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Surgical Strategy in Patients with Atrial Septal Defect and Severe Pulmonary Hypertension

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ABSTRACT

The aim of the study was to review our experience with atrial septal defect (ASD) closure with a fenestrated patch in patients with severe pulmonary hypertension. Between July 2004 and February 2009, 16 patients with isolated ASD underwent closure with a fenestrated patch. All patients had a secundum type ASD and severe pulmonary hypertension. Patients ranged in age from 6 to 57 years (mean ± SD, 34.9 ± 13.5 years). The follow-up period was 9 to 59 months (mean, 34.5 ± 13.1 months). The ranges of preoperative systolic and pulmonary arterial pressures were 63 to 119 mm Hg (mean, 83.8 ± 13.9 mm Hg) and 37 to 77 mm Hg (mean, 51.1 ± 10.1 mm Hg). The ranges of preoperative values for the ratio of the pulmonary flow to the systemic flow and for pulmonary arterial resistance were 1.1 to 2.7 (mean, 1.95 ± 0.5) and 3.9 to 16.7 Wood units (mean, 9.8 ± 2.9 Wood units), respectively. There was no early or late mortality. Tricuspid annuloplasty was performed in 14 patients (87.5%). The peak tricuspid regurgitation gradient and the ratio of the systolic pulmonary artery pressure to the systemic arterial pressure were decreased in all patients. The New York Heart Association class and the grade of tricuspid regurgitation were improved in 13 patients (81.2%) and 15 patients (93.7%), respectively. ASD closure in patients with severe pulmonary hypertension can be performed safely if we create fenestration. Tricuspid annuloplasty and a Cox maze procedure may improve the clinical result. Close observation and follow-up will be needed to validate the long-term benefits.

INTRODUCTION

Pulmonary hypertension is frequently encountered in patients with left-to-right shunt lesions, such as atrial septal defect (ASD), ventricular septal defect, or patent ductus arteriosus. If left untreated, the pulmonary vascular resistance may rise to systemic levels, or even higher, and become irreversible pulmonary vascular disease (Eisenmenger syndrome) [Wood 1958]. When patients with pulmonary hypertension undergo surgery for a congenital heart defect, they have an increased risk of a pulmonary hypertensive crisis or right heart failure. Although ASD closure is known to increase survival prospects even when carried out at an advanced age, it may still cause significant mortality or morbidity in patients with severe pulmonary hypertension [Gault 1968; Steele 1987; Konstantinides 1995; Attie 2001].

Recent advances in the medical management of pulmonary hypertension have led surgeons and cardiologists to close an ASD even in patients with severe pulmonary hypertension, who are usually considered as high risk or inoperable [Beghetti 2009; Hirabayashi 2009]. If there is a residual shunt between the atria, we can avoid hemodynamic instability caused by a pulmonary hypertensive crisis. Because these patients frequently have tricuspid regurgitation (TR) and atrial fibrillation, tricuspid valve repair and a Cox maze procedure may improve right heart function. Therefore, we have closed the ASD with a fenestrated patch and aggressively repaired the tricuspid valve in patients with an ASD and severe pulmonary hypertension. The aim of the present study was to evaluate the safety of closing an ASD with a fenestrated patch in patients with ASD and severe pulmonary hypertension.

PATIENTS AND METHODS

Our institutional review board approved this study and waived the need for individual consent from patients or relatives. We retrospectively reviewed and analyzed the data of patients who underwent ASD closure with fenestration. Follow-up data were obtained from patients' medical records.

Patient Characteristics

Between July 2004 and February 2009, 19 patients with an ASD underwent fenestrated patch closure at our institution. The indication for making a fenestration on the patch was severe pulmonary hypertension, which was defined as a systolic pulmonary arterial pressure (SPAP) >60 mm Hg. We excluded 3 patients who had other congenital heart problems,

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such as patent ductus arteriosus or pulmonary vein stenosis, that might cause pulmonary hypertension. All 16 patients had a secundum type ASD. Three patients had another congenital heart anomaly: interruption of the inferior vena cava, bilateral superior vena cava, and single coronary artery. Surgical inclusion criteria were a pulmonary-to-systemic flow ratio (Qp/Qs) 1.5, a response to nitric oxide (n = 3), or a test occlusion of the ASD (n = 7), which was defined as a >20% decrease in the SPAP. These patients were taking a selective pulmonary vasodilator before surgery, such as sildenafil, beraprost, or bosentan. The mean patient age at the time of surgery was 34.9 ± 13.5 years (range, 6-57 years). There were 12 female patients (75%). The mean follow-up period was 34.5 ± 13.1 months (range, 9-59 months). The ASD size measured by echocardiography ranged from 19 to 43 mm (mean, 28.2 ± 7.1 mm). The mean preoperative SPAP was 83.8 ± 13.9 mm Hg (range, 63-119 mm Hg). The mean pulmonary arterial pressure (PAP) was 51.1 ± 10.1 mm Hg (range, 37-77 mm Hg). The mean preoperative Qp/Qs ratio and the mean pulmonary arterial resistance (Rp) were 1.95 ± 0.5 (range, 1.11-2.7) and 9.8 ± 2.9 Wood units (range, 3.9-16.7 Wood units), respectively (Table). Atrial fibrillation was present before the operation in 2 patients (12.5%).

Surgical Technique

ASD closure was performed with standard cardiopulmonary bypass under mild to moderate systemic hypothermia. Intermittent cold crystalloid cardioplegia was administered for myocardial protection via an antegrade route. The ASD was closed in all patients with glutaraldehyde-fixed autologous pericardium. Fenestration of the patch was made by punch. The size of the fenestration was determined by the patient's body surface area and was >4.5 mm. The mean size of the fenestration was 6.34 ± 1.01 mm (range, 4.5-8 mm). Concomitant procedures were tricuspid annuloplasty in 14 patients (87.5%), the modified Cox maze III procedure in 2 patients (12.5%), and mitral valve repair in 1 patient (6.3%). Tricuspid annuloplasty was performed with the modified DeVega method (n = 2). The choice of annuloplasty technique was according to the surgeon's preference.

Patient Characteristics from Preoperative and Postoperative Catheterization

Patient No.	Age, y	SPAP, mm Hg	MPAP, mm Hg	Qp/Qs	Rp (Wood units)	SPAP/SAP
1	26	99	57	2.64	9.7	0.79
2	27	93	51	2.45	7.4	0.58
3	34	119	77	1.3	16.7	0.92
4	22	100	68	2.48	8.7	0.72
5	41	63	37	1.62	8.88	0.58
6	36	80	47	1.72	NA	0.70
7	22	83	52	2.05	9.3	0.76
8	57	90	48	1.6	12.9	0.87
9	52	75	41	2.7	3.9	0.52
10	54	71	43	2.3	6.2	0.70
11	34	77	44	1.94	9.7	0.65
Postoperative		48	32	1.38	4.7	0.40
12	26	84	54	1.5	11.4	0.80
Postoperative		53	35	1.07	8.0	0.46
13	28	76	46	2.15	10.5	0.64
Postoperative		37	22	1.14	6.0	0.35
14	37	84	54	2.49	9.53	0.68
Postoperative		53	35	1.30	9.4	0.48
15	49	69	44	2.26	9.5	0.58
Postoperative		57	40	NA	NA	NA
16	6	78	54	1.11	12.21	0.74
Postoperative		48	32	NA	6.7	0.51
Mean ± SD†	34.9 ± 13.5	83.8 ± 13.9	51.1 ±10.1	1.95 ± 0.5	9.8 ± 2.9	0.70 ± 0.11
Range†	6-57	63-119	37-77	1.11-2.7	3.9-16.7	0.52-0.92

*SPAP, systolic pulmonary artery pressure; MPAP, mean pulmonary artery pressure; SAP, systolic systemic arterial pressure; Qp/Qs, pulmonary-to-systemic flow ratio; Rp, pulmonary arterial resistance.

†Preoperative values.

Postoperative Management, Echocardiography, and Catheterization

In the intensive care unit, the PAP was monitored continuously. To lower the PAP, nitric oxide inhalation, sildenafil, or beraprost was used. Anticoagulation therapy was started in patients who had risk factors for thromboembolism, such as preoperative atrial fibrillation, a history of cerebral infarction, or transient ischemic attack. Echocardiography was performed before discharge and annually after surgery. The severity of TR was estimated by the area of the distal TR jet. Moderate TR was defined as TR with a distal jet area 5 cm2, and severe TR was defined as TR with a distal jet area 10 cm2 [Zoghbi 2003]. The peak TR gradient was determined by the maximal velocity of the TR jet by means of a modified Bernoulli equation. Postoperative cardiac catheterization was performed in 6 patients (37.5%).

Statistical Analysis

All measurements are expressed as the mean ± SD and the range, or as frequencies and proportions. The Wilcoxon signed rank test was used to assess differences in mean values. P values <.05 were considered statistically significant, and statistical analyses were carried out with the statistics software package SPSS Statistics 17.0 (SPSS, Chicago, IL, USA).

RESULTS

Changes in the Ratio of SPAP to the Systolic Systemic Arterial Pressure

The mean preoperative ratio of the SPAP to the systolic systemic arterial pressure (SAP) was 0.70 ± 0.11 (range, 0.64-0.76). The mean SPAP/SAP ratio decreased to 0.47 ± 0.15 (range, 0.39-0.55; P = .001) after weaning from cardiopulmonary bypass, to 0.48 ± 0.16 (range, 0.38-0.58; P = .002) by 30 minutes after arrival in the intensive care unit, to 0.44 ± 0.12 (range, 0.37-0.51; P = .001) before extubation, and, finally, to 0.44 ± 0.09 (range, 0.39-0.50; P = .001) after extubation.

Clinical Outcomes

There were no early or late deaths. Except for postoperative bleeding in 2 patients, there were no operative complications. One patient received a diagnosis of constrictive pericarditis and underwent pericardiectomy 22 months after the operation. No patient experienced a thromboembolic event during follow-up. The mean hospital stay after the operation was 9.4 ± 3.1 days (range, 6-18 days). The preoperative New York Heart Association (NYHA) class was II in 14 patients (87.5%) and III in 2 patients (12.5%). The NYHA class at the last follow-up visit was I in 11 patients (68.8%) and II in 5 patients (31.3%). The changes in NYHA class are shown in Figure 1.

Hemodynamic Data from Echocardiography

A follow-up echocardiography evaluation was performed at the outpatient clinic in 15 patients (93.8%), and the mean time of the evaluation was 33.1 ± 17.0 months (range, 12-60 months) after the operation. Preoperative echocardiography

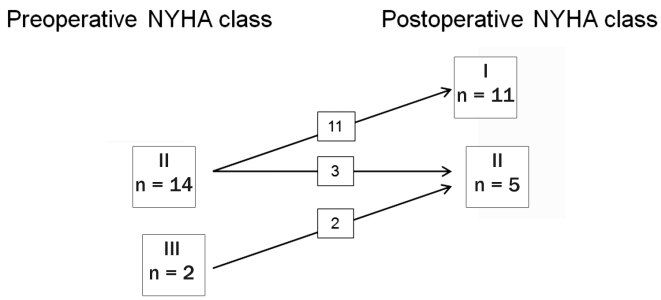

Figure 1. Changes in New York Heart Association (NYHA) class. Postoperative NYHA class was checked at the last outpatient visit.

results showed the presence of moderate or severe TR in 11 patients (68.8%). The severity of TR at the last echocardiography evaluation was trace or mild in 14 patients (87.5%); however, 1 patient, who had severe TR preoperatively and underwent ring annuloplasty, still had moderate TR at this visit (Figure 2). The mean peak TR gradient was significantly decreased after the operation (87.4 ± 21.8 mm Hg preoperatively versus 38.4 ± 14.5 mm Hg at the last echocardiography evaluation; P = .001). The changes in the peak TR gradient are shown in Figure 3. The direction of the shunt through the fenestration before discharge was right to left in 1 patient (6.3%), bidirectional in 1 patient (6.3%), and left to right in 14 patients (87.5%). At the last echocardiography evaluation, the shunt direction was left to right in 15 patients (93.7%) and invisible in 1 patient (6.3%).

Follow-up Catheterization

Postoperative catheterization was performed in 6 patients (37.5%) at 7 to 36 months postoperatively. With the exception of 1 patient, all hemodynamic data from catheterization,

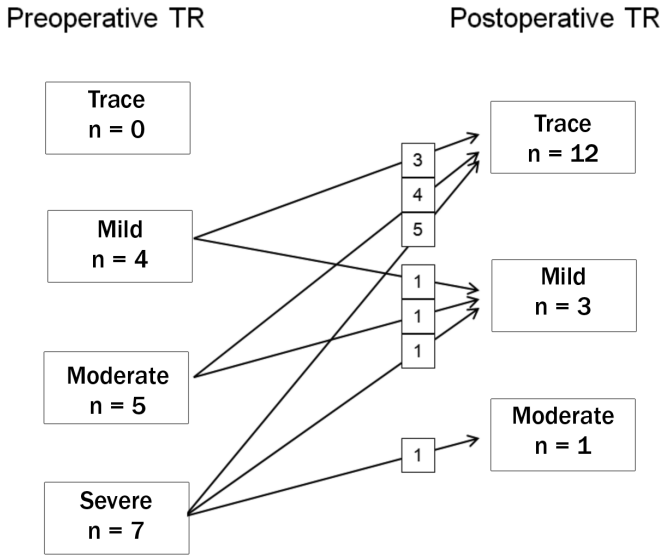

Figure 2. Changes in tricuspid regurgitation (TR) grades. Postoperative TR grade was obtained from the most recent echocardiographic data.

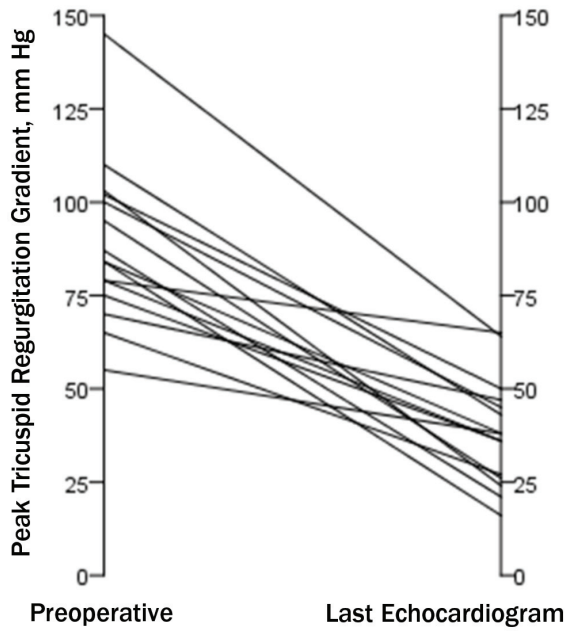

Figure 3. Changes in the peak tricuspid regurgitation (TR) gradient. The peak TR gradient was decreased in all patients after the operation.

such as SPAP, Qp/Qs, Rp, and the SPAP/SAP ratio, were improved. For patient no. 14, the postoperative Rp did not decrease, even though SPAP, Qp/Qs, and the SPAP/SAP ratio had decreased (Table).

Pulmonary Vasodilator

Nitric oxide was used in 3 patients (18.7%) during mechanical ventilation. Sildenafil or beraprost was used in all patients during the early postoperative period and in 5 patients (31.3%) at the last follow-up date. Four patients (25.0%) have taken 50 to 100 mg of sildenafil, and 1 patient (6.2%) has taken 0.04 mg beraprost per day.

DISCUSSION

ASD with a left-to-right shunt causes right ventricular dilatation and excessive pulmonary blood flow. Although the chance of developing pulmonary vascular obstructive disease is much less than in patients with a ventricular septal defect or patent ductus arteriosus, many patients with unrepaired ASD are at risk of developing pulmonary hypertension or even Eisenmenger syndrome [Gault 1968; Vogel 1999]. Konstantinides et al compared the results of surgical closure with those of medical management and concluded that surgical closure significantly increased the 10-year survival rate (95% for surgical closure versus 84% for medical management) and prevented functional deterioration [Konstantinides 1995]. Attie et al also compared surgical and medical treatment for patients older than 40 years with a secundum ASD in a randomized trial [Attie 2001]. They concluded that surgical closure was superior to medical treatment in improving both major cardiovascular events and overall mortality. Additional studies have shown that the severity of pulmonary hypertension is an independent risk factor for mortality. The patients showed excellent early and late results; however, high-risk patients who had low Qp/Qs values, severe pulmonary hypertension, or fixed Rp were excluded in these studies. In these high-risk patients, simple closure of the ASD did not produce consistently favorable surgical outcomes [Gault 1968; Steele 1987; Sachweh 2006]. The reasons for the poor outcomes in these patients were postoperative pulmonary hypertensive crisis and right ventricular failure. The fenestration between the right and left atrium can prevent suprasystemic PAP. Although there have been many studies of patients with ventricular septal defect, there are only a few reports of patients with ASD.

Studies in which an ASD was closed with fenestrated occluders in elderly patients with pulmonary hypertension have shown that this procedure can be an important therapeutic option for elderly and high-risk patients [Althoff 2008; Bruch 2008]. In the present study, we closed ASDs with a fenestrated patch in patients with an ASD and severe pulmonary hypertension. The clinical and hemodynamic outcomes were satisfactory. Although the SPAPs of all patients were >60 mm Hg and the Qp/Qs values of 3 patients were <1.5, there was no early or late mortality. As shown by continuous monitoring of the PAP by Swan-Ganz catheter, the SPAP/SAP ratio decreased significantly immediately after surgery and was stable during recovery. The postoperative SPAP/SAP ratio and the peak TR gradient were significantly decreased in all patients, and the postoperative NYHA class was improved in 13 patients and unchanged at II in 3 patients. The primary role of fenestration is to allow a right-to-left shunt in the event of a pulmonary hypertensive crisis. In the present study, the size of the fenestration varied. Because fenestration was not found by postoperative echocardiography in 1 patient who had a 4.5-mm fenestration, we tried to make it >4.5 mm. Although we created a larger fenestration in larger patients, we do not think that we need such large fenestrations. If there are any concerns that the fenestration is too small, we can enlarge it via a transvenous technique. Taking these considerations together, we think that we can overcome postoperative hemodynamic instability via the fenestration. In addition, pulmonary hypertension and symptoms were improved after surgery by reducing the pulmonary blood flow.

TR is common in patients with an ASD and pulmonary hypertension. Some authors have suggested that the severity of TR is associated with a poor prognosis and that tricuspid surgery may provide some benefit [Nath 2004]. These facts encourage repair of the tricuspid valve during mitral or aortic valve surgery; however, there are few reports about tricuspid annuloplasty and ASD closure. Generally, the severity of TR in patients with an ASD corresponds to the degree of pulmonary hypertension and right ventricular dysfunction. Although TR is usually ameliorated after ASD closure, it can remain or progress in patients with severe pulmonary hypertension. Toyono et al reported that a systolic

PAP >60 mm Hg predicted persistent TR after ASD closure [Toyono 2009]; however, tricuspid annuloplasty can prevent right ventricular dilatation and protect the right atrium from high pressure. Therefore, we performed tricuspid annuloplasty in patients with significant TR. In the present study, postoperative TR was less than a mild degree in 15 patients, but TR was mildly improved in 1 patient from severe to moderate TR (Figure 2). Atrial fibrillation is one of the late complications of an ASD and is common in adult patients with an ASD. In our study, 2 patients who had permanent atrial fibrillation before the operation underwent a modified Cox maze procedure. All patients were in sinus rhythm during follow-up. Although it is unclear that tricuspid valve repair and the Cox maze procedure are related with respect to improving clinical outcome, we believe that decreased TR can protect the right atrium from high pressure and that sinus rhythm restoration may help synchronous contraction of the atria and ventricles.

Although surgical adjuncts such as fenestration and tricuspid annuloplasty may be necessary in high-risk patients, medical management of pulmonary hypertension is also important. We liberally used nitric oxide and sildenafil for these patients, and we carefully tapered sildenafil during follow-up. Approximately one third of our patients are still on sildenafil or beraprost. In the present study, the decreased peak TR gradient after the operation is most likely due to the comprehensive surgical and medical management (Figure 3).

There is no definite surgical indication or standard management strategy for patients with ASD and severe pulmonary hypertension. For high-risk patients, different management strategies should be applied. Because these patients frequently have TR or atrial fibrillation, surgical closure may be a better option than a catheter-based closure procedure that cannot correct TR or atrial fibrillation. Fenestrated ASD closure, tricuspid annuloplasty, the Cox maze procedure for atrial fibrillation, and intensive control of PAP with a pulmonary vasodilator are all good possible management strategies.

Our study is inherently limited by its retrospective nature. We reviewed patients who had undergone ASD closure with a fenestrated patch. All patients had severe pulmonary hypertension, but they also had various degrees of shunt and pulmonary vascular resistance. Although the characteristics of the patients were somewhat heterogeneous, they were all high-risk patients for ASD closure. Therefore, our management strategy for these patients was to close the ASD with a fenestrated patch and, if there was significant TR, to repair the tricuspid valve and use pulmonary vasodilators liberally. In spite of the small number of patients and short follow-up duration, all patients recovered quickly and showed improved functional activity and a decreased peak TR gradient.

Because there are currently no recommendations or guidelines for patients with ASD and severe pulmonary hypertension, this integrated strategy including fenestrated patch closure, tricuspid valve repair, the Cox maze procedure, and use of a pulmonary vasodilator may become a safe and valuable option for these patients. We think that the indication of ASD closure can be extended with this strategy. Longer follow-up periods and further prospective studies are necessary to demonstrate the benefit of fenestrated patch closure of ASDs and tricuspid annuloplasty.

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