Author’s response to reviews

Title: Improved Operative and Recovery Times with Mini-Thoracotomy Aortic Valve Replacement

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Reviewer #1: The Authors report their experience with 503 patients who underwent isolated AVR from 2012-2015 using one of three techniques: 1) Mini-thoracotomy, 267 (53.1%), 2) Mini-sternotomy, 120 (23.8%), 3) Conventional sternotomy, 116 (23.1%). MT patients, compared to MS and CS, had significantly shorter bypass times, lower incidence of prolonged ventilator support and shorter ICU and postoperative stays, resulting in an overall shorter hospitalization. Incidence of other postoperative complications were lower in the MT group compared to mini-sternotomy and conventional sternotomy, without significance. Minimally invasive techniques trended towards better survival [MT 1.5%, MS 1.67%, and CS 5.17% (p=0.13)]. The Authors conclude that the MT mini-thoracotomy approach showed decreased operative times, decreased lengths of stay, decreased incidence of prolonged ventilator time, and a trend towards lower mortality when compared to MS and CS.
Question 1: The Authors do not specify how the patients were chosen for one approach instead than another. However, patients' selection is biased toward lower risk patients in the MT group. Lower complications rate can be expected.

- Answer 1: All patients requiring isolated AVR are considered candidates for mini-AVR through a right anterior mini-thoracotomy approach. Our preferred approach for minimally invasive AVR is mini-thoracotomy. If patients are unable to undergo mini-thoracotomy due to anatomical reasons or body habitus, then the mini-sternotomy approach is used. This occurs in a small number of patients. We acknowledge that mini-thoracotomy patients had lower STS scores. However, this should not impact cardiopulmonary bypass and cross-clamp times, which were lower for mini-thoracotomy patients, and which is our main point of interest for the manuscript. In addition, the STS scores in all three groups were within the same low-risk range, all with scores of 3.0% or less. Thus, the significant difference may not be clinically relevant. (see added text in discussion, page 10).

Question 2: It is not clear why cross clamping time is lower in MT group. In CS patients vision is good and there is no reason, if patients are the same, that any difference exists in any technical aspect. I am wondering if CS patients are operated on by younger surgeons and trainees, and the MT patients by more expert surgeons.

- Answer 2: These patients' operations were performed by the same small group of surgeons. The mini-thoracotomy approach is not performed by all surgeons, in which case the mini-sternotomy approach would be performed for a minimally invasive approach. We recognize that differences in surgeon experience account for selection for patients to undergo mini-thoracotomy AVR, but we argue that mini-thoracotomy AVR may be the superior approach for surgeons who have experience with the technique and have mastered the learning curve. (see added text in methods, patients selection on page 4 and surgical procedure on page 5)

Question 3: I think that this paper is missing a correct patients' selection. At least, propensity matching has to be performed, including surgeons' experience. The final message is not correct.

- Answer 3: Based on the number of patients, we did not feel that there were enough patients to match. We recognize that the STS scores of the MT group are lower than those of the CS group. However, the main message of this paper is that with improved experience performing MT AVR, operative times can be lower, in addition to shorter lengths of stay and faster recovery, further promoting the benefit of the MT approach in comparison to CS. Propensity-matching is a good suggestion, but our sample size of mini-thoracotomy patients is larger than that of the conventional sternotomy patients within the same time frame, and we wanted to maintain the same time frame for each approach. In addition, we wanted to explore the differences between conventional sternotomy and both mini-sternotomy and mini-thoracotomy. Propensity-matching will
be a good method to study mini-thoracotomy in high-risk patients in future studies. (see added text in discussion page 10)

Reviewer #2: The paper with title "Improved Operative and Recovery Times with Mini-Thoracotomy Aortic Valve Replacement", despite the interesting topic treated, doesn't apport anything to our surgical knowledge.

For that reason I do not suggest the publication.

Answer 1: The literature focused on minimally invasive AVR almost always cites longer cross-clamp and bypass times as a disadvantage of minimally invasive approaches. This paper was meant to add to the literature to make the point that with more experience performing mini-thoracotomy AVRs, the operative times can be decreased, in addition to the shorter lengths of stay and faster recovery as have been mentioned in other studies. Subsequently, with shorter operative times, patients are subjected to fewer complications from cardiopulmonary bypass and cross-clamping. We believe this is an important point when considering approach, because decreased operative times further reduce postoperative complications. We also argue that mini-thoracotomy can be used for most patients requiring isolated aortic valve replacement with the proper surgeon training.

Reviewer #3: The authors compare the outcomes and perioperative aspects of minimally invasive aortic valve replacement (AVR) surgeries, namely right anterior mini-thoracotomy- and mini sternotomy AVR, to the conventional full sternotomy approach in their retrospective study. 503 adult patients who underwent surgical aortic valve replacement between January 2012 and December 2015 in a single center were involved.

As a result, they found the mini-thoracotomy approach the most favourable because of the following advantages compared to the other two techniques: significantly shorter aortic cross clamping and cardiopulmonary bypass time, significantly shorter ICU-, postoperative- and total hospital length of stay, significantly lower incidence of prolonged ventilator time, lower incidence of stroke, reoperation for bleeding, renal failure and atrial fibrillation. Minimally invasive techniques showed lower 30-day mortality rate than conventional sternotomy.

This study is of great clinical importance as minimally invasive approaches in cardiac surgery have been in the spotlight for many years, but their safety and advantage have been highly questioned due to their complexity. Data are needed to demonstrate if minimally invasive techniques have clear benefit for patients, therefore this research has great value.

In this article the aim is clearly identified and its significance is highlighted. The sample size is large enough to draw conclusions. The article is well written and structured making it easy to read and understand. Both tables provide information not mentioned in the text.

Limitations of this study and suggestions for further investigations are noted by the authors.
Question 1: What were the criteria for patient selection for mini-thoracotomy approach?

Answer 1: For most surgeons in the practice, all patients are considered candidates for mini-thoracotomy AVR via right anterior mini-thoracotomy. If there is a contraindication to mini-thoracotomy due to anatomical reasons or body habitus (mini-thoracotomy AVR may be difficult in morbidly obese patients), mini-sternotomy or full sternotomy is the second choice. (text added to Methods on page 4, section patient selection).

Question 2: How did you decide between mini-thoracotomy and mini-sternotomy?

Answer 2: The mini-sternotomy approach was performed in the early years of our experience performing minimally invasive AVR. Subsequently, almost all minimally invasive approaches are performed with mini-thoracotomy because it provides faster recovery time, and we have seen improved outcomes with mini-thoracotomy compared to mini-sternotomy. Almost all patients undergoing isolated AVR are considered candidates for mini-thoracotomy, and only if they are unable to undergo mini-thoracotomy for anatomical reasons or body habitus, they will undergo mini-sternotomy or conventional sternotomy. A small number of surgeons in our practice use the mini-sternotomy approach as the approach of choice for their patients, but this is the minority. (see added text in methods, page 4, section patient selection, and page 5, section surgical procedure).

Question 3: The STS score was lower in the mini-thoracotomy group than in the other two groups, meaning that they were lower risk patients. How much could this contribute to the better outcomes of this group? How could you take this into consideration when drawing conclusions?

Answer 3: We acknowledge that the STS scores were lower in the mini-thoracotomy group, and we have cited this as a limitation of the analysis of the results. This is due to the selection at the beginning of our experience of lower risk patients for the mini-thoracotomy approach, as we were just starting to use the approach. However, the STS scores in all three groups were within the same low-risk range, all with scores of 3.0% or less. Thus, the significant difference may not be clinically relevant. Subsequently, we have been performing the mini-thoracotomy approach with excellent outcomes in higher risk patients. The main point of this paper is to highlight the shorter operative times with the mini-thoracotomy approach. In addition to the shorter length of stay and recovery times, the bypass and cross-clamp times in the mini-thoracotomy approach were significantly shorter. This provides an encouraging reason to increase usage of the mini-thoracotomy approach. Other studies have demonstrated longer operative times, likely due to inexperience or lack of training in the approach, so we have demonstrated that it is indeed possible to decrease the operative times, leading to fewer related complications. The lower operative times should be independent of preoperative STS scores for the majority of patients. The shorter length of stay can be attributed to the mini-thoracotomy approach due to the ability for patients to recover quicker than those who have undergone conventional sternotomy, regardless of STS score. There was no significant difference in mortality, although the STS
scores were lower in the mini-thoracotomy group. In future studies comparing conventional sternotomy to minimally invasive approaches to AVR, propensity-matching can be performed with a larger group of patients to eliminate differences in STS scores and other preoperative factors. (see added text in Discussion, page 10)

Question 4: When the general condition of a patient does not allow us to carry out conventional sternotomy, could mini-thoracotomy be an option?

Answer 4: If sternotomy is not available, mini-thoracotomy can be possible depending on the specific anatomical reasons and constraints. As long as the anatomy and body habitus allow adequate visualization and exposure, the mini-thoracotomy approach is a viable alternative. (text added to Methods on page 4, section patient selection).

Question 5: Are you planning to compare the results of mini-thoracotomy in low risk patients to a high risk group and mini-thoracotomy to conventional sternotomy in high risk patients? It has been mentioned in the article that this approach is being expanded to include patients with higher risk.

Answer 5: We are planning to perform a follow-up study with an increased sample size to include patients in more recent years. This will include higher-risk patients who have been selected for mini-thoracotomy AVR. We would like to perform a study looking at high-risk mini-thoracotomy patients compared to high-risk conventional sternotomy patients. Our primary goal for the next study will be to compare mini-thoracotomy and conventional sternotomy AVR in patients with similar STS scores, via propensity-matching. At our institution, we currently perform isolated AVRs via mini-thoracotomy in the vast majority of patients of all risk categories. (see added text in discussion on page 11)

Question 6: What is the learning curve like for mini-thoracotomy?

Answer 6: There is a fairly steep learning curve for the mini-thoracotomy approach, but well worth it due to the benefit to patients. Patients often request minimally invasive approaches to heart surgery, and we are able to offer them this approach which gets them out of the hospital and recovered much sooner. (see added text in discussion page 10)

Question 7: Are you planning to follow these patients to investigate their medium-term survival (1-5 years)? So far only a few studies have reported it to be increased.

Answer 7: This is an excellent suggestion, and we are hoping to be able to follow these patients. We agree that the information on medium and long-term survival is limited in the literature, so this would add a great deal to the body of knowledge. (see added text in discussion on page 11)
Question 8: Do you have information on blood transfusion requirements among the three groups? Blood transfusion is considered to decrease medium-term survival.

Answer 8: Unfortunately, this data was not available for us to analyze. This would be an excellent piece of data to add in the future.

Question 9: Did you use any technologies like automated suturing that could have reduced operative time?

Answer 9: For all conventional sternotomy and mini-thoracotomy cases, the CorKnot is used to tie down the valve and facilitated ease of valve placement somewhat. No automated sutures or other similar technologies were used. (see added text in Methods, surgical procedure section on page 5)

I would suggest this article for possible publication after minor revision as it has great potential to add important information to the current literature and can be part of the evidence needed to decide on the best surgical option for aortic valve replacement.