

## Peer Review File

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### Reviewer A

The authors provide a retrospective comparison of 100 aortic valve replacements through partial upper sternotomy with 100 through full sternotomy. The manuscript is focusing on morbidity and mortality at 3 years. The authors fully acknowledge the limitations of this study. The quality of the manuscript will be further enhanced if the authors address the following issues.

Dear Sir or Madam, thank you for your very inspiring comment on our article. I really appreciate your time with our work. I will try to answer your questions and comments fully and satisfactorily.

[1] Subsection, surgical technique, please provide information about whether or not an LV vent was used?

Reply 1: No, we did not use the LV-vent. We have always used the pulmonary artery vent to prevent increased blood return from the pulmonary circulation.

Changes in the text: Please see the changes in subsection surgical technique, page 5, line 116-117

[2] Was epicardial pacing used upon completion of procedure in partial upper sternotomy cases? If so please describe where and how were the epicardial wires placed?

Reply 2: Yes, we have always used ventricular epicardial wires to provide pacing in the event of bradycardia. They were placed on the surface of the right ventricle before removing the cross clamp to gain access to the right ventricle. Atrial pacing has not been routinely used.

Changes in the text: Please see the changes in subsection surgical technique, page 5, line 125-127

[3] How was the pericardial space drained in partial upper sternotomy cases?

Reply 3: We drained the pericardial space in patients with partial upper sternotomy with Blake drains® (Ethicon, Somerville, NJ, USA). As the entrance for the drain we have routinely cut the right paraxiphoid space and have guided the drain to the margoacutus. The drain was placed circumferentially behind the left ventricle with its tip ending at the root of pulmonary artery. In our opinion, the silicone material used to make this drain minimizes the risk of injury to the left ventricle and maximizes the amount of fluid drained from the pericardial cavity.

Changes in the text: Please see the changes in subsection surgical technique, page 5

and 6, line 127-129

[4] Please ensure that errors of grammar and syntax are addressed.

Reply 4: I apologize for my inadequate English, which is not my mother tongue. Thank you for the corrections, I have fully received in the text. The article was newly corrected by a native speaker, both in terms of grammar and syntax.

Changes in the text: all pages.

### Reviewer B

The authors summarized the study results well. However, I would like to point out a few problems.

Dear Sir or Madam, thank you for your very inspiring comment on our article. I really appreciate your time with our work. I will try to answer your questions and comments fully and satisfactorily.

1. The upper sternotomy clearly shows considerable superiority in recovery after surgery. However, the selection of the sternotomy between the 3rd and 4th intercostal spaces is very important to ensure an adequate surgical field of view. It is necessary to describe the selection method of the incised intercostal space and whether there are any examples of extending from the 3rd intercostal space to the 4th intercostal space.

Reply 1: I strongly agree. In some patients the long ascending aorta does not allow to reach aortic annulus safely. For this reason the selection of the intercostal space was based on the standard preoperative chest x-ray, which was performed in all cases. According to the Klein et al: "In general, the aortic valve will be positioned in the proximity of the 4th intercostal space. Furthermore, acute and chronic lung pathologies can be identified." (a) However, this position does not exclude making the incision in the 3th intercostal space, if the aortic annulus is not situated more than 3cm under the level of the planned cut.

In 5 patients we decided for an unplanned extension to the 4th ICS because of very long aortae, compressing the right atrium, preventing safe venous cannulation. These patients were not marked as "conversion".

a) Patrick Klein, Idserd D G Klop, Geoffrey L T Kloppenburg, Bart P van Putte, Planning for minimally invasive aortic valve replacement: key steps for patient assessment, *European Journal of Cardio-Thoracic Surgery*, Volume 53, Issue suppl\_2, May 2018, Pages ii3–ii8

Changes in the text: Please see the changes in subsection Surgical technique, Statistical Analysis and Results, page 5 line 108-111, page 6 line 150-151 and page 8,

2. I wonder if there were any cases where pericardial drainage was inadequate in the upper sternotomy, often suffering from severe pericardial effusion, and in that case, pericardiotomy syndrome may be further combined. The authors were wondering if there was any severe pericardial effusion.

Reply 2: We drained the pericardial space in patients with partial upper sternotomy with Blake drains® (Ethicon, Somerville, NJ, USA). As the entrance for the drain we have routinely cut the right paraxiphoid space and have guided the drain substernally in the direction of the acute margin (margo acutus). The drain has been placed circumferentially behind the left ventricle with its tip ending at the root of pulmonary artery. In our opinion, the silicone material, used to make this drain minimizes the risk of injury to the left ventricle and maximizes the amount of fluid drained from the pericardial cavity.

The severe pericard effusion occurred in 7 cases, 2 in MiniAVR, 5 in the sternotomy group ( $p=0.445$ ) respectively, requesting controlled punktion. No patient was reoperated because of the late pericardial effusion.

Changes in the text: Please see the changes in subsection Surgical technique, page 5 and 6 line 127-129, page 8, line 183-185

3. The Perceval valve took less time and was mainly performed in the partial sternotomy group, and the Trifecta valve took more time and was mainly performed in the full sternotomy group. Nevertheless, the ACC time and CPB time were longer in the partial sternotomy group. An explanation for that and the reason for the longer ACC time in the partial sternotomy group should be described

Reply 3: You are absolutely right. Multiple explanations can be found. It is true that the Perceval valve should have a potential to shorten cross-clamp time; but as already discussed, the running-suture technique allows essential reduction of the time of implantation as well. Furthermore, in the same group of patients we implanted the ATS 3f Enable®, which is also defined as a self expandable, sutureless valve, but it does not really reduce the time of implantation compared to our results. As shown in a multicentric study in 10 European centres: "Implantation of the ATS 3f Enable® Model 6000 Bioprosthesis was successful using only a single guiding suture in 85.6% of patients. Mean aortic cross-clamp and cardiopulmonary bypass times were noted as  $58.1 \pm 25.1$  and  $84.9 \pm 34.2$  min, respectively." (Martens et al.) (a) We have no doubt, that limited access from the partial upper sternotomy and technical difficulty negatively influenced the cross-clamp time. For example the right ventricle epicardial pace-maker wire has been implanted during the cross-clamp time, when the heart was collapsed, preventing LV injury.

a) Martens S, Sadowski J, Eckstein FS, Bartus K, Kapelak B, Sievers HH,

Schlensak C, Carrel T. Clinical experience with the ATS 3f Enable®  
Sutureless Bioprosthesis. Eur J Cardiothorac Surg. 2011 Sep;40(3):749-55.

Changes in the text: Please see the changes in subsection discussion, page 9 and 10  
line 232-236

4. The running suture technique can be a technically advantageous operation in patients with aortic stenosis because it has a strong annulus. However, patients with thin aortic annulus with aortic regurgitation may have more complications such as para-valvular leaks. Is the same surgical method applied to such AR patients? The authors need to explain whether only patients with aortic stenosis were operated on and patients with pure aortic regurgitation were excluded from this study. After surgery, a trivial para-valvular leak may occur. It should show the frequency of its occurrence.

Reply 4: As mentioned in the surgical technique subsection, all the “non-suture-less” valves were implanted using the running-suture technique, regardless of whether stenosis or insufficiency occurred. The interrupted single suture technique was used only in cases of infective endocarditis with an anular abscess. Patients with this etiology were not included in this study. This was not included in the text. It has been completed. (page 4, line 86)

At the time of this study, aortic valve repair was not well established at our department. For this reason, replacement was used to treat aortic regurgitation.

Trivial paravalvular leakage (not requesting any surgical re-intervention) occurred in 4% vs. 13% patients respectively ( $p=0.04$ ). Please, see the Table 4, subsection Results,

Changes in the text: Please see the changes in subsection surgical technique and discussion, page 4 line 86

5. Partial sternotomy may be selected depending on the patient's surgical method (eg, the use of a Perceval valve). The explanation of selection bias should also be added to the limitation of the study.

Reply 5: I agree, the use of self expandable sutureless valves in one group only could, indeed, affect the results. This fact will be mentioned in the Discussion and Limitations of the study.

Changes in the text: Please see the changes in subsection Discussion and Limitation of the study, page 11 line 273, page 9 and 10 line 232-236

6. Some grammar corrections are added in an attached file.

Reply 6: I apologize for my inadequate English, which is not my mother tongue. Thank you for the corrections, I have fully received in the text. The article was newly corrected by a native speaker, both in terms of grammar and syntax.

Changes in the text: all pages.

### Reviewer C

Thank you for the opportunity to review this interesting manuscript. My questions are as follows.

Dear Sir or Madam, thank you for your very inspiring comment on our article. I really appreciate your time with our work. I will try to answer your questions and comments fully and satisfactorily.

1. As the authors have alluded to, the CPB and cross-clamp time differences of a few minutes are negligible although slightly longer on the minimally invasive AVR. What were the cannulation strategies for these?

Reply 1: Our cannulation strategy is already described in the subsection Surgical Technique. Page 5, line 111-116. Moreover, we did not use the LV-vent. We have always used the pulmonary artery vent to prevent increased blood return from the pulmonary circulation. We did not perform venous cannulation through the femoral vein, even though it could make the operation field more clear, because it is associated with the risk of retroperitoneal bleeding.

Changes in the text: Please see the changes in subsection surgical technique Page 5, line 116-117.

2. It would be helpful to perform an analysis that include only conventional prosthetic aortic valves (exclude the sutureless AV). This would yield more comparative operative and postop event data.

Reply 2: You are definitely right. Unfortunately we decided for the consecutive design of the study. The sutureless valves are expected to be easier and faster to implant. The Perceval valve should have a potential to shorten cross-clamp time indeed. But as already discussed, the running-suture technique allows essential reduction of the time of implantation too. In addition, in the same group of patients we implanted the ATS 3f Enable®, which is also defined as a self expandable, sutureless valve, but does not really reduce the time of implantation compared to our results. As shown in a

multicentric study in 10 European centres: “Implantation of the ATS 3f Enable® Model 6000 Bioprosthesis was successful using only a single guiding suture in 85.6% of patients. Mean aortic cross-clamp and cardiopulmonary bypass times were noted as  $58.1 \pm 25.1$  and  $84.9 \pm 34.2$  min, respectively.” (Martens, et. al)(a) These are certainly longer times as published in our study. We have no doubt, that a limited access from the partial upper sternotomy and technical difficulty negatively influenced the cross-clamp time. For example the right ventricle epicardial pacemaker wire has been implanted during the cross-clamp time, when the heart was collapsed, preventing LV injury.

We strongly believe, that the construction of the sutureless valves is essential for the long-term results because of the risk of early degeneration. The long-term results will be the focus of our next analysis, where the sutureless valves will be excluded.

a) Martens S, Sadowski J, Eckstein FS, Bartus K, Kapelak B, Sievers HH, Schlensak C, Carrel T. Clinical experience with the ATS 3f Enable® Sutureless Bioprosthesis. Eur J Cardiothorac Surg. 2011 Sep;40(3):749-55.

Changes in the text: Please see the changes in subsection discussion, page 9 and 10, line 232-236

3. There was more inotrope use in the FS group but this group also had lower LVEF preoperatively. Can the authors pls comment on this and include in discussions?

Reply: Yes, indeed. We have only this explanation for the higher use of inotropes in the FS group, because in other ways the groups are fully comparable, inclusive of EuroSCORE II. Szwerc et al published in their study higher use of inotropes in the MiniAVR group, explaining that fact with an imperfect local cooling.(b) It is in contradiction to our results.

Changes in the text : Please see the changes in subsection discussion, page 10, line 236-240

b) Szwerc MF, Benckart DH, Wiechmann RJ, et al. Partial Versus Full Sternotomy for Aortic Valve Replacement, Ann Thorac Surg 1999;68:2209–14

4. Was there any conversion from miniAVR to full sternotomy? If so, were these considered miniAVR or full sternotomy in the analysis? This should be shown in the manuscript.

Reply: A very important point, thank you for notifying! There were 2 conversions from the miniAVR to the FS group because of periprocedural bleeding from the right ventricle, injured during the pace-maker electrode implantation and the inserting the pericardial drainage. The patients were included in the miniAVR group, and the conversion were rated among the complications.

Changes in the text: Please see the changes in subsection Results **Page 7, line 168-171**

5. Was there any difference in aortic valve size that was placed with a miniAVR versus full sternotomy? The surgeon may lean towards a smaller valve size if access was difficult. This has implications for subsequent transcatheter AVR and needs to be highlighted.

Reply: I agree with your statement, that not only the construction, but also the gradients at the orifice as a consequence of chosen size is responsible for the early degeneration of the biologic valve. As mentioned in the **Table 3: Types of biological valve prosthesis**, the median size of the used valves was 23mm in both groups (IQR 2.0-4.0),  $p=0.312$ . However, the tendency of the surgeons to chose “smaller valve in smaller cut” was not proven.

Please, find in the **Table 3**

#### **Reviewer D**

The authors describe their unit experience with mini-AVR via upper hemi sternotomy versus midline sternotomy. The article raises several major concerns:

Dear Sir or Madam, thank you for your very inspiring comment on our article. I really appreciate your time with our work. I will try to answer your questions and comments fully and satisfactorily.

1. This article does not add anything new. It is retrospective, small sample size single centre study. There are large metaanalyses and RCTs looking at this topic.

Reply: Thank you for your opinion. We strongly believe, that our article has a potential to bring more information about mid-term complications after AVR, expressed in the number of rehospitalisations. The end point is certainly softer than dead, but harder than QOL. That is why we decided for combined endpoint dead+stroke+rehospitalisation. We are aware of the shortcomings of



our study.

Please, find in the Limitations: **Page 11, line 270-274**

2. It is not clear to me how you adjusted in your model for selection bias - e.g. difference in baseline characteristics. The baseline characteristics you provided are only a few - very limited. Still, there are differences between full sternotomy and mini-AVR groups. Some sort of multivariate logistic regression should be applied to assess the effect of co-variables on the binary endpoint you wanted to measure. Another option is propensity matching. Your analysis provides crude, unadjusted outcomes.

Reply: You are definitely right. Unfortunately we decided to use the consecutive design for this study, not randomized but retrospective as you mentioned in the beginning. Among the 11 basic characteristics there are 4 completely identical, 5 are not significantly different and two (arterial hypertension and EF) are significantly different. Mean EF in the MiniAVR group is 2,65% (!) lower. As cardiac surgeons, we both know, that this difference plays no role in clinical practice.

Reply 2: Please, find in the Discussion, **Page: 10, line 236-239**

3. The article needs more editing (English grammar/spelling).

Reply 3: I apologize for my inadequate English, which is not my mother tongue. The article was newly corrected by a native speaker, both in terms of grammar and syntax.

Changes in the text: **all pages.**

4. State clearly the operative mortality at 30 days.

Reply: Thank you for the inspiring comment.

Changes in the text: Please see **the Table 4**

5. If you want to get this article in a better shape, fit for publication I recommend collaboration with someone with statistical expertise/design.

Reply: Thank you for the inspiring comment.

#### **Reviewer E**

I appreciate the author's efforts. This study evaluates the early-outcomes of partial



upper sternotomy for aortic valve replacement compared to the full sternotomy, including the outcomes after discharge. The authors conclude the partial upper sternotomy provided a similar outcomes of survival rate and free from rehospitalization rate compared to the full sternotomy. However, this study may require the major revisions as following reasons.

Dear Sir or Madam, thank you for your very inspiring comment on our article. I really appreciate your time with our work. I will try to answer your questions and comments fully and satisfactorily.

1. Definition of rehospitalization should be described in Material and Methods section. What is the difference of rehospitalization 1, 2, and 3? Please explain about rehospitalization 1, 2, and 3.

Reply 1: Thank you for the comment. The first rehospitalization is the first rehospitalization after discharge from the hospital and the 3<sup>rd</sup> year after surgery. Not all patients were rehospitalized. The 2<sup>nd</sup> rehospitalization is the rehospitalization following the first one but happened before the 3<sup>rd</sup> year after surgery. The second rehospitalization could happen only among those patients who were rehospitalized once before. It is analogous to any further rehospitalization. The number of patients with at least one rehospitalization is therefore the highest and declines with any other rehospitalization. Changes in the text: Please see the changes in subsection Material and Methods [Page 6, line 149-151](#)

2. A main advantage of partial upper sternotomy is a preservation of sternum, which may reduce deep sternal infection and dehiscence of sternum. Were there the patients who had dehiscence of sternum in partial upper sternotomy?

Reply 2: Thank you for the inspiring comment. There was no early deep sternal dehiscency among the patients in MiniAVR group until the day 30. Later, we observed only one wound healing disorder in that group resulting unfortunately in death of the patient.

Changes in the text: Please see the changes in subsection Results [Page 9, line 208-210](#).

3. Transfusion volume is also an important factor about difference between partial upper sternotomy and full sternotomy. Please describe the intraoperative transfusion volume.

Reply 3: Very important point, the results have been completed. The average postoperative bleeding was statistical significant lower in the MiniAVR group: mean 389ml (SD 209.5) vs. 412ml (SD 322), median 300ml (IQR, 25-75% 290) and 365ml (IQR, 25-75% 207),  $p=0.031$  (Mann-Whitney test). We did not record the exact volume of the PRBCs transfusion, but the units only. There was not a statistical significant difference between the groups in the number of units applied. Every unit varied between 230 and 260ml, according to the hematocrit of the donor. Please look at the Table 4.

Changes in the text: Please see the changes in subsection **Results, Page 7, line 174-179 and the Table 4.**

4. IQR should be expressed as IQR, 25%–75%.

Reply 4: Thank you for the correction.

Changes in the text: Please see the changes in the **tables.**