Effects of tricuspid valve surgery on tricuspid regurgitation in patients with hypoplastic left heart syndrome: a non-randomized series comparing surgical and non-surgical cases

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Abstract

OBJECTIVES: Tricuspid regurgitation (TR) remains an important risk factor affecting the survival of patients with hypoplastic left heart syndrome (HLHS). We performed this study to investigate differences in the clinical course based on the timing of the development of TR and the effects of tricuspid valve surgery (TVS).

METHODS: One hundred and five patients of classic HLHS underwent staged operations from May 1991 to July 2010. Forty-four patients (41.9%) exhibited moderate or greater TR during the follow-up. We defined the early TR group (30 patients, around the first palliative surgery) and the late TR group (14 patients, the later period) based on the timing of the appearance of moderate or greater TR. We performed TVS when moderate or greater TR was detected in 28 patients. The follow-up period was 5.5 ± 5.1 (plus/minus values are means ± SD) years (range: 0.01–14.6 years) after the first palliative surgery and 4.9 ± 4.4 years (range: 0.01–13.3 years) after TVS.

RESULTS: The early TR group exhibited poorer survival than the late TR group (42.9 vs 92.9% at 5 years, P = 0.003). However, in the early TR group, the TVS significantly improved survival compared with that observed in the non-TVS cases (52.1 vs 23.3% at 5 years, P = 0.046). The right ventricular ejection fraction (RVEF) significantly decreased (62.7 ± 11.4→57.2 ± 12.6% (plus/minus values are means ± SD), P = 0.040) and the right ventricular end-diastolic diameter (RVDD) became significantly enlarged (27.7 ± 7.6→36.7 ± 3.4 mm, P < 0.001) in association with deterioration of the TR degree. TVS significantly improved the degree of TR (2.5 ± 0.5→1.5 ± 0.9°, P < 0.001) and RVDD (37.7 ± 7.4→30.4 ± 5.0 mm, P = 0.007); however, the RVEF was not improved 1 month after surgery (54.4 ± 12.1→54.3 ± 12.4%, P = 0.931) or at the latest follow-up (53.7 ± 14.9%, P = 0.836).

CONCLUSIONS: The survival of HLHS patients who develop moderate or greater TR around the time of the first palliative surgery is worse than that of HLHS patients who develop moderate or greater TR at a later time. In this study, TVS for early TR improved survival and decreased right ventricular dimensions during the 4.9-year follow-up period.

Keywords: Hypoplastic left heart syndrome • Tricuspid valve • Tricuspid regurgitation

INTRODUCTION

The surgical results of patients with hypoplastic left heart syndrome (HLHS) have dramatically improved over the past two decades. However, tricuspid regurgitation (TR) remains an important risk factor that affects their survival, and there have been many reports regarding the negative impact of TR on the clinical course of HLHS [1–8]. Some patients show significant TR at birth, which may be diagnosed prenatally by fetal echocardiography [9, 10], and tend to present a difficult clinical course. Others show a gradual increase in TR as they grow.

Regarding the timing of tricuspid valve surgery (TVS), there have been some reports that recommend that TVS should be performed at the same time as the bidirectional Glenn procedure (BDG) when moderate or greater TR is present [7, 8, 11]. However, there have not been any reports about the timing of TVS for significant TR present at birth.

This series included patients with early TR. We performed this study in order to investigate differences in the clinical course based on the timing of development of significant TR and the effects of TVS with regard to survival and the right ventricular function.

MATERIALS AND METHODS

Study population

Staged operations were performed for 105 classic HLHS patients between May 1991 and July 2010. Of these, 44 patients (41.9%) who had moderate or greater TR during their overall clinical
course were targeted. We performed TVS when significant TR of moderate or greater degree was detected. The follow-up period after the first palliative surgery was 5.5 ± 5.1 (plus–minus values are means ± SD) years. This study was performed retrospectively and was non-randomized. Operations were performed by a single surgeon at a single institute.

Classification of the early TR group/late TR group and TVS cases/non-TVS cases

Forty-four patients were classified into two groups according to the timing of the appearance of significant TR of moderate or greater degree. The early TR group included 30 patients with significant TR that appeared around the time of the first palliative surgery (bilateral pulmonary artery banding (bPAB) or Norwood procedure). The late TR group included 14 patients whose significant TR appeared immediately before or after the BDG (including the Norwood with Glenn procedure).

In the early TR group, 20 patients underwent TVS at 6.5 ± 9.0 months (TVS cases), while 10 did not (non-TVS cases). In the late TR group, 8 patients underwent TVS at 11.2 ± 7.5 months (TVS cases), while 6 did not (non-TVS cases). In the early TR group, for historical reasons and after considering the surgical risks, we did not attempt to perform TVS simultaneously with the Norwood procedure in some cases, even if moderate or greater TR was found, particularly between 1991 and 2001. Such patients are indicated to undergo TVS according to the current criteria; these patients were designated as non-TVS cases. In the late TR group, some patients whose cardiac function and haemodynamics were well maintained were observed without TVS; these patients were designated as non-TVS cases.

Echocardiography

Transthoracic echocardiography was performed for all patients, and the changes in the degree of TR and cardiac function could be followed at each stage of surgery. The grade of TR was classified by the echocardiographic examination. It was classified as none (0°), mild (1°, narrow regurgitant jet), moderate (2°, wide jet that reaches the back wall of the atrium) or severe (3°, wide jet that bound at the back wall of the atrium). Moreover, the right ventricular ejection fraction (RVEF) and right ventricular end-diastolic diameter (RVDD) were measured to indicate the right ventricular function and size. The changes in the TR degree, right ventricular function and right ventricular size were compared between before TVS and 1 month after the surgery, and the RVEF was evaluated based on the latest data (4.9 ± 4.4 years after TVS).

Chest X-rays

Chest X-rays were performed for all patients, and the changes in cardiothoracic ratio (CTR) could be followed as an indicator of cardiac size at each stage of surgery.

Statistics

Early death was defined as death within 30 days of surgery and late death was defined as death 30 days or more after surgery.

The results are expressed as mean ± SD. A paired Student’s t-test was used to compare the differences in continuous variables between the two groups for the same subject. Estimates of cumulative survival were calculated according to the Kaplan–Meier method and compared using the log-rank test. A two-sided P-value of <0.05 was considered to be statistically significant.

RESULTS

Clinical course

Figure 1 shows the clinical courses of 44 patients who developed moderate or greater TR during the follow-up. These patients underwent their first palliative surgery at a median age of 10.0 days (range, 0–31.0 days). In detail, the Norwood procedure was performed in 35 patients at a median age of 9.5 days (range, 0–31.0 days; right ventricle to pulmonary artery conduit in 21 patients, Blalock–Taussig shunt in 14 patients) and bPAB was performed in 9 patients at a median age of 13.5 days (range, 6.0–28.0 days). After the first palliative surgery, there were 12 deaths until the second palliative surgery, which included 2 early deaths and 7 late deaths after the Norwood procedure, and 2 early deaths and 1 late death after bPAB. Twenty-four patients underwent BDG as a second palliative surgery at a median age of 7.1 months (range, 4.2–12.1 months), while 6 patients underwent the Norwood with the Glenn procedure at a median age of 3.6 months (range, 2.7–4.0 months). After the second palliative surgery, there were 4 late deaths after BDG before Fontan procedure. Twenty-four patients underwent the extracardiac total cavopulmonary connection procedure (TCPC) at a median age of 2.3 years (range, 1.1–3.8 years). There was 1 early death after TCPC.

The timing of TVS for TR

The timing of the first TVS was as follows: at the time of the Norwood procedure in 9 patients, at the second palliative surgery in 13 patients (BDG in 10 patients, Norwood with Glenn procedure in 3 patients), before TCPC in 3 patients and at TCPC in 3 patients.

Reoperations for TR were performed in 3 patients. These were before TCPC in 1 patient and at TCPC in 2 patients.

Types of TVS

For central TR primarily caused by annular dilatation, we performed annuloplasty according to the De Vega method. We chose to perform commissure closure in patients with commissural gap and valvuloplasty, including edge-to-edge repair, in patients with structural valve abnormalities, such as a prolapsed leaflet.

The types of first TVS were as follows: annuloplasty alone was performed in 15 patients (De Vega method in 14 patients, Kay method in 1 patient), annuloplasty (De Vega method) + commissure closure in 7 patients, commissure closure alone in 2 patients, edge-to-edge repair in 2 patients and tricuspid valve replacement (TVR) was performed in 2 patients.

Reoperations for TR were performed in 3 patients, which were a tricuspid valve repair in 2 patients (annuloplasty + commissure closure in 1 case, commissure closure alone in 1 case) and TVR in 1 patient.
The morphological findings of the tricuspid valve during the operations are given in Table 1. This series focused on classic HLHS; therefore, the atrioventricular valve morphology included only the tricuspid valve, not other valves, such as the common atrioventricular valve. Morphological abnormalities were frequently observed in both the early and the later TR groups. There was no significant difference in incidence of tricuspid valve abnormalities between the two groups. In 4 patients, we found hypoplasia of the septal leaflet with shortening of the chordae as a severe structural abnormality. Three of these 4 patients also had prolapsed anterior leaflet, and they underwent edge-to-edge repair, but 2 of them converted to TVR during the same operation.

**Survival**

The survival among all 44 patients was 71.8% at 1 year, 62.0% at 3 years and 62.0% at 5 years. The early TR group exhibited a poorer survival than the late TR group (57.6 vs 100% at 1 year, 42.9 vs 92.9% at 3 years and 42.9 vs 92.9% at 5 years, $P = 0.003$, Fig. 2A). However, in the early TR group, the TVS cases showed significantly superior results compared with the non-TVS cases (73.7 vs 23.3% at 1 year, 52.1 vs 23.3% at 3 years and 52.1 vs 23.3% at 5 years, $P = 0.046$, Fig. 2B). On the other hand, late TR cases showed favourable result in both the TVS and the non-TVS cases.

### Table 1: Morphological findings of tricuspid valve during tricuspid valve surgery

<table>
<thead>
<tr>
<th>Causes of development of TR</th>
<th>Early TR group n = 20 (%)</th>
<th>Late TR group n = 8 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Only annular dilatation</td>
<td>8 (40)</td>
<td>1 (12.5)</td>
</tr>
<tr>
<td>Structural abnormalities</td>
<td>12 (60)</td>
<td>7 (87.5)</td>
</tr>
<tr>
<td>Commissural gap</td>
<td>8 (40)</td>
<td>3 (37.5)</td>
</tr>
<tr>
<td>Thickenig of leaflets</td>
<td>2 (10)</td>
<td>4 (50)</td>
</tr>
<tr>
<td>Prolapse of leaflets</td>
<td>2 (10)</td>
<td>2 (25)</td>
</tr>
<tr>
<td>Hypoplasia of the septal leaflet</td>
<td>2 (10)</td>
<td>2 (25)</td>
</tr>
<tr>
<td>Shortening of the chordae</td>
<td>2 (10)</td>
<td>2 (25)</td>
</tr>
</tbody>
</table>

**Freedom from recurrent TR following TVS**

The rates of freedom from recurrence of moderate or greater TR following TVS of all patients with significant TR, the early TR group and the late TR group were 50.9, 50.9 and 50.0% at 1 year, 42.0, 44.5 and 33.3 at 3 years, respectively. Recurrence of TR occurred at a similar incidence in both groups, and there were no significant differences between the early and the late TR group ($P = 0.474$, Fig. 3).

**The percentage of moderate or greater TR in clinical course of the early TR group**

Figure 4A shows the clinical course of the percentage of moderate or greater TR in the early TR group. In the patients without TVS, 7 of 10 patients (70%) showed moderate TR at birth. Five of these 7 patients underwent the Norwood procedure alone (2 cases underwent bPAB), and 4 of the 5 patients died. Two patients who showed moderate or greater TR after the Norwood procedure also died after the surgery. One moderate TR patient who underwent bPAB died after the surgery.

On the other hand, the patients who underwent TVS simultaneously with the Norwood procedure were also difficult cases. All of the 5 severe TR patients died after the Norwood procedure, because of acute or chronic heart failure. However, 3 of the 5 moderate TR patients survived.

In the patients who underwent TVS between BDG and TCPC, though severe TR patients prior to TVS also showed poor survival,
The percentage of moderate or greater TR in clinical course of the late TR group

In the late TR group, the patients who underwent TVS showed relatively satisfactory results, though there was 1 death in TVR case. The percentage of moderate or greater TR improved after BDG with TVS in many patients; however, several patients showed recurrence of significant TR.

On the other hand, in the patients without TVS, many patients' TR were progressing and they had moderate or greater TR after TCPC, but they exhibited relatively favourable results without death (Fig. 4B).

Correlation between the deterioration of TR and the cardiac function

The changes in the RVEF, CTR and RVDD corresponding to the degree of deterioration in TR over time in 25 patients who exhibited gradual deterioration of TR from none/mild to moderate/severe after birth are given in Table 2. The RVEF significantly decreased with the deterioration of the TR degree (P = 0.040). On the other hand, the CTR in chest X-rays showed a significant increase (P = 0.026), and the RVDD also showed a significant increase (P < 0.001).

Changes in cardiac function after TVS

Compared with before TVS, the degree of TR improved significantly 1 month after the surgery (P < 0.001). Although the CTR decreased significantly (P = 0.003), and the RVDD also decreased significantly (P = 0.007, Table 3), the RVEF did not show a significant change 1 month after TVS (54.5 ± 12.2 → 54.3 ± 12.4%, P = 0.931) or at the latest follow-up (53.7 ± 14.9%, P = 0.836).

DISCUSSION

The major findings of the present study are as follows: the patients with classic HLHS frequently exhibited moderate or greater TR in their clinical course after birth. The early TR group showed poorer survival than the late TR group. However, TVS when moderate or greater TR was detected improved their survival significantly. TVS significantly improved the degree of TR and right ventricular dilatation; however, the right ventricular systolic function was not improved 1 month after surgery or in the mid- to long-term results.

Survival, clinical courses of the TR and strategy for TR

In the early TR group, TVS cases showed results significantly superior to those of the non-TVS cases. The Norwood procedure alone for significant TR cases is supposed to burden the patients with a high volume load due to the systemic-pulmonary shunt, and may lead to increase in TR and acute heart failure in this situation.

Guleserian et al. [12] reported bPAB for high-risk single-ventricle patients with moderate or greater atroventricular valve regurgitation or other risks, as a bridge to conventional Norwood procedure or primary cardiac transplantation. We also performed bPAB
for several patients with significant TR at birth and their clinical courses were relatively stable, who performed TVS with the Norwood with Glenn procedure at 2.5–4 months of age following bPAB [13].

Our current strategy is to perform the Norwood procedure within 2 weeks of age, with TVS for patients with only moderate TR as a risk factor at birth and bPAB for multiple-risk patients with both significant TR and other cardiac or non-cardiac complications as a first palliative surgery. If the TR deteriorates early after bPAB, we plan to perform the Norwood procedure with TVS, because this may indicate the presence of morphological abnormalities of the tricuspid valve.

We also perform TVS for the cases of moderate or greater TR at BDG. In the period at or after BDG, the surgical results in survival were relatively acceptable even in the early TR group, particularly in the moderate TR cases.

Hansen et al. [8] reported that more than moderate TR should be targeted at surgery simultaneously with BDG, as it is a risk factor for adverse outcomes, such as death or the need for cardiac transplantation. Kasnar-Samprec et al. [11] showed that BDG in patients with HLHS promoted the remodelling of the systemic right ventricle but this did not improve the degree of TR. They also recommended that TVS should be considered at the time of BDG in patients with moderate and severe TR.

**Relationship between morphological abnormalities of the tricuspid valve and the development of TR**

The relationships between morphological abnormalities and the development of TR have been described in previous studies [4, 7, 14, 15]. Takahashi et al. [14] found that moderate TR is associated with the tethering and prolapse of the tricuspid valve leaflets in HLHS patients using three-dimensional echocardiography. Also in our findings, the patients with significant TR frequently had morphological abnormalities of the tricuspid valve in both the early TR group (60%) and the late TR group (87.5%). Commisural gaps, prolapse of leaflets, hypoplasia of the septal leaflet and shortened chordae of the septal leaflet were associated with the development of significant TR. In 3 patients, we found hypoplasia of the septal leaflet and shortened chordae complicated with prolapsed anterior leaflet as severe abnormalities of tricuspid valve, and these 3 patients were difficult to correct by edge-to-edge repair and 2 of them needed TVR during the same operation.
Correlation between deterioration of TR and right ventricular function, and the timing of TVS

We observed a significant decrease in the right ventricular function and significant right ventricular dilatation in association with deterioration of TR. After TVS, the right ventricular dilatation improved significantly, whereas the right ventricular systolic function did not change significantly within 1 month or 4.9 ± 4.4 years after TVS.

In studies regarding mitral valve regurgitation as acquired valvular heart disease, it was indicated that when a decrease in the left ventricular ejection fraction (<55%) or an increase in the left ventricular end-systolic diameter (≥40 mm) is detected, mitral valve repair should be considered to preserve the postoperative left ventricular function [16]. From the view point of the systemic ventricular function, it is also supposed that performing TVS before deterioration of the right ventricular function would better help to preserve the function of the systemic right ventricle in HLHS patients. In this study, moderate or greater TR indicated the start of a decrease in the right ventricular function.

Regarding the right ventricular function after TVS, Elmi et al. [6] also described that immediately after surgery (24 h after surgery), the right ventricular performance was no different or even slightly worse compared with that before TVS, and our findings were in agreement with this result. However, their findings indicated that the right ventricular performance improved in the long-term (median follow-up, 5.1 years). In contrast, our results indicated that patients might not show improvement of the right ventricular function in the mid- to long-term after they exhibit functional deterioration.

In this study, TVS for early TR improved the survival of patients with HLHS and decreased the right ventricular dimensions during the 4.9-year follow-up period. Furthermore, to preserve the function of the right ventricle, it may be better for patients who show moderate or greater TR to undergo TVS before deterioration of the right ventricular function.

Study limitations

The present study was limited by the relatively small sample size and non-randomized design, particularly in the classification of the groups between TVS cases and non-TVS cases and of the types of the first palliative surgery (Norwood procedure or bPAB). In addition, this study was performed retrospectively using surgical records, so it is likely that there were more structural abnormalities of the tricuspid valve than we noted. A study with more patients and a longer follow-up is needed to clarify the clinical course of TR and right ventricular function after TVS.

CONCLUSION

The patients with classic HLHS frequently exhibited moderate or greater TR in their clinical course. The survival of patients who develop moderate or greater TR around the time of the first palliative surgery is worse than that of patients who develop this condition at a later time. In this study, TVS for early TR improved the survival and decreased the right ventricular dimensions during the 4.9-year follow-up period.

Conflict of interest: none declared.

REFERENCES