Determinants of Surgical Outcome in Patients With Isolated Tricuspid Regurgitation

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Background**—**We sought to identify preoperative predictors of clinical outcomes after surgery in patients with severe tricuspid regurgitation.

Methods and Results**—**We prospectively enrolled 61 consecutive patients (54 women, aged 57±9 years) with isolated severe tricuspid regurgitation undergoing corrective surgery. Twenty-one patients (34%) were in New York Heart Association functional class II, 35 (57%) in class III, and 5 (9%) in class IV. Fifty-seven patients (93%) had previous history of left-sided valve surgery. Preoperative echocardiography revealed pulmonary artery systolic pressure of 41.5±8.7 mm Hg, right ventricular (RV) end-diastolic area of 35.1±9.0 cm^2, and RV fractional area change of 41.3±8.4%. The median follow-up duration after surgery was 32 months (range, 12 to 70). Six of the 61 patients died before discharge; thus, operative mortality was 10%. Three of the 55 patients who survived surgery died during follow-up, and 6 patients required readmission because of cardiovascular problems. Thus, 46 patients (75%) remained event free at the end of follow-up. In the 54 patients who underwent 6-month clinical and echocardiographic follow-up, RV end-diastolic area decreased by 29%, with a corresponding 26% reduction in RV fractional area change. Thirty-three patients (61%) showed improved functional capacity after surgery. On multivariable Cox regression analysis, preoperative hemoglobin level ($P<0.001$) and RV end-systolic area ($P<0.001$) emerged as independent determinants of clinical outcomes. On receiver operating characteristic curve analysis, we found that RV end-systolic area <20 cm^2 predicted event-free survival with a sensitivity of 73% and a specificity of 67%, and a hemoglobin level >11.3 g/dL predicted event-free survival with a sensitivity of 73% and a specificity of 83%.

Conclusions**—**Timely correction of severe tricuspid regurgitation carries an acceptable risk and improves functional capacity. Surgery should be considered before the development of advanced RV systolic dysfunction and before the development of anemia. **(*Circulation*. 2009;120:1672-1678.)**

Key Words: echocardiography ■ prognosis ■ surgery ■ tricuspid regurgitation ■ valves

Determining the optimal time for corrective surgery remains a difficult clinical problem in patients with severe tricuspid regurgitation (TR). Subjective symptoms are often nonspecific, progress very slowly, and only become evident after irreversible right ventricular (RV) dysfunction occurs. The complex geometry of the RV makes it difficult to attain accurate and reproducible measurements of RV function.[1] Furthermore, TR has long been neglected because of the belief that it is rare and that it is clinically insignificant. However, recent studies have clearly demonstrated that it is not a rare disease because its prevalence is rapidly growing late after mitral valve surgery.[2] The impact of TR on long-term prognosis regardless of left ventricular (LV) ejection fraction or pulmonary artery pressure has been well demonstrated.[3] Moreover, high surgical mortality and morbidity have been reported in these patients.[4–6] Therefore, it is of paramount importance to provide objective measures to predict clinical outcomes after surgery and thus to determine surgical timing in TR. There have been a few studies dealing with this important issue, but they have been limited by small study populations or lack of echocardiographic RV examination.[5,6] In the present study, we prospectively enrolled patients with isolated severe TR to identify preoperative predictors of clinical outcomes after surgery.

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Methods

Study Subjects

We prospectively enrolled consecutive patients with isolated severe TR who underwent corrective surgery between March 2003 and

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January 2008. All patients satisfied the following 3 criteria for severe TR: (1) TR jet area >30% of right atrial area, (2) inadequate cusp coaptation, and (3) systolic flow reversal in the hepatic vein. Inadequate cusp coaptation was associated with tricuspid annular dilation and apical tethering of the leaflets in all patients but 1 who had chordal rupture. Patients with significant left-sided valve disease who underwent concomitant left-sided valve surgery were excluded from the study. Ultimately, 61 patients were enrolled. The mean patient age was 57±9 years; 54 patients (89%) were women. In all patients, clinical and echocardiographic follow-up was performed 6 months after surgery. Occurrence of clinical events was checked by reviewing the hospital records and by telephone interview if needed. This study protocol was approved by the institutional review board of Seoul National University Hospital.

Echocardiographic Examination

All patients underwent comprehensive echocardiographic examination before surgery with commercially available equipment (Sequoia from Siemens Medical Solution or Vivid 7 from GE Medical Systems). LV end-diastolic and end-systolic diameters and LV ejection fraction were measured by M-mode in the parasternal short-axis view at the papillary muscle level. RV end-diastolic and end-systolic areas (ESA) were measured in the apical 4-chamber view, and RV fractional area change (FAC) was calculated.[7] Care was taken to obtain a true nonforeshortened apical 4-chamber view. Right atrial area was measured at end-systole in the apical 4-chamber view. The TR jet/right atrial area ratio was obtained with a highest possible Nyquist limit in a given patient, which was typically 70 to 80 cm/s. Peak systolic transtricuspid pressure gradient was obtained. Systolic tricuspid annulus velocity was obtained by placing the sample volume of the pulse-wave Doppler tissue imaging at the lateral side of the tricuspid annulus. In the subcostal view, the diameter of inferior vena cava and its respiratory variation were measured 1.0 to 2.0 cm from the junction with the right atrium. The percent decrease in the diameter was used to estimate mean right atrial pressure. The right atrial pressure was estimated as normal (50% decrease), mildly elevated (dilated >17 mm with 50% decrease), moderately elevated (dilated with <50% decrease), or severely elevated (dilated without any collapse) as the guideline recommended.[7] Echocardiographic measurements were averaged for 3 beats in patients with normal sinus rhythm and for 5 consecutive beats in those with atrial fibrillation. Echocardiographic examination was repeated 6 months after surgery.

Statistical Analysis

Data are expressed as mean±SD or median (range) for continuous variables and as numbers (percentages) for categorical variables. For comparison of continuous and categorical variables between patients with clinical events and those without clinical events, the Mann-Whitney *U* test and Fisher exact test were employed, respectively. Clinical end points or events were defined as operative mortality (death within 30 days after surgery or before discharge), all-cause death, and readmission due to cardiovascular problems. Using receiver operating characteristic curves, we examined the sensitivities and specificities of various cutoff points that reliably predicted patients' events. Multivariable Cox proportional hazard analysis with the use of forward selection based on the likelihood ratio test was employed to determine independent variables for event-free survival after surgery, with variables showing statistical significance in univariate analysis between patients with clinical events and those without clinical events as covariates. A Kaplan-Meier curve was constructed to demonstrate the survival difference in relation to New York Heart Association (NYHA) functional class, hemoglobin level, and RV ESA according to the presence or absence of clinical events with the use of the log-rank test. SPSS version 13.0 and SAS version 9.1 statistical package were used for statistical analyses. *P* values <0.05 were considered statistically significant.

Results

Baseline Characteristics

Baseline clinical and echocardiographic characteristics are summarized in Table 1. Fifty of the 61 patients (82%) were in atrial fibrillation. The type of TR was functional in 51 patients (84%), rheumatic in 9 (15%), and chordal rupture in 1 (1%). Twenty-one patients (34%) were in NYHA functional class II, 35 (57%) were in class III, and 5 (9%) were in class IV. All but 1 of the patients took diuretics, most of which were loop diuretics (75%). In addition, digitalis was given in 70% of the patients, angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers in 15%, and β-blockers in 15%. Fifty-seven patients (93%) had a previous history of left-sided valve surgery, and 10 (17%) had a previous history of tricuspid annuloplasty. The mean interval between the operations was 175±53 months. Baseline echocardiographic examination showed LV end-diastolic diameter of 45.6±8.4 mm, LV ejection fraction of 57.4±9.2%, pulmonary artery systolic pressure of 41.5±8.7 mm Hg, right atrial area of 52.8±18.6 cm^2, RV end-diastolic area of 35.1±9.0 cm^2, and RV FAC of 41.3±8.4%. Tricuspid annular diameter measured in apical 4-chamber view was 44±8 mm. Peak systolic tricuspid annulus velocity was 9.7±2.6 cm/s. Right atrial pressure was elevated in all patients, to a mild degree in 6, to a moderate degree in 49, and to a severe degree in 6.

Table 1. Baseline Characteristics of Study Patients (n=61)

Variables	Values
Age, y	57.0±8.9
Female, n/N (%)	54/61 (89)
Systolic blood pressure, mm Hg	117±16
Atrial fibrillation, n/N (%)	50/61 (82)
NYHA functional class, II:III:IV	21:35:5
Previous left-sided valve surgery, n/N (%)	57/61 (93)
Tricuspid replacement, n/N (%)	53/61 (87)
Laboratory findings	
Creatinine, mg/dL	1.0±0.3
Urea nitrogen, mg/dL	21.8±14.0
Albumin, mg/dL	4.0±0.6
Total cholesterol, mg/dL	156±42
Hemoglobin, g/dL	12.1±1.7
Echocardiographic parameters	
End-diastolic LV diameter, mm	45.6±8.4
LV ejection fraction, %	57.4±9.2
Pulmonary artery systolic pressure, mm Hg	41.5±8.7
RV end-diastolic area, cm^2	35.1±9.0
RV FAC, %	41.3±8.4
Inferior vena cava, mm	27.3±6.5
Inferior vena cava collapse, %	25.3±15.6
Right atrial area, cm^2	52.8±18.6
TR area, cm^2	24.0±11.3
S'_T, cm/s	9.7±2.6

S'_T indicates peak systolic tricuspid annulus velocity. Data are expressed as mean±SD.

Postoperative Outcomes

Eight patients underwent tricuspid valve repair, and 53 patients underwent tricuspid valve replacement with the use

Table 2. Comparison Between Patients With and Without Cardiovascular Events

	Without Event (n=46)	With Event (n=15)	*P*
Age, y	56.1±9.3	58.7±7.1	0.46
Median (range)	56.8 (29–72)	58.5 (42–71)	
Weight, kg	54.3±9.1	50.7±7.0	0.19
Median (range)	53 (35–75)	50 (38–64)	
Systolic blood pressure, mm Hg	118±17	115±15	0.58
Median (range)	120 (86–154)	118 (95–138)	
Urea nitrogen, mg/dL	19.0±8.4	30.3±22.7	0.08
Median (range)	17 (12–57)	26 (9–99)	
Creatinine, mg/dL	1.0±0.2	1.3±0.5	0.02
Median (range)	0.9 (0.7–1.5)	1.1 (0.8–2.6)	
Albumin, mg/dL	4.1±0.6	3.6±0.6	0.003
Median (range)	4.3 (2.0–4.8)	3.7 (2.7–4.6)	
Hemoglobin, g/dL	12.7±1.6	10.6±1.2	<0.001
Median (range)	12.8 (8.2–15.6)	10.5 (8.8–13.0)	
Platelet $\times 10^3/mm^3$	165±65	117±39	0.005
Median (range)	Median: 161×10^3 (46×10^3–356×10^3)	Median: 114×10^3 (49×10^3–192×10^3)	
Echocardiographic variables			
End-diastolic LV diameter, mm	45.4±8.0	45.6±10.2	0.97
LV ejection fraction, %	57.3±9.0	56.5±9.7	0.67
RV end-diastolic area, cm^2	33.9±7.1	40.0±12.0	0.09
RV ESA, cm^2	19.3±5.0	25.9±8.8	0.009
RV FAC, %	43.1±8.4	36.1±6.6	0.01
Inferior vena cava, mm	27.0±6.3	28.2±7.1	0.61
Inferior vena cava collapse, %	28.3±16.5	18.9±9.9	0.04
Right atrial area, cm^2	51.2±17.8	58.5±21.6	0.29
TR area, cm^2	22.7±10.0	29.4±13.4	0.06
Pulmonary artery systolic pressure, mm Hg	41.4±8.2	43.5±9.6	0.32
S'_T, cm/s	9.4±2.5	10.4±2.8	0.20

Values in parentheses are ranges. S'_T indicates peak systolic tricuspid annulus velocity. Data are expressed as mean±SD unless otherwise indicated.

of tissue valves (n=30) or mechanical valves (n=23). Although combined Maze operation was performed in 8 patients, normal sinus rhythm was restored and maintained in only 1 patient. Therefore, postoperative sinus rhythm was observed in 12 patients (20%). However, atrial fibrillation newly developed during long-term follow-up in 8 of 12 patients. The total cardiopulmonary bypass time was 177±55 minutes, and the aortic cross-clamp time was 95±35 minutes. The median follow-up duration after surgery was 32 months (range, 12 to 70). Six of the 61 patients died before discharge (operative mortality, 9.8%). The median duration of admission was 26 days (range, 8 to 118), with a median intensive care unit stay of 7 days (range, 1 to 99). Two of the 55 patients who survived surgery died of heart failure, and 1 patient died of hemorrhagic stroke. Six patients required readmission because of cardiovascular problems. Thus, 46 patients (75%) remained event free at the end of follow-up.

Patients without cardiovascular events showed a high percentage of preoperative NYHA functional class II (20 [43.5%] versus 2 [9.1%]; $P=0.04$), a lower serum creatinine level (1.0±0.2 versus 1.3±0.5 mg/dL; $P=0.02$), a higher albumin level (4.1±0.6 versus 3.6±0.6 mg/dL; $P=0.003$), a higher platelet count ($165\pm65\times10^3$ versus $117\times\pm39\times10^3/mm^3$; $P=0.006$), and a higher hemoglobin level (12.7±1.6 versus 10.6±1.2 g/dL; $P<0.001$). On echocardiographic examination, patients without cardiovascular events showed lower preoperative RV ESA (19.3±5.0 versus 25.9±8.8 cm^2; $P=0.009$) and higher RV FAC (43.1±8.4% versus 36.1±6.6%; $P=0.01$). However, RV end-diastolic area was not significantly different (33.9±7.1 versus 40.0±12.0 cm^2; $P=0.11$) (Table 2).

Thirty-three (61%) of the 54 patients who survived and underwent 6-month clinical and echocardiographic follow-up showed improved functional capacity after surgery, whereas only 5 patients (9%) showed symptomatic aggravation (Figure 1). RV end-diastolic area decreased by 29% from 35.1±9.0 to 25.0±7.1 cm^2, with a corresponding RV FAC reduction of 26%, from 41.3±8.4% to 30.7±8.9%.

Predictors of Clinical Outcome

Cox regression analysis with the use of forward stepwise selection method demonstrated that preoperative hemoglobin

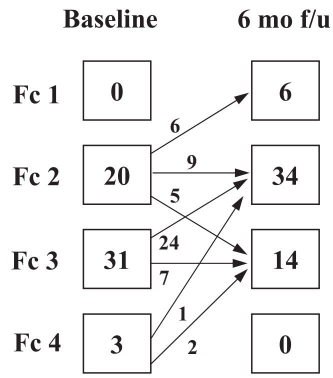

Figure 1. Changes in functional status in 54 patients who completed 6-month clinical follow-up. Fc indicates New York Heart Association functional class; f/u, follow-up.

level and RV ESA were the 2 most important determinants of event-free survival (both $P<0.001$). On receiver operating characteristic curve analysis, we found that preoperative RV ESA <20 cm^2 predicted event-free survival most effectively, with a sensitivity of 73% (95% confidence interval, 0.51 to 0.96) and a specificity of 67% (95% confidence interval, 0.53 to 0.81). Preoperative hemoglobin level >11.3 g/dL predicted event-free survival most effectively, with a sensitivity of 73% (95% confidence interval, 0.51 to 0.96) and a specificity of 83% (95% confidence interval, 0.72 to 0.94).

The 1-year and 2-year event-free survival rates were 91% in patients with RV ESA <20 cm^2, whereas they were 69% and 57%, respectively, in those with RV ESA ≥20 cm^2 (Figure 2A). Whereas the 1-year and 2-year event-free survival rates were 93% and 90%, respectively, in patients with hemoglobin levels >11.3 g/dL, they were only 57% and 44% in those with hemoglobin levels ≤11.3 g/dL (Figure 2B). Although preoperative NYHA functional class failed to demonstrate its independent contribution to predicting event-free survival, a clear difference was noted according to NYHA functional class; the 1-year and 2-year event-free survival rates were 95% and 90%, respectively, in patients with NYHA functional class II, whereas they were 73% and 68% in those with class III or IV (Figure 3). Operative mortality was only 4.8% in patients with NYHA class II, 0% in those with RV ESA <20 cm^2, and 2.4% in those with hemoglobin >11.3 g/dL.

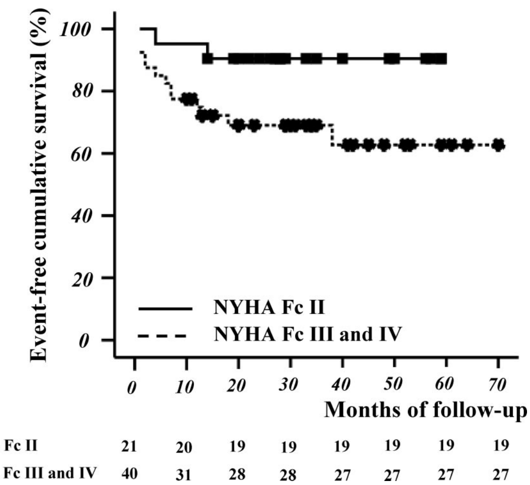

Figure 3. Kaplan-Meier curve showing differences in event-free survival according to preoperative NYHA functional class (Fc).

Discussion

This is the first prospective study to evaluate the surgical outcome and its predictors in a sizable number of patients with isolated severe TR. We found that operative mortality was 9.8% and that the event-free survival rate was 75% during a median follow-up period of 32 months. Most surviving patients showed improved functional capacity after correction of TR. Preoperative hemoglobin level and RV ESA measured by echocardiography were independent predictors of postoperative outcome.

Severe TR induces chronic volume overload in RV, which leads to progressive RV dilation, dysfunction, and finally RV failure. Timely correction of TR will preserve RV function, improve functional capacity, and improve long-term survival.

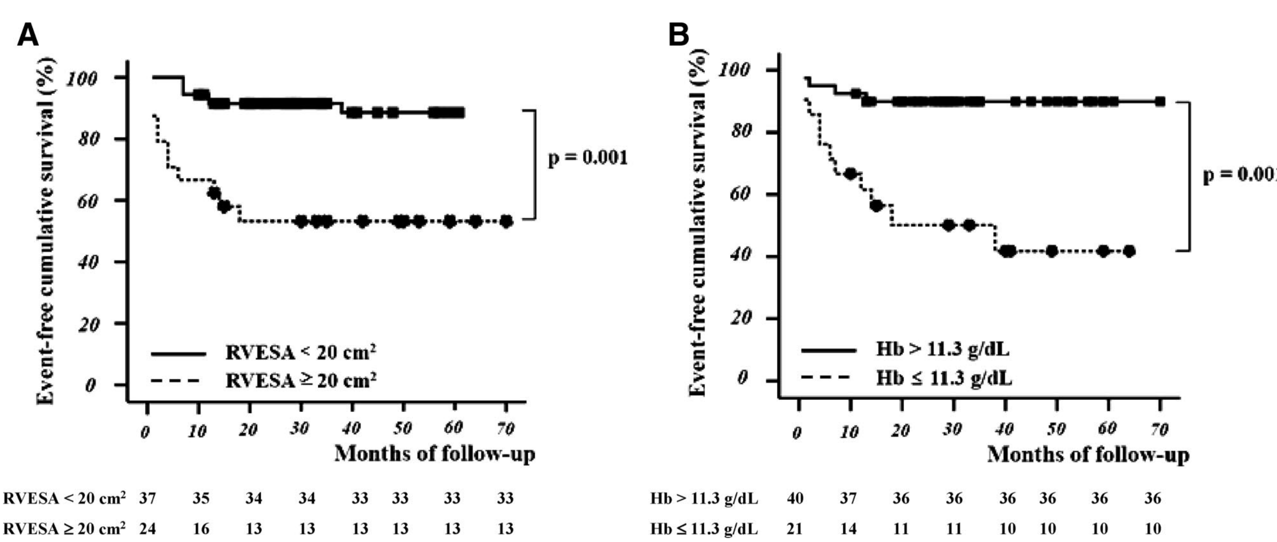

Figure 2. Kaplan-Meier curves showing differences in event-free survival according to preoperative RV ESA (A) and hemoglobin (Hb) level (B).

However, surgical indications in TR are not well established for several reasons. First, severe TR is not common, and thus data on postoperative outcomes are scarce. Common causes of valve diseases mainly involve left-sided valves, and thus the prevalence of TR is much lower than that of mitral disease. However, our group reported late TR in 27% of patients who had shown no more than mild TR at the time of left-sided valve surgery.[8] This finding implies that TR is a growing clinical problem. Hence, objective and reliable predictors of postoperative outcome are critically important. Second, TR has long been regarded as a benign lesion that does not alter exercise capacity or long-term prognosis. This belief originated mainly from animal experiments and clinical experiences with congenital heart disease. However, recent observations strongly suggest that TR considerably reduces exercise capacity[9] and negatively affects long-term survival, irrespective of pulmonary artery pressure or LV ejection fraction.[10,11] Moreover, significant TR can increase morbidity and mortality despite adequate correction of underlying valve disease.[12] Third, evaluation of RV function is problematic because of its complex geometry. Thus, reliable and reproducible parameters representing RV function are not widely available.

Evaluation of RV function is difficult because of complex geometry and the limited definition of the endocardial surface caused by heavy trabeculation. In the present study, we employed RV ESA, RV FAC, and peak systolic tricuspid annulus velocity as echocardiographic markers of RV systolic function because they have been well validated in many previous studies. We found that RV ESA was a reliable indicator of good postoperative outcome on multivariable analysis, although both RV ESA and RV FAC were significant determinants on univariate analysis. These findings are in accordance with the previous observations in patients with mitral regurgitation that ejection phase indexes such as ejection fraction and FAC overestimate ventricular contractility in the presence of regurgitant valve lesions because of favorable loading conditions. In contrast, end-systolic volume (or area) is relatively independent of preload and varies linearly with afterload, as shown in the previous studies with mitral regurgitation.[13,14] A relatively large ESA for a given pulmonary artery pressure indicates less ventricular shortening for a given afterload and therefore indicates decreased myocardial contractility. Because pulmonary artery pressure is not usually significantly elevated in most patients with severe TR, as shown in this study, in which only 3 patients had systolic pulmonary artery pressure >55 mm Hg, we believe that RV ESA is a useful clinical marker and may be of use in clinical decisions in severe TR. Of interest, the cutoff RV ESA value in this study, 20 cm^2, corresponds with the previous definition of moderate RV dilation.[7] Although end-diastolic and end-systolic RV volume would be other important markers of RV systolic function, measurement of infundibular volume remains difficult. Three-dimensional echocardiography and cardiac magnetic resonance imaging may offer a better assessment of RV volume and systolic function, and further studies with these new imaging modalities will be necessary. In our previous study, systolic tricuspid annulus velocity proved to be a prognostic marker in a small number of patients.[4] In the present study, however, it was not a reliable prognostic marker. This discrepancy is likely due to the differences in patient numbers and outcome measures.[4] In the previous study, clinical outcome was defined on the basis of improvement of functional class or increase in the respiratory variation of inferior vena cava diameter because of the small study population.

Another prognostic determinant in the present study was the hemoglobin level. This is not surprising because it is well known that lower hemoglobin levels and anemia are associated with an increased risk of mortality and morbidity in heart failure.[15–17] Although low renal perfusion, malabsorption, nutritional deficiencies, and hemodilution have been proposed as possible mechanisms for anemia in heart failure, the main mechanism in our patients was probably hypersplenism secondary to long-standing systemic venous congestion. Nearly 60% of patients with low hemoglobin showed combined thrombocytopenia ($<120\times10^3/mm^3$), and these patients with both low hemoglobin and thrombocytopenia had a worse 2-year event-free survival rate of 30%. Therefore, we believe that hemoglobin levels in these patients indicate the chronicity and severity of systemic venous hypertension.

Information on the outcome of isolated tricuspid valve surgery is scarce. King et al[18] reported high hospital mortality of 25% and 3- and 5-year actuarial survival rates of 65% and 44% in 32 patients with TR late after mitral valve replacement. Staab et al[6] reported early mortality of 8.8% and 5-year event-free actuarial survival of 41.6% in 34 patients with severe TR after prior left-sided valve surgery. They identified age and the number of prior valve surgeries as independent predictors of poor clinical outcome. These studies were limited by their retrospective design, small population, and lack of objective RV function measures. In the present study, we also noted a high operative mortality of 9.8% and a poor event-free survival rate of 75% during a median follow-up period of 32 months. These results are disappointing because left-sided valve surgeries have shown operative mortality rates as low as 1% to 2% in many cardiac centers.[19] However, we found that operative mortality and event-free survival were much better in patients with preserved RV systolic function. In patients with preoperative RV ESA <20 cm^2, operative mortality and 2-year event-free survival rate were 0% and 91%, respectively. In addition, in patients with NYHA functional class II symptoms, operative mortality was only 4.8%, and 2-year event-free survival rate was 90%. Furthermore, exercise tolerance and RV dilation improved in most patients who completed 6-month clinical and echocardiographic follow-up. These findings imply that poor surgical outcome is mainly due to a failure of optimal surgical timing. Early corrective surgery is mandatory to preserve RV function and exercise capacity and to improve long-term prognosis. Two thirds of our patients had preoperative NYHA functional class III or IV, which suggests that surgical timing was too late in many patients. We believe that the surgical delay was partly due to the absence of guidelines for surgical timing. Therefore, establishment of guidelines with widely used clinical and echocardiographic parameters is critically important. On the basis of our observations, we propose that surgical correction of severe TR should be considered before the development of advanced RV systolic dysfunction (RV ESA $\geq$20 cm^2) and before the development of anemia (hemoglobin level $\leq$11.3 g/dL). In addition, surgery could be considered in all symptomatic patients.

Study Limitations

First, in most of our study subjects, the source of TR was functional late after left-sided valve surgery, and thus our findings may not be directly applicable in TR patients with other organic valve diseases. However, because we prospectively enrolled consecutive patients, we believe that our data represent the real patient population in clinical practice. Second, the median follow-up duration of 32 months might not be enough to determine the long-term benefit and risk of surgery. However, our data clearly demonstrated that timely correction of TR can be performed with acceptable risk and can improve exercise tolerance and RV remodeling, which are well-known prognosticators in various cardiac diseases. Third, because we did not have a comparative group, we cannot conclude that surgery is better than medical therapy. This is an inherent limitation of clinical studies with valvular heart disease because of the relatively low prevalence of the disease and the duration it takes for the hemodynamic disturbance to affect chamber remodeling and function. However, we can assume the benefit of surgery because we could terminate the progressive deleterious effects of chronic TR on RV function with acceptable risk, especially in patients with milder symptoms and less enlarged RV. Fourth, the valve replacement rate is relatively high compared with the previous studies. There are a couple of reasons for the high rate of replacement in our study population. First, most of our patients had inadequate coaptation mainly because of severe leaflet tethering and annular dilation, in which the success rate of repair is relatively low. Second, $>$90% of the patients had prosthetic valve in the aortic or mitral position, and thus the benefit of the repair was partially reduced. There were no significant differences in the outcome between patients with repair and those with replacement, which might be due in part to the low statistical power from the small number of patients. Although tricuspid repair would be better for preserving RV function as shown in mitral regurgitation, there have been no data yet, and further studies are needed in this regard. Finally, cutoff points of hemoglobin level and RV ESA determined by receiver operating characteristic curves could not be validated in a subsequent patient group because of the low prevalence of severe TR. Despite this limitation, we believe that the values suggested in the present study can aid in clinical decision making and can guide future research into this issue. These cutoff values should be validated in future studies for clinical relevance.

Conclusion

Timely correction of severe TR carries acceptable risk and improves functional capacity and RV remodeling. Preoperative hemoglobin level and RV ESA were independent predictors of postoperative outcome. Surgery should be considered before the development of advanced RV systolic dysfunction and before the development of anemia.

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Disclosures

None.

References

1. Bonow RO, Carabello BA, Kanu C, de Leon AC Jr, Faxon DP, Freed MD, Gaasch WH, Lytle BW, Nishimura RA, O'Gara PT, O'Rourke RA, Otto CM, Shah PM, Shanewise JS, Smith SC Jr, Jacobs AK, Adams CD, Anderson JL, Antman EM, Faxon DP, Fuster V, Halperin JL, Hiratzka LF, Hunt SA, Lytle BW, Nishimura R, Page RL, Riegel B. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing committee to revise the 1998 Guidelines for the Management of Patients With Valvular Heart Disease): developed in collaboration with the Society of Cardiovascular Anesthesiologists: endorsed by the Society for Cardiovascular Angiography and Interventions and the Society of Thoracic Surgeons. *Circulation*. 2006;114:e84–e231.
2. Kim HK, Kim YJ, Kim KI, Jo SH, Kim KB, Ahn H, Sohn DW, Oh BH, Lee MM, Park YB, Choi YS. Impact of the maze operation combined with left-sided valve surgery on the change in tricuspid regurgitation over time. *Circulation*. 2005;112:I14–I19.
3. Nath J, Foster E, Heidenreich PA. Impact of tricuspid regurgitation on long-term survival. *J Am Coll Cardiol*. 2004;43:405–409.
4. Kwon DA, Park JS, Chang HJ, Kim YJ, Sohn DW, Kim KB, Ahn H, Oh BH, Park YB, Choi YS. Prediction of outcome in patients undergoing surgery for severe tricuspid regurgitation following mitral valve surgery and role of tricuspid annular systolic velocity. *Am J Cardiol*. 2006;98: 659–661.
5. Kuwaki K, Morishita K, Tsukamoto M, Abe T. Tricuspid valve surgery for functional tricuspid valve regurgitation associated with left-sided valvular disease. *Eur J Cardiothorac Surg*. 2001;20:577–582.
6. Staab ME, Nishimura RA, Dearani JA. Isolated tricuspid valve surgery for severe tricuspid regurgitation following prior left heart valve surgery: analysis of outcome in 34 patients. *J Heart Valve Dis*. 1999;8:567–574.
7. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, Picard MH, Roman MJ, Seward J, Shanewise JS, Solomon SD, Spencer KT, Sutton MS, Stewart WJ. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiogr*. 2005;18:1440–1463.
8. Kwak JJ, Kim YJ, Kim MK, Kim HK, Park JS, Kim KH, Kim KB, Ahn H, Sohn DW, Oh BH, Park YB. Development of tricuspid regurgitation late after left-sided valve surgery: a single-center experience with long-term echocardiographic examinations. *Am Heart J*. 2008;155: 732–737.
9. Groves PH, Lewis NP, Ikram S, Maire R, Hall RJ. Reduced exercise capacity in patients with tricuspid regurgitation after successful mitral valve replacement for rheumatic mitral valve disease. *Br Heart J*. 1991; 66:295–301.
10. Matsuyama K, Matsumoto M, Sugita T, Nishizawa J, Tokuda Y, Matsuo T. Predictors of residual tricuspid regurgitation after mitral valve surgery. *Ann Thorac Surg*. 2003;75:1826–1828.
11. Koelling TM, Aaronson KD, Cody RJ, Bach DS, Armstrong WF. Prognostic significance of mitral regurgitation and tricuspid regurgitation in patients with left ventricular systolic dysfunction. *Am Heart J*. 2002;144: 524–529.
12. Groves PH, Hall RJ. Late tricuspid regurgitation following mitral valve surgery. *J Heart Valve Dis*. 1992;1:80–86.
13. Mahler F, Covell JW, Ross J Jr. Systolic pressure–diameter relations in the normal conscious dog. *Cardiovasc Res*. 1975;9:447–455.
14. Marsh JD, Green LH, Wynne J, Cohn PF, Grossman W. Left ventricular end-systolic pressure-dimension and stress-length relations in normal human subjects. *Am J Cardiol*. 1979;44:1311–1317.
15. Anand IS, Chandrashekhar Y, Ferrari R, Poole-Wilson PA, Harris PC. Pathogenesis of oedema in chronic severe anaemia: studies of body water

and sodium, renal function, haemodynamic variables, and plasma hormones. *Br Heart J*. 1993;70:357–362.
16. Anand IS, Kuskowski MA, Rector TS, Florea VG, Glazer RD, Hester A, Chiang YT, Aknay N, Maggioni AP, Opasich C, Latini R, Cohn JN. Anemia and change in hemoglobin over time related to mortality and morbidity in patients with chronic heart failure: results from Val-HeFT. *Circulation*. 2005;112:1121–1127.
17. Go AS, Yang J, Ackerson LM, Lepper K, Robbins S, Massie BM, Shlipak MG. Hemoglobin level, chronic kidney disease, and the risks of death and hospitalization in adults with chronic heart failure: the Anemia in Chronic Heart Failure: Outcomes and Resource Utilization (ANCHOR) Study. *Circulation*. 2006;113:2713–2723.
18. King RM, Schaff HV, Danielson GK, Gersh BJ, Orszulak TA, Piehler JM, Puga FJ, Pluth JR. Surgery for tricuspid regurgitation late after mitral valve replacement. *Circulation*. 1984;70(pt 2):I193–I197.
19. Gammie JS, O'Brien SM, Griffith BP, Ferguson TB, Peterson ED. Influence of hospital procedural volume on care process and mortality for patients undergoing elective surgery for mitral regurgitation. *Circulation*. 2007;115:881–887.

CLINICAL PERSPECTIVE

Although the impact of tricuspid regurgitation on long-term prognosis has been well demonstrated, determining the optimal time for corrective surgery remains a difficult clinical problem. Therefore, it is of paramount importance to provide objective measures to predict clinical outcomes after surgery and thus to determine surgical timing in tricuspid regurgitation. We prospectively enrolled 61 patients with isolated severe tricuspid regurgitation to identify preoperative predictors of clinical outcomes after surgery. Operative mortality was 10%, and event-free survival rate was 75% during mean follow-up duration after surgery of 35±16 months. In the 54 patients who underwent 6-month clinical and echocardiographic follow-up, right ventricular end-diastolic area decreased by 29%, and 33 patients (61%) showed improved functional capacity after surgery. Preoperative hemoglobin level and right-ventricular end-systolic area measured by echocardiography emerged as independent determinants of clinical outcomes. On receiver operating characteristic curve analysis, we found that preoperative right ventricular end-systolic area <20 cm^2 and preoperative hemoglobin level >11.3 g/dL predicted event-free survival most effectively. Our data suggest that timely correction of severe tricuspid regurgitation carries an acceptable risk and improves functional capacity. Surgery should be considered before the development of advanced right ventricular systolic dysfunction and before the development of anemia.