Long-Term Outcomes of Tricuspid Valve Surgery in Patients With Congenitally Corrected Transposition of the Great Arteries

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Background—Valvuloplasty is generally considered unsuccessful in patients with congenitally corrected transposition of the great arteries. Optimal timing of tricuspid valve surgery in these patients is crucial.

Methods and Results—We retrospectively reviewed 57 patients with congenitally corrected transposition of the great arteries undergoing tricuspid valve surgery at our institution. Eleven patients had tricuspid valve plasty and 46 had tricuspid valve replacement. Mean duration of follow-up was 7.4±5.5 years in the group of tricuspid valve plasty and 5.6±3.6 years in the group of tricuspid valve replacement, respectively (P=0.33). For the total of 57 patients, estimates of 1-, 5-, and 10-year survival or freedom from transplantation were 96.4%, 91.6%, and 75.6%, respectively. Late right ventricular ejection fraction of most patients (90%) remained preserved (≥40%) during the follow-up. In a highly selected group of tricuspid valve plasty recipients, although long-term survival and right ventricular function were similar compared with tricuspid valve replacement, recurrent tricuspid regurgitation was observed in 60% of these patients. Multivariate Cox regression analysis identified preoperative right ventricular end-diastolic dimension (1-cm increment; hazard ratio, 3.22; P=0.02) as an independent predictor of postoperative mortality or need for transplantation. Patients undergoing surgery with a right ventricular end-diastolic dimension ≥60 mm had a significant lower survival rate compared with those with a right ventricular end-diastolic dimension <60 mm (P=0.003).

Conclusions—Tricuspid valve surgery in patients with congenitally corrected transposition of the great arteries could yield satisfactory long-term outcomes. Recurrent tricuspid regurgitation was frequently observed in tricuspid valve plasty recipients. Preoperative right ventricular end-diastolic dimension was a risk factor for late mortality and surgery should be performed before cardiac enlargement and dysfunction for best outcomes. (J Am Heart Assoc. 2018;7:e008127. DOI: 10.1161/JAHA.117.008127.)

Key Words: congenital heart disease • congenitally corrected transposition of the great arteries • systemic right ventricle • tricuspid valve plasty • tricuspid valve replacement

In congenitally corrected transposition of the great arteries (CCTGA), the combination of atroventricular and ventriculoarterial discord maintains the circulatory pathways in series. Given that patients without significant associated intracardiac lesions could remain asymptomatic for a long period,1–5 these patients can be unrecognized until their adulthood, especially in developing countries like China. Meanwhile, even if they are diagnosed in early childhood, more surgeons tend not to intervene surgically in the absence of hemodynamic lesions, but closely monitor them instead.6,7 Consequently, many patients with CCTGA are referred in adulthood. In these patients, incidence and degree of tricuspid regurgitation (TR) increase over time,5,8 and TR has been identified as a major contributor to right ventricular (RV) failure and decreased survival.2,9–12 Traditionally, TR was considered secondary to dysfunction of morphological RV, which cannot sustain the systemic circulation, and tricuspid valve (TV) surgery was mostly described as unbeneﬁcial in the early days.10,13–15 However, several studies proved that TV surgery in the early stage of RV dysfunction could bring favorable short- and long-term outcomes.12,16,17 To date, very few studies have been reported examining the long-term outcomes of TV surgery in patients with CCTGA, and it is still controversial among cardiac surgeons. Among the limited studies, valvuloplasty was not recommended because of unsatisfactory outcomes.12,18–20 The aims of the present study are to compare the long-term results between valvuloplasty and valve replacement in patients with CCTGA, and to identify the risk factors for postoperative mortality in these patients.
Clinical Perspective

What Is New?

- Preoperative right ventricular end-diastolic dimension was an independent predictor of postoperative mortality or need for transplantation.
- Tricuspid valve surgery should be performed before cardiac enlargement and dysfunction in patients with congenitally corrected transposition of the great arteries for best outcomes.

What Are the Clinical Implications?

- Recurrent tricuspid regurgitation was frequently observed in congenitally corrected transposition of the great arteries patients treated with tricuspid valve plasty; therefore, tricuspid valve plasty may be of limited utility in the management of tricuspid regurgitation in CCTGA.

Methods

The data, analytical methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

Patients

Patients with CCTGA who underwent TV surgery (including repair and replacement) between 1999 and 2016 were identified from the database of our hospital. All patients had at least moderate TR preoperatively. Patients aged <14 years or who had an anatomic repair or palliative procedures (such as pulmonary artery banding, Glenn, and Fontan) were excluded. Two patients could not be reached for the follow-up, and they were also excluded. Eventually, 57 patients were included in the present study. The protocol was approved by the Institutional Review Board of Fuwai Hospital, and written informed consent was obtained from all patients involved.

Operative Techniques

Cardiopulmonary bypass was established through median sternotomy. The approach to the TV was through the right atrium and across the atrial septum. TV was carefully inspected, and the decision to repair or replace was made according to the mechanism of regurgitation and the surgeon’s individual preference. Basically, valvuloplasty was only considered when the main mechanism of regurgitation was annular dilatation. In the present study, a total of 11 patients underwent tricuspid valve plasty (TVP), and the techniques included annuloplasty ring implantation (n=5), De vega annuloplasty (n=3), closure of accessory commissure (n=2), and bicuspidization technique (n=1). Forty-six patients underwent tricuspid valve replacement (TVR), and bioprosthesis was used in only 3. The prosthesis was sewn into place with interrupted pledgeted mattress sutures (n=20) or with a continuous suture (n=26). In TVR, the subvalvular apparatus was preserved as much as possible. Transesophageal echocardiography was performed before the cardiopulmonary bypass was weaned.

Data Collection and Follow-up

Medical records were retrospectively reviewed. Mean duration of follow-up for the entire cohort was 5.98±4.07 years. Functional status was evaluated according to the New York Heart Association functional class. For echocardiography, preoperative results closest to surgery and the immediate postoperative and latest results (≥6 months after surgery) were recorded. TR was graded on a scale of 0 to 4 according to its severity: absent or trivial (0), mild (1), moderate (2), moderate to severe (3), and severe (4). Late TR of above mild degree was defined as recurrent TR. Right ventricular ejection fraction (RVEF) was used to assess RV function. An RVEF ≥40% was selected to define preserved RV function on the basis of previous studies.16,17,21 Echocardiography follow-up was not available for 17 patients, who were only included in the survival analysis. The end point was defined as death or heart transplantation. Postoperative complications included complete heart block, perivalvular leak, prosthesis occlusion, low cardiac output, renal insufficiency, infection, embolism, and rethoracotomy.

Statistical Analysis

SPSS software (version 19; SPSS, Inc, Chicago, IL) was used for statistical analysis. Descriptive statistics for categorical variables were reported as frequency and percentage, whereas continuous variables were reported as mean±SD or median (range) as appropriate. To examine differences between the TVP group and the TVR group, categorical variables were compared using chi-square test or Fisher’s exact test, where appropriate, and continuous variables were compared using 2-sample t test or Wilcoxon rank-sum test where appropriate. Survival analysis was performed using the Kaplan–Meier method and log-rank test. Cox regression models were used to find the risk factors for postoperative mortality or need for cardiac transplantation. Univariate Cox regression analysis was performed initially, and only those variables with a probability value <0.10 were considered for the subsequent step-wise multivariate analysis. A P value of <0.05 was considered to be statistically significant.
Results
Preoperative and Operative Characteristics

There were 57 patients, 32 of them (56%) were male, and age at surgery ranged from 14 to 62 years, with a mean age of 36.6±13.8 years. Eleven patients underwent TVP, and 46 underwent TVR. The 2 groups’ preoperative characteristics are presented in Table 1. Patients who underwent TVP were younger. The majority of patients undergoing TVP had moderate TR preoperatively, whereas severe TR was most commonly observed in patients with TVR. Abnormal TV was observed in only 2 patients who underwent TVP, reflecting the fact that valvuloplasty was mostly performed for TR caused by annular dilatation alone. Approximately 90% of patients were in New York Heart Association functional class II or III in both groups. Echocardiography showed a larger left atrial diameter in patients with TVR, whereas right ventricular end-diastolic dimension (RVEDD) and RVEF were comparable between these 2 groups. Preoperative complete heart block was found in only 2 patients, and both of them were in the group of TVR.

The operative characteristics are shown in Table 2. Mean duration of cardiopulmonary bypass and aortic clamping was similar between the 2 groups. Concomitant procedures included atrial septal defect closure, ventricular septal defect closure, pulmonary outflow surgery, mitral valve repair, mitral valve replacement, and aortic root replacement.

### Table 1. Preoperative Characteristics

|                          | TVP (n=11) | TVR (n=46) | P Value |
|--------------------------|------------|------------|---------|
| Age, y                   | 26.3±9.6 (14–43) | 39.1±13.5 (14–62) | 0.005   |
| Male                     | 5 (45.5%)  | 27 (58.7%) | 0.51    |
| TR grade                 |            |            |         |
| Moderate                 | 7 (63.6%)  | 5 (10.9%)  | 0.001   |
| Moderate to severe       | 2 (18.2%)  | 12 (26.1%) |         |
| Severe                   | 2 (18.2%)  | 29 (63%)   |         |
| Abnormal TV              | 2 (18.2%)  | 19 (41.3%) | 0.19    |
| NYHA functional class    |            |            |         |
| I                        | 1 (9.1%)   | 2 (4.3%)   | 0.25    |
| II                       | 8 (81.8%)  | 21 (45.7%) |         |
| III                      | 2 (18.2%)  | 21 (45.7%) |         |
| IV                       | 0          | 2 (4.3%)   |         |
| LA diameter, mm          | 38.8±12    | 49.7±11.9  | 0.02    |
| RVEDD, mm                | 52.9±10    | 57.7±9.1   | 0.15    |
| RVEF (%)                 | 57.4±6.4 (50–66) | 53.9±7.9 (40–77) | 0.2 |
| SPAP >50 mm Hg           | 1 (9.1%)   | 9 (19.6%)  | 0.67    |

### Postoperative Outcomes

Postoperative outcomes are outlined in Table 3. Only 1 patient who underwent TVR died perioperatively, because of refractory heart failure. Early complications included surgically induced complete heart block (n=3) and perivalvular leak (n=5), all in the group of TVR. Mean duration of follow-up was a little longer in patients with TVP, without statistically significant difference compared with TVR. Late mortality occurred in 1 patient with TVP and 5 with TVR, and 1 had cardiac transplantation 7 years after TVP. For the total of 57 patients, estimates of 1-, 5-, and 10-year survival or freedom from transplantation were 96.4%, 91.6%, and 75.6%, respectively (Figure 1A). Comparing the 2 different surgical strategies, we found that postoperative survival was comparable between TVP and TVR (Figure 1B; log-rank test, P=0.83). Among patients who were alive at the latest follow-up, the majority in both groups (89% and 85%) were in New York Heart Association functional class I or II. Also, similar results of left atrial diameter, RVEDD, and RVEF were noticed in both groups according to the latest echocardiography, and only 10% of patients had a late RVEF lower than 40%. However, it is worth noting that, in the group of TVP recipients, recurrent TR was observed in 6 patients (60%), and 1 had severe TR and underwent redo TVR 12 years later. Table 4 presents the outcomes of individual patients in the group of TVP.

### Risk Factors for Postoperative Mortality

To identify the risk factors for postoperative mortality or need for cardiac transplantation, univariate and multivariate Cox regression analysis was performed for all 57 patients (Table 5). In this analysis, preoperative RVEDD (1-cm increment; hazard ratio, 3.22; 95% confidence interval, 1.23–8.4; P=0.02) and bypass time (10-minute increment; hazard ratio, 1.19; 95% confidence interval, 1.07–1.33; P=0.002) emerged as independent predictors of postoperative mortality or need.
for cardiac transplantation. To further evaluate the impact of RVEDD on late survival, patients were grouped according to their preoperative RVEDD (≥60 mm, n=25 or <60 mm, n=32). Kaplan–Meier curves showed a significant lower survival rate in patients with an RVEDD ≥60 mm (Figure 2; log-rank test, \( P=0.003 \)).

### Table 2. Operative Characteristics

|                      | TVP (n=11) | TVR (n=46) | \( P \) Value |
|----------------------|------------|------------|---------------|
| Bypass time, min     | 122.2±34.4 (75–175) | 112.7±61.8 (49–323) | 0.64          |
| Clamping time, min   | 84.1±29.9 (57–128)   | 77.9±44.8 (32–268)  | 0.68          |
| Concomitant procedures |           |            |               |
| ASD closure          | 3 (27.3%)  | 12 (26.1%) | 0.94          |
| VSD closure          | 7 (63.6%)  | 11 (23.9%) | 0.03          |
| Pulmonary outflow surgery | 3 (27.3%) | 7 (15.2%) | 0.39          |
| Mitral valve repair  | 2 (18.2%)  | 5 (10.9%)  | 0.61          |
| Mitral valve replacement | 0       | 2 (4.4%)  | 1.0           |
| Aortic root replacement | 0       | 1 (2.2%)  | 1.0           |

ASD indicates atrial septal defect; TVP, tricuspid valve plasty; TVR, tricuspid valve replacement; VSD, ventricular septal defect.

### Table 3. Postoperative Outcomes

|                      | TVP | TVR | \( P \) Value |
|----------------------|-----|-----|---------------|
| Early mortality      | 11  | 0   | 1.0           |
| Follow-up, y         |     |     |               |
| Vital status         | 11  | 45  | 0.33          |
| Echocardiography     | 10  | 29  | 0.1           |
| Late mortality or transplantation | 11  | 45  | 0.61          |
| NYHA functional class| 9   | 40  | 0.86          |
| I                    | 2 (22.2%) | 5 (12.5%) |               |
| II                   | 6 (66.7%) | 29 (72.5%) |               |
| III                  | 1 (11.1%) | 5 (12.5%)  |               |
| IV                   | 0   | 1 (2.5%) |               |
| Recurrent TR (moderate or more) | 10  | 29  | <0.001        |
| Moderate             | 5 (50%) | 0   |               |
| Severe               | 1 (10%) | 0   |               |
| LA diameter, mm      | 9   | 27  | 0.33          |
| RVEDD, mm            | 9   | 28  | 0.67          |
| RVEF (%)             | 10  | 29  | 0.51          |
| RVEF <40%            | 10  | 29  | 1.0           |
| Atrial fibrillation or flutter | 9   | 30  | 0.32          |
| Complications        | 11  | 45  |               |
| Complete heart block | 0   | 3 (6.7%) | 1.0           |
| Perivalvular leak    | ... | 5 (11.1%) | ...           |
| Prosthesis occlusion | ... | 1 (2.2%) | ...           |
| Stroke               | 0   | 2 (4.4%) | 1.0           |
| Reoperation          | 11  | 45  | 0.49          |

LA indicates left atrial; NYHA, New York Heart Association; RVEDD, right ventricular end-diastolic dimension; RVEF, right ventricular ejection fraction; TVP, tricuspid valve plasty; TVR, tricuspid valve replacement; TR, tricuspid regurgitation.
Discussion

Surgical treatment of CCTGA comprises 2 basic strategies (ie, physiological repair and anatomical repair). Physiological repair targets associated intracardiac lesions, such as ventricular septal defect and TR, and the morphological RV remains the systemic ventricle. On the other hand, anatomical repair, mostly the double-switch procedure in the current era, restores the morphological left ventricle to the systemic position. For pediatric patients associated with TR, an anatomical repair has a superior outcome compared with a physiological repair and is advocated in these patients. However, in adult patients with significant TR, anatomical repair is almost impossible to be achieved, and TV surgery serves as the only surgical option other than heart transplantation. Nevertheless, limited literature about the long-term outcomes of this type of surgery can be found. In this study, we included a group of CCTGA patients who underwent TV surgery at our institution. All of these patients had a preserved RVEF (≥40%) preoperatively, and the long-term outcomes were satisfactory, with an estimated 10-year survival rate of 75%. Late RVEF of most patients (90%) remained preserved during the follow-up.

Table 4. Outcomes of Patients Undergoing TVP

| Patient No. | Pre-Op TR    | Valvuloplasty Technique | Immediate Post-Op TR | Late TR     | Survival (Y) |
|-------------|--------------|------------------------|----------------------|-------------|--------------|
| 1           | Severe       | Anuloplasty ring        | Mild                 | Moderate    | Transplant (7.3) |
| 2           | Moderate to severe | De vega              | Trivial              | Severe      | Redo TVR (12) |
| 3           | Moderate     | Closure of accessory commissure | Mild             | Moderate    | Alive (13.8)  |
| 4           | Moderate     | Closure of accessory commissure | Mild             | Mild        | Alive (13.4)  |
| 5           | Severe       | Anuloplasty ring        | Mild                 | Moderate    | Alive (13)    |
| 6           | Moderate     | De vega                | Mild                 | Mild        | Alive (11.9)  |
| 7           | Moderate     | De vega                | ...                  | ...         | Dead (1)      |
| 8           | Moderate     | Anuloplasty ring        | Trivial              | Mild        | Alive (4.8)   |
| 9           | Moderate     | Bicuspudization         | Mild                 | Mild        | Alive (1.8)   |
| 10          | Moderate to severe | Anuloplasty ring       | Mild                 | Moderate    | Alive (1.7)   |
| 11          | Moderate     | Anuloplasty ring        | Mild                 | Moderate    | Alive (0.9)   |

Post-op indicates postoperative; Pre-op, preoperative; TR, tricuspid regurgitation; TVP, tricuspid valve plasty; TVR, tricuspid valve replacement.
Table 5. Univariate and Multivariate Cox Regression Analysis for Postoperative Mortality or Need for Transplantation (n=57)

|                        | HR    | 95% CI         | P Value |
|------------------------|-------|----------------|---------|
| **Univariate**         |       |                |         |
| Age                    | 0.972 | 0.918 to 1.029 | 0.33    |
| NYHA functional class III to IV | 3.36  | 1.12 to 10.09  | 0.03    |
| Abnormal TV            | 1.92  | 0.67 to 5.49   | 0.23    |
| Preoperative severe TR | 1.72  | 0.4 to 7.3     | 0.46    |
| LA diameter (1-cm increment) | 1.7   | 1.04 to 2.79   | 0.04    |
| RVEDD (1-cm increment) | 2.56  | 1.10 to 5.96   | 0.03    |
| RVEF (5% increment)    | 0.51  | 0.30 to 0.87   | 0.01    |
| SPAP >50 mm Hg         | 1.29  | 0.15 to 11.49  | 0.82    |
| Preoperative atrial fibrillation | 3.22  | 0.62 to 16.68  | 0.16    |
| TVP                    | 0.83  | 0.16 to 4.34   | 0.83    |
| Bypass time (10-min increment) | 1.15  | 1.05 to 1.27   | 0.003   |
| Clamping time (10-min increment) | 1.14  | 1.02 to 1.28   | 0.02    |
| Postoperative complete heart block | 2.53  | 0.29 to 21.85  | 0.4     |
| Perivalvular leak       | 1.64  | 0.19 to 14.19  | 0.65    |
| **Multivariate**       |       |                |         |
| RVEDD (1-cm increment) | 3.22  | 1.23 to 8.40   | 0.02    |
| Bypass time (10 min increment) | 1.19  | 1.07 to 1.33   | 0.002   |

CI indicates confidence interval; HR, hazard ratio; LA, left atrial; NYHA, New York Heart Association; RVEDD, right ventricular end-diastolic dimension; RVEF, right ventricular ejection fraction; SPAP, systolic pulmonary artery pressure; TVP, tricuspid valve plasty; TR, tricuspid regurgitation; TV, tricuspid valve.

term survival and RV function were similar in both groups, the recurrent TR, defined as above mild degree, was observed in 60% of patients undergoing valvuloplasty. Considering that the long-standing RV volume overloading may predispose to systemic RV dilation and dysfunction, the high incidence of recurrent TR is unacceptable. The reason for the comparable outcomes might be the TVP recipients’ younger age and less preoperative TR at baseline. Although valvuloplasty has some inherent advantages over valve replacement, based on our limited experience, it is still difficult to anticipate which group of patients would actually benefit from TVP. Therefore, as for now, we do not recommend TVP in patients with CCTGA.

In this series, valve replacement was associated with a high incidence of postoperative complications, including complete heart block, perivalvular leak, prosthetic occlusion, and stroke. Considering that the conduction tissue lies on the left side of the septum in CCTGA, incidence of complete heart block might be the consequence of mitral valve surgery or ventricular septal defect closure, instead of TVR. In the 3 cases of surgically induced complete heart block, 2 underwent mitral valve surgery and the other 1 had ventricular septal defect closure. Consequently, these procedures should be performed with extreme caution. As for perivalvular leak, the continuous suturing was the selected technique in all the 5 patients with this complication; therefore, we recommend using the interrupted pledgeted mattress sutures in all cases.

Preoperative RVEF has proved to be an important predictor of late mortality and ventricular function.16,17 In a previous study by Mongeon et al,16 patients who underwent TVR with a RVEF <40% had poor outcomes, suggesting that the surgery should be performed earlier to maintain the systemic RV function. In this series, in the absence of severely impaired RVEF (<40%), we identified the RVEDD as another risk factor for postoperative mortality, and patients who underwent surgery with an RVEDD ≥60 mm had a significant lower survival rate compared with those with an RVEDD <60 mm. This result supported the idea that this type of operation should be considered before cardiac enlargement and dysfunction for best outcomes.

In addition to TV competence, the ultimate fate of RV function in CCTGA was influenced by several factors, including adaptability to the systemic afterload, myocardial perfusion,32–35 and arrhythmias.36 Significant individual differences have been noticed in the long-term outcomes of these patients. For a subset of patients undergoing TV surgery, even though the procedure is performed in the early stage, RV is still doomed to fail, and heart transplantation is the final solution. However, it is still difficult to identify such patients to date. Nevertheless, for these unfortunate patients, relief of TR could improve quality of life and survival and, possibly, delay the need for transplantation.
Our study had some limitations. This was a retrospective study. The patients undergoing TVP were a highly selected group (only 11 of 57 patients) and differed in several aspects at baseline from the patients undergoing TVR, who were younger and had lower degree of preoperative TR. With these limitations, we might not be able to reveal some significant differences in the outcomes between the 2 strategies of TV surgery.

In conclusion, we demonstrated that TV surgery in patients with CCTGA could yield satisfactory long-term results. In a highly selected group of TVP recipients, although long-term survival and RV function were similar compared with patients undergoing TVR, recurrent TR was frequently observed in this highly selected group of TVP recipients, although long-term differences in the outcomes between the 2 strategies of TV surgery were highly significant lower survival rate.

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Disclosures

None.

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