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Significance of strictly defined idiopathic tricuspid regurgitation

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Abstract

Background: Moderate to severe tricuspid regurgitation (TR) is known to cause right ventricular (RV) failure and death. Although TR is traditionally classified as primary or secondary, recently, a new class of TR called idiopathic TR has been proposed, with varying definitions among different studies.

Methods: The data were retrospectively collected for the period of January to June 2018 for 8711 patients from the patient cohort of the National Cheng Kung University Hospital echocardiography laboratory. A total of 670 patients (7.7%) with moderate-to-severe TR were included. Idiopathic TR was diagnosed strictly using a new systematic approach.

Results: The distribution of significant TR included 74 (11.0%) primary TR cases, 48 (7.2%) with pacemaker-related TR, 267 (39.9%) with left heart disease, 24 (3.6%) with congenital heart disease, 6 (0.9%) with RV myopathy, 105 (15.7%) with pulmonary hypertension, and 146 (21.8%) with idiopathic TR. The mean age in primary and idiopathic TR groups was older ($p = 0.004$), with lower estimated pulmonary pressure ($p < 0.001$), higher RV fraction area change (FAC, $p < 0.001$), and tricuspid annulus systolic velocity (S', $p = 0.004$) compared with functional TR group. Multivariate analysis showed that idiopathic TR ($p = 0.002$) and primary TR ($p = 0.008$) had better RV FAC than functional TR.

Conclusion: Idiopathic TR was associated with better RV function than the other secondary TRs. Thus, idiopathic TR should be strictly defined and regarded as a distinct type of TR.

Keywords: Echocardiography; Right ventricular function; Tricuspid regurgitation

1. INTRODUCTION

Compared with the aortic and mitral valves, the tricuspid valve (TV) is referred to as the forgotten valve,[1] with limited studies on tricuspid regurgitation (TR). In adults, TR is the most common TV dysfunction,[2] which results from incomplete coaptation of TV leaflets and flow regurgitation into the right atrium (RA) during systole.

TR has been traditionally classified as primary/organic and secondary/functional TR. Primary TR refers to a defect solely in the TV, such as prolapse, flail, perforation, Ebstein's anomaly, carcinoid syndrome, and rheumatic disease, and accounts for 10% of all TR cases in adults.[3] The majority of TRs are secondary, accounting for more than 80% of the cases, but the definition and classification are not uniform. Recently, a third category, idiopathic TR, has been proposed. However, its definition varies among studies.[4–6] Idiopathic TR is defined as the absence of any obvious cause of TR, the diagnosis of which requires that primary and secondary TRs be excluded first.[3,7]

Previous studies found that the functional TR operations did not achieve a therapeutic effect and the outcome was poor, including a high relapse rate.[2,8] It is believed that the poor outcome is due to inaccurate grading and classification of TR. That is, it is critical to individualize the treatments for TR, based on the pathophysiology.

At present, there are different opinions regarding the classification of idiopathic TR. We believe that idiopathic TR requires independent analysis as it cannot be confused with secondary TR. Therefore, the purpose of this study was to strictly define idiopathic TR from echocardiographic images based on a new systematic approach, and to study the characteristics of the disease, as identified by this approach.

2. METHODS

2.1. Study population

A total of 8711 adult patients referred for clinically indicated echocardiography at the National Cheng Kung University Hospital from January 2018 to June 2018, were recruited in a retrospective study setting. We collected all patients who underwent echocardiography during this period, without special screening of patients in a certain group. Significant TR was defined as TR severity equal to or greater than a moderate

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degree. Baseline demographic and echocardiographic variables were recorded, including age, sex, left ventricular ejection fraction (LVEF), concomitant left valvular heart disease (VHD), right ventricle (RV) and RA size, RV systolic function, and other relevant parameters, as well as atrial fibrillation (AF). The study was approved by our research ethics committee (B-ER-408-450).

2.2. Grading of TR severity

According to the recommended guidelines, assessment of TR severity by color flow Doppler includes a critical assessment of the jet area, vena contracta (VC), and flow convergence.[9] In our study, VC color flow Doppler was used to evaluate TR grading. Images were acquired from the apical four-chamber, parasternal short-axis, and RV inflow views. The VC width considered for mild TR, moderate TR, and severe TR are < 0.3 cm, 0.3–0.69 cm, and > 0.7 cm, respectively. In severe TR, with a large flow convergence, color flow jet area >10 cm^2, proximal iso-velocity surface area radius >0.9 cm, and effective regurgitation orifice area ≧40 mm^2. Severe TR is often accompanied by systolic flow reversal in the hepatic vein.[3,9,10]

2.3. Grouping of significant TR

All echocardiographic images of subjects with significant TR were reviewed carefully by two cardiologists to divide into subgroups according to our new systematic approach. In case of inconsistent results, a third cardiologist determined the final classification. The new systematic approach (Fig. 1) was developed, based on a classification from another study,[11] dividing significant TR into seven groups including (1) primary TR (any leaflet pathology, that is, prolapse, flail, perforation, or displacement); (2) pacemaker or other instruments (biopsy)-related TR; TR related to (3) left heart disease such as significant VHD, previous VHD operation on the left side, and LV dysfunction (LVEF <50%), (4) congenital heart disease such as atrial septal defects, ventricular septal defects, and/or after intervention or operation, (5) RV cardiomyopathy (dilated RV, RV hypertrophy, or systolic abnormalities), and (6) Pulmonary hypertension (PH) without other structural heart disease, such as pulmonary artery systolic pressure (PAP) ≥50 mmHg, or other evidence of RV pressure overload when the estimated PAP is 35 to 50 mmHg, or history of PH under treatment; and (7) idiopathic TR. The grouping process consisted of a step-by-step approach as illustrated in Fig. 1.

2.4. Echocardiography measurements

Echocardiographic examinations were performed using a GE and Philips ultrasound system (Vivid7and E9, GE-Vingmed, Horten, Norway; iE33 xMATRIX, Philips, Bothell, USA). A 3.5 MHz transducer was used for conventional 2D echocardiography.

Left heart parameters, including systolic and diastolic function[5,12] and right heart parameters, were measured using standard methods according to current guidelines.[13] RV was measured from the apical four-chamber view. In this study, fractional area change (FAC) and Tissue Doppler Imaging (TDI) of the lateral TA were used to measure RV systolic function. FAC is calculated as the ratio of the difference between RV end-diastolic and end-systolic areas to RV end-diastolic area by tracking the RV endocardial border beneath the trabeculations. RV dysfunction is indicated by an FAC of less than 35 %.[5,13,14] TDI, which measures the velocity of the myocardium during the cardiac cycle, has been used to assess systolic and diastolic function.[15] TDI is used to record the longitudinal motion velocity of the lateral and medial mitral annulus, as well as the lateral TA in the apical four-chamber view.[16] The TDI lateral TA systolic velocity (RV S') was used as another index of RV systolic function. When RV S' is less than 10 cm/s, the possibility of abnormal RV function is raised.[13]

2.5. Statistical analysis

Continuous and categorical variables were expressed as mean ± standard deviation (SD) and number (%), respectively. The χ^2 test was used for categorical variables and the independent *t*-test for continuous variables. By using one-way analysis of variance, it is possible to compare quantitative data between more than two independent groups regarding the distribution of parameters. The confidence interval was set to 95%. Logistic regression analyses were used to study the risk factors of TR. Ordinal logistic regression was used to calculate odds ratios (ORs) for clinically relevant explanatory variables between TR groups. To test for inter- and intra-observer variability in RV FAC measures, 20 studies were randomly selected. The analysis was repeated by an observer at two different time points, with the first analysis performed by another observer. For intra- and inter-observer variability, Bland-Altman analysis was used. Statistical significance was evaluated at $p < 0.05$. All statistical analyses were performed using SPSS version 22.0, for Windows (SPSS, Inc., Chicago, IL, USA).

3. RESULTS

3.1. Comparison between significant and non-significant TR

The study population (8711 subjects) consisted of 670 patients (7.7%) with significant TR, including 473 (70.6%) with moderate TR and 197 (29.4%) with severe TR. The other 8041 patients, without significant TR, were recruited as the comparative group. The mean age was significantly higher in the significant TR group than in the nonsignificant TR group, and there was a higher prevalence of significant TR among female patients. Patients with significant TR demonstrated more impaired LV systolic function and diastolic function (E/e', 13.4 ± 6.9 vs. 10.1 ± 4.6, $p <$ 0.001). The group with significant TR (45.9%) also had a higher proportion of left VHD compared to the nonsignificant group (10.6%) (Table 1). Among 670 patients with significant TR, 105 (15.7%) patients received cardiovascular surgery including 54 (51.4%) valvular surgery, 19 (18.1%) coronary bypass surgery, 7 (6.7%) both, and 25 (23.8%) other surgery. There were 140 (20.9%) patients who had angiographic documented coronary artery disease, including 64 (45.7%) patients who received the percutaneous intervention, 21 (15%) coronary bypass surgery, 5 (3.6%) both, and 50 (35.7%) medical therapy.

3.2. Distribution of significant TR by type and subtypes

The distribution of significant TR included 74 (11.0%) primary TR and 596 (89.0%) secondary TR cases. In the primary TR group, 27 (36.5%) patients had TV flail; 45 (60.8%) had TV prolapse; 1 (1.4%) had TV annuloplasty; and 1 (1.4%) had TV infective endocarditis. Our study did not have patients with Ebstein's anomaly in this period. In secondary TR, 48 (7.2%) patients had pacemaker-related TR; 267 (39.9%) had left heart disease; 24 (3.6%) had congenital heart disease; 6 (0.9%) had RV myopathy; 105 (15.7%) had PH; and 146 (21.8%) had idiopathic TR. Idiopathic TR is the new category of TR as opposed to primary and functional TR (the remaining five secondary TRs). After regrouping into three groups, there were 11.0% primary, 67.2% functional, and 21.8% idiopathic TR cases.

3.3. Comparison between three groups

Most of the echocardiographic parameters were worse in the functional TR group (Table 2). The results showed that the mean age in the primary and idiopathic TR groups was higher, with better diastolic function and LVEF, lower TR velocity, lower estimated PAP and right atrial pressure, thinner RV wall, lower RV end-diastolic area (RVED area), and smaller RA area, higher RV

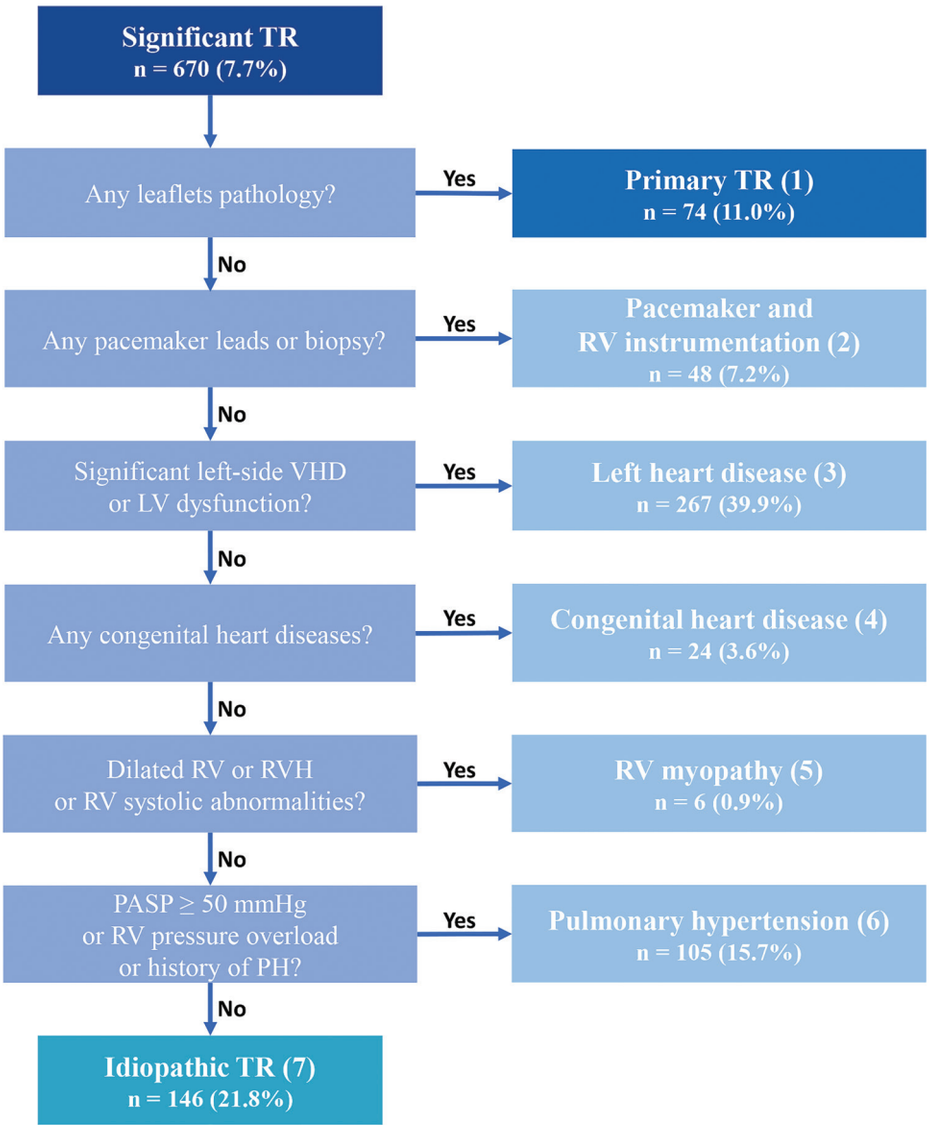

Fig. 1 The figure shows the new systematic approach of classifying significant TR into 7 groups based on etiology. TR = tricuspid regurgitation.

Table 1

Comparison between significant TR and non-significant TR

Variable	Significant TR (n = 670)	Non-significant TR (n = 8041)	*p*
Age (years)	71.0 ± 15.3	63.6 ± 16.7	<0.001*
Male (n,%)	269 (40.1)	4090 (50.8)	<0.001*
LV dysfunction (n,%)	144 (21.5)	745 (9.3)	<0.001*
E/e'	13.4 ± 6.9	10.1 ± 4.6	<0.001*
Left VHD (n,%)	308 (45.9)	859 (10.6)	<0.001*
Significant MR (n,%)	235 (35.0)	390 (4.8)	<0.001*
Significant AR (n,%)	97 (14.4)	372 (4.6)	<0.001*
Significant MS (n,%)	20 (2.9)	27 (0.3)	<0.001*
Significant AS (n,%)	47 (7.0)	170 (2.1)	<0.001*

Data are expressed as mean ± standard deviation or number (%).
AR = aortic regurgitation; AS = aortic stenosis; LV dysfunction = left ventricular ejection fraction <50%; MR = mitral regurgitation; MS = mitral stenosis; VHD = valvular heart disease.
*$p < 0.01$.

Table 2

Comparison between three groups

Variable	Primary TR (n = 74)	Functional TR (n = 450)	Idiopathic TR (n = 146)	*p*
Age (years)	71.2 ± 17.6	69.8 ± 15.5	74.6 ± 12.7	0.004**
Male (n,%)	23 (31.0)	188 (41.7)	58 (39.7)	0.219
HT (n,%)	30 (40.5)	213 (43.7)	84 (57.5)	0.032*
DM (n,%)	15 (20.3)	126 (28.0)	29 (20.0)	0.082
Surgery (n,%)	9 (12.2)	94 (20.9)	2 (1.4)	<0.001**
CAD (n,%)	7 (9.5)	105 (23.3)	28 (19.2)	0.015*
LVEF (%)	68.1 ± 9.6	60.0 ± 15.4	69.8 ± 8.3	<0.001**
E/e'	10.4 ± 4.8	14.8 ± 7.5	10.9 ± 3.7	<0.001**
CLD (n,%)	8 (11)	65 (14)	18/146 (12)	0.617
PE (n,%)	0 (0)	10 (2)	1 (0.7)	0.223
% of moderate TR (n,%)	37 (50)	306 (68)	130 (89)	<0.001**
TR VC (mm)	7.1 ± 3.6	6.9 ± 3.9	5.8 ± 4.0	0.007**
TR V_{max} (m/s)	3.2 ± 0.5	3.5 ± 0.8	3.0 ± 0.3	<0.001**
TV annulus D (cm)	3.24 ± 0.75	3.52 ± 0.79	3.01 ± 0.70	<0.001**
RVs' (m/s)	13.1 ± 4.1	11.3 ± 5.1	12.1 ± 3.2	0.004**
RVFAC (%)	46.7 ± 14.5	37.9 ± 16.2	47.7 ± 13.2	<0.001**
RAP (mmHg)	6.0 ± 4.2	7.7 ± 4.6	4.8 ± 3.1	<0.001**
PAP (mmHg)	47.9 ± 14.3	60.9 ± 24.9	40.7 ± 8.6	<0.001**
% of PH (PAP >35 mmHg)	64 (86)	408 (91)	103 (71)	<0.001**
RV wall (mm)	4.6 ± 1.3	5.1 ± 1.8	4.5 ± 1.3	<0.001**
RVED area (cm^2)	15.6 ± 6.5	18.3 ± 7.3	13.5 ± 4.5	<0.001**
RAA (cm^2)	20.2 ± 9.8	21.6 ± 10.0	17.3 ± 7.3	<0.001**
AF (n,%)	25 (33.7)	206 (45.7)	56 (38.3)	0.072

Data are expressed as mean ± standard deviation or number (%).

AF = atrial fibrillation; CAD = coronary artery disease; CLD = chronic lung disease (asthma, chronic obstructive pulmonary disease, bronchiectasis); DM = diabetes mellitus; HT = hypertension; LVEF = left ventricular ejection fraction; PE = pulmonary embolism; PH = pulmonary hypertension; PAP = pulmonary artery systolic pressure; RAA = right atrial area; RAP = right atrial pressure; RVED area = right ventricular end-diastolic area; RVFAC = right ventricular fractional area change; Surgery = cardiovascular surgery; TR VC = tricuspid regurgitation vena contracta; TR V_{max} = tricuspid regurgitation maximal velocity; TV annulus D = tricuspid valve annulus diameter.

*$p < 0.05$.

**$p < 0.01$.

FAC and tricuspid annulus S', compared with the functional TR group. Rates of hypertension, diabetes mellitus, cardiac surgery, and coronary artery disease were inevitably higher in the functional TR group (Table 2). The rate of hypertension was highest in the idiopathic TR group possibly due to older age. The percentage of moderate TR in the idiopathic TR group was higher, and the value of TR VC and TV annulus diameter was lower in the idiopathic TR group. The above results showed that idiopathic TR was different from other secondary TRs.

3.4. Independent determinants of RV function

After controlling for age, TR severity, maximal velocity of TR, RVED area, RA area, type of TR, and presence of AF, RV FAC was significantly lower in functional TR (ß, –0.109; 95% CI, –8.764 to –1.303; $p = 0.008$) than in primary TR. This result was also found for RV S' (ß, –0.101; 95% CI, –2.711 to –0.183; $p = 0.025$) (Table 3). RV FAC was significantly better in idiopathic TR (ß, 0.123; 95% CI, 1.658-7.393; $p = 0.002$) than in functional TR. However, RV S' did not show this difference (ß, 0.029; 95% CI, –0.639 to 1.279; $p = 0.513$) (Table 3). Between primary and idiopathic TR, RV FAC (ß, 0.029; 95% CI, –1.597 to 2.377; $p = 0.699$) and RV S' (ß, –0.041; 95% CI, –0.697 to 0.394; $p = 0.585$) showed no significant differences (Table 3). RV FAC was poorer in functional TR, and the results were similar between primary and idiopathic TR.

Furthermore, FAC <35% was used as an indicator of RV systolic dysfunction. Functional TR had the highest rate of RV dysfunction, followed by primary TR and idiopathic TR (43.3 vs. 20.3 vs. 9.7 %; $p < 0.001$) (Fig. 2). After controlling for age, TR maximal regurgitation velocity, severity of TR, and presence of AF in multivariate analysis, functional TR had significantly more RV dysfunction than idiopathic TR (OR, 4.399; 95% CI, 2.385-8.114; $p < 0.001$) but not primary TR (OR, 1.882; 95% CI, 0.822-4.307; $p = 0.135$).

3.5. Reproducibility

For FAC, the absolute difference ratios for three repeated measurements for two different observers were –0.004 ± 10.25 (inter-observer variability) and 0.91 ± 8.56 (intra-observer variability), respectively. The intraclass correlation coefficients of the inter-observer and intra-observer reliability were 0.79 (95% CI, 0.53-0.91) and 0.84 (95% CI, 0.64-0.93) for FAC, respectively, showing excellent agreement.

4. DISCUSSION

This is the first report on the prevalence and distribution of TR phenotypes in Taiwan. The major findings of the study are as follows: (1) the prevalence of significant TR was 7.7 %; (2) idiopathic TR, which was defined strictly by our systematic approach, constituted 21.8% of significant TR in this study; and (3) idiopathic TR had better RV function than secondary TR.

4.1. Importance of strictly defined idiopathic TR

The distribution and classification of TR phenotypes in the current study differed from those in previous studies. Yang et al[11] investigated the prevalence and outcomes of moderate to severe TR in the Chinese population. The distribution of moderate to severe TR was 6.1% for primary TR, 92.7% for functional TR, and 1.2% for idiopathic TR. In contrast to our study, the

Table 3

Multivariate analysis for independent variables RV FAC and RV S', between primary, functional, and idiopathic TR groups

Variable	RV FAC Beta (95% CI)	*p*	RV S' Beta (95% CI)	*p*
Multivariate analysis for the RV FAC and RV S' between primary and functional TR				
Age (years)	0.153 (0.069 to 0.244)	<0.001**	0.130 (0.012 to 0.071)	0.007**
AF (%)	−0.144 (−7.670 to −1.662)	0.002**	−0.138 (−2.406 to −0.370)	0.008**
TR severity	0.011 (−2.540 to 3.285)	0.802	0.009 (−0.895 to 1.079)	0.855
TR V_{max} (m/s)	−0.129 (−0.045 to −0.010)	0.003**	−0.025 (−0.008 to 0.004)	0.599
RVED area (cm^2)	−0.254 (−0.793 to −0.346)	<0.001**	−0.002 (−0.077 to 0.074)	0.972
RAA (cm^2)	−0.061 (−0.268 to 0.070)	0.248	−0.021 (−0.068 to 0.047)	0.717
Type of TR	−0.109 (−8.764 to −1.303)	0.008**	−0.101 (−2.711 to −0.183)	0.025*
Multivariate analysis for the RV FAC and RV S' between functional and idiopathic TR				
Age (years)	0.170 (0.098 to 0.261)	<0.001**	0.108 (0.006 to 0.061)	0.016*
AF (%)	−0.149 (−7.439 to −2.092)	<0.001**	−0.183 (−2.619 to −0.831)	<0.001**
TR severity	0.031 (−1.690 to 3.910)	0.437	−0.015 (−1.094 to 0.779)	0.741
TR V_{max} (m/s)	−0.118 (−0.041 to −0.008)	0.003**	−0.040 (−0.008 to 0.003)	0.375
RVED area (cm^2)	−0.278 (−0.848 to −0.428)	<0.001**	−0.016 (−0.081 to 0.059)	0.763
RAA (cm^2)	−0.051 (−0.241 to 0.073)	0.291	−0.009 (−0.057 to 0.048)	0.863
Type of TR	0.123 (1.658 to 7.393)	0.002**	0.029 (−0.639 to 1.279)	0.513
Multivariate analysis for RV FAC and RV S' between primary and idiopathic TR				
Age (years)	−0.017 (−0.137 to 0.107)	0.809	0.054 (−0.021 to 0.046)	0.455
AF (%)	−0.149 (−8.487 to 0.546)	0.085	−0.252 (−3.057 to −0.576)	0.004**
TR severity	−0.045 (−5.884 to 3.205)	0.562	0.080 (−0.599 to 1.897)	0.306
TR V_{max} (m/s)	0.013 (−0.040 to 0.049)	0.848	0.090 (−0.004 to 0.020)	0.207
RVED area (cm^2)	0.071 (−0.230 to 0.585)	0.392	0.161 (−0.003 to 0.221)	0.057
RAA (cm^2)	−0.259 (−0.714 to −0.089)	0.012*	−0.072 (−0.116 to 0.056)	0.493
Type of TR	0.029 (−1.597 to 2.377)	0.699	−0.041 (−0.697 to 0.394)	0.585

TR severity ranges from no, mild, moderate, and severe TR, and TR represents primary and functional TR. Data are expressed as mean ± standard deviation or number (%).
AF = atrial fibrillation; RAA = right atrial area; RVED area = right ventricular end-diastolic area; TR V_{max} = tricuspid regurgitation maximal velocity.
Regression,
*$p < 0.05$.
**$p < 0.01$.

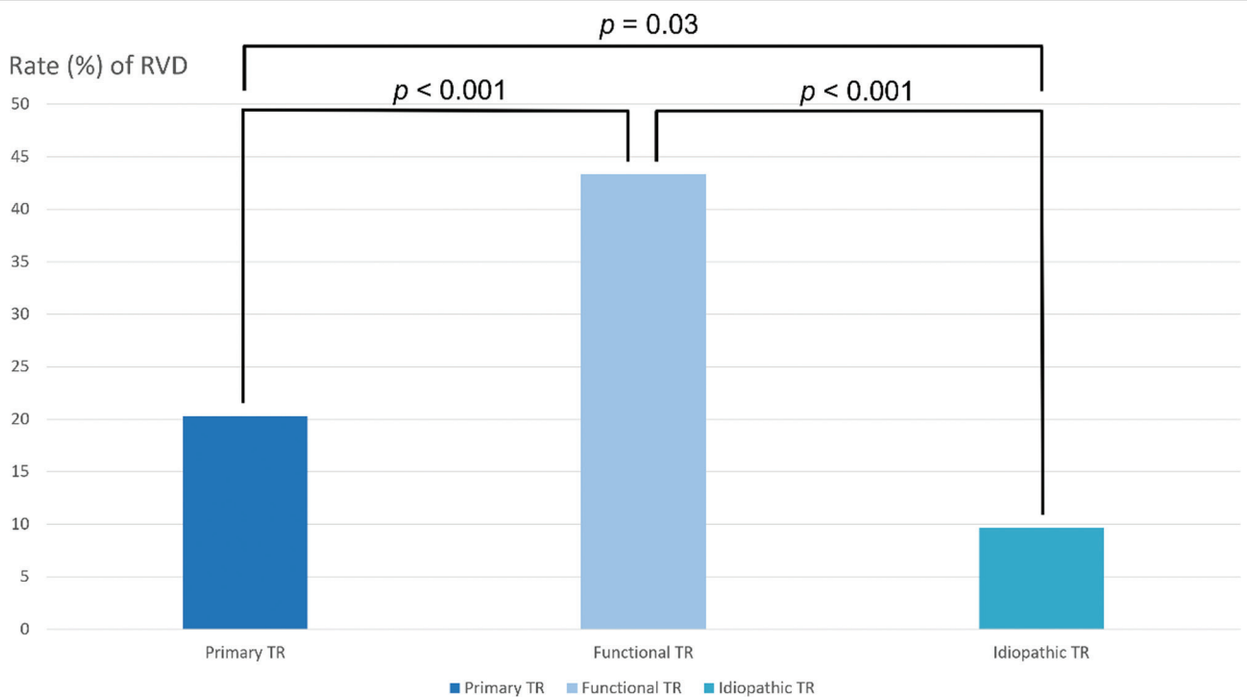

Fig. 2 This figure shows the difference in the rate of RV dysfunction between three groups. Functional TR had the highest rate of RV dysfunction (FAC <35%), followed by primary and idiopathic TR, with significant differences in the rate of RV dysfunction when comparing between groups versus when comparing all three groups together (20.3 vs. 43.3 vs. 9.7 %, $p < 0.001$). FAC = fraction area change; TR = tricuspid regurgitation; RV = right ventricular.

prevalence of idiopathic TR in their study was lower than that of our study, while similar to our study, left heart disease was the most common phenotype in secondary TR despite considering left-side VHD and dilated cardiomyopathy separately. Topilsky et al[6] collected 21 020 residents of Olmsted County, and found 1095 (5.21%) patients with moderate to severe TR, dividing them into six groups: congenital (1.7%), organic (4.8%), left valvular disease (49.5%), LV dysfunction (12.9%), PH related TR (23.0%), and isolated TR (8.1%). Although their classification is different from ours, left VHD-related and PH-related TR were higher in secondary TR as in our study. Despite the different classification categories, isolated (idiopathic TR) was only 8.1 %, which was much lower than that of our study. In Vieitez's study,[17] significant TR was present in 2121 of the 35088 (6.0%) patients with a mean age of 77.1 (SD = 11.6) years, and 62.9% of patients were female. Their patients were older, and the male-to-female ratio was different from our group. The distribution of significant TR (moderate TR, 69.6%; severe TR, 30.4%) was similar to that of our study. Although the classification method is slightly different from ours, isolated TR was the second most common etiology, with 16.0% of cases, similar to our research results. In another study, Bohbot et al[4] collected 208 patients with moderate to severe TR and classified the TR subgroups into primary (n = 31, 14.9%), left valvular surgery (n = 51, 24.5%), no left valvular surgery (n = 55, 26.5%), and idiopathic TR (n = 71, 34.1%). Nishimura et al[18] classified device lead-related TR as primary TR instead of secondary TR. However, according to the classification method adopted by Hahn et al,[19] the presence or absence of leaflet involvement was used to distinguish primary (leaflet pathology) or secondary (non-leaflet pathology) TR. Cardiac-implanted device-induced TR was classified as a unique category because it possibly covered both the primary (direct interaction of the lead on the valve leaflets) and the secondary (pacing-related remodeling) components. Besides, some studies restricted isolated TR only to TR associated with dilation of the tricuspid annulus due to dilation of the RA in the presence of AF.[20] In our study, the annulus diameter of the idiopathic TR group was smaller than that of the others. Therefore, it was still controversial if idiopathic TR was directly equivalent to atrial functional TR. Usually, the size of the annulus of atrial functional TR should be larger.

As could be seen from the above studies, not only was the classification of TR associated with device leads still controversial, but the distribution of idiopathic or isolated TR varies widely across studies. We believe the reason for this conflict was the lack of a uniform definition and standard diagnostic process for idiopathic TR. Our current study provided a systematic approach to significant TR classification, defining idiopathic TR strictly by excluding all other possible causes of secondary TR. This approach could help clarify the true characteristics and natural course of idiopathic TR.

4.2. Effects of TR types on RV function

According to our classification, functional TR (secondary TR excluding idiopathic TR) had worse RV function in the current study. Although the true reasons are not well understood, it was proposed that secondary TR resulted in prolonged pressure overload (shown by increased E/e'), and changes in LV geometry would contribute to this finding. Early intervention of underlying left heart disease or more aggressive treatment of co-existing TR associated with left heart disease would be beneficial to these patients.

Interestingly, our study showed less RV dysfunction in patients with idiopathic TR. In previous studies, idiopathic TR was often considered to have poor RV function, poor prognosis, and poor survival rates.[4] A previous study[4] found that patients with idiopathic TR had a high risk of mortality (Hazzard ratio, 1.83; 95% CI, 1.05-3.21; $p = 0.034$), which was associated with poor outcome and lower survival rate compared to other phenotypes of TR. The poorer RV function in previous studies, may possibly be due to the inclusion of other types of secondary TR, unlike we excluded other possible causes of secondary TR and strictly defined idiopathic TR. Therefore, idiopathic TR should be treated as a distinct category of TR, which is strictly defined in the current study.

The contribution of the study was to strictly define idiopathic TR from echocardiographic images based on a new systematic approach, and to study the characteristics of idiopathic TR, whereby different results were obtained. In previous studies, idiopathic TR was often considered to have a poor prognosis and poor survival rate. After regrouping using our step-by-step approach, idiopathic TR was found to be superior to other groups of secondary TR in terms of RV geometry, the hemodynamics of TR, and RV systolic function. It is proposed that leaflet lesions not revealed by traditional echocardiography may be included in our idiopathic TR group. Other imaging modalities and 3D echocardiography are helpful for a better definition of leaflet lesions.

The limitations of the study are as follows: First, because the study was retrospective, the focus was not specifically on the RV focus view. Second, because the number of patients with subtypes was low in this study, differences between subtypes was not analyzed in functional TR. Third, RV strain was not used in the evaluation of RV function. Because this study was retrospective, with multiple vendors, speckle tracking could not be performed in all cases. Fourth, no prognostic data were included in the current study, and further follow-up is warranted for these subjects for cardiovascular events.

In conclusion, the results of our study showed that there were 21.8% of strictly defined idiopathic TR among significant TR. In contrast to previous studies, idiopathic TR displayed better RV function than secondary TR. Idiopathic TR should be strictly defined and regarded as a distinct type of TR.

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