

Peer Review File

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Reviewer A

Comment 1: This is a retrospective study which compares the outcomes of patch augmentation repair for AFMR with the outcomes of valve replacement. The authors share their single institution experience. Overall it is a well presented study with some interesting pieces of information. The main limitations of the study are its retrospective nature and the small number size which hinders any meaningful analysis.

Reply 1: We appreciate the reviewer's comments. As mentioned by the reviewer, the sample size of this study is small. However, obtaining a large number of patients with AFMR and excluding selection bias because the number of patients with AFMR is relatively small may be difficult. However, the data from only a small number of patients may still be meaningful to obtain information regarding AFMR with long-standing atrial fibrillation. We have already described this information in the limitations of the Discussion section.

Changes in the text: No changes.

Comment 2: Additionally,

-Figures 2-3. The KM curve should be truncated when patients at risk are less than 10 percent of the overall population of the study. Although, the dashed lines representing the CI are informative, overcomplicate the figures so it would be preferable if they were replacement by SEM error bars at specific timepoints only, debulking thus the figures.

Reply 2: We thank the reviewer for the helpful comments. We have revised Figures 2 and 3 by truncating the KM curve when patients at risk are less than 10% of the overall population. As mentioned by the reviewer, SEM error bars at specific time points may be better than the CI. However, we believe that the readers of the Journal might mistake the SEM error for the CI. Therefore, we believe that the CI is the best value to use for the KM curve.

Changes in the text: We have revised Figures 2 and 3.

Comment 3:

-The PA population looks to be less sick than the VR one in terms of cerebrovascular disease, renal disease, tricuspid regurgitation, euroSCORE. Do the authors believe that this difference in baseline characteristics could account for confounding effects on the observed outcomes?

Reply 3: As mentioned by the reviewer, the PA group was less sick than the VR group because the patients who had severe illness tended to undergo mitral valve replacement, which may have affected the outcomes. Therefore, we cannot deny that

this difference did not affect the outcomes as a confounding effect.

Changes in the text: No changes.

Reviewer B

Morisaki et al assessed outcome difference in patients with atrial functional mitral regurgitation who underwent patch augmentation and mitral valve replacement. It is a retrospective analysis, and showed comparable results with either of these procedures. Also, atrial reduction was recommended to reduce thromboembolic events. My concerns relate to the methods and patient selection.

Minor concerns:

Comment 1. Atrial FMR occurs due to LA dilation leading to mitral annular dilation and insufficient leaflet modeling causing insufficient leaflet to annulus ratio and subsequent malcoaptation. Even though management options are limited, medical therapy has been shown to be beneficial in reducing MR severity and LA size. Rhythm control is usually enough and if needed, surgical options may be considered though with variable results. There is no mention of how many patients had atrial fibrillation and if medical management focused at rhythm control was undertaken.

Reply 1: We thank the reviewer for the helpful comments. As mentioned by the reviewer, medication therapies, including rhythm control, are beneficial in reducing the severity of mitral regurgitation and the LA size, and improving congestive heart failure. However, the candidates in this study were patients who developed congestive heart failure caused by AFMR and long-standing atrial fibrillation even after medical management including rhythm control.

Changes in the text: We have added the following text to the Methods section: “The patients who had congestive heart failure caused by AFMR and long-standing atrial fibrillation even after medical management, including rhythm control, were eligible for inclusion in the study.”

Comment 2. Line 54-57: I disagree with author’s statement here, atrial FMR is multifactorial and not every patient has atriogenic restricted/tethered mitral valve leaflet. There are a lot of patients who have insufficient leaflet remodeling, which is often, the main pathophysiologic mechanism. Comments on the main mechanism of FMR in the patients included in the study would be helpful.

Reply 2: As mentioned by the reviewer, AFMR is often caused by insufficient leaflet coaptation by the mitral annulus and left atrial dilatation. However, a recent study showed that some patients who had long-standing atrial fibrillation developed AFMR caused by posterior leaflet tethering due to deviation of the posterior leaflet. This deviation was caused by considerable dilation of the mitral annulus and the left atrium (atriogenic tethering or atrial hamstringing). Therefore, in patients who have AFMR caused by posterior leaflet tethering, using only ring annuloplasty may not be sufficient to achieve a good long-term outcome because of insufficient leaflet coaptation by shortening of the posterior leaflet. We have added the mechanism of

AFMR and long-standing atrial fibrillation to the Introduction section.

Changes in the text: We have added the following text to the Introduction section: “Atrial fibrillation often causes mitral annular and left atrial dilatation, which lead to insufficient coaptation of the mitral leaflets. Some patients who have long-standing atrial fibrillation develop AFMR and posterior leaflet tethering due to deviation of the posterior leaflet. This deviation is caused by considerable dilation of the mitral annulus and the left atrium (atriogenic tethering or atrial hamstringing) (1).”

Comment 3. What was vena contracta and ERAO in both groups? How was leaflet tethering measured?

Reply 3: We apologize that we did not measure the vena contracta in all patients. However, we defined the severity of mitral regurgitation using a multiparametric approach. This approach involved assessment of the color Doppler-derived jet area, effective regurgitant orifice area, mitral regurgitation volume and fraction, and pulmonary vein flow velocity pattern. We measured the P2 posterior leaflet lengths and the posterior leaflet tethering angle in mid-systole. The patients who had coaptation loss and a short length (< 12 mm) of the posterior leaflet with a posterior leaflet tethering angle > 30 degrees were candidates for this study.

Changes in the text: We have added the following text to the Methods section: “We measured the P2 posterior leaflet lengths and the posterior leaflet tethering angle in mid-systole. The posterior leaflet tethering angle was defined as the angle comprising the annular line, and the line drawn between the posterior annulus and the tip of the posterior leaflet [3]. The patients who had coaptation loss and a short length (< 12 mm) of the posterior leaflet with a posterior leaflet tethering angle > 30 degrees were candidates for this study.”

Comment 4. I would be careful with using the term late stage AFMR and its definition that is being limited to posterior leaflet tethering in this manuscript.

Reply 4: As mentioned by the reviewer, defining AFMR with posterior leaflet tethering as late-stage AFMR may be inappropriate.

Changes in the text: We have changed the term “late-stage AFMR” to “AFMR with a tethered posterior leaflet” in the main text.

Comment 5. Was there any reason for INR to be in the lower range?

Reply 5: We had described the INR improperly. We controlled warfarin within 1.8–2.2 of the INR as the standard. If the patients had a bleeding tendency, we controlled the INR to a lower level than that of the standard level.

Changes in the text: We have changed the values “1.6–2.2” to “1.8–2.2” in the anticoagulant therapy subsection of the Methods section. We have also added the following text to the Anticoagulant therapy subsection of the Methods section: “If the patients had a bleeding tendency, we controlled warfarin at a lower level of the international normalized ratio than the standard level.”

Reviewer C

Comment 1. Due to the small sample size of your study, it is imperative to talk about preliminary results, and conditional verb tenses should be used in abstract and conclusions of the manuscript. Also, a summary of concomitant procedures should be included in the methods to explain your X-clamp times, and you must indicate what type of tricuspid repair was performed.

Reply 1: We appreciate the reviewer's comments. As mentioned by the reviewer, stating the conclusions in the abstract and main text may be difficult because of the small sample size. Therefore, we have revised the conclusions in the abstract and main text. Moreover, we have added concomitant procedures in the Methods section and the type of tricuspid repair in the Results section.

Changes in the text: We have revised the conclusions in the abstract and main text with conditional verb tenses. We have added the following information on the surgical techniques to the Methods section: "We performed aortic valve replacement or coronary artery bypass grafting in the conventional fashion during cardiac arrest if necessary." We have also added the following sentence to the "Patients' preoperative and intraoperative characteristics" subsection in the Results section: "Only one patient underwent the DeVega procedure for severe tricuspid valve regurgitation in the VR group, whereas 30 patients underwent ring annuloplasty."

Comment 2. You said that few studies have examined the outcomes of patch augmentation, you should cite those papers.

Reply 2: We thank the reviewer for the helpful comment. We have added some references as suggested.

Changes in the text: We have added some references to the Introduction section as follows: "However, few studies have examined the outcomes of patch augmentation repair for AFMR (3,4),"

Comment 3. What is the reason that the subvalvular apparatus was not preserved in the VR group? Could this be a reason for the higher rates of MACE in this group during follow-up?

Reply 3: We did not preserve subvalvular tissue in the VR group because residual subvalvular tissue might promote pannus formation, which may be associated with limiting prosthetic valve leaflet motion in the future. Moreover, as mentioned by the reviewer, non-preserved subvalvular tissue may not affect the outcomes during follow-up because of a preserved left ventricular ejection fraction. Therefore, we have deleted the sentence regarding non-preserved subvalvular tissue in the Discussion section.

Changes in the text: We have added the following text to the Methods section: "...because residual subvalvular tissue might have pannus formation, which may be associated with limiting prosthetic valve leaflet motion in the future." Furthermore, we have deleted the sentence of "Moreover, our technique of valve replacement without preserving the posterior leaflet and subvalvular tissues may have affected the

outcomes.” in the Discussion section.

Comment 4. Limitations should include heterogeneity of repairs and concomitant procedures.

Reply 4: We have added this information to the discussion on limitations to the study.

Changes in the text: We have added the following text to the limitation part of the Discussion section: “Heterogeneity of repair for AFMR and concomitant operations may also affect the outcomes.”

Comment 5. I assumed that all patients had atrial fibrillation. Why was atrial appendage closure performed in only 68% of patients in the PA group? If all patients had atrial fibrillation, I suggest you include "atrial fibrillation" in the title of the article.

Reply 5: We thank the reviewer for the comment. We only performed left atrial appendage closure in 80.6% of patients because of a weak left atrial wall that had a high possibility of a bleeding. As mentioned by the reviewer, this study evaluated the outcomes between patch augmentation versus valve replacement for AFMR with a tethered posterior leaflet and atrial enlargement due to long-standing atrial fibrillation. We have mentioned “long-standing atrial fibrillation” in the title.

Changes in the text: We have revised the title as follows: “Patch augmentation vs. valve replacement for patients with atrial functional mitral regurgitation and long-standing atrial fibrillation”. We have also added the following text to the Methods section: “We did not perform atrial plication and left atrial appendage closure if the patients had a weak atrial wall that led to severe bleeding.”

Comment 6. On the other hand, preoperative LAVI was higher in the VR group, but postoperative LAVI was lower in this group. Does this mean that atrial plication was less aggressive because few patients in this group underwent atrial plication? Since LAVI was associated with worse outcomes, you should clarify this point.

Reply 6: As mentioned by the reviewer, the VR group had a higher preoperative LAVI and lower postoperative LAVI than those in the PA group. Additionally, 43.8% of patients in the PA group and 60.0% in the VR group underwent atrial plication. However, there was no significant difference in the atrial plication rate between the two groups. Moreover, non-atrial plication may affect the outcomes, but a univariate analysis showed that atrial plication was not associated with thromboembolic events, whereas the postoperative LAVI was significantly associated with thromboembolic events, but not the preoperative LAVI. These findings suggest that the postoperative LAVI is an important indication to predict thromboembolic events. Additionally, if patients have a large LAVI, atrial plication should be performed to prevent thromboembolic events.

Changes in the text: We have revised the sentence of LAVI was associated with thromboembolic events with emphasizing the postoperative in the manuscript.

Comment 7. Intraoperative images of atrial plication procedure should be included in your supplemental material.

Reply 7: We have added intraoperative schema of the left atrial plication procedure.

Changes in the text: Intraoperative schema of left atrial plication have been shown in Supplemental Figure 1.