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ORIGINAL RESEARCH

Preoperative Right Ventricular Free-Wall Longitudinal Strain as a Prognosticator in Isolated Surgery for Severe Functional Tricuspid Regurgitation

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BACKGROUND: Severe tricuspid regurgitation (TR) should be intervened before the development of irreversible right ventricular (RV) dysfunction. However, current guidelines do not provide criterion related to RV systolic function to guide optimal surgical timing. We investigated the prognostic value of RV longitudinal strain in patients undergoing isolated surgery for severe functional TR.

METHODS AND RESULTS: We enrolled 115 consecutive patients (aged 62±10 years; 23.5% men; 62.6% [n=72] with previous left-sided valve surgery) who underwent isolated surgery for severe functional TR at 2 tertiary centers. Preoperative clinical and echocardiographic parameters, including RV free-wall longitudinal strain (RVFWSL), were collected. The primary end point was a composite of cardiac death and unplanned readmission attributable to cardiovascular causes 5 years after surgery. Forty patients (34.8%) reached the primary end point during 333 person-years of follow-up. There were 11 cardiac deaths and 34 unplanned readmissions attributable to cardiovascular causes, with 5 patients experiencing both. An absolute preoperative RVFWSL <24% was associated with the primary end point (hazard ratio, 2.30; 95% CI, 1.22–4.36; *P*=0.011), independent of clinical risk factors, including European System for Cardiac Operative Risk Evaluation II and hemoglobin levels. Meanwhile, other conventional echocardiographic measures of RV systolic function were not significant. The addition of an absolute RVFWSL <24% provided incremental prognostic value to the clinical model for predicting the primary end point.

CONCLUSIONS: Preoperative RVFWSL as an indicator of RV dysfunction was an independent prognosticator in patients undergoing isolated surgery for severe functional TR. Thus, preoperative RVFWSL could help determine the optimal surgical timing for severe functional TR.

Key Words: cardiac surgery procedure ■ echocardiography ■ global longitudinal strain ■ right ventricle ■ tricuspid valve insufficiency

Severe functional tricuspid regurgitation (TR) is increasingly recognized in patients who underwent successful prior left-sided valve surgery or those with long-standing atrial fibrillation.[1] Increasing TR severity is associated with higher morbidity and mortality irrespective of pulmonary hypertension and right ventricular (RV) or left ventricular (LV) dysfunction.[2] Sustained severe TR results in RV systolic dysfunction, which is accepted as an independent predictor of clinical outcomes in patients undergoing corrective TR surgery.[1,3–5] A vicious circle of severe TR, RV volume overload, tricuspid annular dilatation,

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CLINICAL PERSPECTIVE

What Is New?

- Preoperative right ventricular free-wall longitudinal strain is an independent predictor of postoperative outcomes and showed an incremental prognostic value over clinical variables in patients undergoing isolated surgery for severe functional tricuspid regurgitation.

What Are the Clinical Implications?

- Preoperative right ventricular longitudinal strain could be a useful imaging surrogate marker for clinical outcome and could suggest optimal surgical timing for severe functional tricuspid regurgitation.

Nonstandard Abbreviations and Acronyms

EuroSCORE	European System for Cardiac Operative Risk Evaluation
NYHA	New York Heart Association
RV4CSL	right ventricular 4-chamber strain (including the ventricular septum)
RV-ESA	right ventricular end-systolic area
RV-FAC	right ventricular fractional area change
RVFWSL	right ventricular free-wall longitudinal strain
TR	tricuspid regurgitation

and resultant TR aggravation is a pathophysiological pathway leading to a poor TR-associated prognosis.[1,5] Although timely correction of severe TR has been shown to improve functional capacity, hemodynamics, and clinical outcomes,[4,6–8] delaying surgery may result in persistent RV dysfunction,[9] even with percutaneous or surgical correction of severe TR, and subsequently lead to venous congestion, organ damage, and poor clinical outcomes, similar to those observed in mitral regurgitation.[1,3–5,8] Previous studies have consistently demonstrated that RV systolic function is an important determinant of postoperative outcomes.[1,3–6,8,10] Although preoperative conventional echocardiography-based RV assessments have been used,[4,7] echocardiographic assessment of RV systolic function has long been clinically challenging and technically difficult because of the complex geometry of the RV.

Myocardial strain measurement using speckle tracking echocardiography is a well-established and reproducible method that is used to reflect the systolic function of the ventricles. Preoperative LV global longitudinal strain was recently shown to be helpful for predicting postoperative outcomes and may guide the optimal surgical timing in patients with severe mitral regurgitation.[11,12] Although prognostic value of the RV longitudinal strain was demonstrated in patients with ischemic heart disease[13] and pulmonary hypertension,[14] it is unclear if RV longitudinal strain plays an important role in patients with severe isolated functional TR requiring surgical correction. Therefore, the purpose of this study was to investigate the prognostic value of RV longitudinal strain and its ability to predict the clinical outcomes of patients undergoing isolated surgery for severe functional TR.

METHODS

The data that support the findings of this study are available from the corresponding author on reasonable request.

Study Subjects

Between January 2005 and April 2019, consecutive patients undergoing isolated corrective surgery for severe functional TR were prospectively enrolled from 2 tertiary centers. We systematically excluded patients with primary TR based on imaging, surgical, and/or pathological findings. All patients satisfied the following criteria for severe TR on preoperative echocardiography[4–6,15–17]: (1) a TR jet area >30% of the right atrial area, (2) vena contracta width >7 mm, and (3) systolic flow reversal in the hepatic veins. Patients who underwent index echocardiography before 2005 were excluded because digitized echocardiographic images were unavailable (n=23). We also excluded patients with severe TR secondary to LV failure with reduced ejection fraction (defined as LV ejection fraction ≤45%) or severe pulmonary hypertension (defined as systolic pulmonary artery pressure ≥70 mm Hg),[18,19] and those with coronary artery disease that required intervention based on preoperative coronary angiography. Only patients with isolated severe functional TR as a single hemodynamically significant lesion were included, and patients with significant left-sided valve disease necessitating concomitant surgical correction were excluded. A total of 115 patients with severe isolated functional TR were included in the final analysis. The study protocol was approved by the institutional review boards of both centers. Informed consent was waived because of the retrospective nature of the study.

Data Collection and Outcomes

Clinical data, including the preoperative and postoperative New York Heart Association (NYHA) functional class, were collected. Preoperative blood test results were obtained, and the glomerular filtration rate was estimated using the Chronic Kidney Disease–Epidemiology Collaboration equation. Cardiac operative risk was estimated using European System for Cardiac Operative Risk Evaluation (EuroSCORE) II.[20]

The index date was defined as the day when TR surgery was performed. Echocardiography was performed a median of 12 days (interquartile range [IQR], 4–39 days) before the surgery. The primary end point was a composite of major postoperative cardiac events, which was defined by cardiac death or unplanned readmission attributable to cardiovascular causes within 5 years. Data on all-cause death and cardiac death during the postoperative follow-up were collected. Operative mortality, defined as death within 30 days of the surgery or before hospital discharge, was assessed separately. Unplanned readmission attributable to cardiovascular causes was defined as readmission attributable to heart failure, coronary artery disease, stroke, infective endocarditis at the repaired or prosthetic tricuspid valve (TV), or arrhythmia.

Patients were followed up until they reached the primary end point, were lost to follow-up or death, or until 5 years after surgery. Outcomes were assessed by thorough review of medical records, and mortality was confirmed using the nationwide official data on death certification provided by the National Statistical Office of Korea. Telephone interviews were systematically performed in a blinded manner by one trained research nurse to monitor the development of clinical events in patients who did not return to the clinic.

Conventional Echocardiography

Comprehensive echocardiographic examination was performed before surgery in all patients with commercially available equipment (General Electric Healthcare, Milwaukee, WI; Philips, Bothell, WA; and Siemens, Erlangen, Germany). LV end-systolic/end-diastolic dimensions, LV end-diastolic interventricular septal/posterior wall thickness, and LV ejection fraction were measured according to the guidelines.[21] The vena contracta width was measured at the narrowest portion of the tricuspid regurgitant jet from the zoomed apical 4-chamber view.[16] RV end-diastolic area and RV end-systolic area (RV-ESA) were obtained in the RV-focused apical 4-chamber view, and RV fractional area change (RV-FAC) was calculated as 100×(RV end-diastolic area−RV-ESA)/RV end-diastolic area.[21] Pulmonary artery systolic pressure was estimated from the peak TR velocity using the Bernoulli equation, $4v^2$+right atrial pressure.[22] The maximum diameter of the inferior vena cava and its respiratory variation were measured at 1 to 2 cm from the junction with the right atrium in the subcostal view. The percentage decrease in the inferior vena cava diameter was used to estimate mean right atrial pressure.[21,22] Echocardiographic measurements were averaged for 3 consecutive heart beats in sinus rhythm and for 5 in atrial fibrillation.

RV Longitudinal Strain Measurement

All digitized echocardiographic images were sent to a core laboratory, and RV longitudinal strain was measured using vendor-independent 2-dimensional Cardiac Performance Analysis software (TomTec Imaging System, Munich, Germany) by one experienced sonographer blinded to patient clinical information. In brief, the endocardial border of the RV was manually traced on the end-systolic frame in an RV-focused apical 4-chamber view, with end systole defined as the smallest RV volume observed during the cardiac cycle. The software tracks speckles along the RV endocardial border and myocardium throughout the cardiac cycle.[23] RV free-wall longitudinal strain (RVFWSL) was calculated at the RV free wall, which was used as the main measure for RV longitudinal strain, according to the guidelines.[24] Also, RV 4-chamber strain (including the ventricular septum) (RV4CSL) was calculated at the total RV wall that includes the ventricular septum and RV free wall. Because longitudinal strain values are negative by definition, we used absolute values for a simpler comparison throughout the article, with "lower" or "worse" values denoting smaller absolute strain values.

Measurement Reproducibility

Intraobserver and interobserver variabilities for RVFWSL and RV4CSL measurements were assessed in 30 randomly selected patients. To determine intraobserver variability, the same observer, who was blinded to the former results, repeated RVFWSL and RV4CSL measurements for each selected patient at a separate time point. To determine interobserver variability, another experienced sonographer independently measured RVFWSL and RV4CSL while blinded to the previous results.

Statistical Analysis

Continuous variables were presented as mean±SD, or as median (IQR) if normality assumption was rejected by the Shapiro-Wilk test. Categorical variables were presented as numbers and percentages. Comparisons of continuous data were made using the Student *t* test or Mann-Whitney *U* test. Categorical data were compared using the χ^2 test or the Fisher exact test. For statistical comparison, NYHA class was divided into 2 groups (NYHA class I and II versus NYHA class III and IV) and compared before and after surgery using the McNemar test. To ascertain the optimal cutoff value of RVFWSL and RV4CSL for the clinical end point, receiver operating characteristic curve analysis was performed on the basis of the Youden index,[25] and was confirmed using spline regression curves. Kaplan-Meier survival curves for the study end point, according to the RVFWSL and RV4CSL cutoff values, were constructed and compared using the log-rank test. After checking the proportional hazards assumption, Cox regression analyses were performed to assess predictors of the study end point. EuroSCORE II and other significant clinical variables on univariate Cox regression were incorporated into the multivariable models. The predictive value of echocardiographic parameters of RV systolic function, including RV-ESA, RV-FAC, RVFWSL, and RV4CSL, were assessed with multivariable adjustment for clinical variables. Because they are physiologically associated with one another, the RV-ESA, RV-FAC, and RV longitudinal strain values were not simultaneously entered into the same multivariable model. The incremental values of RV echocardiographic parameters for predicting the primary end point were assessed by exploring changes in the global χ^2 values in the sequentially constructed multivariable models, starting with the clinical model, including EuroSCORE II and hemoglobin levels. The performance of each survival model was statistically compared using net reclassification improvement and integrated discrimination improvement. All *P* values were 2 sided, and $P<0.05$ was considered statistically significant. All statistical analyses were performed using R version 3.6.1 software (R Development Core Team, Vienna, Austria) with "rcompanion," "pROC," "survminer," and "survNRI" packages.

RESULTS

Baseline Characteristics

Of 115 patients (mean age, 62.3±9.9 years), 88 (76.5%) were women. Seventy-two patients (62.6%) had previously undergone valve surgery; 16 of these had previously undergone concomitant tricuspid annuloplasty. The mean length of time between the operations was 17.0±6.3 years. For the index TR surgery, 84 patients (73.0%) received tricuspid valve replacement, whereas 31 (27.0%) received tricuspid valve repair. Combined maze operation was performed in 40 patients (34.8%).

Patients were followed up for 5 years after the index TR surgery, and 40 patients (34.8%) reached the primary end point during 333 person-years of follow-up. There were 11 cardiac deaths and 34 cases of unplanned readmission attributable to cardiovascular causes. Five patients experienced both hospitalization and cardiac death, in whom the first event (ie, hospitalization) was included in the primary end point analysis.

There were no significant differences in age, sex, traditional cardiovascular risk factors, atrial fibrillation, previous cardiac surgery and its type, and the index TR surgery type between patients who did and did not reach the primary end point (Table 1). However, patients reaching the primary end point had a lower hemoglobin level, lower estimated glomerular filtration rate, and higher EuroSCORE II.

Echocardiographic parameters are summarized in Table 2. Patients who reached the primary end point tended to have worse RV longitudinal strain values compared with those who did not (24.8% versus 26.5% for RVFWSL [P=0.051]; 21.8% versus 23.6% for RV4CSL [P=0.051]). The RV-FAC, RV-ESA, vena contracta width, LV ejection fraction, and pulmonary pressures were not different between the groups (Table 2).

Outcomes

All-cause and cardiac mortality during the follow-up were 14.8% (n=17) and 9.6% (n=11), respectively. Specific causes of cardiac death included heart failure in 6 patients, documented ventricular fibrillation in 1 patient, and sudden cardiac death in 4 patients. Causes of noncardiac death included postoperative hypoxic brain damage, subdural hematoma, and infection. Operative mortality was 5.2% (n=6); 4 of these patients experienced cardiac death, but no patient died during the surgery. Unplanned readmission attributable to cardiovascular causes was attributable to heart failure in 23 patients, stroke in 4 patients, infective endocarditis in 1 patient, and arrhythmia in 6 patients.

The median lengths of intensive care unit and hospital stay were 5 days (IQR, 2.0–6.5 days) and 22 days (IQR, 15.0–31.5 days), respectively.

The NYHA functional class 6 months after discharge was available in 108 patients, excluding those who died within 6 months (n=7). Significant improvements in the functional capacity were observed after surgery (Figure 1); ie, the proportion of NYHA class III/IV was dramatically decreased after TR surgery (from 48.7% [n=56] to 4.6% [n=5]). More specifically, the NYHA class improved in 88.0% (n=95), remained the same in 10.2% (n=11), and worsened in 1.8% (n=2). Postoperatively, only 5 patients (4.6%) had NYHA class III dyspnea, whereas the rest (95.4%) had NYHA class I or II dyspnea (Figure S1).

Prognostic Impact of RV Longitudinal Strain

The best cutoff value with the highest Youden index on the receiver operating characteristic curve

Table 1. Baseline Clinical Characteristics, According to the Primary End Point

Characteristic	Primary End Point (+) (n=40)	Primary End Point (–) (n=75)	*P* Value
Demographics			
Age, y	63.4±9.9	61.8±9.9	0.421
Female sex	28 (70.0)	60 (80.0)	0.330
Body mass index, kg/m^2	22.0±3.6	23.2±3.2	0.083
Preoperative NYHA functional class			0.106
Class I	2 (5.0)	1 (1.3)	
Class II	14 (35.0)	42 (56.0)	
Class III	22 (55.0)	31 (41.3)	
Class IV	2 (5.0)	1 (1.3)	
Cardiovascular risk factors			
EuroSCORE II, %	3.7 (2.5–5.5)	3.2 (1.6–4.0)	0.028
Hypertension	8 (20.0)	20 (26.7)	0.572
Diabetes mellitus	8 (20.0)	11 (14.7)	0.638
Chronic kidney disease	3 (7.5)	5 (6.7)	0.999
Previous stroke	0 (0.0)	4 (5.3)	0.341
Atrial fibrillation	31 (77.5)	68 (90.7)	0.097
Previous cardiac surgery	29 (72.5)	43 (57.3)	0.162
Mitral valve surgery	27 (67.5)	45 (60.0)	0.556
Aortic valve surgery	10 (25.0)	15 (20.0)	0.703
Tricuspid annuloplasty	7 (17.5)	9 (12.0)	0.597
Maze operation	3 (7.5)	2 (2.7)	0.465
Type of index TR surgery			0.752
Tricuspid valve replacement	28 (70.0)	56 (74.7)	
Mechanical valve	5 (12.5)	14 (18.7)	
Bioprosthetic valve	23 (57.5)	42 (56.0)	
Tricuspid valve repair	12 (30.0)	19 (25.3)	
Combined Maze operation	12 (30.0)	28 (37.3)	0.561
Major laboratory findings			
Hemoglobin, g/dL	12.0±1.9	12.6±1.5	0.049
Platelet, ×10^6/mL	152.5 (106.5–209.0)	147.0 (107.5–191.0)	0.653
Total protein, mg/dL	7.3 (6.6–7.6)	7.0 (6.3–7.7)	0.448
Albumin, mg/dL	4.1 (3.6–4.4)	4.1 (3.6–4.4)	0.895
Total cholesterol, mg/dL	138.0 (116.0–172.0)	154.0 (138.5–173.0)	0.145
GFR, mL/min per 1.73 m^2	65.6 (49.4–78.2)	74.2 (64.9–85.5)	0.011
Preoperative medications			
Antiplatelet	4 (10.0)	6 (8.0)	0.988
RAS blocker	7 (25.9)	20 (74.1)	0.382
β-Blocker	2 (5.0)	15 (20.0)	0.060
Aldosterone receptor blocker	20 (50.0)	42 (56.0)	0.676
Loop diuretics	26 (65.0)	49 (65.3)	0.999
Digoxin	17 (42.5)	37 (49.3)	0.615
Amiodarone	2 (5.0)	7 (9.3)	0.646
Anticoagulant	24 (60.0)	50 (66.7)	0.612

Categorical variables are presented as the number (percentage). Continuous variables are presented as mean±SD or median (interquartile range), as appropriate. EuroSCORE indicates European System for Cardiac Operative Risk Evaluation; GFR, estimated glomerular filtration rate (by Chronic Kidney Disease–Epidemiology Collaboration equation); NYHA, New York Heart Association; RAS, renin-angiotensin system; and TR, tricuspid regurgitation.

Table 2. Baseline Echocardiographic Parameters, According to the Primary End Point

Parameter	Primary End Point (+) (n=40)	Primary End Point (–) (n=75)	*P* Value
RV end-diastolic area, cm^2	30.6±6.9	30.2±6.8	0.787
RV end-systolic area, cm^2	17.3±4.6	17.0±4.1	0.763
RV fractional area change, %	43.2±9.2	43.0±9.6	0.889
Tricuspid annulus diameter, mm	48.0 (42.0–55.0)	48.0 (41.5–53.0)	0.526
LV end-systolic dimension, mm	31.0 (27.5–34.0)	32.0 (27.0–35.0)	0.853
LV end-diastolic dimension, mm	47.8±6.8	46.9±7.3	0.536
LV ejection fraction, %	56.4±7.7	58.1±7.2	0.253
Estimated PA systolic pressure, mm Hg	38.0 (32.5–42.0)	36.0 (32.0–41.0)	0.531
IVC diameter			
Expiratory, mm	26.9±5.5	26.1±6.2	0.513
Collapse, %	66.6 (52.7–75.5)	66.7 (54.4–77.8)	0.810
Vena contracta width, mm	9.4 (8.6–11.5)	10.4 (8.4–11.6)	0.487
RVFWSL, %	24.8±5.0	26.5±4.3	0.051
RV4CSL, %	21.8±4.9	23.6±4.3	0.051

Continuous variables are presented as mean±SD or median (interquartile range), as appropriate. IVC indicates inferior vena cava; LV, left ventricular; PA, pulmonary artery; RV, right ventricular; RV4CSL, RV 4-chamber strain (including the ventricular septum); and RVFWSL, RV free-wall longitudinal strain.

was 24% (sensitivity, 52.5%; specificity, 75.7%) for RVFWSL and 21% (sensitivity, 50.0%; specificity, 77.0%) for RV4CSL. Spline regression curves confirmed that these cutoff values were associated with an increased risk of reaching the primary outcome (Figure S2).

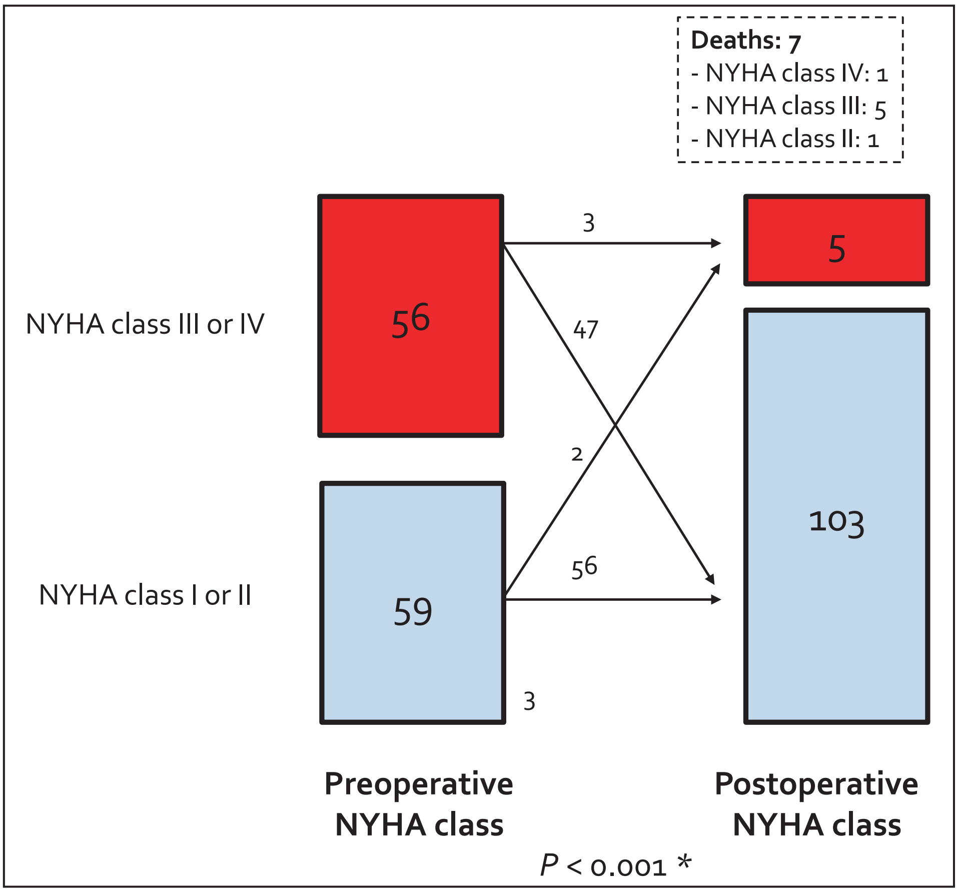

Figure 1. Changes in the New York Heart Association (NYHA) functional class in patients who completed the 6-month clinical follow-up.
For statistical analysis, patients were divided into 2 groups (ie, NYHA class I and II vs NYHA class III and IV). *Using the McNemar test.

Kaplan-Meier event-free survival curves showed significant differences in the primary end point, with the RVFWSL cutoff of 24% and the RV4CSL cutoff of 21% (Figure 2). Event-free survival curves started to separate during the early postoperative period and continued to diverge throughout the follow-up.

Univariate Cox regression analysis with clinical and echocardiographic parameters is shown in Table S1. The cutoff values of RV-ESA ≥20 cm^2 and RV-FAC <35% were selected according to the previous study.[4] Univariate analysis revealed that higher EuroSCORE II, lower estimated glomerular filtration rate, lower hemoglobin levels, higher NYHA class, and worse RVFWSL and RV4CSL were significantly associated with the primary end point, whereas RV-ESA, RV-FAC, LV ejection fraction, and pulmonary artery systolic pressure were not. In the multivariable analysis, the model 1 was constructed using significant clinical factors on univariable analysis (ie, the EuroSCORE II and hemoglobin level). Thereafter, analyses were performed by serially adding echocardiographic parameters reflecting RV systolic function to model 1 (Table 3). RV-ESA and RV-FAC were not associated with the primary end point in multivariable analysis (models 2 and 3 in Table 3, respectively). RVFWSL <24%, however, was independently associated with the primary end point in multivariable analysis (model 4) (hazard ratio [HR], 2.30; 95% CI, 1.22–4.36; P=0.011). In addition, RV4CSL <21% was independently associated with the primary end point (model 5) (HR, 2.36; 95% CI, 1.25–4.47; P=0.008).

Incremental Value of RV Longitudinal Strain for Predicting Clinical Events

The incremental value of RV longitudinal strain to predict the primary end point over clinical risk factors was assessed by sequential Cox analysis (Figure 3). Compared with the clinical model (model 1), adding RV-ESA or RV-FAC did not significantly increase the global χ^2 values. However, adding RVFWSL or RV4CSL significantly improved the global χ^2 values (P=0.012 and P=0.010, respectively). The addition of RVFWSL to model 1 also increased the C-statistic (from 0.619 to 0.692) and showed incremental predictive value for the primary end point with a positive overall continuous net reclassification index of 0.52 (95% CI, 0.16–0.89; P=0.005) and a positive integrated discrimination index of 0.060 (95% CI, 0.016–0.105; P=0.008). Similar data were observed for RV4CSL (Table 4).

Measurement Reproducibility

Analysis of intraobserver variability of the RV longitudinal strain measurement revealed excellent correlations between the repeated measurements. Intraclass correlation coefficients for RVFWSL and RV4CSL were 0.98 (95% CI, 0.96–0.99) and 0.94 (95% CI, 0.89–0.97), respectively. There was also a good correlation between the measurements by 2 independent observers for interobserver variability; intraclass correlation coefficients for RVFWSL and RV4CSL were 0.88 (95% CI, 0.78–0.93) and 0.90 (95% CI, 0.82–0.95), respectively. Bland-Altman plots for interobserver and intraobserver variabilities

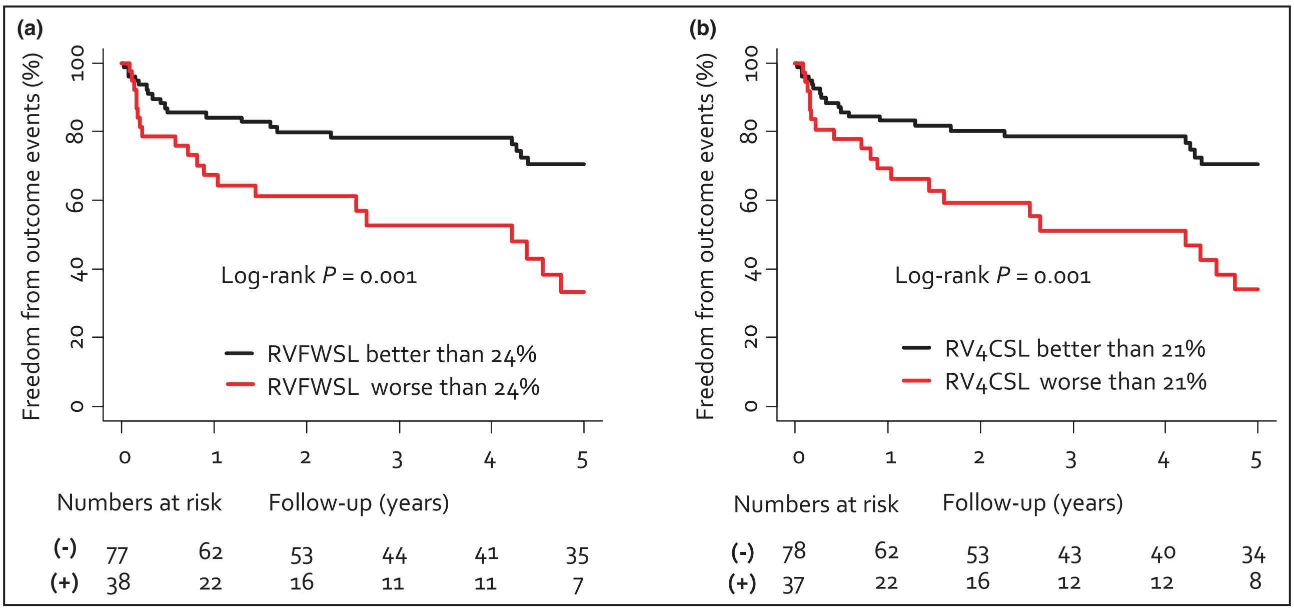

Figure 2. Kaplan-Meier survival curves for the primary end point, according to the right ventricular (RV) longitudinal strain. The primary end point of cardiac death or unplanned readmission attributable to cardiovascular causes according to RV free-wall longitudinal strain (RVFWSL) cutoff value of 24% (**A**) and RV 4-chamber strain (including the ventricular septum) (RV4CSL) cutoff value of 21% (**B**).

Table 3. Multivariable Cox Models for the Prediction of the Primary End Point, Including RV Parameters

Variables	Model 1*		Model 2 (Model 1+RV-ESA)		Model 3 (Model 1+RV-FAC)	
	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
EuroSCORE II	1.14 (1.00–1.31)	0.046	1.14 (1.00–1.30)	0.045	1.14 (0.99–1.31)	0.056
Hemoglobin, g/dL	0.90 (0.82–0.99)	0.035	0.90 (0.82–1.00)	0.040	0.90 (0.82–0.99)	0.035
RV-ESA ≥20 cm^2			1.13 (0.53–2.41)	0.750		
RV-FAC <35%					1.07 (0.46–2.49)	0.884

Variables	Model 4 (Model 1+RVFLSW)		Model 5 (Model 1+RV4CSL)	
	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
EuroSCORE II	1.09 (0.94–1.26)	0.251	1.09 (0.94–1.26)	0.238
Hemoglobin, g/dL	0.84 (0.69–1.01)	0.062	0.83 (0.69–1.00)	0.053
RVFWSL <24%	2.30 (1.22–4.36)	0.011		
RV4CSL <21%			2.36 (1.25–4.47)	0.008

EuroSCORE indicates European System for Cardiac Operative Risk Evaluation; HR, hazard ratio; RV, right ventricular; RV4CSL, RV 4-chamber strain (including the ventricular septum); RV-ESA, RV end-systolic area; RV-FAC, RV fractional area change; and RVFWSL, RV free-wall longitudinal strain.

*Multivariable clinical model includes EuroSCORE II and other significant clinical variables on univariate analysis. For each multivariable model 2 to 5, echocardiographic parameters of RV function were added to the model 1.

of RVFWSL and RV4CSL measurement are shown in Figures S3 and S4.

DISCUSSION

The present study is the first to demonstrate the prognostic value of preoperative RV longitudinal strain in patients undergoing isolated surgery for severe functional TR. The main findings are summarized as follows. First, isolated surgery for severe functional TR resulted in significant improvement in functional capacity (of at least one grade) in 95 patients (88%). However, the operative mortality was still high (5.2%), and the 5-year all-cause and cardiac mortality rates could not be ignored (14.8% and 9.6%, respectively). Second, preoperative RV longitudinal strain was independently associated with the primary end point after

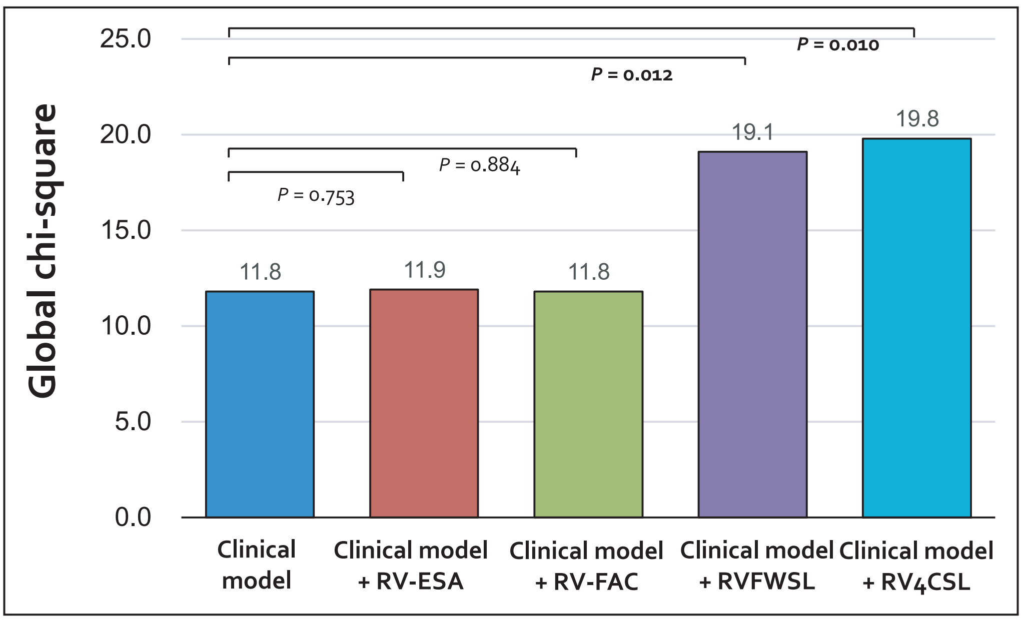

Figure 3. Incremental value of the right ventricular (RV) longitudinal strain over clinical variables for predicting the primary end point by global χ^2 changes in sequential Cox analysis.
The clinical model included European System for Cardiac Operative Risk Evaluation and hemoglobin level. RV4CSL indicates RV 4-chamber strain (including the ventricular septum); RV-ESA, RV end-systolic area; RV-FAC, RV fractional area change; and RVFWSL, RV free-wall longitudinal strain.

Table 4. Incremental Value of RV Echocardiographic Parameters to Clinical Variables for Predicting the Primary End Point

Variable	C-Statistic	Net Reclassification Index		Integrated Discrimination Improvement	
	95% CI	95% CI	*P* Value for Difference*	95% CI	*P* Value for Difference*
Clinical model (model 1)†	0.619 (0.509–0.728)				
Clinical model†+RV-ESA ≥20 cm^2	0.616 (0.506–0.727)		0.886		0.852
Clinical model†+RV-FAC <35%	0.611 (0.501–0.721)		0.876		0.523
Clinical model†+RVFWSL <24%	0.692 (0.582–0.801)	0.52 (0.16–0.89)	0.005	0.060 (0.016–0.105)	0.008
Clinical model†+RV4CSL <21%	0.699 (0.592–0.807)	0.55 (0.18–0.91)	0.003	0.070 (0.021–0.118)	0.005

RV indicates right ventricular; RV4CSL, RV 4-chamber strain (including the ventricular septum); RV-ESA, RV end-systolic area; RV-FAC, RV fractional area change; and RVFWSL, RV free-wall longitudinal strain.
*Compared with model 1.
†Clinical model includes European System for Cardiac Operative Risk Evaluation II and hemoglobin level.

adjusting for clinical variables and showed an incremental prognostic value over clinical variables for the primary end point. These findings suggest that preoperative RV longitudinal strain could be a useful imaging marker for optimizing the timing of isolated surgery for severe functional TR.

Prognosticators of Isolated TR Surgery

Although the prevalence of moderate or greater TR is higher than previously thought and on the rise, only 2.6% of these patients receive corrective surgery.[26] Isolated surgery for significant TR is even less frequently performed, accounting for only 20% of total TR surgeries.[27] Taking a passive stance in isolated TR surgery is likely caused by concerns of high in-hospital mortality (8%–10% reported) and uncertainty of long-term outcomes.[28,29]

Isolated severe TR leads to progressive RV failure and reduces life expectancy[10]; however, timely intervention can induce RV reverse remodeling.[6] According to a recent study, the median length of time from diagnosis to TR surgery was up to 13.5 months (IQR, 4.2–31.7 months) in patients undergoing isolated surgery for severe TR,[29] suggesting delayed surgical referral. Survival rates may decline by delaying intervention; thus, it is plausible to conclude that determining the optimal surgical timing for isolated severe TR surgery before the development of RV dysfunction and end-organ damage is crucial for better clinical outcomes.

Previous studies have demonstrated that clinical factors, such as age, male sex, liver cirrhosis, lower glomerular filtration rate, lower hemoglobin levels, and the presence of severe symptoms, like dyspnea, are associated with adverse outcomes after TR surgery.[4,8,30] In addition, preoperative RV dimensions and systolic function, determined by echocardiography or cardiac magnetic resonance (CMR), were associated with postoperative outcomes. Analogous to LV systolic function in patients with severe mitral regurgitation, RV systolic function in patients with severe TR seems preserved at an earlier stage because of favorable loading conditions.[4,5] Once RV systolic dysfunction is objectively observed on echocardiography or CMR, surgical interventions cannot completely reverse RV systolic function because of irreversible damage to the RV myocardium.[28] However, the current guidelines do not recommend quantitative assessment of RV systolic function by conventional echocardiography for technical reasons.[31] Recently, the LV global longitudinal strain showed some promising data for guiding surgical referral in patients with severe mitral regurgitation.[11,12] A similar concept could be applied to RV longitudinal strain in patients with TR. We herein demonstrated that RVFWSL, with a cutoff of 24%, can predict long-term postoperative outcomes and aid in optimizing the timing of isolated surgery for severe functional TR (Figure 4). Furthermore, the separation of event-free survival curves began from the early postoperative period, emphasizing the role of RV longitudinal strain as an early and late prognosticator.

RV Longitudinal Strain for Measuring RV Systolic Function and Its Prognostic Value

RV longitudinal strain has some advantages over conventional echocardiographic indexes for RV systolic function. First, RV longitudinal strain is measured by tracking the location of speckles on sequential images; thus, it is angle independent.[32] Second, as demonstrated in the present study, RV longitudinal strain showed an additive prognostic value over clinical variables. Third, RV longitudinal strain correlated well with the CMR-derived RV ejection fraction, with lower interobserver and intraobserver variabilities.[33] Although CMR is the gold standard for RV systolic function measurement and provides incremental prognostic information,[5] CMR is an expensive modality and its use is limited in patients with implantable electronic devices, claustrophobia, or severe dyspnea.[5] However,

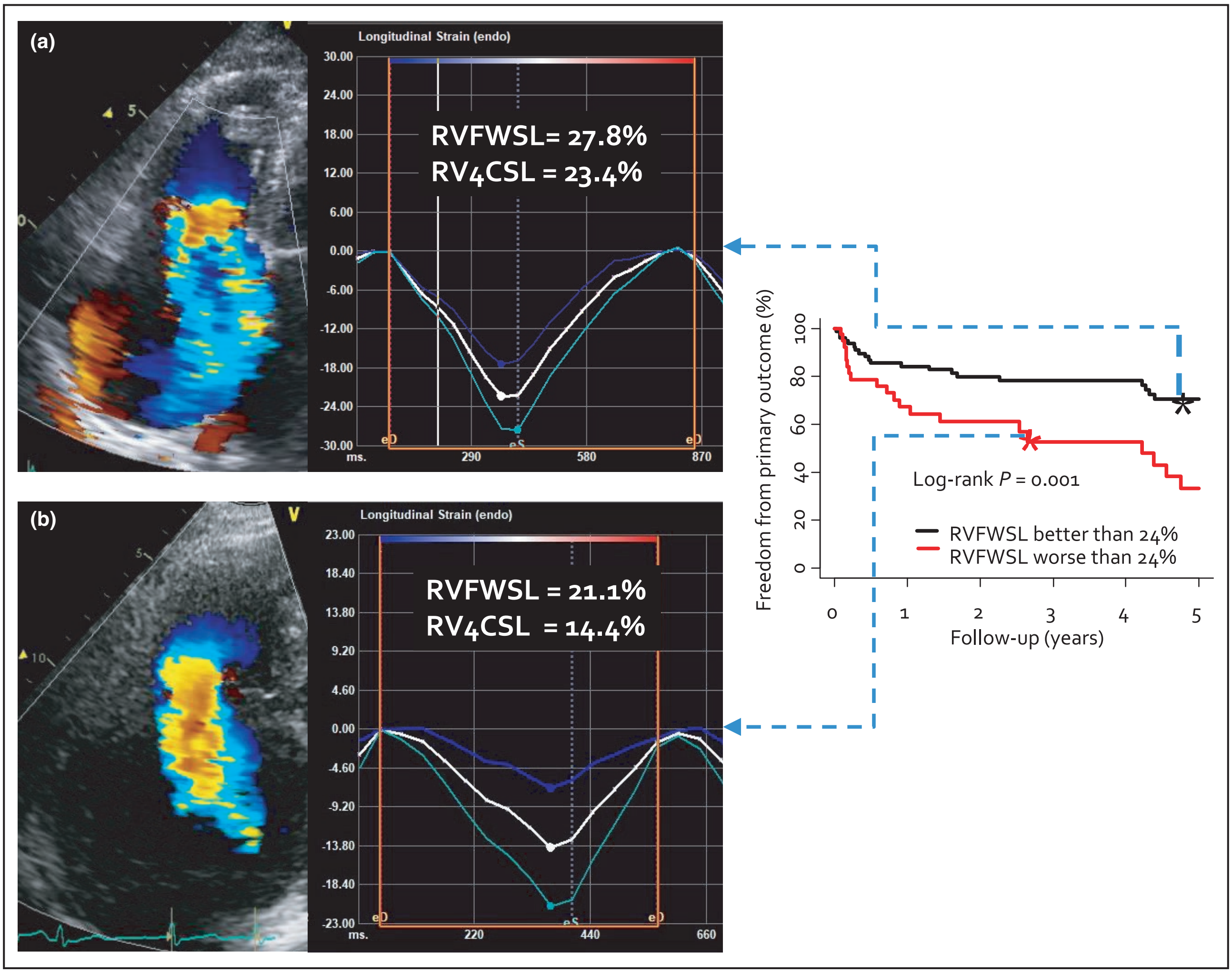

Figure 4. Two representative examples.
A, A 71-year-old woman with a right ventricular free-wall longitudinal strain (RVFWSL) of 27.8% remained event free. **B**, A 50-year-old man with an RVFWSL of 21.1% was readmitted because of heart failure 3 years after surgery. RV4CSL indicates right ventricular 4-chamber strain (including the ventricular septum). Endo indicates endocardium.

echocardiographic RV longitudinal strain can avoid these limitations.

A previous study by Prihadi et al[34] also demonstrated that RVFWSL was a sensitive marker of RV systolic dysfunction and had incremental prognostic value to RV-FAC and tricuspid annular plane systolic excursion for predicting survival in patients with moderate to severe functional TR who were mostly followed up without TR surgery. To note, the RV longitudinal strain values in the earlier study were lower compared with those in the present study (mean, 14.4% versus 25.9%), although a similar cutoff value for RV dysfunction was used (RVFWSL <23%). The difference in the baseline characteristics of the study population may contribute. Specifically, the earlier study included patients with functional TR of moderate or severe grade with or without left-sided valve disease. Those patients were older, had lower LV ejection fractions, and had worse RV systolic function. Apart from the differences in baseline characteristics, different software programs used for strain measurement might contribute to differences in RV longitudinal strain results.

Limitations

A few limitations should be acknowledged. First, this was a retrospective study, and some bias may remain despite adjustments. Second, the sample size was relatively small (n=115); this was attributable to strict inclusion criteria (ie, patients undergoing “isolated” surgery for severe functional TR). However, this is the first study to investigate the decisive role of RV longitudinal strain in optimizing the timing of isolated surgery for severe functional TR, with careful long-term follow-up in all patients. Third, patients without digitized echocardiographic images (n=23) were excluded, which might have introduced selection bias. Fourth, there may be a concern about intervendor differences in RV longitudinal strain measurements.[35] To avoid this issue, we used a single, vendor-independent, commercialized software to measure the RV longitudinal strain. Finally, the cutoff value for RVFWSL and RV4CSL may be variable, depending on population of interest and the strain analysis program used; external validation is thus required to confirm the cutoff value of the present study.

CONCLUSIONS

RVFWSL with a cutoff value of 24% is independently associated with postoperative cardiac death and unplanned readmission attributable to cardiovascular causes in patients undergoing isolated surgery for severe functional TR. Impaired RV systolic function, as assessed by RVFWSL and RV4CSL, has incremental prognostic value to a clinical variables–based multivariable model. Incorporating preoperative RV longitudinal strain into clinical practice may be helpful for predicting postoperative outcomes and for optimizing surgical timing in severe functional TR.

ARTICLE INFORMATION

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Supplementary Material

Table S1
Figures S1–S4

REFERENCES

1. Kim HK, Lee SP, Kim YJ, Sohn DW. Tricuspid regurgitation: clinical importance and its optimal surgical timing. *J Cardiovasc Ultrasound*. 2013;21:1–9. DOI: 10.4250/jcu.2013.21.1.1.
2. Wang N, Fulcher J, Abeysuriya N, McGrady M, Wilcox I, Celermajer D, Lal S. Tricuspid regurgitation is associated with increased mortality independent of pulmonary pressures and right heart failure: a systematic review and meta-analysis. *Eur Heart J*. 2019;40:476–484. DOI: 10.1093/eurheartj/ehy641.
3. Dietz MF, Prihadi EA, van der Bijl P, Goedemans L, Mertens BJA, Gursoy E, van Genderen OS, Ajmone Marsan N, Delgado V, Bax JJ. Prognostic implications of right ventricular remodeling and function in patients with significant secondary tricuspid regurgitation. *Circulation*. 2019;140:836–845. DOI: 10.1161/CIRCULATIONAHA.119.039630.
4. Kim Y-J, Kwon D-A, Kim H-K, Park J-S, Hahn S, Kim K-H, Kim K-B, Sohn D-W, Ahn H, Oh B-H, et al. Determinants of surgical outcome in patients with isolated tricuspid regurgitation. *Circulation*. 2009;120:1672–1678. DOI: 10.1161/CIRCULATIONAHA.109.849448.
5. Park J-B, Kim H-K, Jung J-H, Klem I, Yoon YE, Lee S-P, Park E-A, Hwang H-Y, Lee W, Kim K-H, et al. Prognostic value of cardiac MR imaging for preoperative assessment of patients with severe functional tricuspid regurgitation. *Radiology*. 2016;280:723–734. DOI: 10.1148/radiol.2016151556.
6. Kim H-K, Kim Y-J, Park E-A, Bae J-S, Lee W, Kim K-H, Kim K-B, Sohn D-W, Ahn H, Park J-H, et al. Assessment of haemodynamic effects of surgical correction for severe functional tricuspid regurgitation: cardiac magnetic resonance imaging study. *Eur Heart J*. 2010;31:1520–1528. DOI: 10.1093/eurheartj/ehq063.
7. Kim JH, Kim HK, Lee SP, Kim YJ, Cho GY, Kim KH, Kim KB, Ahn H, Sohn DW. Right ventricular reverse remodeling, but not subjective clinical amelioration, predicts long-term outcome after surgery for isolated severe tricuspid regurgitation. *Circ J*. 2014;78:385–392. DOI: 10.1253/circj.CJ-13-0790.
8. Kim JB, Jung SH, Choo SJ, Chung CH, Lee JW. Surgical outcomes of severe tricuspid regurgitation: predictors of adverse clinical outcomes. *Heart*. 2013;99:181–187. DOI: 10.1136/heartjnl-2012-302856.
9. Fortuni F, Dietz MF, Butcher SC, Prihadi EA, van der Bijl P, Ajmone Marsan N, Delgado V, Bax JJ. Prognostic implications of increased right ventricular wall tension in secondary tricuspid regurgitation. *Am J Cardiol*. 2020;136:131–139. DOI: 10.1016/j.amjcard.2020.09.022.
10. Topilsky Y, Nkomo VT, Vatury O, Michelena HI, Letourneau T, Suri RM, Pislaru S, Park S, Mahoney DW, Biner S, et al. Clinical outcome of isolated tricuspid regurgitation. *JACC Cardiovasc Imaging*. 2014;7:1185–1194. DOI: 10.1016/j.jcmg.2014.07.018.
11. Kim HM, Cho GY, Hwang IC, Choi HM, Park JB, Yoon YE, Kim HK. Myocardial strain in prediction of outcomes after surgery for severe mitral regurgitation. *JACC Cardiovasc Imaging*. 2018;11:1235–1244. DOI: 10.1016/j.jcmg.2018.03.016.
12. Namazi F, van der Bijl P, Hirasawa K, Kamperidis V, van Wijngaarden SE, Mertens B, Leon MB, Hahn RT, Stone GW, Narula J, et al. Prognostic value of left ventricular global longitudinal strain in patients with secondary mitral regurgitation. *J Am Coll Cardiol*. 2020;75:750–758. DOI: 10.1016/j.jacc.2019.12.024.
13. Antoni ML, Scherptong RW, Atary JZ, Boersma E, Holman ER, van der Wall EE, Schalij MJ, Bax JJ. Prognostic value of right ventricular function in patients after acute myocardial infarction treated with primary percutaneous coronary intervention. *Circ Cardiovasc Imaging*. 2010;3:264–271. DOI: 10.1161/CIRCIMAGING.109.914366.
14. Mukherjee M, Mercurio V, Tedford RJ, Shah AA, Hsu S, Mullin CJ, Sato T, Damico R, Kolb TM, Mathai SC, et al. Right ventricular longitudinal strain is diminished in systemic sclerosis compared with idiopathic pulmonary arterial hypertension. *Eur Respir J*. 2017;50:1701436. DOI: 10.1183/13993003.01436-2017.
15. Hahn RT, Thomas JD, Khalique OK, Cavalcante JL, Praz F, Zoghbi WA. Imaging assessment of tricuspid regurgitation severity. *JACC Cardiovasc Imaging*. 2019;12:469–490. DOI: 10.1016/j.jcmg.2018.07.033.
16. Zoghbi WA, Adams D, Bonow RO, Enriquez-Sarano M, Foster E, Grayburn PA, Hahn RT, Han Y, Hung J, Lang RM, 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. DOI: 10.1016/j.echo.2017.01.007.
17. Arsalan M, Walther T, Smith RL II, Grayburn PA. Tricuspid regurgitation diagnosis and treatment. *Eur Heart J*. 2017;38:634–638. DOI: 10.1093/eurheartj/ehv487.
18. Elwing J, Panos RJ. Pulmonary hypertension associated with COPD. *Int J Chron Obstruct Pulmon Dis*. 2008;3:55–70.
19. Hirachan A, Maskey A, Shah RK, Kc B, Shareef M, Roka M, Manandhar R, Sherpa K, Pandey R, Yadav D, et al. Echocardiographic right heart study in patients with chronic obstructive pulmonary disease. *Nepal Heart J*. 2017;14:9–12. DOI: 10.3126/njh.v14i2.18496.
20. Nashef SA, Roques F, Sharples LD, Nilsson J, Smith C, Goldstone AR, Lockowandt U. EuroSCORE II. *Eur J Cardiothorac Surg*. 2012;41:734–745. DOI: 10.1093/ejcts/ezs043.

21. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr*. 2015;28:1–39.e14. DOI: 10.1016/j.echo.2014.10.003.
22. Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K, Solomon SD, Louie EK, Schiller NB. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. *J Am Soc Echocardiogr*. 2010;23:685–713; quiz 786-788. DOI: 10.1016/j.echo.2010.05.010.
23. Lee JH, Park JH. Strain analysis of the right ventricle using two-dimensional echocardiography. *J Cardiovasc Imaging*. 2018;26:111–124. DOI: 10.4250/jcvi.2018.26.e11.
24. Badano LP, Kolias TJ, Muraru D, Abraham TP, Aurigemma G, Edvardsen T, D'Hooge J, Donal E, Fraser AG, Marwick T, et al. Standardization of left atrial, right ventricular, and right atrial deformation imaging using two-dimensional speckle tracking echocardiography: a consensus document of the EACVI/ASE/Industry Task Force to standardize deformation imaging. *Eur Heart J Cardiovasc Imaging*. 2018;19:591–600. DOI: 10.1093/ehjci/jey042.
25. Yin J, Tian L. Joint confidence region estimation for area under ROC curve and Youden index. *Stat Med*. 2014;33:985–1000.
26. Topilsky Y, Maltais S, Medina Inojosa J, Oguz D, Michelena H, Maalouf J, Mahoney DW, Enriquez-Sarano M. Burden of tricuspid regurgitation in patients diagnosed in the community setting. *JACC Cardiovasc Imaging*. 2019;12:433–442. DOI: 10.1016/j.jcmg.2018.06.014.
27. Vassileva CM, Shabosky J, Boley T, Markwell S, Hazelrigg S. Tricuspid valve surgery: the past 10 years from the Nationwide Inpatient Sample (NIS) database. *J Thorac Cardiovasc Surg*. 2012;143:1043–1049. DOI: 10.1016/j.jtcvs.2011.07.004.
28. Fender EA, Zack CJ, Nishimura RA. Isolated tricuspid regurgitation: outcomes and therapeutic interventions. *Heart*. 2018;104:798–806. DOI: 10.1136/heartjnl-2017-311586.
29. Axtell AL, Bhambhani V, Moonsamy P, Healy EW, Picard MH, Sundt TM III, Wasfy JH. Surgery does not improve survival in patients with isolated severe tricuspid regurgitation. *J Am Coll Cardiol*. 2019;74:715–725. DOI: 10.1016/j.jacc.2019.04.028.
30. Topilsky Y, Khanna AD, Oh JK, Nishimura RA, Enriquez-Sarano M, Jeon YB, Sundt TM, Schaff HV, Park SJ. Preoperative factors associated with adverse outcome after tricuspid valve replacement. *Circulation*. 2011;123:1929–1939. DOI: 10.1161/CIRCULATIONAHA.110.991018.
31. Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, Iung B, Lancellotti P, Lansac E, Rodriguez Muñoz D, et al. 2017 ESC/EACTS guidelines for the management of valvular heart disease. *Eur Heart J*. 2017;38:2739–2791. DOI: 10.1093/eurheartj/ehx391.
32. Langeland S, D'Hooge J, Wouters PF, Leather HA, Claus P, Bijnens B, Sutherland GR. Experimental validation of a new ultrasound method for the simultaneous assessment of radial and longitudinal myocardial deformation independent of insonation angle. *Circulation*. 2005;112:2157–2162. DOI: 10.1161/CIRCULATIONAHA.105.554006.
33. Freed BH, Tsang W, Bhave NM, Patel AR, Weinert L, Yamat M, Vicedo BM, Dill K, Mor-Avi V, Gomberg-Maitland M, et al. Right ventricular strain in pulmonary arterial hypertension: a 2D echocardiography and cardiac magnetic resonance study. *Echocardiography*. 2015;32:257–263. DOI: 10.1111/echo.12662.
34. Prihadi EA, van der Bijl P, Dietz M, Abou R, Vollema EM, Marsan NA, Delgado V, Bax JJ. Prognostic implications of right ventricular free wall longitudinal strain in patients with significant functional tricuspid regurgitation. *Circ Cardiovasc Imaging*. 2019;12:e008666. DOI: 10.1161/CIRCIMAGING.118.008666.
35. Farsalinos KE, Daraban AM, Unlu S, Thomas JD, Badano LP, Voigt JU. Head-to-head comparison of global longitudinal strain measurements among nine different vendors: the EACVI/ASE Inter-Vendor Comparison Study. *J Am Soc Echocardiogr*. 2015;28:1171–1181, e1172. DOI: 10.1016/j.echo.2015.06.011.

SUPPLEMENTAL MATERIAL

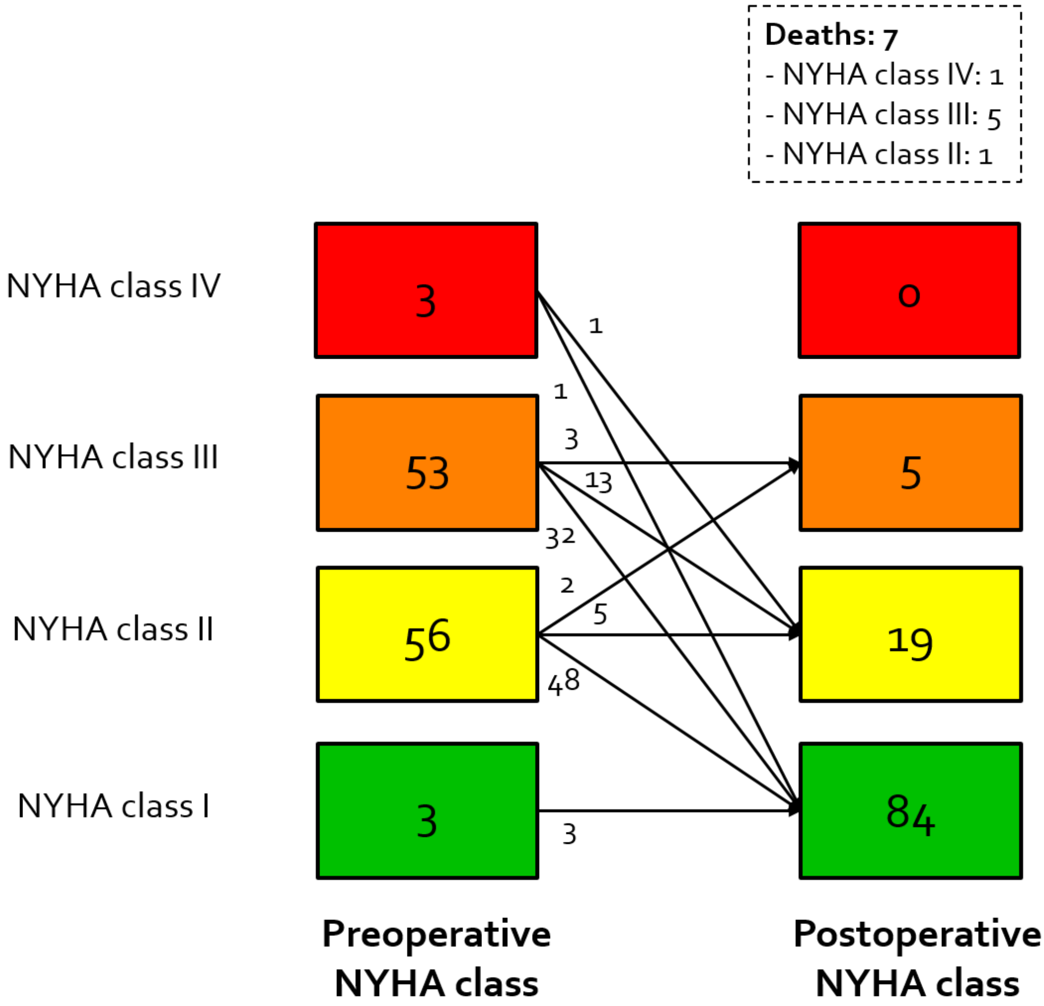
Table S1. Univariate analysis for the prediction of the primary endpoint.

	Univariate analysis	
	HR (95% CI)	***P* value**
Age*	1.16 (0.98–1.37)	0.085
Male sex	1.72 (0.87–3.40)	0.121
Body mass index, kg/m^2	0.90 (0.81–1.01)	0.065
EuroSCORE II	1.19 (1.05-1.35)	**0.008**
Hypertension	0.90 (0.41–1.95)	0.783
Diabetes mellitus	1.52 (0.70–3.33)	0.291
Atrial fibrillation	0.50 (0.24–1.05)	0.069
GFR†	0.89 (0.83–0.96)	**0.002**
Hemoglobin, g/dL	0.77 (0.64–0.93)	**0.006**
NYHA Fc, per class	1.81 (1.05-3.13)	**0.034**
NYHA Fc III-IV	2.01 (1.07-3.79)	**0.031**
LV ejection fraction, %	0.98 (0.94-1.02)	0.349
PASP, mmHg	1.00 (0.96-1.04)	0.996
RV ESA ≥20 cm^2	1.31 (0.62-2.77)	0.475
RV FAC <35%	1.24 (0.55-2.82)	0.602
RVFWSL, %	1.07 (1.00-1.15)	**0.047**
RV4CSL, %	1.07 (1.00-1.14)	**0.043**
RVFWSL <24%	2.68 (1.44-5.00)	**0.002**
RV4CSL <21%	2.66 (1.43-4.96)	**0.002**

* per 5-year increase. † per 5 mL/min/1.73m^2 increase.

HR, hazard ratio; CI, confidence interval; NYHA Fc, New York Heart Association functional class; GFR, estimated glomerular filtration rate; RV, right ventricle; ESA, end-systolic area; FAC, fractional area change; RVFWSL, RV free wall longitudinal strain; RV4CSL, RV 4-chamber strain including the ventricular septum.

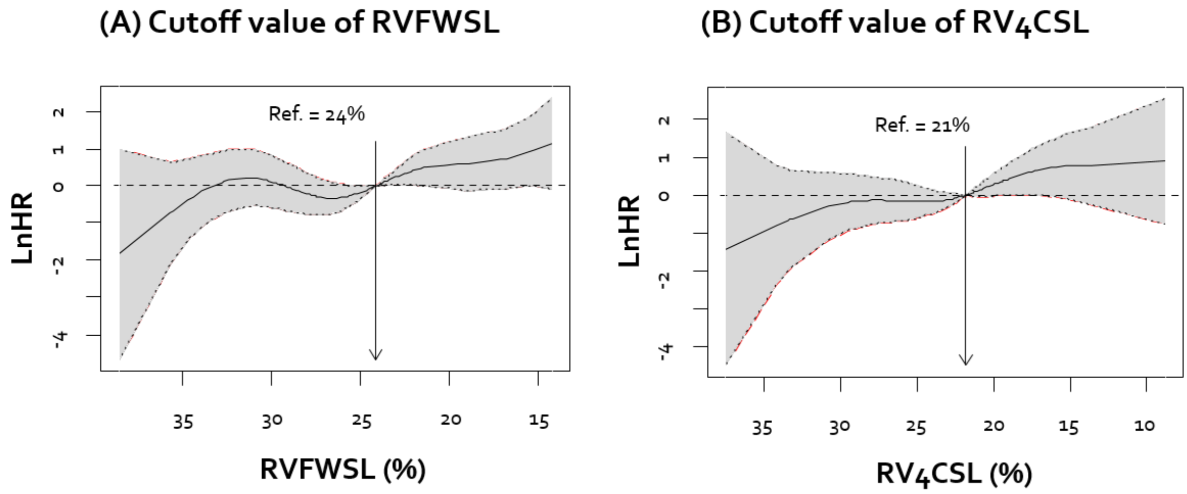
Figure S1. Changes in the NYHA functional class in patients who completed the six-month clinical follow-up.



Values are presented as numbers. Of 115 patients who underwent surgery for isolated severe functional tricuspid regurgitation, 7 died within 6 months, while 108 survived. The preoperative NYHA class of the 7 patients who died were class IV in one, class III in five, and class II in one.

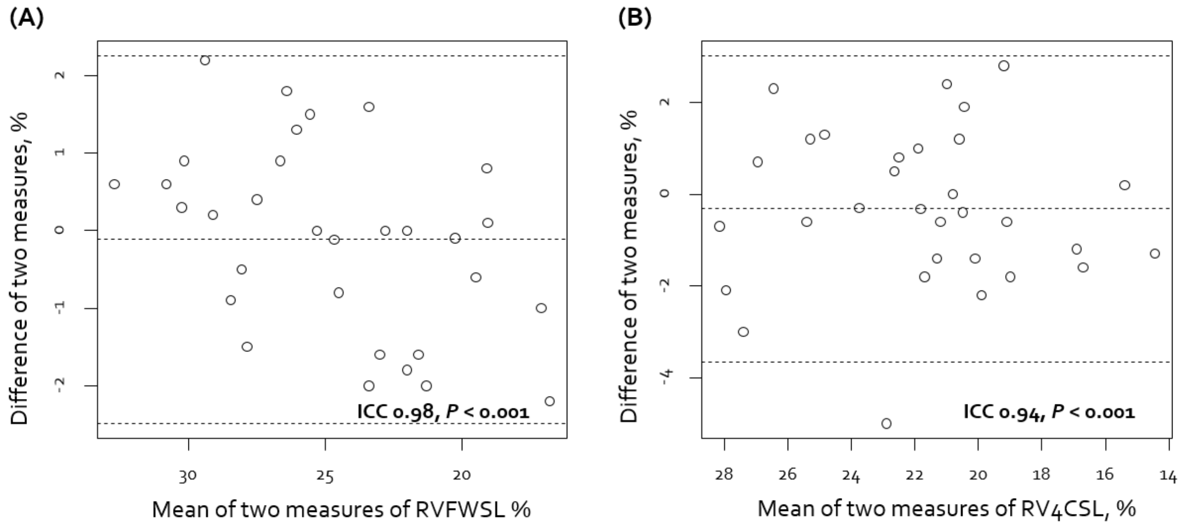
NYHA, New York Heart Association.

Figure S2. Cutoff values of RVFWSL and RV4CSL for the prediction of the primary endpoint.



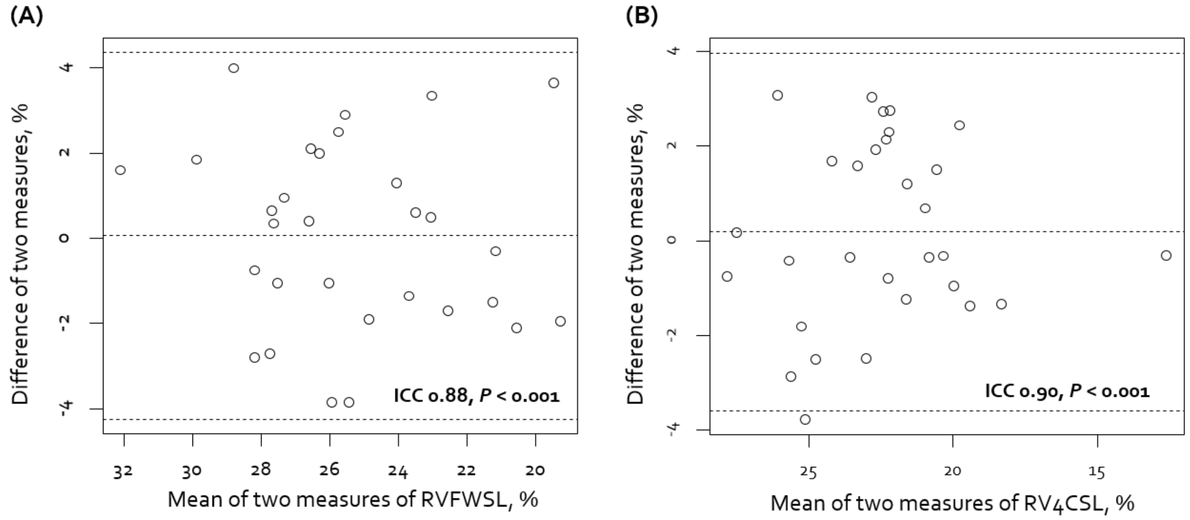
RVFWSL, RV free-wall longitudinal strain; RV4CSL, RV 4-chamber strain (including the ventricular septum).

Figure S3. Bland-Altman plot for comparing intra-observer variability of RV longitudinal strain measurement.



ICC, intra-class correlation coefficient; RVFWSL, RV free-wall longitudinal strain; RV4CSL, RV 4-chamber strain (including the ventricular septum).

Figure S4. Bland-Altman plot for comparing inter-observer variability of RV longitudinal strain measurement.



ICC, intra-class correlation coefficient; RVFWSL, RV free-wall longitudinal strain; RV4CSL, four-chamber strain (including the ventricular septum).