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ORIGINAL ARTICLE

Prognostic value of right atrial function in patients with significant tricuspid regurgitation

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Abstract

Aims Although right ventricular (RV) dysfunction is associated with adverse outcomes in tricuspid regurgitation (TR), the potential role of right atrial (RA) function is unknown. We aimed to investigate the relationship between RA function and clinical outcomes in patients with significant TR.

Methods This retrospective study included 169 outpatients with moderate or severe TR due to left-sided heart diseases who underwent transthoracic echocardiography between June 2020 and April 2023 (average age, 75 ± 10 years; male, 40%). Patients with atrial fibrillation were excluded from this study due to the inaccuracy of the evaluation using 2D speckle-tracking echocardiography. RA function was compared between patients with and without events, which were defined as all-cause mortality or hospitalization due to heart failure. RA function was calculated as RA global longitudinal strain (RAGLS) with the 2D speckle-tracking echocardiography.

Results During a median follow-up of 13 months, 19 patients had events (all-cause mortality: 14 cases, hospitalization due to heart failure: 5 cases). RAGLS was lower in patients with events than in those without events (13% ± 10% vs. 18% ± 9%, $P = 0.02$). When the patients were categorized into two groups [low RAGLS $\leq$ 16.2% vs. high RAGLS $>$ 16.2%, high RA volume index (RAVI) $\geq$ 50 mL/m^2 vs. low RAVI $<$ 50 mL/m^2], Kaplan–Meier curves showed that patients with low RAGLS had higher event rates than those with high RAGLS (log-rank test, $P = 0.003$). Patients with high RAVI had higher event rates than those with low RAVI (log-rank test, $P < 0.001$). In the multivariate Cox regression analysis, low RAGLS (≤16.2%) was significantly associated with events in a model that included RV dysfunction (RV fractional area change $\leq$ 35%) or high RAVI (≥50 mL/m^2) (hazard ratio: 4.55, 95% confidence interval: 1.51–13.71, $P < 0.01$; hazard ratio: 4.57, 95% confidence interval: 1.52–13.79, $P < 0.01$, respectively).

Conclusions RAGLS is associated with all-cause mortality and hospitalization due to heart failure in patients with significant TR. Our results suggest that RA function is a sensitive marker for identifying the risk stratification of significant TR.

Keywords echocardiography; prognosis; right atrial function; tricuspid regurgitation

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Introduction

Tricuspid regurgitation (TR) is a common disease in clinical practice. TR usually occurs as a result of annular dilation and leaflet tethering caused by right ventricular (RV) remodelling due to volume overload related to left-sided heart diseases.[1,2] Significant TR is associated with impaired survival and worsening heart failure (HF).[3–5] Adverse outcomes in TR have been reported to be affected by RV performance.[6,7]

The volume overload caused by regurgitation also induces right atrial (RA) remodelling. RA dilatation and dysfunction lead to worsening regurgitation, which progresses with right-sided HF. RA performance is often impaired in patients with TR. The evaluation of RA function may be important for determining clinical outcomes in significant TR. However, the potential role of RA function is unknown. Recently, 2D speckle-tracking echocardiography (2D-STE) has been used to assess RA function. This method non-invasively and auto-

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matically tracks specified myocardial speckles to evaluate myocardial motion. Therefore, we hypothesized that the RA function calculated by the 2D-STE is useful for predicting adverse outcomes. This study investigated whether RA function is associated with clinical outcomes in patients with significant TR.

Methods

Study population and design

This retrospective, single-centre observational study was conducted at Okayama University Hospital, Japan. *Figure* 1 shows a flow diagram of the study design. The inclusion criterion was the presence of moderate or severe TR due to left-sided heart diseases among patients who underwent transthoracic echocardiography between June 2020 and April 2023. We excluded the following: (A) a history of adult congenital heart disease, pulmonary arterial hypertension or pacemaker implantation; (B) atrial fibrillation; and (C) insufficient tracking of RA walls due to poor echocardiographic image quality. Finally, 169 patients were included in this study. All these patients had clinical symptoms or signs of HF, according to the 2016 European Society of Cardiology guidelines.[8] Details of clinical characteristics, comorbidities, drug therapy, laboratory values and echocardiographic findings were collected from a review of medical records. Among blood test measurements, haemoglobin, albumin, serum creatinine and plasma B-type natriuretic peptide levels were obtained.

This study was conducted following the principles of the Declaration of Helsinki and reviewed and approved by the ethics committee of the Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences (2309-027). Furthermore, the requirement for informed patient consent was waived because of the low-risk nature of the study and the inability to obtain consent directly from all patients.

Echocardiographic examination

Transthoracic echocardiography was performed using commercially available equipment (Vivid E95; GE Healthcare, Milwaukee, WI, USA; and Aplio i900; Canon Medical Systems, Otawara, Japan). The images were acquired with a breath hold and recorded for three consecutive heart cycles. Echocardiographic measurements were performed according to the guidelines.[9] Left ventricular (LV) end-diastolic volume, LV end-systolic volume, LV ejection fraction, LV stroke volume and left atrial (LA) volume index were calculated. The tissue Doppler-derived early diastolic mitral annular velocity was measured at the septal and lateral wall sites. The ratio of early diastolic transmitral inflow velocity to early diastolic mitral annular velocity was calculated. The severity of mitral regurgitation or TR was evaluated by a qualitative assessment using colour Doppler flow imaging. The TR pressure gradient was measured from the peak velocity. RV end-diastolic area, RV end-systolic area and RV fractional area change were measured from an RV-focused apical four-chamber view. RV basal diameter was measured in the basal third of the right ventricle, parallel to the tricuspid annulus at end-diastole.

RA parameters

RA function and volume analyses were performed using vendor-independent software (TOMTEC Imaging System, Unterschleissheim, Germany) (*Figure* 2). All echocardio-

Figure 1 Study flow diagram. RA, right atrial; TR, tricuspid regurgitation.

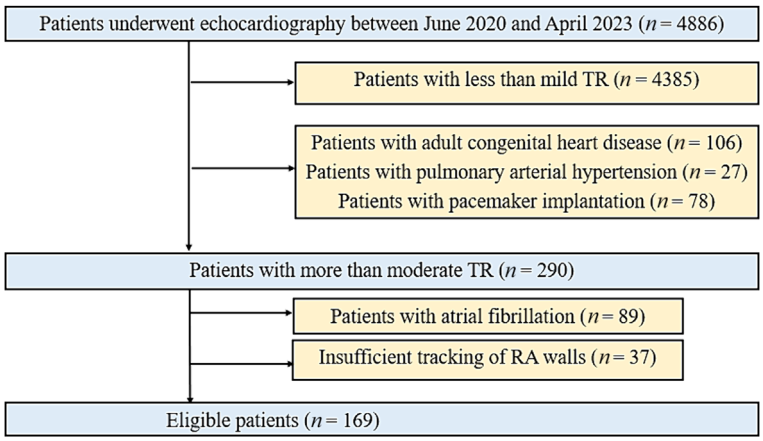

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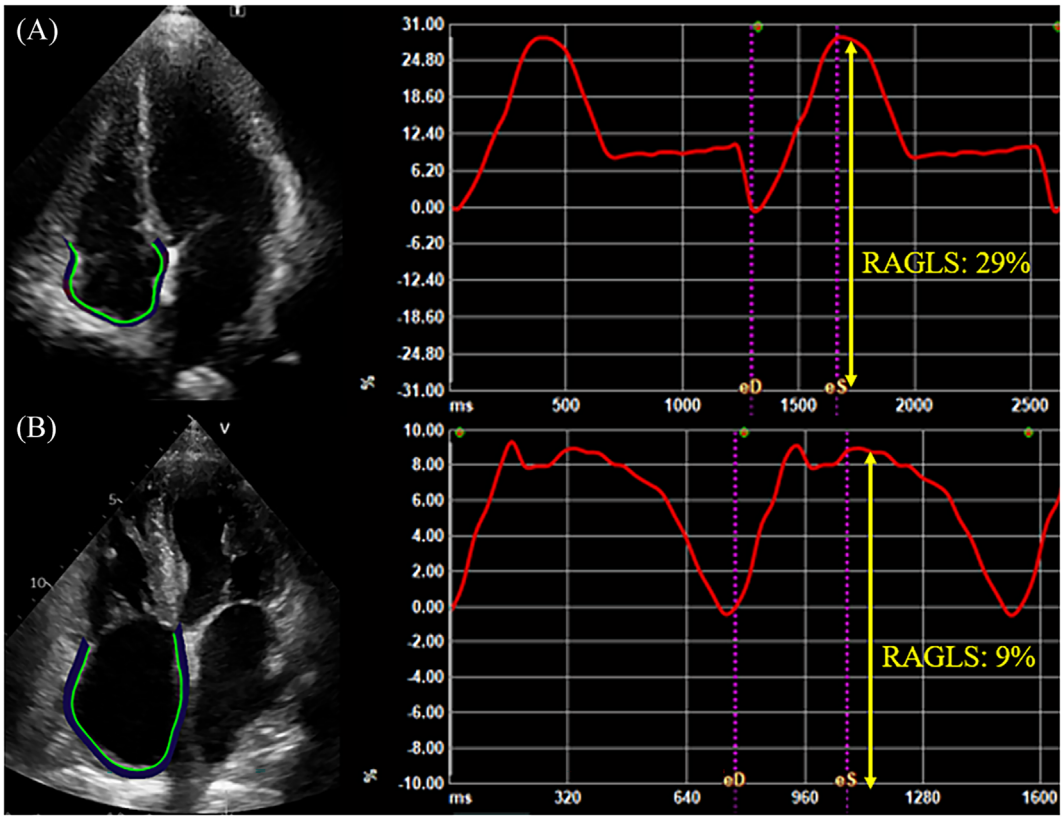
Figure 2 Representative case of right atrial function measured as right atrial global longitudinal strain (RAGLS) in a patient with tricuspid regurgitation. (A) A case with a high value of RAGLS (29%). (B) A case with a low value of RAGLS (9%).



graphic images were sent in DICOM format to the core laboratory. The 2D-STE analyses were performed offline from apical four-chamber view images. Three reference points were placed at the tricuspid annulus and the roof of the right atrium. The software automatically determined the RA endocardial border and performed speckle-tracking analysis through one complete cardiac cycle. When an inaccurate RA endocardial border was detected, manual adjustment was performed to ensure optimal tracking. The 2D-STE provided the values of the average RA global longitudinal strain (RAGLS), RA volume, RA fractional area change and RA ejection fraction. RA volume index (RAVI) was calculated by body surface area. The 2D-STE analyses were performed by a single experienced and independent cardiologist who was blinded to clinical information.

Clinical outcomes

The endpoint was all-cause mortality or hospitalization due to HF. We reviewed the medical records and conducted telephone interviews to collect follow-up information.

Statistical analysis

The Shapiro–Wilk test was used to determine the normality of continuous variables. Continuous variables are represented as mean ± standard deviation or median (interquartile range) according to the distribution. Categorical variables are presented as numbers and percentages. Continuous and categorical variables were compared using the paired Student's *t*-test or Mann–Whitney *U* test and the χ^2 or Fisher's exact test, respectively. Cumulative survival estimates were calculated using the Kaplan–Meier method and compared using the log-rank test. Univariable and multivariable Cox proportional hazard regression analyses were used to clarify variables associated with the occurrence of events. Multivariable models were constructed, including age, gender, New York Heart Association class, LV ejection fraction, RV fractional area change and RA parameters. The results are reported as hazard ratios (HRs) with 95% confidence intervals (CIs). Receiver operating characteristic analysis was performed to identify the optimum cut-off for RAGLS or RAVI to discriminate patients with events using the Youden J statistic. Statistical significance was set at $P < 0.05$. All statistical analyses were performed using the Statistical Package for the Social

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Sciences software (Version 24; IBM Corp., Armonk, NY, USA) and the R statistical package (Version 4.0.2; R Foundation for Statistical Computing, Vienna, Austria).

Results

Patients' characteristics

The mean age of the patients was 75 ± 10 years, and 40% of the patients were males. During a median follow-up of 13 months, 19 patients had events (14 cases of all-cause mortality and 5 cases of hospitalization due to HF). Baseline characteristics at the timing of transthoracic echocardiographic examination are shown in *Table* 1. The patients' prevalence rates of hypertension, dyslipidaemia, diabetes mellitus and chronic kidney disease were 36%, 24%, 16% and 14%, respectively. Patients with events had a significantly higher prevalence of chronic kidney disease than those without events. With respect to HF, patients with events had a significantly higher prevalence of a history of admission for HF than those without events, and the symptom of HF was more severe in patients with events. Patients with events had higher levels of plasma B-type natriuretic peptide than those without events. The use of tolvaptan was more frequent in patients with events than in those without events. After transthoracic echocardiographic examination, 17 out of 19 (89%) patients with events had at least taken diuretic drugs.

Echocardiographic characteristics

Baseline echocardiographic findings in patients with and without events are shown in *Table* 2. Patients with events had a lower LV ejection fraction than those without events. There was no significant difference in RV dimension or RV fractional area change between the two groups. RAGLS was lower in patients with events than in those without events; meanwhile, no significant difference was observed in RA fractional area change or RA ejection fraction between the two groups. RAVI was higher in patients with events than in those without events.

Table 1 Clinical characteristics of the study population.

	All (n = 169)	Events		P-value
		Present (n = 19)	Absent (n = 150)	
Age, years	75 ± 10	75 ± 7	75 ± 11	0.76
Male gender, n (%)	68 (40)	13 (68)	55 (37)	0.01
Body surface area (m^2)	1.5 ± 0.2	1.5 ± 0.1	1.5 ± 0.2	0.77
Hypertension, n (%)	60 (36)	7 (37)	53 (35)	0.90
Dyslipidaemia, n (%)	40 (24)	2 (11)	38 (25)	0.15
Diabetes mellitus, n (%)	26 (16)	3 (16)	23 (15)	0.97
Chronic kidney disease, n (%)	24 (14)	6 (32)	18 (12)	0.02
Current smoker, n (%)	5 (3)	0 (0)	5 (3)	0.42
Aetiology of HF, n (%)				0.70
Ischaemic heart disease	22 (13)	3 (16)	19 (13)	
Non-ischaemic heart disease	147 (87)	16 (84)	131 (87)	
HF stage, n (%)				0.01
B	113 (67)	7 (37)	106 (70)	
C	55 (33)	12 (63)	43 (29)	
D	1 (1)	0 (0)	1 (1)	
New York Heart Association class, n (%)				<0.01
I	50 (30)	1 (5)	49 (33)	
II	93 (55)	8 (42)	85 (57)	
III	25 (15)	10 (53)	15 (10)	
IV	1 (1)	0 (0)	1 (1)	
Previous admission for HF, n (%)	31 (18)	9 (47)	22 (15)	<0.01
Angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, n (%)	53 (31)	3 (16)	50 (33)	0.12
Beta-blocker, n (%)	71 (42)	9 (47)	62 (41)	0.62
Loop diuretics, n (%)	48 (28)	8 (42)	40 (27)	0.16
Tolvaptan, n (%)	11 (7)	6 (32)	5 (3)	<0.01
Thiazide, n (%)	6 (4)	1 (5)	5 (3)	0.67
Potassium-sparing diuretics, n (%)	38 (23)	6 (32)	32 (21)	0.31
Sodium glucose transporter 2 inhibitor, n (%)	22 (13)	4 (21)	18 (12)	0.27
Haemoglobin, g/dL	12.0 ± 2.0	10.6 ± 2.2	12.2 ± 1.9	<0.01
Albumin, g/dL	3.6 ± 0.7	3.4 ± 0.5	3.7 ± 0.7	0.12
Estimated glomerular filtration rate, mL/min/1.73 m^2	56 ± 22	51 ± 26	57 ± 22	0.28
B-type natriuretic peptide, pg/mL	476 ± 1231	1103 ± 1249	388 ± 1208	0.04

Note: Values are expressed as mean ± standard deviation or number (%).
Abbreviation: HF, heart failure.

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Table 2 Baseline echocardiographic characteristics.

		Events		
	All (n = 169)	Present (n = 19)	Absent (n = 150)	P-value
Left chambers				
LV end-diastolic volume, mL	90 ± 41	101 ± 50	89 ± 40	0.23
LV end-systolic volume, mL	37 ± 31	51 ± 39	35 ± 29	0.11
LV stroke volume, mL	54 ± 18	50 ± 15	54 ± 18	0.4
LV ejection fraction, %	64 (60, 66)	56 (47, 65)	64 (61, 66)	0.01
LA volume index, mL/m^2	48 ± 18	54 ± 23	48 ± 18	0.16
Early diastolic transmitral inflow velocity/early diastolic mitral annular velocity	14 (10, 19)	17 (11, 26)	14 (10, 19)	0.19
Mitral regurgitation				
Non/mild/moderate/severe, n (%)	67/58/37/7 (40/34/22/4)	4/6/8/1 (21/32/42/5)	63/52/29/6 (42/35/19/4)	0.11
Aortic regurgitation				
Non/mild/moderate/severe, n (%)	112/38/16/3 (66/23/9/2)	12/5/2/0 (63/26/11/0)	100/33/14/3 (67/22/9/2)	0.90
Right ventricle				
RV basal diameter, mm	45 ± 6	44 ± 5	45 ± 6	0.71
RV end-diastolic area, cm^2	17 ± 6	19 ± 6	17 ± 6	0.12
RV end-systolic area, cm^2	11 ± 4	12 ± 4	11 ± 4	0.12
RV fractional area change, %	38 ± 8	37 ± 6	38 ± 8	0.61
Tricuspid annular plane systolic excursion, mm	21 ± 7	20 ± 5	21 ± 7	0.71
Right atrium				
RAVI, mL/m^2	57 ± 31	75 ± 39	55 ± 29	0.04
RAGLS, %	18 ± 10	13 ± 10	18 ± 9	0.02
RA fractional area change, %	23 ± 11	19 ± 12	23 ± 10	0.16
RA ejection fraction, %	28 ± 14	27 ± 17	28 ± 14	0.72
TR				
TR moderate/severe, n (%)	155/14 (92/8)	16/3 (84/16)	139/11 (93/7)	0.21
TR pressure gradient, mmHg	29 (25, 36)	36 (25, 43)	29 (24, 34)	0.07
Inferior vena cava, mm	13 ± 6	16 ± 8	12 ± 5	0.01

Note: Values are expressed as mean ± standard deviation, number (%) or median (interquartile range).
Abbreviations: LA, left atrial; LV, left ventricular; RA, right atrial; RAGLS, right atrial global longitudinal strain; RAVI, right atrial volume index; RV, right ventricular; TR, tricuspid regurgitation.

Association of RA function and volume with events

The corresponding optimal cut-off values of RAGLS and RAVI for discriminating the events from the receiver operating characteristic curve were 16.2% and 50 mL/m^2, respectively. Based on these cut-off values, we categorized the patients into two groups (low RAGLS $\leq$ 16.2% vs. high RAGLS $>$ 16.2%, high RAVI $\geq$ 50 mL/m^2 vs. low RAVI $<$ 50 mL/m^2). Kaplan–Meier curves showed that patients with low RAGLS had higher event rates than those with high RAGLS (log-rank test, P = 0.003; *Figure* 3A). Kaplan–Meier curves showed that patients with high RAVI had higher event rates than those with low RAVI (log-rank test, $P < 0.001$; *Figure* 3B). When all the patients were categorized according to the combination of high/low RAGLS and/or RAVI, Kaplan–Meier curves showed that patients with low RAGLS and high RAVI had the highest event rates compared with the other groups (log-rank test, $P < 0.001$; *Figure* 4).

Cox proportional hazard regression analyses were performed to evaluate the determinants of events (*Table* 3). In univariate Cox regression analysis, male, New York Heart Association class, LV ejection fraction $\leq$ 50%, RAVI $\geq$ 50% and RAGLS $\leq$ 16.2% were significant determinants of events. In multivariate Cox regression analysis, RAGLS $\leq$ 16.2% was associated with events in Model 1 including age and gender (HR, 4.45; 95% CI, 1.46–13.55; P = 0.01), in Model 2 including New York Heart Association class (HR, 3.27; 95% CI, 1.05–10.18; P = 0.04), in Model 3 including LV ejection fraction $\leq$ 50% (HR, 3.87; 95% CI, 1.27–11.81; P = 0.02), in Model 4 including RV fractional area change $\leq$ 35% (HR, 4.55; 95% CI, 1.51–13.71; $P < 0.01$) and in Model 5 including RAVI $\geq$ 50% (HR, 4.57; 95% CI, 1.52–13.79; $P < 0.01$).

Discussion

The present study showed that low RAGLS and high RAVI were associated with mortality and HF in patients with significant TR. RAGLS remained a predictor after adjusting for LV function, RV function and RA volume. A cut-off value of $\leq$16.2% for RAGLS showed the best accuracy to predict events. Our results offer additional insights into the evaluation of clinical outcomes in patients with significant TR.

TR and RA function

Significant TR is observed in 0.55% of the general population, and its prevalence increases with age, affecting approxi-

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Figure 3 Kaplan–Meier curves of cumulative probability of event-free survival. (A) Kaplan–Meier curves according to high or low right atrial global longitudinal strain (RAGLS). (B) Kaplan–Meier curves according to high or low right atrial volume index (RAVI).

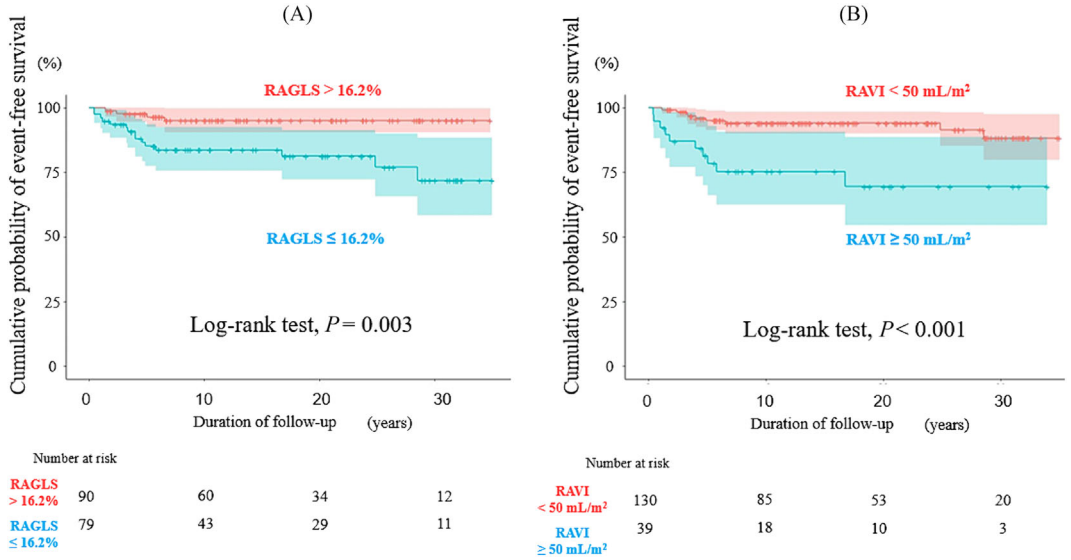
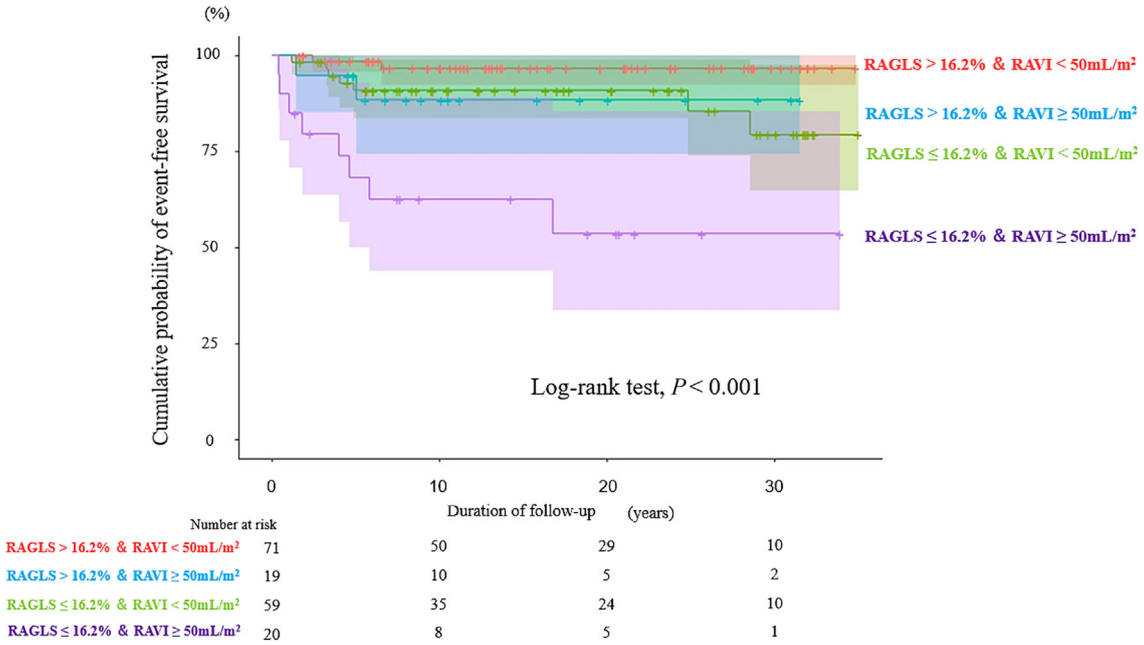


Figure 4 Kaplan–Meier curves of cumulative probability of event-free survival according to the combination of high/low right atrial global longitudinal strain (RAGLS) and/or right atrial volume index (RAVI).



mately 4% of patients aged 75 years or older.[10] More than moderate TR has been reported to be associated with a poor prognosis.[3–5] TR is related to remodelling of the right ventricle, which induces RV dilatation and dysfunction. The impairment of RV function progresses with worsening regurgitation.[11] RV dysfunction has been demonstrated to be a predictor of clinical outcomes in patients with TR.[7]

TR imposes volume overload on the right atrium as well as the right ventricle. This volume overload causes not only atrial dilatation but also impaired atrial stiffness and compli-

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Table 3 Univariate and multivariate analyses of the prediction of the outcome endpoints.

	Univariate		Multivariate 1		Multivariate 2		Multivariate 3		Multivariate 4		Multivariate 5	
	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Age, years	1.01 (0.97–1.06)	0.6	1.00 (0.95–1.05)	0.99								
Male	3.52 (1.34–9.27)	0.01	3.41 (1.28–9.09)	0.01								
New York Heart Association class	4.11 (2.22–7.60)	<0.01			3.31 (1.80–6.11)	<0.01						
LV ejection fraction ≤ 50%	5.61 (2.13–14.78)	<0.01					4.37 (1.64–11.67)	0.01				
RV fractional area change ≤ 35%	1.32 (0.54–3.25)	0.55							1.26 (0.51–3.10)	0.62		
RAVI ≥ 50 mL/m^2	4.51 (1.83–11.15)	<0.01									4.52 (1.82–11.23)	<0.01
RAGLS ≤ 16.2%	4.58 (1.52–13.81)	<0.01	4.45 (1.46–13.55)	0.01	3.27 (1.05–10.18)	0.04	3.87 (1.27–11.81)	0.02	4.55 (1.51–13.71)	<0.01	4.5 (1.52–13.79)	<0.01

Abbreviations: CI, confidence interval; HR, hazard ratio; LV, left ventricular; RAGLS, right atrial global longitudinal strain; RAVI, right atrial volume index; RV, right ventricular.

ance due to inflammation, hypertrophy and fibrosis, leading to atrial dysfunction.[12] The right atrium serves as a reservoir for systemic venous return and has an important role in modulating RV filling. Thus, RA impairment develops worsening congestion. RA myocardial fibrosis also affects the electromechanical properties. In addition, the neurohormonal disturbance caused by RA fibrotic stretch manifests as excessively defective atrial natriuretic peptide synthesis, inducing volume overload.[13] Therefore, the deterioration of RA function may lead to worse clinical outcomes. Although RA remodelling is not uncommon in patients with TR, the potential role of RA function is unknown.

Influence of RA function on clinical outcomes

There is growing interest in understanding the contribution of atrial function to cardiac mechanics. The performance of the left atrium is well known to be associated with clinical outcomes in HF.[14,15] LA function has been reported to decline from the moderate stage of mitral regurgitation and provide incremental prognostic value.[16,17] The prognostic implication of RA performance has not been fully elucidated, but its clinical importance has recently been highlighted in HF. Ivanov *et al*. reported that RA volume measured by cardiac magnetic resonance imaging was an independent predictor of mortality in patients with HF with preserved ejection fraction.[18] Jain *et al*. showed that RA function measured by strain analysis on cardiac magnetic resonance imaging was impaired in patients with HF and was associated with mortality, independent of LV or RV function.[19] Hasselberg *et al*. showed that RA function measured by strain analysis on transthoracic echocardiography, representing the RA reservoir strain, was associated with 5 year mortality in patients with precapillary pulmonary hypertension.[20]

The 2D-STE can assess RA function as RAGLS by measuring the atrial deformation profile during the cardiac cycle. The evaluation of RA function using the 2D-STE has been shown to be feasible and reproducible. A systemic review and meta-analysis of 4111 subjects from 21 studies indicated a normal reference value of 44% (95% CI, 25%–63%) for the RA reservoir strain,[21] which was represented as RAGLS in the present study.

Regarding the association of RA remodelling with TR, Muraru *et al*. reported the role of RA volume as a mechanism of tricuspid annular dilatation and a predictor of TR severity, irrespective of cardiac rhythm and RV loading conditions.[22] Hinojar *et al*. reported that RA strain indices were related to TR, with a gradual decline in RA strains with increasing severity of TR.[23] They also showed that an RA reservoir strain of <9.4% predicted mortality and HF hospitalization in patients with TR. However, data on the influence of RA function are limited in patients with TR.

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Present study

The present study showed that RAGLS had a prognostic value in patients with significant TR. Atrial volume reflects the chronic effect of ventricular filling pressure over time, whereas atrial function more accurately reflects dynamic ventricular filling pressure. Atrial functional changes occur before the progression of atrial dilatation. RA function can be useful for assessing clinical outcomes in the earlier stages of disease. A previous study reported a cut-off value of $<$9.4% for the RA reservoir strain for predicting adverse outcomes,[23] whereas our study showed a cut-off value of $<$16.2% for RAGLS. This difference between studies appeared to be due to the difference in study populations. The previous study included patients with severe, massive or torrential TR who had advanced RA dysfunction,[23] unlike our study, which included patients with moderate or severe TR. Further studies are required to investigate the adequate cut-off of RAGLS for identifying clinical outcomes. In addition, RV dysfunction was not a prognostic factor in the present study. RV dysfunction is a late consequence of changes in the pulmonary circulation in HF. RA function responds early to changes in RV compliance.[19] RA function can be a sensitive marker for assessing disease severity.

With regard to the treatment of TR, the first choice is drug therapy, mainly diuretics. In the 2021 European Society of Cardiology/European Association for Cardio-Thoracic Surgery guidelines, tricuspid valve interventions are recommended when RV dilatation or dysfunction occurs.[24] However, exact thresholds have not yet been defined because clinical evidence on indications for treatments is lacking. In clinical practice, tricuspid valve interventions may be underused and often initiated too late. Recently, transcatheter repair has emerged as a less invasive treatment option for TR. Therefore, the optimal timing of tricuspid valve interventions needs to be considered before irreversible RV dysfunction and organ damage occur. Our findings suggest that the evaluation of RA function is useful for identifying the risk stratification in patients with significant TR, which may help in selecting patients who would benefit from treatment.

Study limitations

The present study has certain limitations. First, this study was conducted retrospectively at a single centre. The number of events was limited. This could lead to no significant difference in the ratio of early diastolic transmitral inflow velocity to early diastolic mitral annular velocity or RV function between patients with events and those without events. Long-term follow-up was lacking. Second, because we performed not the quantitative assessment but the qualitative assessment, we did not evaluate the TR severity in detail. Third, because we had no data on follow-up transthoracic echocardiography, we could not assess the influence of the medical therapy for HF. Fourth, RA volume and function were calculated from apical four-chamber view images. The assessment of RA remodelling might be less accurate. Finally, this study excluded patients with atrial fibrillation but included patients with atrial and functional TR.

Conclusions

RAGLS is an independent predictor of all-cause mortality and HF hospitalization in patients with significant TR. The assessment of RAGLS could improve risk stratification in significant TR.

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Conflict of interest statement

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None declared.

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