMra2216709

2. Alqahtani F, Berzingi CO, Aljohani S, Hijazi M, Al-Hallak A, Alkhouli M. Contemporary trends in the use and outcomes of surgical treatment of tricuspid regurgitation. *J Am Heart Assoc*. 2017;6:e007597. https://doi.org/10.1161/JAHA.117.007597

3. Otto CM, Nishimura RA, Bonow RO, et al. 2020 ACC/AHA guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Joint Committee on clinical practice guidelines. *J Am Coll Cardiol*. 2021;77:e25–e197.

4. Alkhouli M, Lopez JJ, Mathew V. Transcatheter therapy for severe tricuspid regurgitation: learning to understand the forgotten valve. *J Am Coll Cardiol*. 2019;74:3009–3012. https://doi.org/10.1016/j.jacc.2019.09.029

5. Grapsa J, Praz F, Sorajja P, et al. Tricuspid regurgitation: from imaging to clinical trials to resolving the unmet need for treatment. *JACC Cardiovasc Imaging*. 2024;17:79–95. https://doi.org/10.1016/j.jcmg.2023.08.013

6. Kawsara A, Alqahtani F, Nkomo VT, et al. Determinants of morbidity and mortality associated with isolated tricuspid valve surgery. *J Am Heart Assoc*. 2021;10:e018417. https://doi.org/10.1161/JAHA.120.018417

7. Lara-Breitinger KM, Scott CG, Nkomo VT, et al. Tricuspid regurgitation impact on outcomes (TRIO): a simple clinical risk score. *Mayo Clin Proc*. 2022;97:1449–1461. https://doi.org/10.1016/j.mayocp.2022.05.015

8. Welle GA, Hahn RT, Lindenfeld J, et al. New approaches to assessment and management of tricuspid regurgitation before intervention. *JACC Cardiovasc Interv*. 2024;17:837–858. https://doi.org/10.1016/j.jcin.2024.02.034

9. Hahn RT, Badano LP, Bartko PE, et al. Tricuspid regurgitation: recent advances in understanding pathophysiology, severity grading and outcome. *Eur Heart J Cardiovasc Imaging*. 2022;23:913–929. https://doi.org/10.1093/ehjci/jeac009

10. Hahn RT, Weckbach LT, Noack T, et al. Proposal for a standard echocardiographic tricuspid valve nomenclature. *JACC Cardiovasc Imaging*. 2021;14:1299–1305. https://doi.org/10.1016/j.jcmg.2021.01.012

11. Weckbach LT, Orban M, Kitamura M, et al. Tricuspid valve morphology and outcome in patients undergoing transcatheter tricuspid valve edge-to-edge repair. *JACC Cardiovasc Interv*. 2022;15:567–569. https://doi.org/10.1016/j.jcin.2021.12.028

12. Maffessanti F, Gripari P, Pontone G, et al. Three-dimensional dynamic assessment of tricuspid and mitral annuli using cardiovascular magnetic resonance. *Eur Heart J Cardiovasc Imaging*. 2013;14:986–995. https://doi.org/10.1093/ehjci/jet004

13. Park JB, Kim HK, Jung JH, et al. Prognostic value of cardiac MR imaging for preoperative assessment of patients with severe functional tricuspid regurgitation. *Radiology*. 2016;280:723–734. https://doi.org/10.1148/radiol.2016151556

14. Hinojar R, Gomez AG, Garcia-Martin A, et al. Impact of right ventricular systolic function in patients with significant tricuspid regurgitation. A cardiac magnetic resonance study. *Int J Cardiol*. 2021;339:120–127. https://doi.org/10.1016/j.ijcard.2021.07.023

15. Ahn Y, Koo HJ, Kang JW, et al. Prognostic implication of right ventricle parameters measured on preoperative cardiac MRI in patients with functional tricuspid regurgitation. *Korean J Radiol*. 2021;22:1253–1265. https://doi.org/10.3348/kjr.2020.1084

16. Driessen MMP, Schings MA, Sieswerda GT, et al. Tricuspid flow and regurgitation in congenital heart disease and pulmonary hypertension: comparison of 4D flow cardiovascular magnetic resonance and echocardiography. *J Cardiovasc Magn Reson*. 2018;20:5. https://doi.org/10.1186/s12968-017-0426-7

17. Feneis JF, Kyubwa E, Atianzar K, et al. 4D flow MRI quantification of mitral and tricuspid regurgitation: reproducibility and consistency relative to conventional MRI. *J Magn Reson Imaging*. 2018;48:1147–1158. https://doi.org/10.1002/jmri.26040

18. Zhan Y, Senapati A, Vejpongsa P, Xu J, Shah DJ, Nagueh SF. Comparison of echocardiographic assessment of tricuspid regurgitation against cardiovascular magnetic resonance. *JACC Cardiovasc Imaging*. 2020;13:1461–1471. https://doi.org/10.1016/j.jcmg.2020.01.008

19. Medvedofsky D, Leon Jimenez J, Addetia K, et al. Multi-parametric quantification of tricuspid regurgitation using cardiovascular magnetic resonance: a comparison to echocardiography. *Eur J Radiol*. 2017;86:213–220. https://doi.org/10.1016/j.ejrad.2016.11.025

20. Spiewak M, Klopotowski M, Kowalik E, et al. Comparison of mitral regurgitation severity assessments based on magnetic resonance imaging and echocardiography in patients with hypertrophic cardiomyopathy. *Sci Rep*. 2021;11:19902. https://doi.org/10.1038/s41598-021-99446-y

21. Krieger EV, Lee J, Branch KR, Hamilton-Craig C. Quantitation of mitral regurgitation with cardiac magnetic resonance imaging: a systematic review. *Heart*. 2016;102:1864–1870. https://doi.org/10.1136/heartjnl-2015-309054

22. Uretsky S, Gillam L, Lang R, et al. Discordance between echocardiography and MRI in the assessment of mitral regurgitation severity. *J Am Coll Cardiol*. 2015;65:1078–1088. https://doi.org/10.1016/j.jacc.2014.12.047

23. Lopez-Mattei JC, Ibrahim H, Shaikh KA, et al. Comparative assessment of mitral regurgitation severity by transthoracic echocardiography and cardiac magnetic resonance using an integrative and quantitative approach. *Am J Cardiol*. 2016;117:264–270. https://doi.org/10.1016/j.amjcard.2015.10.045

24. Penicka M, Vecera J, Mirica DC, Kotrc M, Kockova R, Van Camp G. Prognostic implications of magnetic resonance–derived quantification in asymptomatic patients with organic mitral regurgitation: comparison with Doppler echocardiography-derived integrative approach. *Circulation*. 2018;137:1349–1360.

25. Zhan Y, Debs D, Khan MA, et al. Natural history of functional tricuspid regurgitation quantified by cardiovascular magnetic resonance. *J Am Coll Cardiol*. 2020;76:1291–1301. https://doi.org/10.1016/j.jacc.2020.07.036

26. Zoghbi WA, Adams D, Bonow RO, et al. Recommendations for noninvasive evaluation of native valvular regurgitation: a report from the American Society of Echocardiography developed in collaboration with the Society for Cardiovascular Magnetic Resonance. *J Am Soc Echocardiogr*. 2017;30:303–371. https://doi.org/10.1016/j.echo.2017.01.007

27. Topilsky Y, Bae R, Nkomo V, Gavazzoni M. An integrative, multiparametric approach to tricuspid regurgitation evaluation: a case-based illustration. *JACC Case Rep*. 2023;25:102050. https://doi.org/10.1016/j.jaccas.2023.102050

28. Wang TKM, Reyaldeen R, Akyuz K, et al. Echocardiography versus magnetic resonance imaging quantification and novel algorithm for isolated severe tricuspid regurgitation. *Am J Cardiol*. 2023;211:40–48. https://doi.org/10.1016/j.amjcard.2023.10.062

29. Renella P, Aboulhosn J, Lohan DG, et al. Two-dimensional and Doppler echocardiography reliably predict severe pulmonary regurgitation as quantified by cardiac magnetic resonance. *J Am Soc Echocardiogr*. 2010;23:880–886. https://doi.org/10.1016/j.echo.2010.05.019

30. Hahn RT. State-of-the-Art Review of echocardiographic imaging in the evaluation and treatment of functional tricuspid regurgitation. *Circ Cardiovasc Imaging*. 2016;9:e005332. https://doi.org/10.1161/CIRCIMAGING.116.005332

31. Wang TKM, Unai S, Xu B. Contemporary review in the multi-modality imaging evaluation and management of tricuspid regurgitation. *Cardiovasc Diagn Ther*. 2021;11:804–817. https://doi.org/10.21037/cdt.2020.01.06

32. Seo J, Hong YJ, Batbayar U, et al. Prognostic value of functional tricuspid regurgitation quantified by cardiac magnetic resonance in heart failure. *Eur Heart J Cardiovasc Imaging*. 2023;24:742–750. https://doi.org/10.1093/ehjci/jeac224

33. Correction to: 2020 ACC/AHA guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Joint Committee on clinical practice guidelines. *Circulation*. 2023;148:e8. https://doi.org/10.1161/CIR.0000000000001177

34. Gavazzoni M, Heilbron F, Badano LP, et al. Corrigendum: the atrial secondary tricuspid regurgitation is associated to more favorable outcome than the ventricular phenotype. *Front Cardiovasc Med*. 2023;10:1169907. https://doi.org/10.3389/fcvm.2023.1169907

35. Cain MT, Schafer M, Ross LK, et al. 4D-flow MRI intracardiac flow analysis considering different subtypes of pulmonary hypertension. *Pulm Circ*. 2023;13:e12307. https://doi.org/10.1002/pul2.12307

36. Barker N, Fidock B, Johns CS, et al. A systematic review of right ventricular diastolic assessment by 4D flow CMR. *Biomed Res Int*. 2019;2019:6074984. https://doi.org/10.1155/2019/6074984

37. Kodali S, Hahn RT, Makkar R, et al. Transfemoral tricuspid valve replacement and one-year outcomes: the TRISCEND study. *Eur Heart J*. 2023;44:4862–4873. https://doi.org/10.1093/eurheartj/ehad667

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