Outcomes of Totally Endoscopic Atrial Septal Defect Closure Using a Glutaraldehyde-Treated Autologous Pericardial Patch

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Background: We evaluated the outcomes of totally endoscopic minimally invasive surgery for atrial septal defect (ASD) using a glutaraldehyde-treated autologous pericardial patch in the transcatheter interventional era.

Methods and Results: We retrospectively reviewed 37 consecutive patients who underwent totally endoscopic ASD closure with a glutaraldehyde-treated autologous pericardial patch between June 2011 and April 2015. All patients had been deferred from catheter-based intervention for clinical or anatomical reasons. We analyzed operative outcomes and postoperative echocardiographic data. The mean age was 45.7±16.5 years, and 25 patients (67.6%) were women. The mean ratio of pulmonary to systemic flow was 2.4±0.7. Six patients (16.2%) underwent concomitant tricuspid valve repair, and 3 patients (8.1%) underwent concomitant atrial fibrillation surgery. There were no operative deaths, and the median length of hospital stay was 5 days. Postoperative echocardiography revealed trivial residual shunt in 1 patient. During the follow-up period, there were no re-interventions for ASD or readmission for heart failure. Follow-up echocardiography revealed no recurrent shunt or calcification of the autologous pericardial patch.

Conclusions: Totally endoscopic ASD closure with a glutaraldehyde-treated autologous pericardial patch demonstrated excellent outcomes. It is a useful option for patients with unfavorable anatomy or other reasons excluding transcatheter intervention.

Key Words: Congenital heart disease; Pericardium; Surgery

Trial septal defect (ASD) is a common congenital heart disease. The current guideline recommends ASD closure for patients developing right atrial and ventricular enlargement regardless of the presence of symptoms (Class I) and in those who have a history of paradoxical embolism or documented orthodoxia-platypnea (Class IIa). Open heart surgery was the standard treatment of ASD for many years, but these days transcatheter closure of ASD has demonstrated excellent outcomes, and has become the new standard treatment of ASD. However, transcatheter closure is not feasible for patients with any of the following: large defect (diameter >39 mm), multiple defects, non-ostium secundum defect, short rim (<5 mm), concomitant congenital anomaly, concomitant valve disease or allergy to the metal of the closure device. Such patients are candidates for surgical ASD closure.

Surgical ASD closure has demonstrated excellent early and late outcomes. A minimally invasive approach is feasible for this procedure, and provides faster postoperative recovery and other benefits to patients. However, a standard direct-vision minithoracotomy approach requires rib spreading with a metal retractor, which causes postoperative pain. Thus, we prefer a totally endoscopic approach using only a soft-tissue retractor. In terms of the material of the closing patch, we prefer to use glutaraldehyde-treated autologous pericardium, which is easy to handle, visualize on screen, durable, and cost-effective.

The aim of this study was to evaluate the outcomes of totally endoscopic minimally invasive ASD closure using a glutaraldehyde-treated autologous pericardial patch in the transcatheter interventional era.

Methods

Patients and Study Design
Between June 2011 and April 2015, 37 consecutive patients underwent surgical closure for ASD using a glutaraldehyde-treated autologous pericardial patch with a totally endoscopic minimally invasive approach at Sakakibara Heart Institute and Tokyo Bay Urayasu-Ichikawa Medical Center. All patients were deferred from catheter-based intervention for the following reasons: insufficient rim in 25 patients, multiple defects in 5 patients, metal allergy in 2 patients and concomitant procedure in 1 patient. We analyzed the perioperative clinical and echocardiographic data to assess the safety and effectiveness of this procedure. The institutional review boards approved this study.
sure is a right minithoracotomy in which the ribs are widely spread with a metal retractor so the surgeon can see directly into the chest (Figure 1). The other options are totally endoscopic and robotic approaches. We defined a totally endoscopic approach as operation through a right minithoracotomy with \( \leq 5 \) cm skin incision, no use of metal retractors, use of an endoscopic system to visualize the operative field and no use of a surgical robot (Figure 1).

A double-lumen endotracheal tube was used for single-lung ventilation. A 14 or 17 Fr venous tube and central venous line were placed in the right internal jugular vein by the anesthetist. After draping the patient, the common femoral artery and vein were cannulated, and cardiopulmonary bypass (CPB) established with vacuum-assisted bicaval venous drainage. We made a 4 or 5 cm incision to create a right 4th intercostal minithoracotomy and used only a soft-tissue retractor to restrain muscle and fat. We place a 5-mm port for the endoscopic camera and another port for the vent and carbon dioxide tubes in the 5th or 6th intercostal space (Figure 1). Needle holders and forceps were inserted through the minithoracotomy.

After the establishment of CPB, the pericardium was opened 3 cm away from the right phrenic nerve, and the correct amount of pericardium resected from the opposite side of the phrenic nerve. The resected pericardium was preserved in 0.625% glutaraldehyde solution for 10 min and then rinsed twice with saline for 1 min. Fresh pericardium curls up and is difficult to handle in a limited space, whereas glutaraldehyde-treated pericardium retains its shape and is easy to handle (Figure 2).

Both the superior and inferior venae cavae were taped. A vent tube was placed in the left atrium via the right superior pulmonary vein, and the antegrade cardioplegia cannula was placed in the ascending aorta. During administration of the cardioplegia solution, both venae cavae were snared and the right atrium was opened. The ASD can be well visualized with a couple of traction sutures on the right atrial wall. The left atrial vent is useful for obtaining a bloodless operative field. Next, we trimmed the pericardial patch to the appropriate size and shape, and closed the ASD with the patch and 5-0 running polypropylene suture. The glutaraldehyde-treated pericardium can be seen through the endoscopic system because it does not reflect the endoscopic light (Figure 3).

We routinely performed intraoperative transesophageal echocardiography to evaluate the absence of residual shunt. If we found significant residual shunt, we re-opened the right atrium on CPB with the heart beating, and placed additional sutures to close the shunt. Postoperatively, no antiplatelet or anticoagulation drugs were used unless the patient developed atrial fibrillation (AF).

**Statistical Analysis**
All data analyses were performed with JMP 11.0 software (SAS Institute Inc., Cary, NC, USA). Data are expressed as mean±standard deviations or median (range) for continuous variables and as numbers (percentages) for categorical variables. Long-term survival was plotted using the Kaplan-Meier method.

**Results**

**Preoperative Background**
The preoperative patients’ characteristics were shown in...
Early Outcomes
There were no operative deaths in this series. Moreover, there were no cerebrovascular accidents, perioperative myocardial infarctions, respiratory insufficiency including pneumonia, wound infections or re-exploration for bleeding. Postoperative renal insufficiency, defined as $\geq 2.0 \text{ mg/dL}$, occurred in 1 patient (2.7%) and left atrial appendage closure in 1 patient (2.7%). The mean operation time was $184.0 \pm 37.2 \text{ min}$, CPB time was $103.8 \pm 27.4 \text{ min}$ and aortic cross-clamping time was $58.6 \pm 23.5 \text{ min}$. No patients required conversion to a full sternotomy; 2 patients required a second pump run because of residual shunt in 1 patient and injury of the right pulmonary artery in the other.

Long-Term Outcomes
The follow-up rate was 100%. The mean follow-up was 32.6±16.1 months. There was 1 late death during the follow-up period; the patient died of gastric cancer 40 months ASD surgery. Actuarial survival was 100% at 3 years and 93.8% at 5 years. During the follow-up period, there were no re-interventions for the ASD or tricuspid valve, no readmission for heart failure, no thromboembolic events and no infective endocarditis.

All patients underwent 1-year echocardiography and the mean echocardiographic follow-up period was 26.6±16.3 months. Follow-up echocardiography showed no new recurrent shunts. In the 1 patient with a trivial residual shunt, the shunt volume was unchanged 3 years after surgery. Moreover, follow-up echocardiography showed no sign of structural deterioration of the glutaraldehyde-treated autologous pericardial patches, including perforation, calcification and thrombus formation.

Discussion
In this report, we have shown excellent surgical outcomes and durability of totally endoscopic ASD closure using a glutaraldehyde-treated autologous pericardial patch. To the best of our knowledge, this is the first report to show the effectiveness and safety of totally endoscopic ASD closure using glutaraldehyde-treated autologous pericardium. The totally endoscopic approach is even less invasive than the standard direct-vision minimally invasive approach. In this transcatheter interventional era, a smaller skin incision and less postoperative pain are what patients expect. Some previous studies have shown that small skin incision and not using metal retractors lead to less postoperative pain and greater patient satisfaction. Glutaraldehyde treatment of autologous pericardium has been controversial, but in our experience it is easier to handle and visualize endoscopically.

Outcomes of Transcatheter and Surgical ASD Closure
ASD is the most common congenital heart disease in adults. ASD closure is recommended for patients developing right atrial and right ventricle enlargement regardless of the presence of symptoms (Class I) and in those who...
have a history of paradoxical embolism or documented orthodeoxia-platypnea (Class IIa). There are surgical and transcatheter options for ASD closure. Open heart surgery with a median sternotomy had been the standard treatment for many years and demonstrated excellent long-term outcome.6,7 Harvath and colleagues reported their experience of 166 consecutive patients who underwent surgical ASD closure. There were no operative deaths, reoperation for ASD in 1 patient and 10-year survival rate was 94%.5 Murphy and colleagues reviewed their 123 patients undergoing surgical ASD closure; the overall 30-year actuarial survival rate was 74% and reoperation for ASD was required in 1 patient during the follow-up period.6

In the 1970s, King and colleagues reported the first successful transcatheter closure of ostium secundum ASD.16 Following their success, several transcatheter trials were conducted for ostium secundum ASD closure.17,18 Recent studies have reported that the procedural mortality is nearly zero and the rate of successful closure is greater than 95%.1,3,19,20 In terms of long-term outcomes, Katório and colleagues reported a 5-year re-intervention rate of 7.9% and 5-year mortality rate of 5.3%.23 Masura and colleagues reported no re-interventions during their median follow-up of 78 months.24 Takaya and colleagues reported no procedure-related complications during a median follow-up of 36 months.23 Those findings show the safety and effectiveness of transcatheter ASD closure, which has become the new standard treatment for the ostium secundum type of ASD. On the other hand, some adverse events have been reported. DiBardino and colleagues have reported adverse events and their incidences among 18,333 cases: device infection (0.011%), thromboembolic event (0.06%), residual shunt (0.049%), embolization (0.62%), cardiac perforation/erosion (0.28%).21

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Surgical closure is the standard treatment for the ostium secundum type of ASD (Class I), and is a good alternative to transcatheter closure of the ostium secundum type when patients have a large defect, insufficient rim, multiple defects or metal allergy.4,5 Surgical closure is also a reasonable option when concomitant tricuspid repair is necessary (Class IIa).1

Minimally invasive approaches are feasible for surgical ASD closure, and have several advantages over the conventional approach, such as faster postoperative recovery, less blood product required, better cosmesis and quality of life.23–25 Vistarini and colleagues reported their early and late outcomes of 116 cases of minimally invasive ASD closure.7 There were no conversions to a median sternotomy or hospital deaths; 6 patients (3.6%) had re-exploration for bleeding from the thoracic wall, but there were no other re-interventions during 51 months. Based on all these findings, including ours, minimally invasive surgical ASD closure can be the standard option for patients who are unsuitable for transcatheter ASD closure. There have been no comparative studies of the different minimally invasive approaches: direct-vision, totally endoscopic, and robotic. However, it is rational that a smaller skin incision and no rib spreading are beneficial in terms of postoperative pain.

It is obvious that the endoscopic system is much less costly than the robotic system.

Advantages of Autologous Pericardium

There are several materials used for the closing patch, such as fresh autologous pericardium, glutaraldehyde-treated autologous pericardium, bovine pericardium, expanded polytetrafluoroethylene (ePTFE) and Dacron patch. It is unknown which material provides the least complications and best durability for ASD closure. Thrombus formation has been reported with bovine pericardium and Dacron patches.26,27 In our experience with autologous pericardium, thrombus formation did not occur even without antiplatelet or anticoagulation therapy.

We prefer to use glutaraldehyde-treated autologous pericardium for several reasons. First, it is easy to handle in a limited space compared with fresh autologous pericardium, which always curls up and shrinks (Figure 2). Second, it does not reflect endoscopic light, unlike the ePTFE patch, and so is well visualized on the endoscopic screen (Figure 3). Also, there is no oozing from punctures, as is often seen with the ePTFE patch, and it is less costly than the ePTFE patch. Some surgeons may prefer to use a costly patch to cover the heart after harvesting the pericardium. Instead, we use fat tissue on the pericardium to cover the heart or just leave it unless we have enough fat tissue.

It is controversial whether autologous pericardium should be treated with glutaraldehyde or not. Untreated autologous pericardium has been used for mitral valve repair. Some researchers showed degeneration of fresh autologous pericardium such as retraction, calcification and thickening.28–30 Ross and Olsen reported 11 cases of mitral valve repair using untreated autologous pericardium and very high reoperation rate (64%) in the 58 months after surgery.28 They harvested the pericardial patches at the time of redo surgery. Histological examination of the samples showed prominent degeneration associated with thickening and fibrotic change.28 Chauvaud and colleagues reported their experience of 64 patients who underwent mitral valve repair using glutaraldehyde-treated autologous pericardium.31 There were 6 patients who required reoperation during the follow-up period (6 months to 9 years after primary surgery). Intraoperative macroscopic findings showed that the pericardial patch remained pliable without any calcification in all 6 patients.31 Glutaraldehyde-treated autologous pericardium has been used for complex mitral valve repair and excellent durability, freedom from calcification and low thrombogenicity have been reported.11–13 These data legitimize the use of glutaraldehyde-treated autologous pericardium in ASD closure.

Study Limitations

We did not compare the outcomes of totally endoscopic ASD closure with those of the conventional approach or standard direct-vision minimally invasive approach, or compare the outcomes of ASD closure using glutaraldehyde-treated autologous pericardium with closure using other materials, because we used a totally endoscopic approach and glutaraldehyde-treated autologous pericardium in almost all cases. The sample size was small because nowadays most ASD patients are treated with transcatheter surgery. The follow-up period was not long enough to evaluate the long-term durability of this procedure. Further follow-up is necessary.

In conclusion, totally endoscopic ASD closure with a glutaraldehyde-treated autologous pericardial patch demonstrated low mortality and morbidity, fast postoperative recovery and excellent 3-year durability. This procedure is an excellent alternative to transcatheter ASD closure if the...
patient is anatomically or clinically unsuitable for transcatheter therapy.

**Conflict of Interests**

The authors declare that they have no conflicts of interest related to the manuscript.

**References**


