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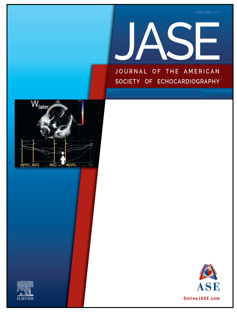

Implication of Right Atrial Pressure Estimated by Echocardiography in Patients with Severe Tricuspid Regurgitation

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ORIGINAL RESEARCH ARTICLE

TITLE PAGE

Implication of Right Atrial Pressure Estimated by Echocardiography in Patients with Severe Tricuspid Regurgitation

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Declaration of interest

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ABSTRACT

Background: Little is known about how tightly right atrial pressure (RAP) is associated with prognosis in patients with severe tricuspid regurgitation (TR). The aim of this study was to investigate the association of RAP estimated by echocardiography (RAP-echo) with cardiovascular events in patients with severe TR.

Methods: We retrospectively studied 240 outpatients (median 75 years, 130 female) who underwent 2-dimensional transthoracic echocardiography and were diagnosed with severe TR. According to RAP-echo using the diameter of inferior vena cava and its response to a sniff, patients were classified into 2 groups: low/middle and high RAP-echo. Cardiovascular events were defined as cardiovascular death or admission for heart failure.

Results: During follow-up (median, 428［87–1229］ days), 64 patients experienced a cardiovascular event. By multivariate analysis, high RAP-echo was independently associated with cardiovascular events (hazard ratio, 2.46［1.17 – 5.18］). Also, jugular vein distention and leg edema were not independently associated with cardiovascular events.

Conclusions: The significant and stronger association of RAP-echo with clinical outcome compared to estimates of RAP on physical examination suggests that recognition of high RAP-echo can be a valuable surrogate for the clinical management of severe TR patients.

Key words:

Severe Tricuspid Regurgitation

Right Atrial Pressure

Transthoracic Echocardiography

Prognosis

INTRODUCTION

People with tricuspid regurgitation (TR) are often asymptomatic, but with more advanced disease, patients show symptoms or signs of heart failure.[1] Past studies reported that, in patients with significant TR, heart failure symptoms or signs were associated with an increase risk of poor prognosis.[2-4] Thus, recognition of the presence of heart failure symptoms or signs caused by TR is essential for the management of TR patients.

It was reported that increased central venous pressure (CVP), which is one of the major signs of heart failure, was independently related to mortality in a broad spectrum of patients with cardiovascular disease.[5-8] However, although severe TR can easily cause CVP and right atrial pressure (RAP) elevation by a large regurgitant flow from the right ventricle into the right atrium, little is known about how tightly RAP is related to poor prognosis in patients with severe TR.

Echocardiography, which is an essential tool for grading the severity of TR, is routinely used to noninvasively estimate RAP. Therefore, in this study, we sought to investigate the impact of RAP estimated by echocardiography (RAP-echo) on cardiovascular events in patients with severe TR.

METHODS

Study Population

We retrospectively reviewed 972 consecutive 2-dimensional TTE that included diagnosis of severe TR at our heart institution between January 2014 and December 2015 and excluded repeat examinations of the same patient (n=239). Also, we excluded patients who underwent TTE during hospitalization (n=486). After excluding patients without a valid RAP-echo assessment (n=7), the remaining 240 severe TR outpatients were included (**Figure 1**). The Cedars-Sinai Institutional Review Board approved this retrospective study with a waiver of informed consent.

Clinical Data

All data were collected from the medical charts and our echocardiographic database. Baseline patient characteristics were collected for the same date as TTE or when not possible within 3 days before or after TTE. Jugular vein distention (JVD) was deemed present if right internal jugular vein pressure was estimated to be over 9 cm above the right atrium.[9-11] Leg edema was deemed present if patients had edema around or above ankle.[12] Renal function was estimated as glomerular filtration rate by using the simplified Modification of Diet in Renal Disease equation.[13]

Echocardiography

2-dimensional and Doppler echocardiography was performed according to American Society of Echocardiography guidelines by experienced sonographers using an ultrasound system (iE33; Philips, Andover, Massachusetts, USA) with S5-1 phased array transducer.[14] Analysis of TTE images was performed by experienced cardiologists. Left ventricular ejection fraction (LVEF) by using biplane Simpson method, left atrial (LA) volume by using the biplane disk summation method and right atrial (RA) volume by using the single disk summation method were measured.[15] LA and RA volume index was calculated dividing LA volume by body surface area. LV stroke volume was calculated using LV outflow tract diameter and the velocity time integral at LV outflow tract obtained by pulse-wave Doppler. The right ventricle was imaged from multiple views, including the right ventricular (RV)-focus and RV-modified apical 4-chamber views. RV end-diastolic/end-systolic area and RV fractional area change were obtained.[15,16] The severity of any valvular heart diseases was defined according to the current recommendation.[17,18] Significant left-heart valvular disease was defined as moderate or severe grade of any left-heart valvular diseases. TR severity was defined by an integration approach using multiple parameters including dilation of RA/RV, vena contracta width, dense and shape of continuous-wave Doppler, and hepatic vein flow reversal.[17] Primary TR was diagnosed by careful tricuspid valve examination for any structural leaflet abnormality. By using the diameter of inferior vena cava (IVC) and its response to a sniff, RAP-echo was classified into three grades as follows: low [3 mm Hg (range, 0−5)], middle [8 mm Hg (range, 5−10)] and high [15 mm Hg (range, 10−20)] according to the current recommendation.[15] Then, we categorized severe TR patients into 2 groups: high grade of RAP-echo (high RAP-echo) and middle/low grade of RAP-echo (middle/low RAP-echo). Systolic pulmonary artery pressure (sPAP) was obtained by adding the systolic pressure gradient between RV and RA calculated by applying the modified Bernoulli equation to RAP-echo.[16] RV-PA coupling was assessed by RV fractional area change/sPAP ratio.

Follow-Up and Clinical Outcomes

The primary end point was defined as cardiovascular death or admission for heart failure and were ascertained through careful review of patients' medical charts written by the cardiologists. If a patient experienced multiple events, the event which was occurred earlier was chosen. The date when a patient underwent TTE was defined as the starting of the follow-up time. Patients' follow-up was censored at the time of any tricuspid valve surgery/intervention or cardiac transplantation.

Statistical Analysis

Normality of distribution was tested by the histograms and the Shapiro-Wilk test. Continuous variables are presented as median and interquartile range regardless of the normality. The student's *t* test or Mann-Whitney U-test was used to assess statistical significance of continuous variables with or without normally distributed variables. Blood pressure and heart rate at the time of TTE or RHC were compared using a paired *t* test. Categorical data were presented as numbers (percentages) and compared between groups using the chi-square test or Fisher exact test. The Kaplan-Meier curve and log-rank test were used to describe the occurrence of adverse events during the follow-up period. Age, female, JVD, leg edema, LVEF, LV stroke volume index, RV fractional area change, sPAP, RV fractional area change/sPAP, and high RAP-echo were included in the multivariate analysis by Cox proportional hazards model. The risk of a given variable was expressed by a hazard ratio (HR) corresponding with 95% confidence interval (CI). All two-sided *P* values were used, taking P <0.05 to be statistically significant. All data were statistically analyzed using the SPSS software package, version 26.0 (Chicago, Illinois).

RESULTS

Patients Characteristics and Echocardiographic Findings

In the 240 severe TR patients, 144 (60%) patients showed high RAP-echo (**Figure 1**). There was no significant difference in age, comorbidities and medical treatments between patients with high RAP-echo and those without, although patients with high RAP-echo had significantly smaller percentage of females than those without (**Table 1**). Also, patients with high RAP-echo had significantly higher prevalence of dyspnea or fatigue, JVD and leg edema, and showed lower estimated glomerular filtration rate compared to those without (**Table 1**). The duration between physical examination and TTE was a median of 0 (range 0 – 5) days.

On echocardiographic findings, patients with high RAP-echo had significantly lower LVEF, larger LA volume index, and higher sPAP than those without (**Table 2**). Also, patients with high RAP-echo showed significantly larger RV end-diastolic/end-systolic area and lower RV fractional area change than those without. In addition, patients with high RAP-echo showed significantly larger RA volume index, vena contracta width of TR, and IVC diameter compared to those without (**Table 2**). **Figure 2** shows the representative cases of echocardiographic images according to the RAP-echo assessment.

Clinical Outcomes for Patients with or without High RAP-echo

Outcome data were available in 228 of 240 (95%) patients. During follow-up [median 428 days (range, 87−1229)], 64 (28%) of the patients experienced cardiovascular events (7 cardiovascular death and 57 admission for heart failure) (**Table S1**). Univariate analysis showed that JVD, leg edema, LVEF, LV stroke volume index, RV fractional area change and high RAP-echo were associated with cardiovascular events (**Table 3**). The multivariate analysis showed that high RAP-echo was independently associated with cardiovascular events [HR, 2.46 (95% CI 1.17 – 5.18)] (**Table 4**). Another multivariate model which included eGFR and total bilirubin also showed that high RAP-echo was independently associated with outcomes [HR, 2.50 (95% CI 1.07 – 5.85)] (**Table S2**). Kaplan-Meier curves revealed that there was a higher risk of cardiovascular events in patients with high RAP-echo than those without (**Figure 3**).

Relationship between high RAP-echo and JVD

In this study cohort, 233 of 240 (97%) patients allowed JVD assessment on physical examination. **Figure S1** shows the distribution of severe TR patients according to the combination of RAP-echo and JVD. In the 233 patients, the number of patients who had high RAP-echo but not JVD was the largest proportion of patients (n=76, 33%).

DISCUSSION

This study investigated the impact of high RAP-echo on cardiovascular events in patients with severe TR. The results demonstrated that high RAP-echo was significantly associated with cardiovascular events in severe TR patients. In addition, this study results showed that high RAP-echo had a stronger association with prognosis than JVD or leg edema.

Association of RAP-echo with Outcome in Severe TR Patients

Higher CVP/RAP has significant implications regarding patients' prognosis.[5,7,8] Previous studies reported that an increased RAP was associated with a poor prognosis in patients with heart failure.[6,7,19] Also, in other cohorts such patients who underwent Fontan surgery or lung transplantation, greater CVP/RAP were strong predictors of outcome.[20,21] Conversely, the prognostic importance of increased CVP/RAP in patients with severe TR has not been reported previously. In this study, we demonstrated the independent association of RAP with cardiovascular outcome in patients with severe TR.

The main mechanism of the harm associated with RAP elevation is splanchnic congestion and organ failure caused by impeded venous return.[22] Congestion can only be managed appropriately if it is recognized. However, accurately quantifying congestion is not easy, and may commonly be missed unless it is obvious.[23,24] RAP-echo is a simple and non-invasive method to identify patients with congestion.[25] Also, severe TR can cause RAP elevation and organ failure such as renal and liver dysfunction regardless of left ventricular function or pulmonary artery pressure. Thus, RAP-echo can identify severe TR patients with congestion with relative ease. Based on this study, RAP-echo had a significant importance on cardiovascular events in patients with severe TR.

Estimates of RAP by Echocardiography and Physical Examination

RAP elevation manifests in JVD, which was reported as a prognostic marker in heart failure patients.[5,9,10] However, we found a significant discordance in RAP estimation between RAP-echo and JVD assessment on physical examination. Many discordant cases showed high RAP-echo but not JVD (**Figure S1**). This finding and significant association of RAP-echo with outcomes suggested that JVD assessment on physical examination tended to underestimate RAP, consistent with previous studies demonstrating underestimation of jugular venous pressure on physical examination when RAP elevated.[26] JVD assessment on physical examination may be inaccurate if the jugular vein is constricted or torturous and may be difficult to assess in patients with short neck or with prior neck surgery.[27] Moreover, JVD assessment on physical examination is subjective. These may explain the limited clinical utility of JVD assessment on physical examination in patients with severe TR and may be a reason why JVD assessment on physical examination showed a weaker association with prognosis than RAP-echo in this study.

Similar to JVD, leg edema is one of the common signs that suggests CVP/RAP elevation. However, leg edema represents extravascular rather than intravascular volume and can be the result of other conditions such as venous insufficiency or obesity. Furthermore, it occurs later than CVP elevation in the process of decompensation.[25] These may be the reasons why leg edema was not associated with outcomes in our study cohort.

Echocardiography or Ultrasound Assessment of RAP

RAP-echo using the most recent criteria based on IVC size and collapsibility indices are appropriate to define whether RAP is high or not.[27] Recently, the usefulness of a method using ultrasound assessment of the internal jugular vein respiratory fluctuation for estimating CVP have been reported.[28,29] Previous studies reported that internal jugular vein diameter and its variations with respiratory maneuvers can be accurately measured using ultrasound and that it can identify patients with congestion who have a higher risk of an adverse outcome.[28] This method may also be a good way to estimate patients' CVP/RAP. However, this method is still not common in daily clinical practice. On the other hand, TTE is a vital examination for the detection and grading of any valvular heart disease, and RAP estimation is a routine component of TTE. Thus, RAP-echo is a much simpler and more efficient method than ultrasound jugular vein assessment in clinical practice.

Clinical Implication

To better define determinants of mortality or morbidity will lead to better patients' management. Our study results of the significant association between RAP-echo and cardiovascular outcome in severe TR patients indicate that recognition of severe TR patients with high RAP-echo is essential for clinical management. One may focus on the improvement of RAP for better outcome in severe TR patients. Additionally, our study results suggest that changes before and after treatment of RAP-echo may be a reasonable surrogate for predicting clinical benefit to severe TR patients in clinical studies such as interventional tricuspid valve repair or replacement.

Limitations

First, our study has some selection bias, in particular, referral bias because it is a single tertiary care center retrospective study. Second, assessment of pulmonary artery pressure and RV function with TTE can be suboptimal in patients with severe TR.[16,30] That may be a reason why sPAP, RV fractional area change, and RV fractional area change/sPAP were not associated with outcomes in this study. Third, we are reporting on outpatients in order to allow for more focused insight into the specific effects of severe TR. Our findings, therefore, might be better to avoid applying to every severe TR patient's cohort. Fourth, we did not have telephone calls with patients to ascertain outcomes. Fifth, physical examination was performed on the day of echocardiography in only 131 of 240 (55%) patients. Sixth, JVD was not prospectively assessed and outpatient clinician may check the echo findings before the physical examination in some cases. Thus, information bias cannot be ruled out. Seventh, only 127 of 240 (53%) patients had the information of natriuretic peptide. Thus, we regrettably did not include natriuretic peptide in our study data. Eighth, although right heart catheterization data were available, these were not included because only 10 patients had TTE and right heart catheterization within 48 hours. Finally, additional Doppler echocardiographic parameters, which have been proposed to better qualify RAP to overcome its limitation such as low compliance with deep inspirations or dilation in individuals with normal RAPs,[27] did not be applied in our study because of lack of data. Furthermore, measurement of the superior vena cava flow velocity from the subcostal view, which was reported as a useful parameter for estimating RAP, also did not apply in our study because we did not measure the parameter routinely[31].

Conclusions

High RAP-echo was significantly associated with cardiovascular outcomes in patients with severe TR. Furthermore, the association of RAP-echo with outcomes was stronger than that of estimates of RAP on physical examination such as JVD or leg edema.

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Supplementary Material

Table S1-2 and Figure S1

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TABLES

Table 1. Patient characteristics

	All patients (n=240)	RAP-echo High (n=144)	RAP-echo Middle/Low (n=96)	*P* value
Age (years)	75 (66 – 84)	75 (65 – 84)	75 (66 – 84)	0.81
Female	130 (54)	70 (49)	60 (63)	0.021
Body mass index (kg/m^2)	24 (21 – 27)	25 (22 – 28)	23 (20 – 27)	0.053
Hypertension	152 (63)	93 (65)	59 (61)	0.57
Dyslipidemia	148 (62)	89 (62)	59 (61)	0.90
Diabetes mellitus	63 (26)	42 (29)	21 (22)	0.21
COPD	20 (8)	14 (10)	6 (6)	0.36
Chronic atrial fibrillation	122 (51)	81 (56)	41 (43)	0.054
Coronary artery disease	69 (29)	44 (31)	25 (26)	0.45
RAS inhibitor	99 (41)	59 (41)	40 (42)	0.84
Beta channel blocker	124 (52)	75 (52)	49 (51)	0.96
Loop diuretic	167 (70)	106 (74)	61 (64)	0.13
Dyspnea or Fatigue	138 (58)	94 (65)	44 (46)	0.003
JVD	89 (37)	63 (44)	26 (27)	0.006
Leg edema	80 (33)	59 (41)	21 (22)	0.002
eGFR (ml/min/1.73 m^2)	49 (36 – 64)	47 (31 – 59)	57 (41 – 72)	0.006
Total bilirubin (mg/dl)	0.7 (0.5 – 1.1)	0.7 (0.5 – 1.2)	0.7 (0.5 – 0.9)	0.27
Albumin (g/dl)	4.0 (3.7 – 4.3)	4.0 (3.6 – 4.3)	4.0 (3.8 – 4.3)	0.79

Data are median (interquartile range) or number (percentage).

RAP-echo = right atrial pressure evaluated by echocardiography; COPD = chronic obstructive pulmonary disorder; RAS = renin-angiotensin system; JVD = jugular vein distention; eGFR, estimated glomerular filtration rate

Table 2. Echocardiographic findings

	All patients (n=240)	RAP-echo High (n=144)	RAP-echo Middle/Low (n=96)	*P* value
LVEF (%)	56 (40 – 64)	54 (35 – 62)	60 (51 – 66)	0.001
Significant LHVD	144 (60)	93 (65)	51 (53)	0.076
LV stroke volume index (ml/m^2)	26 (19 – 36)	26 (18 – 35)	27 (21 – 37)	0.19
LA volume index (ml/m^2)	53 (39 – 75)	55 (43 – 76)	48 (36 – 69)	0.017
RV end-diastolic area (cm^2)	26 (20 – 32)	29 (23 – 33)	22 (16 – 27)	<0.001
RV end-systolic area (cm^2)	15 (11 – 20)	17 (13 – 22)	12 (8 – 16)	<0.001
RV fractional area change (%)	41 (32 – 49)	39 (30 – 48)	43 (36 – 52)	0.019
RA volume index (ml/m^2)	53 (41 – 74)	63 (46 – 79)	46 (30 – 62)	<0.001
Primary TR	26 (11)	15 (10)	11 (11)	0.80
Vena contracta of TR (mm)	12 (9 – 15)	12 (10 – 15)	11 (8 – 13)	0.005
TR peak velocity (m/s)	3.3 (2.9 – 3.9)	3.3 (2.8 – 3.9)	3.3 (3.0 – 3.9)	0.25
IVC diameter (cm)	2.4 (2.0 – 2.7)	2.6 (2.4 – 3.0)	1.9 (1.6 – 2.0)	<0.001
sPAP (mmHg)	55 (43 – 72)	61 (47 – 74)	49 (40 – 65)	0.001
RV fractional area change/sPAP (%/mm Hg)	0.69 (0.51 – 1.06)	0.63 (0.46 – 0.89)	0.92 (0.59 – 1.14)	<0.001
Hepatic vein flow reversal *	150 (84)	93 (89)	57 (78)	0.059

Data are median (interquartile range) or number (percentage).

RAP-echo = right atrial pressure evaluated by echocardiography; LVEF = left ventricular ejection fraction; LHVD = left heart valvular disease; LA = left atrial; RV = right ventricular; RA = right atrial; TR = tricuspid regurgitation; IVC = inferior vena cava; sPAP = systolic pulmonary artery pressure;

* n=178

Table 3. Univariate analysis for cardiovascular events

	HR (95% CI)	*P* value
Age (years)	0.99 (0.98 – 1.01)	0.28
Female	0.97 (0.59 – 1.59)	0.91
Body mass index (kg/m^2)	1.03 (0.97 – 1.10)	0.32
Hypertension	0.71 (0.43 – 1.18)	0.19
Dyslipidemia	0.78 (0.47 – 1.31)	0.35
Diabetes mellitus	1.17 (0.67 – 2.04)	0.59
Chronic atrial fibrillation	0.68 (0.41 – 1.12)	0.13
Coronary artery disease	1.09 (0.63 – 1.89)	0.76
Dyspnea or Fatigue	1.27 (0.77 – 2.11)	0.35
JVD	2.14 (1.30 – 3.53)	0.003
Leg edema	1.75 (1.04 – 2.94)	0.036
eGFR (ml/min/1.73m^2)	1.00 (0.99 – 1.01)	0.69
Total bilirubin (mg/dl)	1.20 (0.78 – 1.60)	0.54
LVEF (%)	0.97 (0.96 – 0.99)	<0.001
LV stroke volume index (ml/m^2)	0.95 (0.93 – 0.98)	0.002
Significant LHVD	1.06 (0.64 – 1.74)	0.83
LA volume index (ml/m^2)	1.00 (0.99 – 1.01)	0.61
RV end-diastolic area (cm^2)	1.00 (0.99 – 1.02)	0.77
RV end-systolic area (cm^2)	1.03 (0.99 – 1.06)	0.050
RV fractional area change (%)	0.97 (0.95 – 0.99)	0.012
RA volume index (ml/m^2)	1.00 (0.99 – 1.01)	0.51
High RAP-echo	2.23 (1.29 – 3.85)	0.004
TR peak velocity (m/s)	1.00 (0.99 – 1.01)	0.63
sPAP (mmHg)	1.01 (0.99 – 1.02)	0.059
RV fractional area change/sPAP (%/mm Hg)	0.49 (0.23 – 1.03)	0.059
Hepatic vein flow reversal	1.59 (0.70 – 3.49)	0.27

HR = hazard ratio; CI = confidence interval; JVD = Jugular vein distention; eGFR, estimated glomerular filtration rate; LVEF = left ventricular ejection fraction; LHVD = left heart valvular disease; LA = left atrial; RV = right ventricular; RA = right atrial; RAP-echo = right atrial pressure evaluated with echocardiography; TR = tricuspid regurgitation; sPAP = systolic pulmonary artery pressure

Table 4. Multivariate analysis for cardiovascular events

	HR (95% CI)	*P* value
Age (years)		0.49
Female		0.46
JVD		0.46
Leg edema		0.58
LVEF (%)		0.35
LV stroke volume index	0.96 (0.92 – 0.99)	0.012
RV fractional area change (%)		0.86
sPAP (mm Hg)		0.64
RV fractional area change/sPAP (%/mm Hg)		0.88
High RAP-echo	2.46 (1.17 – 5.18)	0.018

HR = hazard ratio; CI = confidence interval; JVD = Jugular vein distention; LVEF = left ventricular ejection fraction; RV = right ventricular; RAP-echo = right atrial pressure evaluated with echocardiography; sPAP = systolic pulmonary artery pressure

FIGURE LEGENDS

Figure 1. Flowchart of the study population

TR = tricuspid regurgitation; TTE = transthoracic echocardiography; RAP-echo = right atrial pressure evaluated by echocardiography

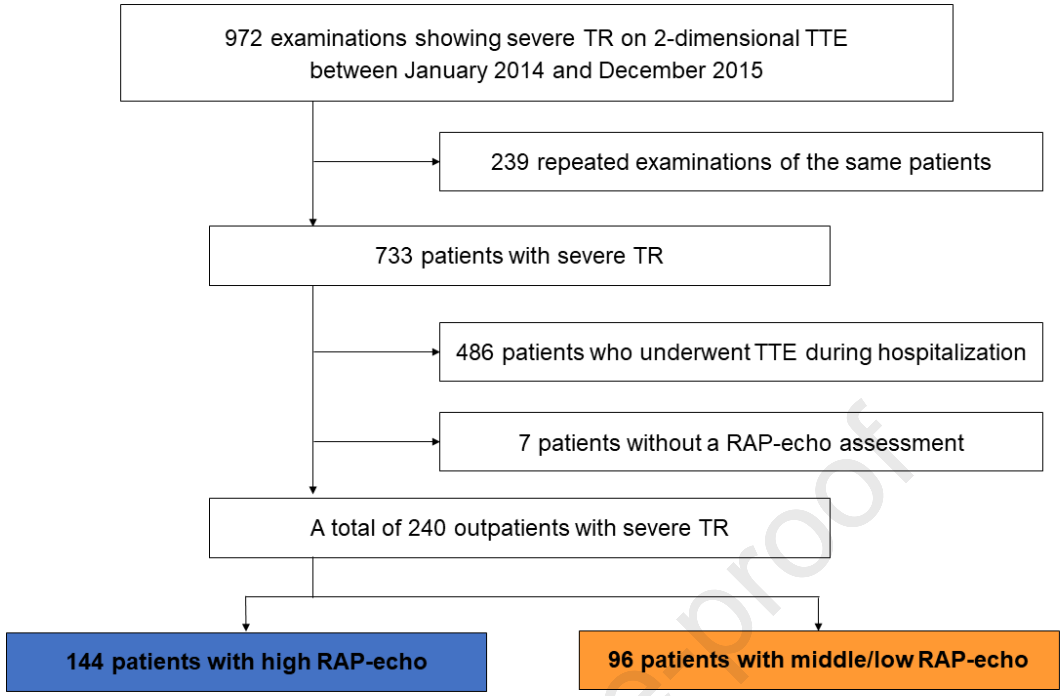
Figure 2. Representative cases

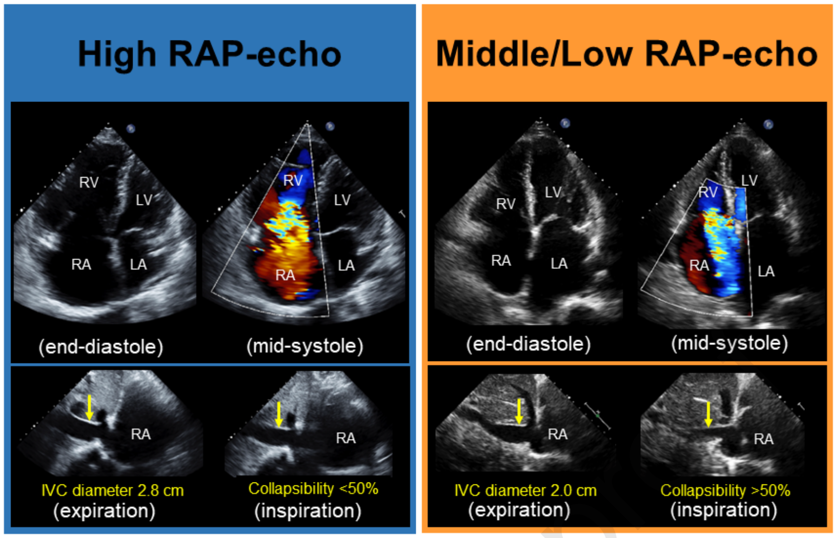
A patient with high RAP-echo (left panel) showed larger RV/RA size, smaller RV fractional area change and larger IVC diameter than that without (right panel). Yellow arrows show the response of IVC diameter to a sniff.

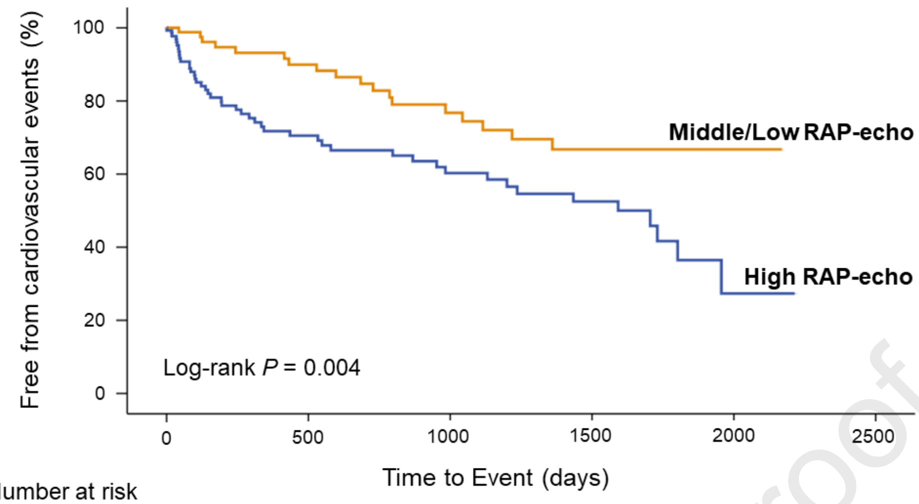
RAP-echo = right atrial pressure evaluated by echocardiography; RV = right ventricle; RA = right atrium; LV = left ventricle; LA = left atrium; IVC = inferior vena cava;

Figure 3. Kaplan-Meier curves according to RAP-echo

RAP-echo = right atrial pressure evaluated by echocardiography


972 examinations showing severe TR on 2-dimensional TTE between January 2014 and December 2015
239 repeated examinations of the same patients
733 patients with severe TR
486 patients who underwent TTE during hospitalization
7 patients without a RAP-echo assessment
A total of 240 outpatients with severe TR
144 patients with high RAP-echo
96 patients with middle/low RAP-echo


High RAP-echo
Middle/Low RAP-echo
RV
LV
RA
LA
(end-diastole)
(mid-systole)
RA
IVC diameter 2.8 cm
(expiration)
Collapsibility <50%
(inspiration)
IVC diameter 2.0 cm
Collapsibility >50%



Number at risk

Middle/Low	92	54	34	19	2
High	136	54	37	25	2

Highlights

- Little is known about whether RAP is associated with outcome in severe TR patients.
- RAP estimated by TTE was independently associated with cardiovascular events.
- Estimates of RAP on physical exam were not significantly associated with outcome.
- RAP estimated by TTE may be more useful for predicting severe TR patients' outcome.

SUPPLEMENTAL MATERIAL

Table S1. Outcome data

	All patients (n=228)	RAP-echo		*P* value
		High (n=136)	Middle/Low (n=92)	
Follow-up period (days)	428 (87 – 1229)	259 (46 – 1131)	692 (154 – 1423)	<0.001
Clinical cardiovascular event	64 (28)	46 (34)	18 (20)	0.019
Cardiovascular death	7 (3)	6 (4)	1 (1)	0.15
Admission for HF	57 (25)	40 (29)	17 (18)	0.043

Data are median (interquartile range) or number (percentage).

RAP-echo = right atrial pressure evaluated by echocardiography; HF = heart failure

Table S2. Multivariate analysis for cardiovascular events

	HR (95% CI)	*P* value
Age (years)		0.67
Female		0.87
JVD		0.32
Leg edema		0.97
eGFR (ml/min/1.73m^2)		0.17
Total bilirubin (mg/dl)		0.78
LVEF (%)		0.46
LV stroke volume index	0.95 (0.91 – 0.99)	0.011
RV fractional area change (%)		0.80
sPAP (mm Hg)		0.82
RV fractional area change/sPAP (%/mm Hg)		0.95
High RAP-echo	2.50 (1.07 – 5.85)	0.035

HR = hazard ratio; CI = confidence interval; JVD = Jugular vein distention; LVEF = left ventricular ejection fraction; RV = right ventricular; RAP-echo = right atrial pressure evaluated with echocardiography; sPAP = systolic pulmonary artery pressure

Figure S1. Distribution according to the combination of RAP-echo and JVD

JVD = jugular vein distention; RAP-echo = right atrial pressure evaluated by echocardiography

Supplemental Figure 1

JVD	RAP−echo: Middle/Low	RAP−echo: High
(−)	n = 68 (29%)	n = 76 (33%)
(+)	n = 26 (11%)	n = 63 (27%)