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Repair of the tricuspid valve in hypoplastic left heart syndrome

Richard G. Ohye,[1] Carlen A. Gomez,[2] Caren S. Goldberg,[2] Holly L. Graves,[1] Eric J. Devaney,[1] Edward L. Bove[1]

[1]*Division of Pediatric Cardiovascular Surgery, and* [2]*Division of Pediatric Cardiology, University of Michigan Medical School, Ann Arbor, Michigan, United States of America*

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THE OUTLOOK FOR PATIENTS WITH HYPOPLASTIC left heart syndrome has dramatically improved over the past two decades. Universally fatal only 25 years ago, since that time outcomes for staged palliation have shown consistent improvement. Recent reports show that eight to nine patients from every ten can now leave the hospital after the Norwood procedure.[1] Attrition following the Norwood procedure, nonetheless, remains significant, with from five to fifteen percent of patients dying between the first and second stages of the Norwood sequence.[1–4] Only three-quarters of the patients undergoing surgery for hypoplastic left heart syndrome survive after five years, even at the centres reporting the best outcomes for the Norwood procedure.[1,5] In addition to the deaths, some patients are unable to progress through the three stages of reconstruction, and may require cardiac transplantation, or have no options for further therapy. There are many causes for these mortalities and morbidities following the Norwood procedure, including elevated pulmonary vascular resistance, cardiac arrhythmias, coronary arterial insufficiency, right ventricular failure, right ventricular volume overload due to shunt-dependent physiology, and tricuspid valvar regurgitation. Many of these factors are interrelated, and may form feedback loops, which serve to propagate their adverse effects on patients with hypoplastic left heart syndrome.

Regurgitation across the tricuspid valve is of particular interest, as it is one potential area in which surgical intervention may improve outcomes. Such regurgitation may be due to an intrinsic anatomic abnormality of the valve, or it may be due to any of the factors outlined above, such as right ventricular dysfunction or dilation. In addition, the morphologically tricuspid valve is subjected to systemic pressures after the Norwood procedure, rather than pulmonary workloads. Due to the multi-factorial nature of the etiology of tricuspid regurgitation, simple repair of the valve may not address the underlying problem, and hence fail to improve either the regurgitation itself, or the outcome for the patients. To address this issue, we performed a retrospective review of all patients undergoing repair of the tricuspid valve to assess early and late outcomes, as well as procedural and anatomic variables predictive of successful repair.

Correspondence to: Richard G. Ohye MD, F7830 Mott/0223, 1500 East Medical Center Drive, Ann Arbor, Michigan 48109, United States of America. Tel: +734 936 4978; Fax: +734 763 7353; E-mail: ohye@umich.edu

Methods

Design of the study

To determine the results of repair of the tricuspid valve in patients undergoing surgery for hypoplastic left heart syndrome, we performed a retrospective analysis of all patients undergoing such repair following a Norwood operation. We hypothesized that repair of the valve is an effective means of treating tricuspid regurgitation in patients with hypoplastic left heart syndrome. The primary endpoint was the degree of regurgitation present at last follow-up, irrespective of death unrelated to the valve, or transplantation. A successful outcome was defined as less than moderate, and an adverse outcome as greater than moderate tricuspid regurgitation, as defined by the standard grading scale from zero to four, taking a score of 2 as the discriminating value. Right ventricular function was graded on a subjective scale as normal, mildly depressed, moderately depressed, and severely depressed. We noted any anatomic malformations responsible for the regurgitation, such as prolapse or

tethering of the leaflets. The diameter of the tricuspid valve, expressed as a z value, was also recorded for all patients, using standard calculations to assess the degree of annular dilation.[6] The variables of the degree of tricuspid regurgitation, right ventricular function, valvar anatomy, and z-score for the tricuspid valve were all assessed pre-operatively, at discharge following repair, and at latest follow-up. A single echocardiographer reviewed all echocardiograms.

Secondary aims involved comparing the groups with successful and unsuccessful results as defined above. Variables for comparison included patient demographics, valvar anatomy, operative technique, right ventricular function, and immediate post-operative result. The other secondary aims were to evaluate the durability of successful repair and survival. The review was approved by the Institutional Review Board of the University of Michigan Health System.

Patients

From August 1994 to December 2002, we performed surgery in 475 patients with hypoplastic left heart syndrome at the C.S. Mott Children's Hospital of the University of Michigan Health System. Of these patients, 28 had undergone repair of the tricuspid valve for greater than moderate tricuspid regurgitation, graded at greater than 2 on the sliding scale, following a Norwood procedure. Only patients with classic hypoplastic left heart syndrome, as defined by right ventricular-dependent systemic circulation and atresia or hypoplasia of the aortic valve, were enrolled. The demographics recorded included the age and weight at repair, the stage of palliation, and the length of follow-up. Surgical variables included the type of repair, concomitant procedures, and operative morbidity or mortality.

Surgical techniques

Surgical techniques were individualized to the valvar pathology based upon the opinion of the operating surgeon. Standard methods of cardiopulmonary bypass were utilized, with initial examination of the tricuspid valve performed by filling the right ventricle with saline. Intra-operative determination was made of the location of regurgitation, the diameter of the annulus, and the presence of either prolapse or tethering of the leaflets. Coupled with the evidence available from the pre-operative and/or intra-operative echocardiograms, the surgeon then selected the most appropriate methods for repair. Partial annuloplasty was commonly used for patients with prolapse of the anterior leaflet, or annular dilation with failure of coaptation of the leaflets and generalized central regurgitation. This technique involves running parallel mattress sutures along the annulus supporting the inferior leaflet between its zones of apposition with the anterior and septal leaflets (Fig. 1). The annuloplasty essentially obliterates the inferior leaflet, forming a bifoliate valve. Localized areas of prolapse were repaired using partial closure of the zones of apposition with adjacent leaflets, and individual clefts or defects in the leaflets were closed directly. Ring annuloplasty was also employed using a flexible partial ring. Less frequently employed techniques included shortening of tendinous cords in 3 patients, advancement of a papillary muscle in one, and mobilization of the septal leaflet in another. The techniques were not mutually exclusive, and any individual patient may have undergone more than one method of repair.

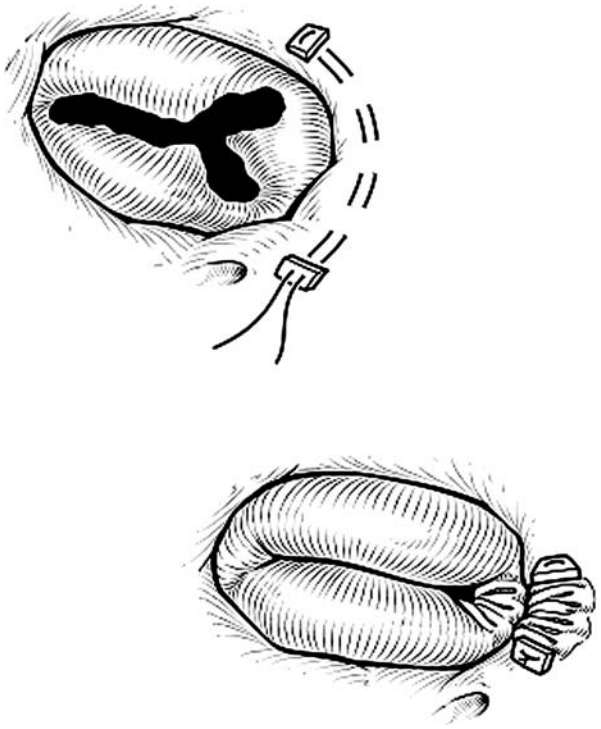

Figure 1.
The technique for partial annuloplasty, which effectively obliterates the inferior leaflet of the tricuspid valve.

Statistical analysis

Differences in dichotomous variables were compared using Fisher's exact test. The Wilcoxin Rank Sum was performed to compare the differences in ordinal variables, such as tricuspid regurgitation and right ventricular dysfunction. Tricuspid regurgitation in the post-operative period was dichotomized to greater or less than 2 on the chosen scale. The sensitivity, specificity, and positive and negative predictive values were then calculated for the finding of greater than moderate post-operative tricuspid regurgitation.

Results

Patients

Of the 28 patients who underwent repair for significant tricuspid regurgitation following a Norwood procedure, 27 (96 percent) were available for follow-up. Median follow-up for the entire group was 20 months, with a range from 1 to 82 months. The patients were subsequently divided into groups based upon whether they had a successful late outcome, as defined by less than moderate tricuspid regurgitation at last follow-up, or an adverse outcome, defined by greater than moderate tricuspid regurgitation. Of the patients, we found that 17 (63 percent) had achieved a successful outcome at a median follow-up of 26 months, with a range from 1 to 82 months. It follows that 10 patients (37 percent) had a poor outcome at a median follow-up of 13 months, with a range from 1 to 75 months. Median age at repair, weight at repair, stage of palliation, tricuspid valvar pathology, and length of follow-up were found not to be significantly different between the two groups. Patients with an unsuccessful outcome tended to require repair earlier in their palliation. Two-thirds of the patients having a successful repair had progressed at least to the hemi-Fontan procedure before requiring repair, compared with only one-third of those with unsuccessful procedures (p value equal to 0.12). Concomitant repair of the valve at either the hemi-Fontan or Fontan procedures was common in both groups. In the 9 patients making up the group achieving a successful late result, 6, who were at the stage of the hemi-Fontan at the time of their valvar repair, were able to undergo a successful concomitant Fontan procedure.

Technique of repair

Partial annuloplasty, used in 17 patients, was the most frequently employed technique. Partial closure of zones of apposition with adjacent leaflets for localized areas of prolapse was used in 6 patients. Ring annuloplasty was performed in 5 patients, inserting rings with a median size of 28 millimetres, and a range from 25 to 31 millimetres. Cordal shortening was employed in 3, and advancement of a papillary muscle and mobilization of the septal leaflet in one each. The technique of partial annuloplasty alone, when compared to any other method or combination of methods, significantly predicted less than moderate tricuspid regurgitation at late follow-up (p value equal to 0.04 – Fig. 2).

Tricuspid valvar regurgitation

All patients had greater than moderate regurgitation prior to operation. There was no difference between the pathology primarily responsible for the regurgitation

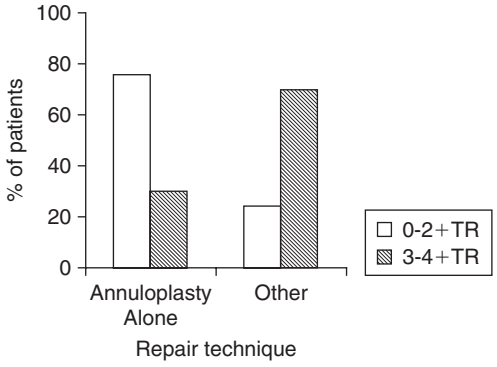

Figure 2.
Comparison of patients achieving a successful as opposed to an adverse outcome, revealing a significant difference between partial annuloplasty alone and the need for any other repair technique or combination of techniques ($p = 0.04$). Abbreviation: TR: tricuspid regurgitation.

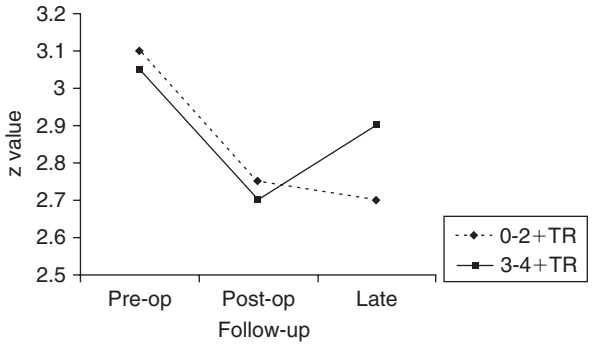

Figure 3.
Comparison of pre-operative, early post-operative and late z values for the tricuspid valve between the patients achieving late success as opposed to those failing. Abbreviation: TR: tricuspid regurgitation.

as assessed by cross-sectional and Doppler echocardiography. Similar degrees of annular dilation were seen in both groups pre-operatively, early post-operatively and at late follow-up. In both groups, nonetheless, the median z value decreased following the repair. The z value then tended to stay stable in those maintaining late success, while it increased slightly in the patients that failed late (Fig. 3). Following repair, 23 patients had an early successful result as defined by presence of less than moderate tricuspid regurgitation in the immediate post-operative period. Of these 23 patients, 17 maintained a durable repair at late follow-up, while 6 subsequently had late failure. In 6 patients, early repair proved unsuccessful, with 4 continuing to have a poor result at late follow-up. The remaining 2 patients with an unsuccessful repair in the early post-operative period underwent re-repair, with a successful late outcome. Early successful repair was predictive of late success (p value equal to 0.012), with a sensitivity of 76 percent, a specificity of 70 percent,

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a positive predictive value of 81 percent, and a negative predictive value of 64 percent.

Right ventricular function

All patients had similar right ventricular function pre-operatively, with a median functional grading of normal, ranging from normal to mildly depressed. There was no significant difference between the patients achieving late success and those subsequently failing with respect to the early post-operative or late follow-up right ventricular function. While differences failed to reach statistical significance, interesting trends were noted when comparing the groups. These trends were particularly apparent when comparing the four groups with early post-operative success and late follow-up success, early success and late failure, early failure and late success due to successful re-repair, and early failure and continued late failure, as outlined in Figure 4. Those patients with early success and continued late success of repair had preserved right ventricular function both early post-operatively and at late follow-up. Similarly, those patients with an early failure, who were salvaged with a re-repair to a successful late outcome, had preserved right ventricular function throughout. Conversely, patients with an early success, but late failure, had poor right ventricular function even in the early post-operative period, which was persistent at late follow-up. The last group, those patients with both early and late failure, initially had preserved right ventricular function in the early post-operative period, which deteriorated at late follow-up (Fig. 4).

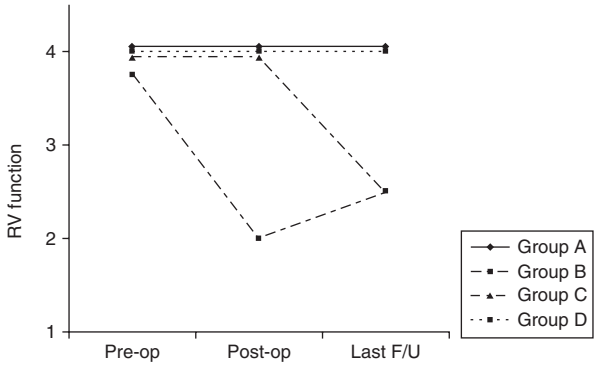

Figure 4.
Right ventricular function, as assessed on a scale of 4, with 4 being normal, 3 mildly depressed, 2 moderately depressed, and 1 severely depressed. The patients were segregated into groups, with Group A having early and late success, Group B having early failure but late success, Group C having early and late failure, and Group having early success but late failure. Abbreviations: RV: right ventricular; F/U: follow-up.

Outcomes and survivals

Of the 17 patients with a successful repair at late follow-up, 15 proceeded to conversion to the Fontan circulation. Among this group, there were 14 long-term survivors, while one patient died suddenly 2 years following conversion to the Fontan circulation with mild tricuspid regurgitation and mild-to-moderate right ventricular dysfunction. Of the other patients, two were at a hemi-Fontan stage. One awaits conversion to the Fontan circulation, having been deemed a good candidate for this procedure. The other patient underwent cardiac transplantation for diastolic dysfunction, with normal right ventricular systolic function and minimal tricuspid regurgitation.

There were 10 patients with an unsuccessful repair at late follow-up, and 8 of these patients died. Two of the deaths occurred early after surgery, one due to an intra-operative injury to a coronary artery, and the other to post-operative right ventricular failure. The other 6 patients died late, all having required an attempted re-repair or replacement with a mechanical valve. Of the 2 late survivors, both have successfully been converted to the Fontan circulation, one having a mechanical prosthetic valve. The other patient has had a single repair, but has greater than moderate residual tricuspid regurgitation, albeit with normal right ventricular function and is functional class one of the grading system devised by the New York Heart Association.

Overall, 18 of the 27 patients making up our cohort have survived (67 percent). For patients undergoing successful late repair, 16 of 17 survived (94 percent). In contrast, only 2 of 10 patients survived with greater than moderate tricuspid regurgitation at follow-up, this difference being statistically significant, with a p value equal to 0.0002. With respect to right ventricular function, 18 of 21 patients with normal to mildly depressed right ventricular function survived, as compared to none of the 6 with moderate to severe dysfunction, this again being a significant difference in survival, with the p value equal to 0.000. Of the 18 late survivors, 17 are functional class one of the system devised by the New York Heart Association, and one is in class two.

Limitations of the study

The limitations are primarily related to the retrospective nature of the analysis, and to the limited number of patients. In addition, the complex and multi-factorial nature of tricuspid regurgitation in patients with hypoplastic left heart syndrome makes it difficult to define the specific variables responsible for the outcomes of repair and other late outcomes.

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Discussion

Overall, our data demonstrates that repair of the tricuspid valve can be successfully accomplished in the majority of patients with hypoplastic left heart syndrome, even in the face of severe regurgitation. Repair can be performed as a sole procedure, or in conjunction with a hemi-Fontan or Fontan procedure. Successful repair in the early post-operative period is significantly predictive of continued excellent valvar function and preserved right ventricular performance at late follow-up. Partial annuloplasty was found to be significantly associated with a successful late outcome. Partial annuloplasty, however, may be a surrogate for other factors, which were not detected. These factors might include variables such as fine differences in tricuspid valvar anatomy not delineated by echocardiography, subclinical right ventricular dysfunction, or subtle coronary arterial insufficiency. Several different repair techniques were successfully employed, and the method of repair should be individualized to the particular anatomy encountered. Similarly, the trend towards earlier operation in the group with an unsuccessful late outcome likely represents a surrogate for a worse subgroup of tricuspid regurgitation that tends to present earlier, rather than an indication that repair should be delayed at all costs.

Tricuspid valvar regurgitation, particularly in the setting of hypoplastic left heart syndrome, is the result of several complex and interrelated variables. Right ventricular function appears to be one of the variables that has an important role in the natural history of tricuspid regurgitation. Comparing patients with a successful early post-operative result that either continued to have less than moderate tricuspid regurgitation, or went on to late failure, those patients who maintained a successful repair had significantly better right ventricular function. The contribution of any given factor, such as right ventricular function, to the development of tricuspid regurgitation is likely variable from patient to patient. This variable influence of right ventricular function on tricuspid regurgitation may be illustrated by trends that were demonstrated in comparing the early post-operative results to the late outcomes of the various groups. Patients with both an early post-operative and late successful outcome had preserved right ventricular function throughout the period of follow-up. Similarly, patients with an initial unsuccessful repair, who achieved a successful late result with re-repair, also had preserved right ventricular function, both demonstrating the importance of right ventricular function in tricuspid valvar competence. In contrast, patients with an early successful repair, followed by late failure had more depressed right ventricular function in both early and late follow-up, suggesting that right ventricular dysfunction may have played an important role in the late deterioration of the tricuspid valve. Conversely, in patients with poor tricuspid valvar competence both immediately after repair and at late follow-up, right ventricular function was initially preserved and later declined, implying an adverse effect of tricuspid regurgitation on right ventricular function.

Despite remarkable improvements in survivals for patients with hypoplastic left heart syndrome over the past two decades, mortality between stages, and at 5 years, remains significant.[1–5] An important factor in this ongoing attrition is the development of significant tricuspid regurgitation, which has been reported to occur in up to one-sixth of patients.[7,8] In a previous publication from our institution,[9] this proportion of patients developed greater than moderate tricuspid regurgitation following a Norwood procedure for hypoplastic left heart syndrome. Such regurgitation has long been recognized as a risk factor for survival after conversion to the Fontan circulation, and has even been suggested as a relative contraindication to pursuing staged palliation for hypoplastic left heart syndrome.[7,8,10] As we have shown, however, repair of the valve can be successfully performed, and contributes to improved outcomes. Overall, the percentage of patients progressing successfully to conversion to the Fontan circulation, and the overall survivals following valvar repair, are excellent in this subpopulation of patients with hypoplastic left heart syndrome at very high risk.

Patients with an initially successful repair, but poor right ventricular function, tended to do poorly as a group as the function of the tricuspid valve often continued to deteriorate. Patients with an initial poor result from repair, but preserved right ventricular function, can achieve a good result with a re-repair. When right ventricular dysfunction develops over time in those patients with residual tricuspid regurgitation, however, the prognosis is poor. The poor outcome associated with this latter subgroup suggests that these patients may benefit from early consideration for cardiac transplantation.

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