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ORIGINAL RESEARCH

Right Ventricular Dysfunction and Short-Term Outcomes Following Left-Sided Valvular Surgery: An Echocardiographic Study

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BACKGROUND: The prognostic value of echocardiographic evaluation of right ventricular (RV) function in patients undergoing left-sided valvular surgery has not been well described. The objective of this study is to determine the role of broad echocardiographic assessment of RV function in predicting short-term outcomes after valvular surgery.

METHODS AND RESULTS: Preoperative echocardiographic data, perioperative adverse outcomes, and 30-day mortality were analyzed in patients who underwent left-sided valvular surgery from 2006 to 2014. Echocardiographic parameters used to evaluate RV function include RV fractional area change, tricuspid annular plane systolic excursion, systolic movement of the RV lateral wall using tissue Doppler imaging (S'), RV myocardial performance index, and RV dP/dt. Subjects with at least 3 abnormal parameters out of the 5 aforementioned indices were defined as having significant RV dysfunction. The study included 269 patients with valvular surgery (average age: 67±15, 60.6% male, 148 aortic, and 121 mitral). RV dysfunction was found in 53 (19.7%) patients; 30-day mortality occurred in 20 patients (7.5%). Compared with normal RV function, patients with RV dysfunction had higher 30-day mortality (22.6% versus 3.8%; P=0.01) and were at risk for developing multisystem failure/shock (13.2% versus 3.2%; P=0.01). Multivariate analyses showed that preexisting RV dysfunction was the strongest predictor of increased 30-day mortality (odds ratio: 3.5; 95% CI, 1.1–11.1; P<0.05).

CONCLUSIONS: Preoperative RV dysfunction identified by comprehensive echocardiographic assessment is a strong predictor of adverse outcomes following left-sided valvular surgery.

Key Words: echocardiography ■ right ventricle ■ valvular surgery

Right ventricular (RV) function affects the prognosis of patients undergoing valvular cardiac surgery. The development of RV failure represents a significant clinical challenge in the postoperative setting because of associated high morbidity and mortality.[1] Preoperative RV dysfunction (RVD) also predicts postoperative adverse events. Preoperative RV failure correlates with increased mortality in the postoperative period with only 28% of patients surviving at 75 months of follow-up.[2] Similarly, RV ejection fraction (EF) of 20% or less before valvular surgery was strongly associated with late postoperative mortality.[3]

Postoperative outcome is a significant determinant of the surgical candidacy. Currently, a number of risk stratification models are used for estimating the risk for adverse events. The 2 commonly used models, Society of Thoracic Surgeons (STS) and European System for Cardiac Operative Risk Evaluation II surgical

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CLINICAL PERSPECTIVE

What Is New?

- Preoperative right ventricular dysfunction assessed by a composite of echocardiographic variables is independently associated with 3.5-fold increased risk of 30-day mortality after left-sided heart valve surgery.
- In addition, it is associated with 4.2-fold increased risk of multiple postoperative adverse events.

What Are the Clinical Implications?

- Incorporation of right ventricular dysfunction in preoperative surgical risk scores like Society of Thoracic Surgeons or European System for Cardiac Operative Risk Evaluation II can help improve surgical risk stratification and can prevent postoperative adverse outcomes.

Nonstandard Abbreviations and Acronyms

MPI	myocardial performance index
RVD	right ventricular dysfunction
STS	Society of Thoracic Surgeons
TAPSE	tricuspid annular plane systolic excursion
TDI	tissue doppler image

risk scoring models, do not incorporate preoperative RVD in the overall estimation of risk of adverse postoperative outcomes.[4,5]

Echocardiography has been the core reference cardiac imaging modality for the assessment of RV volume and function. However, quantitative measures of RV function have not been consistently used in previous studies.[6–8] Most of the studies have used RV fractional area change (RVFAC) to quantify RV function. RVFAC provides a good estimate of global RV function, but its sensitivity is limited. Recent studies have demonstrated that echocardiographic indices such as tricuspid annular plane excursion (TAPSE), peak systolic tricuspid annular velocity by tissue Doppler imaging (TDI) (S'), and RV myocardial performance index (RV MPI) can increase the overall sensitivity of identifying RVD.[6,7] In this study, we sought to identify whether a composite of multiple preoperative RV echocardiographic parameters used to assess RV function can help in predicting short-term adverse postoperative events.

METHODS

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

Study Population

This was a retrospective observational cohort study conducted at the University of Toledo Medical Center, Toledo, Ohio. Institutional review board approval for this study was obtained and the informed consent requirement was waived. We reviewed data on consecutive patients undergoing left-sided valvular cardiac surgery between January 2006 and December 2014. We included all patients over 18 years of age who had left-sided valvular surgery.

Patients who did not have a preoperative echocardiogram within 3 months of the index surgery, had combined coronary artery bypass graft and valvular surgery, or had inadequate or missing echocardiographic data were excluded from the final analysis (Figure 1). Any echocardiogram with limited acoustic windows and inadequate color or tissue Doppler pattern was considered inadequate.

Echocardiographic Parameters

All preoperative echocardiograms were performed on Phillips IE33 and GE Vivid 7 machines and analyzed with Echo PAC workstation (GE, Milwaukee, WI). The images were reviewed, and all echocardiographic variables were remeasured by 2 readers who were both formally trained in echocardiography (A.T., E.S.). A comprehensive echocardiographic examination including all the standard views was done on all patients. To reduce bias, both readers were blinded to the postoperative outcomes during the measurement process. The echocardiographic measurement protocol and reference cutoffs were based on recommendations by the American Society of Echocardiography.[9–12] Left ventricular (LV) EF and LV volumes were measured by the biplane method of disks (modified Simpson's rule) from the apical 2- and 4-chamber views. The LV volume was indexed to the patient's body surface area. Reduced LV function defined as LVEF <40% and enlarged LV volume defined as LV end diastolic volume >74 mL/m^2 for men and >61 mL/m^2 for women and LV end systolic volume >31 mL/m^2 for men and >24 mL/m^2 for women. Left atrial volume was measured by the biplane area length method and indexed to patient's body surface area. Moderately enlarged left atrium was our abnormal cutoff defined as left atrial volume index ≥42 mL/m^2. Mitral peak E and A wave velocities were measured from the apical 4-chamber view by placing the pulsed wave Doppler sample volume between the mitral leaflet tips, and pulsed wave TDI

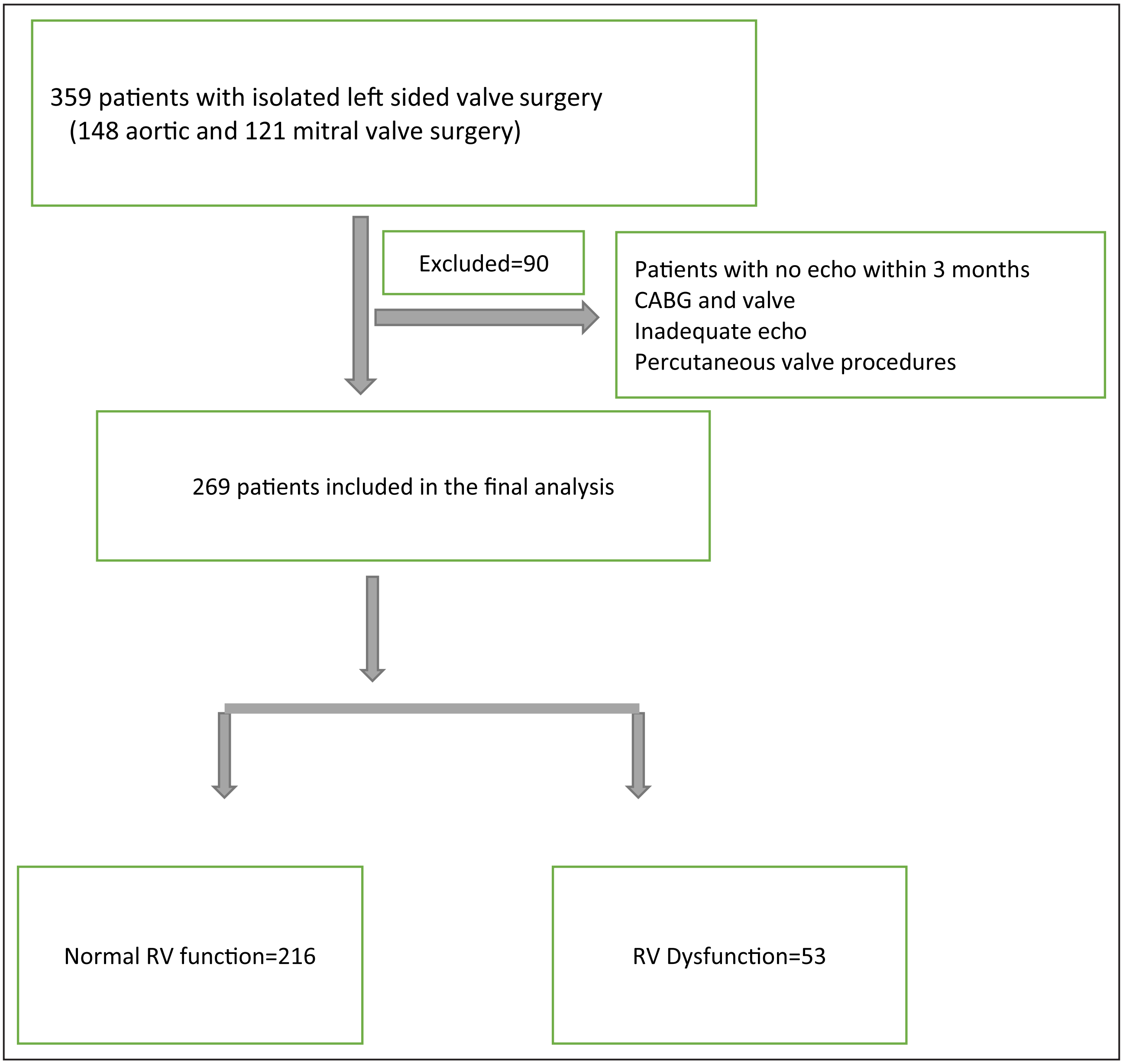

Figure 1. Flow chart of study sample selection based on inclusion and exclusion criteria.
Echo indicates echocardiogram; CABG, coronary artery bypass graft; and RV, right ventricle.

e' velocity was obtained by placing the pulsed wave Doppler sample volume at the base of the anterolateral wall at the mitral level. Grade III diastolic dysfunction was defined as E/A >2 and increased left atrial pressure was suggested by E/e' >14. Right atrial (RA) area was obtained by planimetry in the apical 4-chamber view at end systole. Enlarged RA size was defined as RA area >18 cm^2. Basal RV diameter was measured in the basal one third of RV inflow at end diastole in the RV focused view. RV enlargement was defined by basal RV diameter >4.2 cm. RVFAC was measured by tracing the RV endocardial border in the RV focused view at end diastole and end systole (Figure 2A) and using the formula 100×(end diastolic area-end systolic area)/end diastolic area, with an abnormal cutoff of <35%. RV function was also assessed visually and classified as normal, mildly, moderately, or severely reduced. RV dP/dt was assessed from the ascending limb of the tricuspid regurgitation continuous wave Doppler signal. The time interval between 1 and 2 m/s (Figure 2B) was measured and RV dP/dt was estimated using the formula 12 mm Hg/measured time, abnormal cutoff was defined as RV dP/dt <400 mm Hg/s. Abnormal tricuspid regurgitation was defined as having at least moderate tricuspid regurgitation. TAPSE was measured by placing

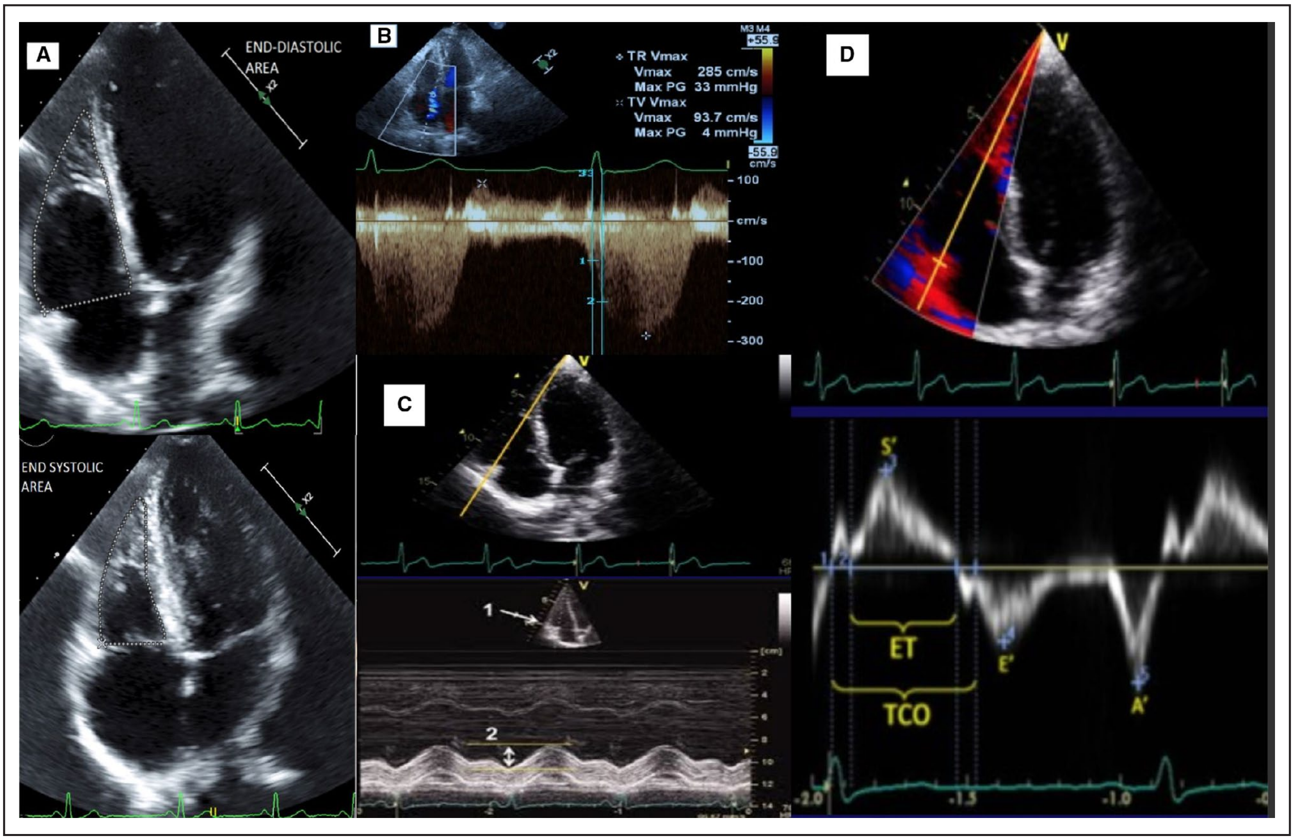

Figure 2. Echocardiographic illustration of RV echocardiographic parameters.
(**A**) RVFAC, (**B**) RV dP/dt, (**C**) TAPSE, (**D**) TV e', S', and MPI. ET indicates ejection time; RV, right ventricle; RVFAC, right ventricular fractional area change; TCO, tricuspid valve closure-opening time; and TR, tricuspid regurgitation.

the M-mode cursor through the tricuspid annulus and measuring the longitudinal excursion between end diastole and peak systole (Figure 2C), and abnormal cutoff was defined as TAPSE <17 mm. Tricuspid peak E and A wave velocities were recorded in the apical 4-chamber view by placing the pulsed wave Doppler sample volume between the tricuspid leaflet tips. Tricuspid pulsed wave TDI e', S' velocity, and RV MPI was obtained by aligning the pulsed wave Doppler sample volume with the basal RV free wall at the tricuspid annulus (Figure 2D) and RV MPI was obtained by using the formula (tricuspid valve closure to opening time - ejection time)/ejection time. We chose to use the tissue Doppler method for estimating RV MPI in all patients rather than the pulsed Doppler method in order to avoid matching the R-R intervals of the analyzed beats in patients with irregular heart rate.

RV diastolic dysfunction was suggested by tricuspid valve E/A >2.1, elevated RA pressures were suggested by tricuspid valve E/e' >6, abnormal tricuspid TDI S' was defined as <10 cm/s, and abnormal RV MPI was defined as >0.55. Tricuspid regurgitation peak velocity was used to estimate the maximal systolic difference between RV and RA pressures. RA pressure was estimated from the inferior vena cava diameter and its change in diameter with respiration, abnormal cutoff defined as RA pressure >10 mm Hg. RV systolic pressure was estimated by adding the RA pressure to the RV and RA systolic pressure difference. In the absence of gradient between the pulmonic valve and the RV outflow tract, the RV systolic pressure was assumed to be equivalent to the systolic pulmonary artery pressure. The cutoff for pulmonary hypertension was systolic pulmonary artery pressure ≥36 mm Hg.

A total of 31 patients (11%) had atrial fibrillation during the time of their echocardiogram. In this group, both mitral E/a and tricuspid E/a were kept as missing variables in the final analysis.

The following echocardiographic parameters were used to evaluate the RV function: RV fractional area change, TAPSE, systolic movement of the RV lateral wall using TDI (S'), RV MPI, and RV dP/dt. Subjects with at least 3 abnormal RV parameters out of the 5 (>50%) aforementioned RV indices were defined as having RVD.[7,13] All chosen RV parameters are load dependent indices and can be abnormal in patients with systemic or RV pressure or volume overload and abnormal heart rate.[14]

Outcome Variables

The primary aim of the study was to assess the association between RVD and 30-day mortality. Secondary objective was to assess the correlation between RVD and other postoperative adverse events within 30 days of surgery, which included prolonged mechanical ventilation (>48 hours), reintubation, intensive care unit readmission, postoperative atrial fibrillation, myocardial infarction, renal failure, stroke, cardiopulmonary arrest, multisystem failure, cardiogenic shock, readmission for either congestive heart failure, myocardial infarction, or arrhythmia. Postoperative myocardial infarction was defined as per the fourth universal definition.[15]

Statistical Analysis

Echocardiographic parameters on all patients were correlated with prospectively collected institutional cardiac surgical database as defined by the STS Adult Cardiac Surgery Database. Baseline patient characteristics and echocardiographic data was compared pairwise for normal RV function against RVD. Continuous variables were reported as mean±SD and categorical variables were reported as count (percent). Two-sample *t* tests were used to assess differences in continuous variables and discrete variables were assessed with Fisher's exact tests or chi-square test as appropriate. Univariate analyses were performed to find the potential predictors of 30-day adverse outcomes using binary logistic regression. Multiple logistic regression was then performed. Variables in the univariate analysis with a $P<0.10$ were included in the model. Interactions between predictor variables were included in the multivariable model and were not significant.

To assess intraobserver agreement and satisfy the power requirement, 29 patients were randomly selected, and the right-sided parameters were remeasured by the first reader (A.T.). Interobserver agreement was assessed by repeating the measurements from those same patients by a second reader (E.S.) who was blinded to any previous measurements. Interclass correlation coefficients were used to assess for intraobserver and interobserver variability. There was good agreement between readers for all measures of RVD (Table 1 and 2). A P value of <0.05 (2 sided) was considered statistically significant. IBM SPSS Statistics for Windows (Version 25.0. Armonk, NY: IBM Corp) was used to conduct the statistical analysis.

Table 1. Interobserver Variability

RV Parameter	Interobserver	Interclass Coefficient
Right atrial size (cm^2)	−0.38±2.39	0.88
Basal RV diameter (cm)	−0.035±0.42	0.88
RV fractional area change (%)	4.85±10.3	0.84
Tricuspid annular plane systolic excursion (cm)	0.01±0.24	0.92
Tissue doppler index S' (cm/s)	0.1±2.29	0.90
Tricuspid valve E/e'	0.26±1.3	0.93
RV systolic pressure (mmHg)	4.44±8.59	0.94
RV myocardial performance index	−0.01±0.1	0.83

RV indicates right ventricular.

RESULTS

Baseline Characteristics and Descriptive Statistics

A total of 359 patients underwent left-sided valve surgery at our institution from January 2006 to December 2014; 198 patients underwent aortic valve surgery (55.2%) and 161 patients underwent mitral valve surgery (44.8%). A total of 269 patients had echocardiographic data of adequate quality for the assessment of various parameters, representing the study population of the present analysis (Figure 1). Based on the criteria chosen to define RVD in our study, 53 (19.7%) patients were diagnosed with RVD. Figure S1 depicts the prevalence of RVD depending on the number of RV parameters chosen to define RVD. The accuracy of predicting RVD does not change significantly if more than 3 parameters out of 5 are abnormal. Next, correlation between RVD by our definition and RVD by visual estimation was assessed. It was found that, by using our objective method, 33% of patients with RVD by visual estimation did not have RVD by our metric. At the same time, approximately 32% of patients who had RVD by our metric were classified as being normal by visual estimation. This is in concordance with prior studies showing that visual estimation of RVD is not very accurate when compared with other advanced imaging modalities such as magnetic resonance imaging.[16–18] The baseline clinical characteristics comparing patients with normal RV function and RVD are outlined in Table 3. Compared with patients with normal RV function, patients with RVD at baseline were more often hospitalized for heart failure within the preceding 2 weeks (84.8% versus 54.8%; $P<0.001$) and had higher rates of moderate to severe chronic obstructive pulmonary disease (24.5% versus 4.6%; $P<0.001$). Other baseline variables were not significantly different between subjects with and without RVD.

Echocardiographic Assessment

Patients with RVD at baseline were found to have a lower LVEF (44.6±17.6% versus 56±15.3%; $P<0.001$) and larger LV end diastolic volume (86±41 mL versus 68.4±30 mL; $P=0.001$). Patients with RVD also had larger basal RV diameter(3.9±0.9 cm versus 3.6±0.8 cm; $P=0.004$), RA area (20.1±7 cm^2 versus

Table 2. Intraobserver Variability

RV Parameter	Intraobserver Variability	Interclass Coefficient
Right atrial size (cm^2)	0.09±0.98	0.98
Basal RV diameter (cm)	−0.08±0.228	0.95
RV fractional area change (%)	1.7±9.2%	0.89
Tricuspid annular plane systolic excursion (cm)	0.07±0.2	0.95
Tissue Doppler index S' (cm/s)	0.05±0.22	0.99
Tricuspid valve E/e'	−0.09±0.59	0.98
RV systolic pressure (mmHg)	1±3	0.99
RV myocardial performance index	0.01±0.04	0.98

RV indicates right ventricular.

17.8±6 cm^2; *P*=0.02) and higher RV systolic pressure (45±16.2 mm Hg versus 36.5±18.3 mm Hg; *P*=0.002). The various echocardiographic parameters at baseline in the 2 groups are shown in Table 4.

Postoperative Adverse Outcomes

Twenty patients died within 30 days of valve surgery (7.4% out of 269 patients who had isolated left-sided valve surgery). Within the 30 days following surgery; 14 (5.2%) patients had multisystem failure, of whom 11 died (78%), and 11 (4.1%) patients had cardiopulmonary arrest, of whom 6 died (54%). Compared with normal RV function, patients with RVD had higher 30-day mortality (22.6% versus 3.8%; *P*=0.01) and were found to be at higher risk for developing multisystem failure/shock (13.2% versus 3.2%; *P*=0.01).

On univariable analysis, preoperative RVD, diabetes mellitus, atrial fibrillation, low LVEF, and higher STS score were all predictors of increased 30-day mortality. RVD was found to be the strongest predictor of the primary outcome (adjusted odds ratio [OR], 3.0; 95% CI, 1.2–7.7; *P*=0.02) (Table 5).

In a multivariable regression analysis including history of diabetes mellitus, low EF, history of atrial fibrillation, STS score, and RVD were independent predictors of 30-day mortality (adjusted OR, 3.5; 95% CI, 1.1–11.1; *P*=0.03) (Table 6).

Patients with preexisting RVD undergoing surgery were also observed to have 30-day secondary composite outcome (postoperative adverse events) (OR, 4.2; 95% CI, 2.1–8.3; *P*<0.01]. Postoperative atrial fibrillation was the most common postoperative adverse event, followed by prolonged ventilation duration, 29.4% and 23.2% respectively (Figure 3 and Table 7).

DISCUSSION

The main finding of this study are as follows: (1) preoperative RVD assessed by a composite of

Table 3. Baseline Characteristics

Baseline Clinical Characteristics	All patients (n=269)	Normal RV Function (n=216)	RV Dysfunction (n=53)	*P* Value
Age (Mean±SD), y	67.4±14.9	68.1±14.6	64±16.2	0.13
Men, n (%)	161 (60.2)	124 (58)	37(69.8)	0.12
Women, n (%)	106 (39.7)	56 (42)	16(30.2)	
Body surface area, m^2	1.96±0.3	1.96±0.3	1.97±0.3	0.84
Diabetes mellitus, n (%)	91 (33.8)	71 (33.2)	20 (37.7)	0.90
Dyslipidemia, n (%)	183(68.5)	145 (67.7)	38(71.6)	0.58
Hypertension, n (%)	230 (86.1)	185(86.4)	45(84.9)	0.77
Peripheral arterial disease, n (%)	68 (25.4)	51 (23.8)	17 (32)	0.21
Heart failure admission 2 wks before procedure, no. (%)	158 (59.2)	113 (52.8)	45 (84.9)	<0.001
History of prior myocardial infarction, n (%)	89(33.3)	67 (31.3)	22 (41.5)	0.16
Chronic obstructive pulmonary disease, n (%)	23(8.6)	10(4.6)	13(24.5)	<0.001
Atrial fibrillation, n (%)	31(12)	23(11)	08(16)	0.33
Society of Thoracic Surgeons predicted morbidity and mortality score, (Mean±SD), %	6±8	6.1±8.4	5.2±4.8	0.50

no indicates Number; and RV, right ventricular.

Table 4. Echocardiographic Parameters

Echocardiographic Variable	All Patients (n=269)	Normal RV Function (n=216)	RV Dysfunction (n=53)	*P* Value
Left ventricular ejection fraction (Mean±SD), %	53.7±16.4	56±15.3	44.6±17.6	<0.001
Left atrial volume index (Mean±SD), mL/m^2	41.2±18.4	40.2±18.7	45.4±16.6	0.07
Left ventricular end diastolic volume (Mean±SD), mL/m^2	71.8±33.1	68.4±30	86±41	0.001
Left ventricular end systolic volume (Mean±SD), mL/m2	35.3±26.1	31.8±21.7	49.4±36	<0.001
E/a (Mean±SD)	1.57±0.9	1.5±0.9	1.8±0.8	0.04
E/e' (Mean±SD)	14.3±8.3	13.9±7.9	16.5±10.1	0.05
Right atrial area (Mean±SD), cm^2	18.2±6.3	17.8±6	20.1±7	0.02
Basal RV diameter (Mean±SD), cm	3.6±0.8	3.6±0.7	3.9±0.9	0.004
RV fractional area change (Mean±SD), %	42±12	44.5±10.8	31.7±10.5	<0.001
dP/dt (Mean±SD), mm Hg/s	545±267	579±270	429±222	<0.001
Tricuspid annular plane systolic excursion (Mean±SD), cm	1.9±0.6	2.1±0.6	1.4±0.5	<0.001
Tissue Doppler index S' (Mean±SD), cm/s	12.7±4	13.7±3.8	9.3±3	<0.001
TV E/a (Mean±SD)	1.4±2.6	1.5±2.9	1.3±0.5	0.73
TV E/e' (Mean±SD)	6.3±3.8	5.9±3.3	8.2±4.8	<0.001
Right atrial pressure (Mean±SD), mm Hg	8.5±5	8.5±4	8.6±5.3	0.001
RV systolic pressure (Mean±SD), mm Hg	38±18	36.5±18.3	45±16.2	0.002
Myocardial performance index (Mean±SD),	0.65±1.9	0.7±2.2	0.6±0.2	0.80

RV indicates right ventricular; and TV, tricuspid valve.and MPI, M.

echocardiographic variables is independently associated with 3.5-fold (95% CI, 1.1–11.1) increased risk of 30-day mortality after left-sided heart valve surgery; (2) preoperative RVD is present in approximately 20% of subjects undergoing left-sided valve surgery; (3) subjects with RVD had similar baseline characteristics as subjects without RVD but can be identified with comprehensive echocardiographic assessment; (4) RVD was associated with 4.2 fold (95% CI, 2.1–8.3; *P*<0.01) increased risk of multiple postoperative adverse events; and (5) a strong consideration should be given to incorporation of RVD in preoperative surgical risk scores like STS or European System for Cardiac Operative Risk Evaluation II to improve surgical risk stratification.

RV anatomy is complex and RV function can be difficult to assess. Given the complex 3-dimensional geometry of the right ventricle, 1 parameter may not be sufficient to identify RVD, but a composite of multiple parameters may prove superior. In our study we used 5 parameters of RV function that are easily obtainable by the vast majority of current echocardiographic machines, including RVFAC, TAPSE, systolic movement of the RV lateral wall using TDI (S'), RV MPI, and RV dP/dt to assess RVD. All these parameters have been used on an individual basis for estimating RV function in the past but there are no studies looking at their role when assessed together in predicting adverse outcomes after standard cardiac valve surgery.[6,7] Prior studies on this topic have largely focused on RVFAC, TAPSE, peak systolic RV lateral wall velocity by TDI, or RV MPI.[6] Most of the studies have used a single measuring tool when quantifying the RV function, which in most instances has been RV FAC.[19] RVFAC requires an accurate delineation of RV borders but because of the complex 3-dimensional RV structure is a simple method to assess global radial and longitudinal RV function. This can be directly correlated with RVEF, although RVEF is less sensitive for detecting early impairment of RV function.[20]

Damy et al published a study regarding the accuracy of longitudinal markers for assessing RVD in patients with heart failure and based on their findings, TAPSE (area under the curve=0.80, *P*<0.0001) and peak systolic RV lateral wall velocity by TDI (area under the curve=0.82, *P*<0.0001) are more accurate than RVFAC (area under the curve=0.76, *P*<0.0001) to predict cardiac outcomes.[7,21] An abnormal TAPSE with value of <17 mm, estimated via traditional 1-dimensional M mode of the RV free wall has been proven to be a strong predictor of RVD in a number of studies and has been shown to correlate quite well with adverse outcomes. RV MPI globally estimated via either via tissue Doppler tricuspid annulus or Doppler inflow of tricuspid valve has been shown to provide an accurate estimate of both the systolic and diastolic function of the RV. Because of its calculation mainly from the Doppler parameters it is independent of geometric assumptions that are usually made because of the complex 3-dimensional nature of RV. In a group of 50 patients Haddad et al showed that a preoperative RV MPI of >0.5 improved the risk stratification of patients

Table 5. Univariate Logistic Regression for 30-Day Mortality

Variable	Odds Ratio	99% CI	*P* Value
Age (y)	1.1	0.9–1.1	0.24
Women	1.3	0.5–3.2	0.59
Body mass index (kg/m^2)	0.9	0.9–1.0	0.45
Diabetes mellitus	2.2	0.9–5.7	0.07
Dyslipidemia	1.4	0.5–4	0.51
Hypertension	1.5	0.3–6.8	0.58
Peripheral arterial disease	1.2	0.4–3.5	0.61
LV end diastolic volume/body surface area (ml/m^2)	0.9	0.9–1	0.24
LV ejection fraction <40%	2.7	1.1–7.2	0.06
Society of Thoracic Surgeons score per 1% increase	1.1	1.0–1.1	0.002
Heart failure-2 weeks	2.2	0.7–6.2	0.14
Prior myocardial infarction	2.1	0.8–5.3	0.10
Chronic obstructive pulmonary disease	1.2	0.5–2.9	0.61
Atrial fibrillation	3.1	1.1–9.6	0.04
Right ventricular dysfunction	3.0	1.2–7.7	0.02

LV indicates left ventricular.

undergoing valvular heart surgery and could have an incremental value in predicting the postoperative adverse outcomes.[6] Despite the evidence RV MPI continues to be one of the underreported indices in routine echocardiography studies. In our study compared with patients with normal RV function, patients with RVD had higher 30-day mortality (22.6% versus 3.8%; *P*=0.01) with RVD being the strongest predictor when assessed by a composite of the different parameters.

RVD could represent a marker for more severe valvular heart disease or concomitant pulmonary disease or coronary artery disease. As outlined in Table 1, patients with RVD defined by our criteria had a higher prevalence of chronic obstructive pulmonary disease and congestive heart failure. Although patients with moderate-severe chronic obstructive pulmonary disease had higher rates of 30-day adverse outcomes, this was not found to be an independent predictor of

Table 6. Multivariate Logistic Regression for 30-Day Mortality

Variable	Odds Ratio	99% CI	*P* Value
Diabetes mellitus	2.1	0.7–6.2	0.17
Left ventricular ejection fraction <40%	1.8	0.6–5.8	0.31
Society of Thoracic Surgeons score per 1% increase	1.1	1.0–1.1	0.009
Atrial fibrillation	2.2	0.6–7.7	0.22
Right ventricular dysfunction	3.5	1.1–11.1	0.03

Multivariable model included predictor variables from univariate analysis using *P*<0.10.

30-day mortality. Some of the factors that contribute to RVD in these conditions include pulmonary hypertension, ventricular interdependence, and RV myocardial ischemia.[22,23] Cardiopulmonary interaction and pathophysiology of pulmonary hypertension in LV heart failure are believed to be owing to the backward transmission of elevated LV filling pressures into the pulmonary circulation (postcapillary hemodynamic profile), which with time causes pulmonary vascular remodeling and elevated pulmonary vascular resistance. This increases RV afterload and eventually results in some degree of RVD. RV dilation and increase in wall stress/tension (internal RV afterload) result in elevated myocardial oxygen consumption, which with concomitant reduction in coronary perfusion gradient leads to RV ischemia and progressive RV failure.[24]

Pulmonary pressures can also be increased by a number of other factors such as systemic inflammatory response, pulmonary reperfusion syndrome, and blood transfusions. Protamine administration can result in pulmonary vasoconstriction in 1.8% of patients and institution of positive pressure ventilation after cardiopulmonary bypass could also increase pulmonary pressures. These sudden changes in pulmonary pressure during cardiac surgery could increase the workload of an already decompensated right ventricle resulting in RV failure. Acute RV failure leads to systemic congestion and eventually results in circulatory failure.

Earlier studies have also shown that presence of RVD is not fully explained by pulmonary pressure changes alone. Multiple studies have shown that many patients with pulmonary hypertension have normal RV function indices. It is also been shown that prevalence of RVD is dependent on the kind of valvular heart disease. Prior studies have hinted toward lower incidence of RVD in patients with aortic stenosis and mitral regurgitation versus mitral stenosis.[25,26] The culprits of postoperative RV failure are sudden increase in pulmonary arterial pressures and RV ischemia. Acute onset pulmonary hypertension can be because of pulmonary vasoconstriction after removal of cardiopulmonary bypass, ischemia reperfusion syndrome, reaction to protamine, transfusions, or metabolic abnormalities. RV ischemia can be caused by air embolism, thromboembolic events, graft dysfunction, or hypotension.[27] A normal RV might be able to tolerate the new onset pulmonary hypertension and RVD. However, patients with preoperative RVD are often not able to endure these sudden changes and develop RV insufficiency, which leads to a low cardiac output syndrome. The failing RV will affect LV function by ventricular interdependence and decrease the LV preload, eventually resulting in circulatory collapse.[28]

Comprehensive assessment of RV function over standard RV systolic indices may be particularly

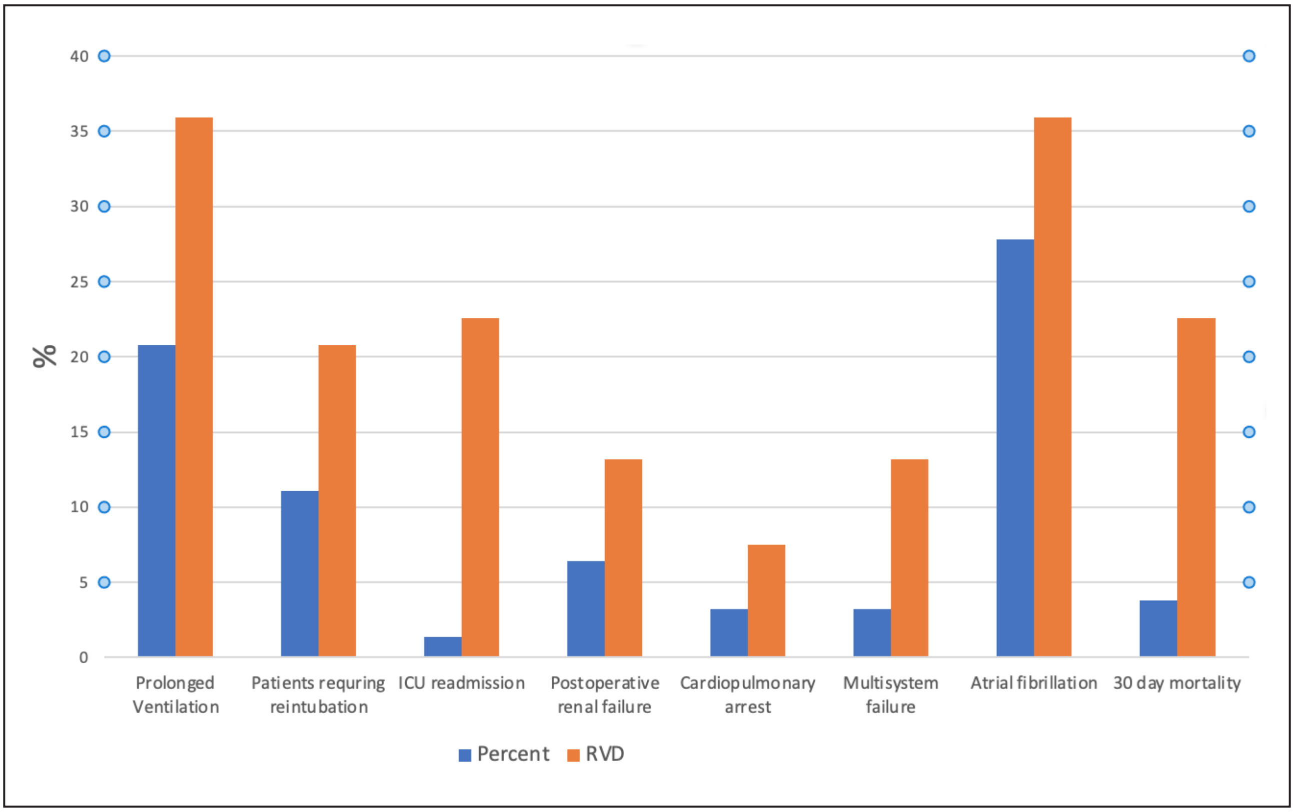

Figure 3. Postoperative adverse outcomes and their frequency (%).
ICU indicates intensive care unit.

interesting for detecting early RVD in patients commonly viewed as free of significant RVD. The presence of severe RVD may modify the medical strategy in the postoperative management. Alternative treatments, such as percutaneous procedures, that do not affect RV function to the same extent as the surgical procedure may be considered in patients who are high risk.[29] This may also help in preparing the intensive care teams and surgeons by making them more cognizant of the risk of refractory postoperative shock and mortality. Cardiac mechanical circulatory support devices may be taken into consideration and scheduled before the surgery in case of high likelihood of predicted complications. The presence of subclinical RVD will increase the predisposition for hemodynamic instability due to pericardiotomy and cardiopulmonary bypass. Multiple earlier studies have shown that increased cardiopulmonary bypass time is associated with increased rate of postoperative complications.[19,30] Therefore, the identification of preoperative RVD, as outlined in this study, may lead to modification of the surgical strategy or the overall treatment plan.

Table 7. Postoperative Adverse Outcomes

Postoperative Adverse Outcomes at 30 days	All Patients (n=269)	Normal RV (n=216)	RVD (n=53)	*P* value
Prolonged ventilation duration (>48 hours), no. (%)	64 (23.8)	45(20.8)	19(35.9)	0.07
Patients requiring reintubation, no. (%)	35(13.0)	24(11.1)	11(20.8)	0.06
Intensive care unit readmission, no. (%)	15(5.6)	3(1.4)	12(22.6)	0.98
Postoperative renal failure, no. (%)	21(7.8)	14(6.4)	7(13.2)	0.19
Cardiopulmonary arrest, no. (%)	11(4.1)	7(3.2)	4(7.5)	0.24
Multisystem failure/shock, no. (%)	14(5.2)	7(3.2)	7(13.2)	0.01
Postoperative atrial fibrillation, no. (%)	79 (29.4)	60(27.8)	19(35.9)	0.49
Mortality within 30 days of surgery, no. (%)	20(7.5)	8(3.8)	12(22.6)	0.01

RV indicates right ventricle; and RVD, right ventricular dysfunction.

LIMITATIONS

This study has a number of limitations that should be acknowledged. It is a retrospective, observational research study and therefore has all of the limitations of this study type. Associations may not be causal and baseline differences between subjects with and without RVD may explain some or all of the observed association. We did perform univariate and multivariate analyses to control for baseline differences, but these methods have known limitations in observational research. In addition, we have a moderate sample size and the study was conducted in a single center. Also, we did not assess 3-dimensional echo or strain imaging for measurement of RV function, because these techniques were not routinely available during the period of data collection. Despite these limitations, we believe the comprehensive echocardiographic assessment of RV function and the strong association between RVD and 30-day mortality after cardiac surgery are noteworthy and make a novel contribution to the literature on this topic.

CONCLUSIONS

In subjects undergoing left-sided heart valve surgery, a comprehensive preoperative echocardiographic assessment of RVD was able to identify RVD in approximately 20% and RVD was an independent predictor of 30-day mortality. Our study enforces the need for a comprehensive assessment of RV function before cardiac surgery. Identification of preoperative RVD may help to reduce postoperative adverse events and postoperative mortality. Furthermore, the STS risk score may be improved with incorporation of an RVD assessment. Measures of RVD may provide useful prognostic information and should be further incorporated in risk prediction models.

ARTICLE INFORMATION

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Disclosures

None.

Supplementary Material

Figure S1

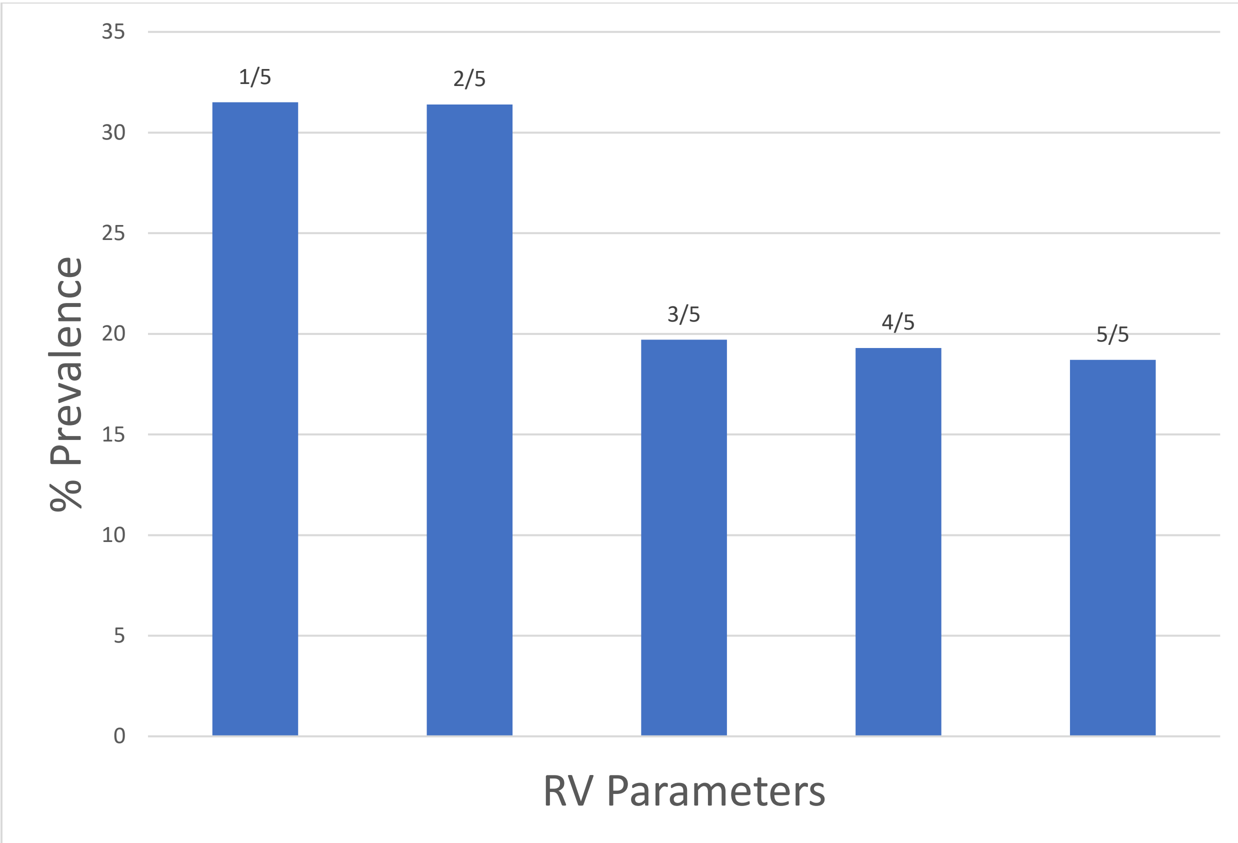
REFERENCES

1. Reichert CL, Visser CA, van den Brink RB, Koolen JJ, van Wezel HB, Moulijn AC, Dunning AJ. Prognostic value of biventricular function in hypotensive patients after cardiac surgery as assessed by transesophageal echocardiography. *J Cardiothorac Vasc Anesth*. 1992;6:429–432. DOI: 10.1016/1053-0770(92)90008-U.
2. Pinzani A, de Gevigney G, Pinzani V, Ninet J, Milon H, Delahaye JP [Pre- and postoperative right cardiac insufficiency in patients with mitral or mitral-aortic valve diseases]. *Arch Mal Coeur Vaiss*. 1993;86:27–34.
3. Wencker D, Borer JS, Hochreiter C, Devereux RB, Roman MJ, Kligfield P, Supino P, Krieger K, Isom OW. Preoperative predictors of late postoperative outcome among patients with nonischemic mitral regurgitation with 'high risk' descriptors and comparison with unoperated patients. *Cardiol*. 2000;93:37–42. DOI: 10.1159/000007000.
4. Ambler G, Omar RZ, Royston P, Kinsman R, Keogh BE, Taylor KM. Generic, simple risk stratification model for heart valve surgery. *Circulation*. 2005;112:224–231. DOI: 10.1161/CIRCULATIONAHA.104.515049.
5. Vahanian A, Baumgartner H, Bax J, Butchart E, Dion R, Filippatos G, Flachskampf F, Hall R, Iung B, Kasprzak J, et al. Guidelines on the management of valvular heart disease: the task force on the management of valvular heart disease of the European Society of Cardiology. *Eur Heart J*. 2007;28:230–268.
6. Haddad F, Denault AY, Couture P, Cartier R, Pellerin M, Levesque S, Lambert J, Tardif JC. Right ventricular myocardial performance index predicts perioperative mortality or circulatory failure in high-risk valvular surgery. *J Am Soc Echocardiogr*. 2007;20:1065–1072. DOI: 10.1016/j.echo.2007.02.017.
7. Damy T, Viallet C, Lairez O, Deswarte G, Paulino A, Maison P, Vermes E, Gueret P, Adnot S, Dubois-Randé J-L, et al. Comparison of four right ventricular systolic echocardiographic parameters to predict adverse outcomes in chronic heart failure. *Eur J Heart Fail*. 2009;11:818–824. DOI: 10.1093/eurjhf/hfp111.
8. Kammerlander AA, Marzluf BA, Graf A, Bachmann A, Kocher A, Bonderman D, Mascherbauer J. Right ventricular dysfunction, but not tricuspid regurgitation, is associated with outcome late after left heart valve procedure. *J Am Coll Cardiol*. 2014;64:2633–2642.
9. 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.
10. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF 3rd, Dokainish H, Edvardsen T, Flachskampf FA, Gillebert TC, Klein AL, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr*. 2016;29:277–314.
11. 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. DOI: 10.1016/j.echo.2010.05.010.
12. Bossone E, D'Andrea A, D'Alto M, Citro R, Argiento P, Ferrara F, Cittadini A, Rubenfire M, Naeije R. Echocardiography in pulmonary arterial hypertension: from diagnosis to prognosis. *J Am Soc Echocardiogr*. 2013;26:1–14. DOI: 10.1016/j.echo.2012.10.009.
13. Asami M, Stortecky S, Praz F, Lanz J, Räber L, Franzone A, Piccolo R, Siontis GCM, Heg D, Valgimigli M, et al. Prognostic value of right ventricular dysfunction on clinical outcomes after transcatheter aortic valve replacement. *JACC Cardiovasc Imaging*. 2019;12:577–587. DOI: 10.1016/j.jcmg.2017.12.015.
14. Kossaify A. Echocardiographic assessment of the right ventricle, from the conventional approach to speckle tracking and three-dimensional imaging, and insights into the "right way" to explore the forgotten chamber. *Clin Med Insights Cardiol*. 2015;9:65–75. DOI: 10.4137/CMC.S27462.

15. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, White HD. Fourth universal definition of myocardial infarction (2018). *J Am Coll Cardiol*. 2018;72:2231–2264.
16. Ling LF, Obuchowski NA, Rodriguez L, Popovic Z, Kwon D, Marwick TH. Accuracy and interobserver concordance of echocardiographic assessment of right ventricular size and systolic function: a quality control exercise. *J Am Soc Echocardiogr*. 2012;25:709–713. DOI: 10.1016/j.echo.2012.03.018.
17. Bellsham-Revell HR, Simpson JM, Miller OI, Bell AJ. Subjective evaluation of right ventricular systolic function in hypoplastic left heart syndrome: how accurate is it? *J Am Soc Echocardiogr*. 2013;26:52–56.
18. Margossian R, Schwartz ML, Prakash A, Wruck L, Colan SD, Atz AM, Bradley TJ, Fogel MA, Hurwitz LM, Marcus E, et al. Comparison of echocardiographic and cardiac magnetic resonance imaging measurements of functional single ventricular volumes, mass, and ejection fraction (from the Pediatric Heart Network Fontan Cross-Sectional Study). *Am J Cardiol*. 2009;104:419–428.
19. Maslow AD, Regan MM, Panzica P, Heindel S, Mashikian J, Comunale ME. Precardiopulmonary bypass right ventricular function is associated with poor outcome after coronary artery bypass grafting in patients with severe left ventricular systolic dysfunction. *Anesth Analg*. 2002;95:1507–1518. DOI: 10.1097/00000539-200212000-00009.
20. Mor-Avi V, Sugeng L, Lindner JR. Imaging the forgotten chamber: is the devil in the boundary? *J Am Soc Echocardiogr*. 2010;23:141–143. DOI: 10.1016/j.echo.2009.12.021.
21. Haddad F, Couture P, Tousignant C, Denault AY. The right ventricle in cardiac surgery, a perioperative perspective: II. Pathophysiology, clinical importance, and management. *Anesth Analg*. 2009;108:422–433. DOI: 10.1213/ane.0b013e31818d8b92.
22. Le Tourneau T, Deswarte G, Lamblin N, Foucher-Hossein C, Fayad G, Richardson M, Polge A-S, Vannesson C, Topilsky Y, Juthier F, et al. Right ventricular systolic function in organic mitral regurgitation: impact of biventricular impairment. *Circulation*. 2013;127:1597–1608. DOI: 10.1161/CIRCULATIONAHA.112.000999.
23. Borer JS, Hochreiter C, Rosen S. Right ventricular function in severe non-ischaemic mitral insufficiency. *Eur Heart J*. 1991;12:22–25. DOI: 10.1093/eurheartj/12.suppl_B.22.
24. Rosenkranz S, Gibbs JS, Wachter R, De Marco T, Vonk-Noordegraaf A, Vachiery JL. Left ventricular heart failure and pulmonary hypertension. *Eur Heart J*. 2016;37:942–954. DOI: 10.1093/eurheartj/ehv512.
25. Morrison DA, Lancaster L, Henry R, Goldman S. Right ventricular function at rest and during exercise in aortic and mitral valve disease. *J Am Coll Cardiol*. 1985;5:21–28. DOI: 10.1016/S0735-1097(85)80080-2.
26. Wroblewski E, James F, Spann JF, Bove AA. Right ventricular performance in mitral stenosis. *Am J Cardiol*. 1981;47:51–55. DOI: 10.1016/0002-9149(81)90288-5.
27. Estrada VH, Franco DL, Moreno AA, Gambasica JA, Nunez CC. Postoperative right ventricular failure in cardiac surgery. *Cardiol Res*. 2016;7:185–195. DOI: 10.14740/cr500e.
28. Voelkel NF, Quaife RA, Leinwand LA, Barst RJ, McGoon MD, Meldrum DR, Dupuis J, Long CS, Rubin LJ, Smart FW, et al. Right ventricular function and failure: report of a National Heart, Lung, and Blood Institute working group on cellular and molecular mechanisms of right heart failure. *Circulation*. 2006;114:1883–1891. DOI: 10.1161/CIRCULATIONAHA.106.632208.
29. Kempny A, Diller G-P, Kaleschke G, Orwat S, Funke A, Schmidt R, Kerckhoff G, Ghezelbash F, Rukosujew A, Reinecke H, et al. Impact of transcatheter aortic valve implantation or surgical aortic valve replacement on right ventricular function. *Heart*. 2012;98:1299–1304. DOI: 10.1136/heartjnl-2011-301203.
30. Salis S, Mazzanti VV, Merli G, Salvi L, Tedesco CC, Veglia F, Sisillo E. Cardiopulmonary bypass duration is an independent predictor of morbidity and mortality after cardiac surgery. *J Cardiothorac Vasc Anesth*. 2008;22:814–822. DOI: 10.1053/j.jvca.2008.08.004.

SUPPLEMENTAL MATERIAL

Figure S1. Comparison of rate of abnormal RV parameters.



RV: right ventricle.