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Outcomes of Reparative and Transplantation Strategies for Multilevel Left Heart Obstructions With Mitral Stenosis

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Abstract

Background—Conventional management for multilevel left heart obstructions and mitral stenosis (Shone's complex) involves multiple operations that carry additive risks. This study reviews our experience with reconstructive and transplantation approaches for Shone's complex.

Methods—Between 1987 and 2007, 43 patients with mitral stenosis and one or more left-sided obstructions were identified: supramitral ring ($n = 13$), subaortic stenosis ($n = 25$), aortic stenosis ($n = 24$), hypoplastic arch ($n = 20$), and coarctation ($n = 38$). Thirty patients underwent a staged reparative approach, including 27 mitral and 51 left ventricular outflow tract operations. Thirteen patients were referred for transplantation. Patients with severe hypoplasia of the left ventricle were excluded.

Results—There was one in-hospital death (2.5%) and six late deaths (14.2%). Actuarial 5- and 10-year survival for staged surgical and transplantation was 88% vs 61.3% and 83.1% vs 61.3% ($p = 0.035$). At a mean follow-up of 7.9 years, freedom from mitral reoperation was 83.3% and freedom from reoperation for subaortic stenosis was 78.0%. Wait-list mortality was 13.3% (2 of 13). Wait-list time exceeding 90 days was an incremental risk factor for death after transplantation ($p = 0.005$).

Conclusions—Despite the challenges of a reparative strategy for Shone's complex, favorable survival and durability outcomes can be expected. Heart transplantation, although avoiding the pitfalls of staged repair, confers increased risks from ongoing physiologic derangements due to uncorrected left heart inflow and outflow obstructions during the wait for donor heart availability.

Surgical management of congenital multilevel left-sided heart obstructive lesions with mitral involvement poses a formidable challenge. In 1963 Shone and colleagues [1] described a complex of lesions causing obstruction to left-sided inflow and outflow, including supramitral ring, parachute deformity of the mitral valve, subaortic obstruction, and aortic coarctation. In reality, these patients exist along a spectrum in which the presence and severity of these lesions varies. Not infrequently, other cardiovascular defects, including valvar aortic stenosis, aortic arch hypoplasia, and borderline left ventricular size contribute to the added complexity of this patient population.

Multiple operations during infancy and childhood are often necessary to address the left ventricular inflow and outflow lesions. Moreover, because of the complex pathology

affecting the mitral subvalvar apparatus and hypoplasia of the mitral annulus, mitral valve-sparing procedures are often not possible or durable. Options for pediatric valve replacement are usually limited to mechanical prostheses; thus, the inherent risks of anticoagulation and thromboembolic complications must be accepted.

With the prospect of multiple operations on the inlet and outlet of the left ventricle, and the potential need for prosthetic valve replacement, cardiac transplantation may be an attractive option in selected patients with Shone's complex. Indeed, the presence of Shone's complex has been demonstrated to be a predictor of death for mitral valve replacement in children aged younger than 5 years [2]. Transplantation, however, is not without major drawbacks: Lengthy waiting times for an organ, acute and chronic rejection, and immunosuppression-related complications are variables that contribute to important morbidity and graft failure.

To gain an improved understanding of the optimal management strategies for patients with Shone's complex, we reviewed our experience with this patient population managed either by a staged repair (SR) or transplantation (TX) strategy. The review of the SR cohort focused on the cumulative effect on patient outcomes of both the multiple operations required and the morbidity associated with prosthetic valve complications. For the TX group, the morbidity of waiting time for organ availability and transplant-related complications were specifically analyzed to accurately assess outcomes of transplantation for Shone's complex.

Patients and Methods

During a 20-year period, between June 1987 and May 2007, 43 consecutive patients presented to Children's Hospital, Denver, with mitral stenosis and multiple levels of left heart obstruction. Patient records, including operative reports, diagnostic reports, inpatient records, and outpatient clinic visit notes were reviewed in accordance with an approved protocol from the Colorado Multiple Institutional Review Board. Individual patient or parental consent was waived because of the retrospective nature of the study. Patients requiring a single-ventricle management pathway were excluded. Echocardiography was used to characterize the cardiovascular anatomy in all patients. In patients who underwent transplantation, additional anatomic data were obtained from pathologic examination of the explanted heart.

Patient Groups

The SR group comprised 30 patients (17 boys, 13 girls) with mitral stenosis and multiple left-sided obstructive lesions who underwent a staged reparative approach. In 27 patients (90%), the initial operation was performed when they were aged younger than 1 year.

The TX group comprised 13 patients (7 boys, 6 girls) with Shone's complex who were listed for transplantation. The median age at first operation was 22 days (range, 2 to 76 days). Of these, 11 (85%) survived to transplantation. Median age at transplantation was 5 months (range, 1 to 20 months).

Mitral Valve Morphology

The specific mitral lesions are summarized in Table 1. All patients had structural abnormalities of the mitral valve. A mean gradient across the left ventricular inflow greater than 6 mm Hg was present in 37 children (86%). Parachute deformity of the mitral subvalvar apparatus was present in 15 (35%), and a supralvalvar mitral ring was present in 13 (30%). Severe deformities of the subvalvar apparatus such as the hammock or arcade malformations, as described by Uva and colleagues [3] with a combination of papillary muscle hypertrophy and foreshortened chordae, were found in 14 patients (33%).

Left-Sided Outflow Obstructions

Left-sided heart obstructive lesions are reported in Table 2. Coarctation of the aorta was the most prevalent left-sided obstructive lesion and was present in 38 of 43 patients (88%). Hypoplasia of the aortic arch was present in 20 (47%) with coarctation. Significant sub-aortic stenosis affected 25 patients (58%). Important valvar aortic stenosis developed in 24 patients (56%), supraaortic stenosis occurred in 3 (7%), and an associated ventricular septal defect was present in 20 (47%).

Surgical Procedures

In the SR group, 30 patients underwent a total of 72 operations. There were 31 left ventricular inflow procedures in 22 patients. Twenty-seven patients underwent 56 procedures to address outflow obstructive lesions.

The median age at first operation was 6.5 days (range, 1 day to 1.6 years). Coarctation repair was the initial operative procedure in 24 of 30 patients (80%). Aortic arch hypoplasia was addressed in 5 patients undergoing coarctation repair. Other procedures performed at time of coarctation repair included pulmonary artery banding (PAB) in 4 and aortic valvotomy in 2. Other procedures performed at the initial presentation include subaortic resection in 2, Ross-Konno and mitral valve repair (MVP) in 1, Ross-Konno and mitral valve replacement (MVR) in 1, supraannular mitral ring resection in 1, and aortic valvotomy in 1.

A second surgical procedure was performed in 25 of 30 patients (83%). The median age at the second operation was 11 months (range, 1 month to 10.8 years). The median interval between the first and second operation was 10.4 months (range, 24 days to 10.6 years). Procedures performed at the second operation included MVP in 10, ventricular septal defect closure in 8, subaortic membrane resection in 7, aortic valvotomy in 4, supraannular mitral ring resection in 7, Ross-Konno in 2, and 1 each with extended homograft aortic root replacement, PAB, and heart transplantation.

A third operation was required in 11 patients (37%) at a median age of 1.9 years (range, 1.0 to 9.5 years). The median interval between the second and third operations was 12.7 months (range, 4.2 months to 5.7 years). Procedures performed at the third operation include subaortic membrane resection in 4, Konno-aortic valve replacement (AVR) in 3, MVP in 2, MVR in 2, and in 1 patient each, Ross-Konno procedure, Ross II procedure, ventricular septal defect closure, and extended homograft aortic root replacement.

A fourth operation was required in 4 patients (13%). The median age at the fourth procedure was 6.3 years (range, 2.9 to 13.3 years), during which four MVRs and one Konno-AVR were performed. A fifth operation was performed in 1 patient (3%), who received a heart transplant at 3.7 years.

In the TX group, 13 patients underwent 26 procedures. Coarctation repair was performed in 10 patients as the initial operation at a median age of 15 days (range, 2 to 74 days). Primary coarctation balloon angioplasty was performed in 2 additional patients. Concomitant procedures included PAB in 4 and aortic arch augmentation in 1. Another patient underwent a PAB as the sole initial procedure. One patient underwent MVR at 6 months while on the waiting list. Heart transplantation was successfully performed in 11 patients (85%) at a median age of 5 months (range, 1 to 23 months). The median time on the waiting list was 73 days (range, 5 to 297 days).

Statistical Analysis

Statistical analysis was performed with Prism 5.0 software (GraphPad Inc, San Diego, CA). Data are described as median with ranges, or mean with standard deviation. Serial data were compared between groups using the Student *t* test and Fisher exact test. Risk factors were assessed using log-rank analysis. Survival and freedom from reoperation were determined by actuarial Kaplan-Meier analysis. Values of $p < 0.05$ were considered statistically significant.

Results

Mortality Rate

For the entire series of 43 patients, there was one in-hospital death for an operative mortality rate of 2.3%. Eight additional late deaths occurred, resulting in an overall mortality rate of 20.9% (9 of 43).

In the SR group, there was one operative death for an operative mortality rate of 3.5%. There were three late deaths. The overall mortality rate for the SR cohort was 13.3% (4 of 30). End-stage cardiomyopathy developed in 3 patients with progressive mitral stenosis despite operative intervention, and they required heart transplantation. Two of the three late deaths in the SR cohort occurred after heart transplantation as a result of complications of chronic rejection.

No operative deaths occurred in the TX group. There were five late deaths among the 13 patients listed for transplantation, for an overall mortality of 38.5%. Two of these patients died before receiving a transplant, for a wait-list mortality of 15.4%. The three posttransplant deaths in the TX group were due to severe chronic rejection.

Actuarial survival at 1, 5, and 10 years was, respectively, 96.2%, 88.0%, and 83.1% for the SR group, and 84.6%, 61.3%, and 61.3% for the TX group (Fig 1).

Mitral Valve Reoperation

In the SR group, 22 patients underwent operative intervention on the left ventricle inflow. MVP was performed in 17 and MVR was performed in 5 patients. Actuarial 5- and 10-year freedom from mechanical MVR for the entire SR group was 81.4% and 73.2%, respectively (Fig 2). The rate of reoperation on the MV was 22.7% (5 of 22). Of the 17 MVP patients, 2 ultimately required MVR, 1 underwent a Ross II procedure, and 1 had a mechanical MVR. Repeat MVR was required in 2 of 7 patients. There were no recurrences of a supraannular mitral ring in the 8 patients who underwent resection.

Left Ventricular Outflow Tract Reoperation

Operations were done in 18 patients to relieve obstruction at the subaortic or aortic valvar level. Actuarial 5-year freedom from left ventricular outflow tract (LVOT) reoperation was 60.6% (Fig 3). After subaortic resection, 5 of 10 patients (50%) required reoperation, including Konno-AVR in 3, repeat subaortic resection in 1, and AVR in 1. After surgical aortic valvotomy, 4 of 5 patients (80%) required complex aortic valve or aortic root replacement. These procedures included extended homograft aortic root replacement in 2, Ross-Konno procedure in 1, and Konno-AVR in 1. To date, none of the 5 patients who underwent a Ross-Konno procedure has required reoperation for recurrent LVOT obstruction. One patient required arterioplasty of the left coronary artery secondary to ischemia.

Staged Repair Group Complications

Progressive cardiomyopathy requiring cardiac transplantation occurred in 3 of 30 patients (10%). The mechanical valve complication rate was 25% (2 of 8). Valve thrombosis requiring repeat MVR occurred in 1 patient. There was one warfarin-related bleeding complication in a patient who sustained a subarachnoid hemorrhage. Pacemaker implantation was required in 5 of 30 patients (16.7%).

Impact of Wait-List Duration on Transplant Outcome

Time on the waiting list (> 90 days) was an important risk factor for posttransplantation death in the TX group ($p = 0.005$). The 3 patients who died after receiving a transplant in the TX group all had waited more than 90 days. When patients undergoing transplantation from both groups were analyzed, wait-list duration remained an incremental risk factor for death ($p = 0.012$): 5 of the 6 patients (83.3%) who died after transplantation had waited more than 90 days (Fig 4).

Transplantation Group Complications

Six patients (46.2%) required more than one hospitalization for severe rejection episodes. Recurrent infectious complications occurred in 7 patients (53.8%). Significant neurologic complications occurred in 2 patients.

Clinical Status at Follow-up

Follow-up was complete in 28 of 30 (93.3%) of the SR group and in all (100%) of the TX group. Average follow-up was 7.9 ± 5.8 years. Of survivors in the SR group, 82.6% were in New York Heart Association (NYHA) class I. Echocardiographic follow-up demonstrated that mitral regurgitation was mild or less in 66.7%, LV function was normal in 79.2%, and 91.7% were free from significant LVOT gradient.

Of the transplant survivors, 87.5% were in NYHA class I. At follow-up, all patients who received a transplant had normal systolic function by echocardiography, and all were free of significant coronary vasculopathy.

Comment

This report highlights the numerous challenges that accompany staged reparative and transplantation approaches to Shone's complex. The highly variable nature of the lesion set and severity of individual lesions requires an individualized approach. If the inlet, ventricular, and outflow components of the left heart are sufficient to pursue biventricular repair, these data suggest that favorable outcomes can be expected with a surgical approach.

The degree of structural mitral valve deformity dictates the outcome with either approach. The transplantation option is severely limited by the unpredictable wait for available donor hearts. Mitral stenosis, with additional obstructive lesions, leads to rapidly progressive pulmonary hypertension and cardiomyopathy. This has been implicated as a factor for previous reports of operative mortality rates of 25% to 43% for mitral interventions in this patient population [4, 5]. Isolated pediatric mechanical MVR has been associated with 30-day mortality rates of 18% to 25% [2, 6, 7]. The prospect of these disappointing early results, along with the likelihood of multiple future operations and the potential need for mechanical valve replacements in young patients, led to the referral of some of these patients for transplantation. At the same time, lengthy wait-list times have a profoundly negative effect on transplantation outcomes for Shone's complex resulting from the pulmonary vascular derangements caused by this constellation of lesions.

Timing of mitral intervention is of central importance to the surgical management of Shone's complex. Consistent with previous series of Shone's complex [8, 9], we found that mitral operations were rarely required in early infancy. If possible, it is preferable to defer mitral operation because fragility of mitral valve tissue may preclude successful repair, and replacement options at this age carry extraordinary risk [10]. Most patients initially present for coarctation repair. Because coarctation repair can unmask effects of intra-cardiac obstructive lesions, it is advisable to closely monitor patients with structurally abnormal mitral valves with serial echocardiograms to prevent delayed intervention. Ikemba and colleagues [11] identified that the presence of thickened leaflets and shortened chordae by echocardiography were predictive of the need for mitral operation as well as death.

An aggressive reparative approach to the mitral valve should be followed, if only to delay MVR until the child is larger. At reoperation, repair should be attempted to prevent or delay MVR. In our series, MVP was possible in greater than three-fourths of patients who required mitral intervention. After MVP, freedom from MVR approached 90%. However, patients with severe deformities of the subvalvar apparatus pose the greatest challenge to a durable repair. The cases of hammock or parachute valve that cannot be addressed by chordal separation or lengthening techniques will often require initial prosthetic replacement. MVR poses challenges in young children with Shone's complex because the mitral annulus is often hypoplastic. In our experience, supraannular placement of the prosthesis, along with patch augmentation of the atrial septum, is helpful to insert a larger prosthesis and to avoid LVOT obstruction.

Reoperation for outflow tract lesions in this series was relatively common. The reintervention rate was 80% after simple aortic valvotomy and 50% after sub-aortic resection. Described initially for the relief of tunnel subaortic stenosis [12], favorable results have been reported for the use of the Konno aortoventriculoplasty in combination with homograft aortic root replacement or the Ross procedure [13, 14]. In cases of complex LVOT obstruction, the Konno aortoventriculoplasty proved to be highly effective in preventing recurrent LVOT obstruction. None of the 10 LVOT reconstructions performed with the Konno aortoventriculoplasty, whether in combination with a pulmonary autograft, a homograft, or mechanical AVR, have required reoperation. These data demonstrate that the Konno operation is the optimal procedure for relief of complex LVOT obstruction in Shone's complex.

In conclusion, the optimal management of Shone's complex is achieved by a staged reparative approach. Despite the need for multiple operations and the possibility of prosthetic valve replacement of either or both of the left-sided valves, favorable long-term results can be achieved. The utility of heart transplantation for Shone's complex is limited because of the severe shortage of the pediatric donor supply. Extended time on the waiting list places the Shone's complex patient at serious risk because the uncorrected obstructive defects result in congestive failure and unrelenting pulmonary hypertension. Transplantation should be reserved for those Shone's complex patients in whom severe cardiomyopathy develops. Although transplant survivors enjoyed excellent functional status at follow-up, the wait-list duration is too unpredictable to recommend transplantation as a first-line treatment option for Shone's complex.

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Fig 1. Actuarial survival at 1, 5, and 10 years is shown for staged repair (solid line) and transplantation (dashed line) approaches. For the transplant group, survival data are based on patients who underwent heart transplantation. Patients at risk for each group are listed.

Fig 2. Freedom from mechanical mitral valve replacement (MVR) is shown in the staged repair group. The actuarial 5-year freedom from mechanical MVR was 81.4%.

Fig 3. Freedom from left ventricular outflow tract (LVOT) reoperation is shown in 18 patients. The actuarial 5-year freedom from LVOT reoperation was 60.6%.

Fig 4.

Impact of wait-list duration on transplantation outcome: A wait of more than 90 days was an incremental risk factor for death (light gray bars) after transplantation ($p = 0.012$), with the dark bars indicating patients who were alive.

Table 1

Spectrum of Left-Sided Heart Inflow Lesions

Pathology	SR	TX	Total
Structurally abnormal MV	30	13	43
Predominant mitral stenosis ^a	26	11	37
Predominant mitral regurgitation	4	2	6
Hammock or arcade MV	9	5	14
Parachute mitral valve	12	3	15
Supraannular mitral ring	11	2	13

^a Gradient > 6 mm Hg.

MV = mitral valve; SR = staged repair; TX = transplantation.

Table 2

Distribution of Left-Sided Outflow Obstructive Lesions

Diagnosis	SR	TX
Coarctation	26	12
Subaortic obstruction	17	8
Valvar aortic stenosis	16	8
Hypoplastic aortic arch	14	6
Supravalvar aortic stenosis	2	1

SR = staged repair; TX = transplantation.