Title

Mid-term results after seamless patch mitral reconstruction

Running Head

Mid-term results of seamless patch reconstruction

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Central picture legend: Mitral valve reconstruction with seamless patch technique.

Central Message: Mitral valve reconstruction with seamless patch technique provides an excellent long-term result, when applied to the pathologies involving the commissure or up to two segments.

Perspective statement: Durable repair of mitral valves with active endocarditis, small leaflet, or restrictive leaflet remains challenging. This approach is easily accessible technically and augments surgeons’ armamentarium, especially in young patients to avoid valve replacement.

Abbreviations

IQR = interquartile range
SD = standard deviation
SRT = seamless patch reconstruction technique
MR = mitral regurgitation
MS = mitral stenosis
Abstract

Objectives: Some pathologies, including infective endocarditis or sclerotic changes of the mitral leaflet, make the conventional mitral valve repair challenging. Our previously described technique for reconstruction with a seamless pericardial patch makes the repair feasible in some of such difficult pathologies. However, the extent of mitral leaflet segments that could be safely repaired using this technique remains unknown. We investigated the association between mid-term outcome and the extent of mitral leaflet segments replaced by pericardial patch.

Methods: From January 2009 to January 2022, patients underwent mitral valve repair with seamless one-patch reconstruction technique were included. The glutaraldehyde-treated pericardium was trimmed and anchored at the papillary muscle. The edge was sewn to the leaflet and the annulus.

Results: 49 patients (60±15 years old) underwent mitral valve repair with this technique. Totally endoscopic approach was utilized in 27 (55%) patients. No patient was converted to valve replacement. No operative mortality or disabling stroke was observed during the early postoperative period. In the mid-term follow-up, redo surgery was required in 9 patients (18%). Freedom from mitral valve reintervention rates at 1, 5, and 10 years were 84%, 82%, and 82% for all patients. Freedom from reoperation at 5 years were 100%,
92%, and 46% for commissural lesion, 1-2 segment involvement, and 3-segment involvements, respectively. There was a significant difference between the three groups with regard to mitral valve reoperation rate (p=0.002).

Conclusion: Mitral valve seamless patch reconstruction provides excellent mid-term results if applied to commissural lesions or lesions involving up to two segments.

Keywords: Mitral valve, autologous pericardium, mitral valve reconstruction, mitral valve repair
Introduction

Mitral valve repair is the standard of care for degenerative mitral regurgitation (MR) meeting operative indications (1,2). Numerous techniques for mitral repair have been reported with good long-term outcomes (3,4,5). However, durable repair of mitral valves with active endocarditis, small leaflet, or restrictive leaflet remains challenging. The difficulties are often related to the lack of sufficient leaflet tissue to provide adequate coaptation. To repair such pathologies, we reported our technique of ‘seamless’ patch reconstruction utilizing glutaraldehyde-treated autologous pericardium (6,7). This technique uses a single piece of pericardium patch to cover the defective or diseased mitral leaflet with a good early outcome. As we have broadened the application of our technique to more extensive valve pathologies, we aimed to characterize the association between the long-term outcome and the extent of segments repaired.

Materials and Methods

Patient selection

This report was approved by the Institutional Review Board of the Japanese Red Cross Nagoya First Hospital (2021-429) April 1st 2021. The individual informed consent was waived. We retrospectively reviewed our database and included all the patients who
underwent seamless patch reconstruction technique (SRT). All the patients who were planned preoperatively to undergo SRT successfully underwent SRT and were included in this series. Patients were considered as a candidate for SRT when the defect or sclerotic mitral leaflet was limited to one leaflet (regardless of the number of involved segments). We excluded patients who received leaflet repair by means other than autologous pericardium. We did not attempt SRT when the lesions were in both anterior and posterior leaflets. We investigated our perioperative and long-term outcomes stratified by the extent of leaflet replaced with SRT. Patients were divided into three groups: commissure leaflets replaced, 1-2 segment replaced, and 3 segment replaced. We analyzed the long-term outcomes in terms of the valve function.

Surgical technique

Median sternotomy or endoscopic approach was chosen based on patients’ anatomy. All patients underwent cardiopulmonary bypass. Totally endoscopic procedures were performed through a right mini-thoracotomy without rib spreading (8). The autologous pericardium was harvested at the time of pericardiotomy. The harvested pericardium was soaked in 0.6% glutaraldehyde solution for ten minutes and rinsed twice with normal saline for ten minutes.
The left atrium was opened at the Waterson groove. The mitral valve was repaired utilizing the harvested pericardium. The edge of the prepared pericardium is attached to the base of the papillary muscle with a pledgetted 4-0 Gore-tex (W. L. Gore & Associates Inc., Newark, DE, USA) suture. We refer the length or width of the leaflet to the adjacent leaflets and try not to shorten the leaflet or the length to the annulus. The pericardium was sewn to the native leaflet with a single interrupted 5-0 polypropylene sutures (Figure 1 A-D, Video) according to the valve anatomy. The annuloplasty was made if there is an annular dilatation. The details of the technique are also described in our previous reports (6,7).

After confirming the valve competency with saline injection to the left ventricle, the left atrium was closed with single-layer polypropylene sutures. The cardiopulmonary bypass was weaned after the resumption of the heart rhythm.

Patient follow-up

Transthoracic echocardiography was performed preoperatively and before the hospital discharge. All the studies were reviewed by a cardiologist specialized in cardiac imaging (Y.M.). The degree of mitral regurgitation was according to the American society of echocardiography guideline. Each measured parameter was recorded at preoperative and
at the time of long-term follow-up. The patients are followed at our clinic with an annual
echocardiography. All patients received warfarin and aspirin for the first three months
after the procedure and aspirin was continued thereafter.

Statistical analysis

Data were summarized as means +/- standard deviation (SD) for continuous variables
and number (%) for categorical variables. Echocardiographic characteristics of the mitral
valve were compared pre- and postoperatively in echocardiographic measurements
utilizing the 2-tailed paired t-test for ejection fraction, mitral regurgitation degree, and
mean gradient across the mitral valve. Overall survival, freedom from redo-surgery, and
freedom from significant mitral regurgitation (more than mild) were displayed in Kaplan-
Meier plots and statistical significances were tested using the log-rank test. We also
performed competing risk analysis for freedom from significant mitral regurgitation and
freedom from redo-surgery to account for the competing mortality risk. The analysis was
performed using SPSS 21 (IBM Corp, Armonk, NY) and ‘cmprsk’ package for R Studio
4.2.1 (R Foundation, Vienna, Austria).

Results
Preoperative variables

From January 2009 to January 2022, 49 patients underwent SRT in our institution using the described technique. During the same time period, 831 cases of mitral valve procedures (surgical repair and/or replacement) were performed in our institutions. Their mean age was $60 \pm 15$ years old at the index surgery. All patients had moderate or severe mitral regurgitation, and one patient (2.0%) had moderate mitral stenosis. Preoperative variables are summarized in Table 1.

Mitral valve pathologies and type of the patch

Details of the mitral valve pathologies and the Carpentier classification are shown in Table 1. The most common pathology was type II disease (26 patients, 53%). The posterior leaflet involvement was the majority in the group (28 patients, 57%). 38 patients (78%) had triangle- or pentagon-shaped patch, and 11 patients (22%) received a double pentagon attached to both anterolateral and posteromedial papillary muscle. 12 patients (24%) received the patch around the commissure. 26 patients (53%) had one or two segments replaced with triangle or pentagon shaped patch (Figure 1). 11 patients (22%) had three segments covered with the double pentagon shaped patch. Four patients (8.2%) were treated with a loop technique for the co-existing type II lesion in addition to SRT.

All the patients received glutaraldehyde-treated autologous pericardium described above.
Perioperative variables

Intraoperative and early postoperative characteristics are shown in Table 2. Seven patients (14%) underwent concomitant aortic valve replacement with a standard stented bioprosthesis. One patient (2.0%) had a concomitant root replacement, and two patients (4.1%) had coronary artery bypass grafting simultaneously. Tricuspid repair, maze procedure, and left atrial appendage closure were performed in 18 (37%), 13 (27%), and 24 patients (49%), respectively. Annuloplasty was performed in 41 patients (84%) including 3 patients had annuloplasty ring from the previous surgery.

Mean aortic cross-clamp time and cardiopulmonary bypass time were 143 ± 46 and 198 ± 61 minutes, respectively. All patients underwent mitral valve repair without the need for replacement. There was no 30-day mortality. Ischemic stroke occurred in one patient (2.0%). There was no conversion to sternotomy in patients planned for totally endoscopic approach (27 patients, 55%).

Mid-term result

The mean duration of the follow-up from the index surgery was 69±41 months (range:
The follow up was completed in 100% of the patients. Postoperative trans-thoracic echocardiographic (TTE) results at latest follow-up are shown in Table 3. The mean duration of the TTE was 55±40 months (range: 1-159, 96% completeness in the mid-term follow-up).

In the mid-term follow-up, redo surgery was required in 9 patients (18%). Of those, double pentagon patch for three segment lesion was used in 6 patients (67%) at the initial operation. The reasons for redo surgery were a tear in the patch in two patients (4.1%), sclerotic change in remnant leaflet tissue in two patients (4.1%), hemolysis in two patients (4.1%). One patient had redo for mitral stenosis eight years after the repair. The details of the redo surgery are shown in Supplemental Table 1. No recurrence of mitral regurgitation was found in the cases of commissural involvement. There were three patients requiring reoperations (12%) among those who had one or two segments replaced, and there were six requiring reoperations (55%) among those who had three segments replaced.

The 1-, 5- and 10-year survival rates were 96%, 80%, and 80% for all patients, and free from cardiac mortality were 96%, 90%, and 90% for all patients, respectively. Long-term survival was not significantly different in the three subgroups of commissural lesion, 1-2
segment involvement, and three segment involvements. (p=0.35, Figure 2).

Freedom from mitral valve reintervention rates at 1, 5, and 10 years were 84%, 82%, and 82% for all patients. There was a significant difference between the 3 groups with regard to mitral valve reoperation in competing risk of death and reoperation by the extent of leaflet involvement (p=0.005, Supplemental Figure 1). Freedom from reoperation rates at 5 years were 100%, 92%, and 46% for commissural lesion, 1-2 segment involvement, and 3-segment involvement, respectively. In terms of freedom from more-than-mild mitral valve regurgitation, there was a significant difference between the 3 groups in competing risk of death and reoperation by the extent of leaflet involvement (p=0.019, Supplemental Figure 2). Freedom from more-than-mild mitral regurgitation rates at 5 years were 100%, 84%, and 58% for commissural lesion, 1-2 segment involvement, and 3-segment involvement, respectively.

Comment

We previously described our technique and early outcome of this seamless patch reconstruction (6, 7). Our previous study demonstrated its effectiveness and reproducibility in short-term. The results of our current study are consistent with previous reports of the fresh autologous pericardium (9, 10, 11). The rate of freedom from
reoperation in patients who underwent SRT was 82% at 5 years, comparable to those
previous studies vary 82-89% at 5 years. Our study represents one of the largest series of
mitral repair utilizing autologous pericardium.

Our data demonstrated that the anatomic location of the SRT application was associated
with mid-term durability of the repair. The SRT patch implanted at the commissure had
no recurrence in the mid-term. The SRT patch covered one to two segments also had
excellent mid-term outcomes. On the other hand, if applied more than two segments, SRT
had a higher incidence of recurrence compared to the less extensive repair. We applied
this technique for patients who otherwise would have received a valve replacement, such
as infective endocarditis or type III lesion. We consider the mid-term result acceptable
when applied to the limited lesion to salvage the native valve. A limitation of our study is
that the included population is heterogenous and the variation in outcomes may partly
owe to the variation in pathology. Based on the repair durability data presented, the extent
of segments involved may be a unifying variable that could guide the patient selection for
appropriate SRT candidates, regardless of the valve pathologies or etiologies. The study
investigates a small number of patients retrospectively and a larger number of patients
are necessary to corroborate our findings. Also a learning curve effect may play a relevant
role in this setting.
A possible drawback of this technique is the potential inflow obstruction by the pericardial patch, as described in previous reports (6). In fact, in our series, three patients had more-than-moderate mitral stenosis in the mid-term, including a patient with rheumatic mitral morphologies. In most of the patients (94%), although the mitral stenosis was negligible with the mean pressure gradient of 3.9 mmHg. The use of fresh autologous pericardium in mitral repair has been reported to rarely incur calcification in the long-term (10, 11). Our series corroborates this observation with no patients showing signs of calcification in the leaflet.

This approach is easily accessible technically and augments surgeons’ armamentarium, especially in young patients to avoid valve replacement. We have performed SRT in a totally endoscopic manner in the majority of the patients (55%) using three-port technique (8) (Video) without any mortalities or major complications. We now routinely perform SRT with an endoscopic platform. Mitral valve reconstruction with seamless patch technique provides an excellent mid-term result, when applied to the pathologies involving the commissure or up to two segments.

Conflict of interest statement

Toshiaki Ito received proctor fee from Edwards Lifescience, Inc. and lecture fee from
Medtronic, Inc. and Abbott, Inc. (no direct conflict with this manuscript). All other authors declared no conflict of interest.
References


Figure legends

Figure 1 (A-D),
Schema of seamless patch reconstruction technique applied to one or two-segment involvement.

Figure 2,
Actuarial overall survival and cardiac death after seamless patch mitral reconstruction, in the commissural, up to two segments, and three-segment involvement.
Freedom from reoperation after seamless patch mitral reconstruction in the commissural, up to two segments, and three-segment involvement with Competing risk of death and reoperation by the extent of leaflet involvement.

Supplemental Figure 2,

Freedom from reoperation after seamless patch mitral reconstruction between the commissural, up to two segments, and three-segment involvement with Competing risk of death and reoperation by the extent of leaflet involvement.

Video legend

A video demonstrating the totally 3D-endoscopic mitral valve repair utilizing seamless patch reconstruction technique after converting two-dimensional view. Video shows a mitral valve repair for active endocarditis. 32-year-old man, previously diagnosed moderate mitral valve regurgitation with the anterior leaflet prolapse, presented with intractable fever after the treatment for pyogenic spondylitis. Urgent surgery was carried out for the large vegetation after a week of antibiotic treatment. The infective tissue was found at the P3 to posterior commissure. After the debridement, triangular shaped autologous pericardium was prepared to cover the whole P3-to PC area. Myxomatous
change in anterior mitral leaflet was found and corrected with a loop technique.
Tables
Table 1, Preoperative Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years ± SD)</td>
<td>60±15</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>23 (47)</td>
</tr>
<tr>
<td>BMI (mean ± SD)</td>
<td>21 ± 3.7</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>16 (33)</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>15 (31)</td>
</tr>
<tr>
<td>Dyslipidemia, n (%)</td>
<td>10 (20)</td>
</tr>
<tr>
<td>History of CVD, n (%)</td>
<td>5 (10)</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>16 (33)</td>
</tr>
<tr>
<td>Chronic kidney disease, n (%)</td>
<td>8 (16)</td>
</tr>
<tr>
<td>Hemodialysis, n (%)</td>
<td>3 (6)</td>
</tr>
<tr>
<td>History of atrial fibrillation, n (%)</td>
<td>22 (45)</td>
</tr>
<tr>
<td>Ejection fraction (mean ± SD)</td>
<td>59±14</td>
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<tr>
<td>Low EF, n (%)</td>
<td>2 (4.1)</td>
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<tr>
<td>NYHA (mean ± SD)</td>
<td>2.7±0.6</td>
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<tr>
<td>Previous cardiac surgery, n (%)</td>
<td>3 (6)</td>
</tr>
<tr>
<td>Endocarditis, n (%)</td>
<td>14 (29)</td>
</tr>
<tr>
<td>Active endocarditis, n (%)</td>
<td>8 (16)</td>
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<tr>
<td>Posterior leaflet lesion, n (%)</td>
<td>28 (57)</td>
</tr>
<tr>
<td>Anterior leaflet lesion, n (%)</td>
<td>9 (18)</td>
</tr>
<tr>
<td>Commissure lesion, n (%)</td>
<td>12 (24)</td>
</tr>
</tbody>
</table>
Degenerative mitral regurgitation, n (%) 26 (53)
Functional mitral regurgitation, n (%) 23 (47)
Atrial functional mitral regurgitation, n (%) 6 (12)
Ventricular functional mitral regurgitation, n (%) 9 (18)
Carpentier classification
Type I, n (%) 0
Type II, n (%) 26 (53)
Type IIIa, n (%) 8 (16)
Type IIIb, n (%) 15 (31)

SD, standard deviation; BMI, body mass index; CVD, cerebrovascular disease; EF, ejection fraction; NYHA, New York Heart Association

Table 2, Perioperative variables

<table>
<thead>
<tr>
<th>Procedure</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Totally endoscopic surgery, n (%)</td>
<td>27 (55)</td>
</tr>
<tr>
<td>Mitral annuloplasty, n (%)</td>
<td>41 (84)</td>
</tr>
<tr>
<td>Concomitant aortic valve replacement, n (%)</td>
<td>6 (12)</td>
</tr>
<tr>
<td>Concomitant root replacement, n (%)</td>
<td>1 (2.0)</td>
</tr>
<tr>
<td>CABG, n (%)</td>
<td>2 (4.1)</td>
</tr>
<tr>
<td>Left ventricular restoration, n (%)</td>
<td>2 (4.1)</td>
</tr>
<tr>
<td>Tricuspid valve repair, n (%)</td>
<td>18 (37)</td>
</tr>
<tr>
<td>Maze procedure, n (%)</td>
<td>13 (27)</td>
</tr>
<tr>
<td>Left atrial appendage closure, n (%)</td>
<td>24 (49)</td>
</tr>
<tr>
<td>Cardiopulmonary bypass time, min (mean ± SD)</td>
<td>198 ± 61</td>
</tr>
<tr>
<td>Variables</td>
<td>Predischarge</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Ejection fraction, % (mean ± SD)</td>
<td>52±15</td>
</tr>
<tr>
<td>Mean pressure gradient, mmHg (mean ± SD)</td>
<td>3.8±2.7</td>
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<tr>
<td>Mean pressure gradient &gt;5mmHg, n (%)</td>
<td>5 (10)</td>
</tr>
</tbody>
</table>

CABG, coronary artery bypass grafting; ICU, intensive care unit; hrs, hours; EF, ejection fraction; MS, mitral stenosis; IQR, interquartile range

Table 3.

Last follow-up transthoracic echocardiographic findings

SD, standard deviation