Peer review file

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Reviewer A

Comment: I think you have an interesting study and your unit seems to perform good volume of MIMS. your reported outcomes are great but your analysis is not valid. You can't compare isolated MV vs MV + TV surgery, the CPB and ACx will be longer by default. This is like comparing apples and oranges. if the FTR was severe then surgery should have been offered. I suggest you to focus on one of them only and not to compare these two different cohorts.

Reply: I am sorry for our misleading description. We are comparing isolated MV vs MV + TV surgery in the context of totally endoscopic. Actually, there are quite a few studies comparing the outcome of concomitant tricuspid valve surgery during mitral valve surgery, and the review I cite below can prove and already included many relevant studies. (Bianchi G, Solinas M, Bevilacqua S, Glauber M. Which patient undergoing mitral valve surgery should also have the tricuspid repair?. *Interact Cardiovasc Thorac Surg*. 2009;9(6):1009-1020.)

However, most of these studies are in the context of median sternotomy open heart surgery. In contrast, our study compares the hospital outcome of concomitant tricuspid annuloplasty during totally endoscopic mitral valve surgery, and this study has both novel and clinical implications. Current clinical guidelines do not address the efficacy of totally endoscopic tricuspid valve repair during totally endoscopic mitral valve surgery, and our study adds to those aspects that are not addressed in the guidelines.

As we mentioned, the severity of TR was carried out in integrative approach as current guidelines recommend. The decision to perform tricuspid repair was depended on the severity of TR, the diameter of tricuspid annular, cardiac function, intra-operative saline testing, and the existence of atrial fibrillation, but the final decision was determined with the attending surgeon.

Because the decision to perform surgery is influenced by the surgeon, there may be cases where mild to moderate tricuspid insufficiency is not repaired intraoperatively, as there is a belief that tricuspid regurgitation will improve with

treatment of left heart disease, while some surgeons believe that if tricuspid repair is not performed intraoperatively at the same time during the left heart surgery, it will affect right heart function in the long term or even aggravate tricuspid regurgitation, so there are various degrees of tricuspid insufficiency with and without surgery. However, in patients with severe tricuspid valve insufficiency, most surgeons prefer surgery; in patients with mild tricuspid valve insufficiency, some surgeons also will perform surgery, so we have performed a propensity score matching to allow for a comparative study.

We conclude that compared with isolated mitral valve replacement, tricuspid valve repair performed concurrently with totally endoscopic mitral valve surgery does not change mortality or stroke rates, although the duration of CPB time and cross-clamp time is prolong, but pulmonary artery pressure and degree of tricuspid regurgitation are significantly reduced. In addition, it cannot be ignored that MIMVS+TAP has great advantages over isolated MIMVS due to reduce TR progression with decreases in right ventricular dysfunction. Seen in reference 4,22,29,30.

Changes in the text: we have modified our text as advised (see in the Introduction part and Page 4, line 2-18).

Reviewer B

Comment: Congratulations on the good results regarding the addition of TAP during totally endoscopic mitral valve surgery. We know that the correction of combined tricuspid regurgitation would be better for the patients. However, the problem is the prolonged cardiopulmonary bypass or cross-clamping times since it requires additional right atrial opening, as a result of which needs superior vena cava or inferior vena cava blocking procedures. This manuscript showed comparable outcomes in terms of the CPC or ACC times.

I recommend the authors to explain the detailed surgical techniques to open the right atrium, such as venous cannulation, SVC or IVC block, tips to make better drainage & surgical field.

Reply: I apologize for our imperfect expressions. We used peripheral femoral

cannulation. Using a single two stage venous cannula. We preferred to incise the pericardium close to the sternum to create a large flap. The pericardial margin was retracted by silk stay sutures which are then brought through the chest wall to hold the right lung back, so created a large cavity for operating. When full bypass flow and moderate hypothermia were achieved, the cava tapes were used to secure the vena cava, and the ascending aorta was occluded with Chitwood clamp. Afterwards, the antegrade HTK solution was administered and the right atrium was opened. Consecutively, the stay sutures were made on either side to retract the margin of the right atrium, which were pulled outside of the thoracic cage and were fixed on the chest wall with curved forceps. Then set the femoral venous cannula in correct position until the atrial septum can be seen. The left atrium was entered via the atrial septum, two sets of stay sutures were used to snare the margin of the atrial septum and were pulled out of the port and secured properly. After assessment, mitral valve surgery and even tricuspid valve surgery was performed (after mitral valve surgery and closure of the atrial septal). After carefully de-airing of the heart was performed and after a TEE evaluation of the heart, CPB was disconnected and all incisions were closed.

Details to position the cannula can be seen in the below references: Michele Murzi, Enkel Kallushi, Marco Solinas, Mattia Glauber, Video-assisted right atrial surgery with a single two-stage femoral venous cannula, Interactive CardioVascular and Thoracic Surgery, Volume 9, Issue 1, July 2009, Pages 9–10.
Changes in the text: we have modified our text as advised (see Page 7, line 17 to Page 8, line 15).

Reviewer C

Comment 1: This study aimed to evaluate the impact of concomitant TV repair in the setting of minimally invasive mitral surgery. The study involved 143 patients—92 in MV surgery alone and 51 in concomitant TAP groups. Subject patients were heterogeneous with regard to preoperative TR degree, in that 27 presented with mild TR, 59 with moderate, 60 with > moderate TR, and the degree of TR was significantly higher with TV repair group. To address for selection bias, the authors used

propensity score matching, and the matching yielded even small number of patients (27 vs. 25).

Reply 2: we are sorry for our misleading expression. we have a total of 40 pairs (80 cases) were successfully matched. And after PS matching, in MIMVS group 27 were female, in MIMVS-TAP group 25 were female.

Changes in the text: Details can be seen in Page 9, line 4-6).

Comment 2: The issue of whether to concomitantly repair TR in the setting of MV surgery generally relates to its impact on long-term clinical outcomes, and this needs (1) sound sample sizes to compare as well as (2) long-enough follow-up duration to capture enough numbers of clinical events.

The major limitations of this study are lack of these two aspects—enough sample size and late follow-up clinical data. Other major comments are as follows:

Reply 2: To solve this problem, we consulted the relevant literature, according to this review: Bianchi G, Solinas M, Bevilacqua S, Glauber M. Which patient undergoing mitral valve surgery should also have the tricuspid repair?. Interact Cardiovasc Thorac Surg. 2009;9(6):1009-1020. The number of cases in which tricuspid valvuloplasty was performed concurrently with mitral valve surgery is generally small, mostly are single-centre studies. Our study was mainly focused on the clinical outcomes of concomitant management of the tricuspid valve with totally endoscopic mitral valve surgery, with a 1:1 propensity match, resulting in a sample of 40 matched pairs, which is not a small sample size for any single centre study worldwide. Limited by our centre's surgical volume and financial resources, it would be difficult to expand the sample size and the duration of follow-up without funding from the natural science foundation.

However, our study does have clinical implications in that the duration of CPB time and cross-clamp time is prolong, and pulmonary artery pressure and degree of tricuspid regurgitation are significantly reduced.

And, we are in the process of applying for a natural science foundation on this topic, and if we are successful in our application, we will be able to conduct a larger sample size, longer follow-up, and even RCT study in the longer follow-up term.

Changes in the text: Details can be seen in the introduction part and particular in Page 4, line 10-18).

Comment 3: Are any significant interaction expected with regard to the differing impact of TV repair depending on the surgical approach?—sternotomy vs. MICS. I would expect the similar long-term impact of TV repair regardless of the surgical approach if data are analyzed fairly in homogeneous settings. Please elaborate this issue more clearly.
Reply 3: We have relevant ideas and are writing relevant articles. Thank you for your suggestions.

Comment 4: There is a mixture of TR severity from mild to severe in the data. Rather, TVP impacts should differ depending on preoperative TR grade. Most relevant researches separately analyze the impacts of TR based on the TR degrees. Unfortunately, the sample sizes are too small in each of the TR degrees in this study.
Reply 4: We are sorry for our incomplete expression. As we have already explained, there is a lack of relevant multi-centre studies, none in the field of totally endoscopic cardiac surgery, and we have completed this study with limited financial and material resources and have presented a convincing conclusion.
Changes in the text: Details can be seen in the introduction part and particular in Page 4, line 10-18).

Comment 5: What is the rationale to repair TV if it is mild? Most functional TR resolves after MV surgery, and TR worsens very infrequently in the setting of mild TR. Was there any sign of annular dilatation?
Reply 5: Recent studies have indicated that untreated FTR can develop in patients who only undergo isolated mitral valve surgery, and the progression of FTR can lead to high morbidity and mortality rates (seen in reference 8-10 and page4 3-5). Operative indications for secondary tricuspid regurgitation which need for mitral valve surgery were as follows according to expert and guidelines recommend: 1) severe TR; 2) significant tricuspid annular dilatation (>40 mm or >21mm/m^2) or signs of right heart failure; or 3) direct assessment during the valve procedure, intra-operative saline testing, and comparison of the anterior and posterior leaflet surface area with the annulus size.

The decision to perform tricuspid annuloplasty was depended on the severity of

TR, the diameter of tricuspid annular, cardiac function, and the existence of atrial fibrillation, but the final decision was determined with the attending surgeon.

Because the decision to perform surgery is influenced by the surgeon, there may be cases where mild to moderate tricuspid insufficiency is not repaired intraoperatively, as there is a belief that tricuspid regurgitation will improve with treatment of left heart disease, while some surgeons believe that if tricuspid repair is not performed intraoperatively at the same time, it will affect right heart function in the long term or even aggravate tricuspid regurgitation, so there are various degrees of tricuspid insufficiency with and without surgery. However, in patients with severe tricuspid valve insufficiency, most surgeons prefer surgery; in patients with mild tricuspid valve insufficiency, some surgeons will perform surgery, so we have performed a propensity score matching to allow for a comparative study.
Changes in the text: Details can be seen in the METHOD section and particular in Page 6, line 16 to Page 7, line 2).

Comment 6: Propensity score analysis:
(1) It is usual to include ALL measurable variables for PS modelling, but the authors only selected 10 variables. Please explain the rationale.
Reply 6: I apologize for our imperfect expressions. In retrospective studies, whether patients received MIMVS or MIMVS+TAP was influenced by baseline characteristics, e.g. surgeons were more likely to consider performing MIMVS+TAP in patients with more severe tricuspid valve insufficiency.

Propensity score matching does just that. It is scientifically described as matching the propensity (i.e. odds, purpose) of two groups of patients to undergo TAP surgery, thus reaching a balance between groups of confounding factors as in the RCT study.

The basic rationale behind this approach is that the factors that determine a particular patient's propensity to undergo TAP surgery can only be something that existed before the surgery.

Some may say no. The surgeon's decision to perform MIMVS or MIMVS + TAP also takes into account what may happen during and after the procedure, such as the amount of CPB time. Yes, but the surgeon anticipates what might happen during and after surgery, not by guessing, but by speculating based on the pre-surgical situation, i.e. the baseline characteristics.

Therefore, the inclusion of a propensity score must be something that is available prior to surgery, specifically including demographic and baseline characteristics.

Therefore, if something other than baseline characteristics, such as the inclusion of extracorporeal circulation time, are included in the propensity score, then the study is fundamentally untenable.

In addition, it has been noted in the literature that there are no clear selection criteria for choosing control variables in PSM, so how we researcher determine which variables qualify often based on previous literature and reseacher's own scientific understanding of the reality of the situation.

(2) Using standardized mean difference is the standard for balancing testing after PS matching. At least, the authors should appropriate tests to compare variables under paired assumptions.
Student's t, Mann-Whitney U-, Chi-square and Fisher's tests should be replaced by Paired T-, Wilcoxon signed rank, McNemar or marginal homogeneity tests in the PS matched cohort.was applied.
Reply 6: SPSS 22 and above comes with a 1:1 PSM and after matching a balance test is performed between groups, which can be seen in Table 1. According to your kindly advice, we used the paired T-test, Wilcoxon signed rank and McNemar's test to replace the student's t test after PSM.
Changes in the text: We have added the corresponding statistical descriptions and re-run the statistics and particular in (see Page 9, line 10-12 and table 2 and 3).

(3) To my knowledge, PS matching is not available in standard SPSS, but only doable by the use of macro in SPSS. Please detail more on this.
Reply 6: I apologize for our imperfect expressions. We applied 1:1 propensity score matching, a feature that comes with IBM SPSS Statistics 22 and above version.

Reviewer D

Comment 1: Title. I would change the title from asking to telling the reader.
Use this. Hospital Outcome concomitant mitral and tricuspid valve repair is similar. A

propensity score analysis.

Reply 1: I agree with your comments and really thank you for the title.

Changes in the text: we have modified our text as advised (see Page 1, line 1-2).

Comment 2: The authors reveal a change in systolic PA pressure. they state that tricuspid valve insufficiency was reduced. Please provide this information before and after surgery

Reply 2: We apologise for our oversight and we have added the relevant information. As mentioned in our text, it cannot be ignored that MIMVS+TAP has great advantages over isolated MIMVS due to reduce TR progression with decreases in right ventricular dysfunction. Seen in reference 4,22,29,30.

Changes in the text: we have modified our text as advised (see Page 15, line 2-4 and Table 3).

Comment 3: The authors state the criteria to intervene on tricuspid valve insufficiency however they also state that repair was based on the surgeon's decision. Please state the criteria this patient cohort had in terms of its qualifiers such as preop dilated annulus (e.g. annulus greater than 40mm), RV dysfunction, etc pertaining to this patient population.

Reply 3: Usually our pre-operative plan is based on the ultrasound results and the patient's condition. The decision to perform tricuspid annuloplasty was depended on the severity of TR, the diameter of tricuspid annular, cardiac function, intra-operative saline testing, and the existence of atrial fibrillation, but the final decision was determined with the attending surgeon.

Changes in the text: Details can be seen in the METHOD section and particular in Page 6, line 16 to Page 7 line 2).

Comment 4: The paper needs to be edited in good English for example Sentence 224 is not accurate.

Reply 4: I am sorry for our English language expression. I have made the formal English language editing.

Comment 5: Can the authors include a concomitant 3rd comparison cohort of patients.

Sternotomy patients undergoing tricuspid and mitral valve. This will help the reader as most surgeons do not perform endoscopic surgery and the 3rd group comparison (sternotomy group) can be timely and context helpful (include the similar outcome data as well as blood transfusion requirement).
Reply 5: We have relevant ideas and have been writing a relevant article. Thank you for your suggestions.

Comment 6: A color figure should be added. showing the site of the ports, size of the camera (angled, right thoracotomy incision straight and instruments will empower the article and reader.
Reply 6: I have added the relevant images in the supplementary material, thank you for your advice.

Reviewer E

Comment 1: The author presents a single center experience on totally endoscopic mitral and tricuspid surgery. The aim of the study is to demonstrate the benefits of totally endoscopic surgery for concomitant tricuspid annuloplasty. I my opinion the follow-up time is too short and the cohort size is still too small. Therefore, a great statistical comparison is not possible yet and I believe that the questions that the author is intending to answer can not be responded yet with the results of the current work. I recommend increasing the number of patients and definitely prolonging the follow-up previous to publication. There is already plenty of published literature on both totally endoscopic cardiac surgery and concomitant tricuspid annuloplasty. Therefore, I currently don’t see the additional value that this paper is adding to the literature and to the clinical practice.
Reply 1: According to the article review: Bianchi G, Solinas M, Bevilacqua S, Glauber M. Which patient undergoing mitral valve surgery should also have the tricuspid repair?. Interact Cardiovasc Thorac Surg. 2009;9(6):1009-1020. The number of cases in which tricuspid annuloplasty was performed concurrently with mitral valve surgery is generally small, mostly are single-centre studies. Besides, we specially focused on the clinical outcomes of concomitant management of the

tricuspid valve with totally endoscopic mitral valve surgery, with a 1:1 propensity match, resulting in a sample of 40 matched pairs, which is not a small cohort size.

In addition, we could not find any similar studies in the pubmed. We reviewed the relevant literature and concluded that we found no relevant studies of tricuspid annuloplasty performed concomitant with totally endoscopic mitral valve surgery. However, with the increase in thoracoscopic cardiac surgery in recent years and due to the unique features of thoracoscopic surgery, it is of great clinical interest to study this topic. There are quite a few studies comparing the hospital outcome of concomitant tricuspid repair during mitral valve surgery, and the review I cite below includes many relevant studies. (Bianchi G, Solinas M, Bevilacqua S, Glauber M. Which patient undergoing mitral valve surgery should also have the tricuspid repair?. Interact Cardiovasc Thorac Surg. 2009;9(6):1009-1020.) But most of these studies are in the context of median sternotomy open heart surgery. In contrast, our study compares the hospital outcome of concomitant tricuspid annuloplasty during totally endoscopic mitral valve surgery, and this study has both novel and clinical implications. Current clinical guidelines do not address the efficacy of totally endoscopic tricuspid valve repair, and our study adds to those aspects that are not addressed in the guidelines.

Changes in the text: we have modified our text as advised (see Page 4, line 10-18).

Comment 2: Most of the postoperative outcomes occurred 1 time. The incidence is too low and therefore it could be just random events. Therefore, a real comparison cannot be performed between groups. Conclusions cannot be derived from this study yet.

Reply 2: Our sample size is already one of the largest in the extant literature, and the statistics on postoperative complications are all based on actual conditions

Some other comments:

Comment 3: The article is in general well written but some language improvements are still required.

Reply 3: I have made the formal English language editing.

Comment 4: Abbreviations in the abstract must be avoided. The abstract must be

improved. It doesn’t really catch the interest of the reader. I personally needed a lot of time and really required to read further to get more interested about the article. More background could be helpful. If the abstract is not good by selling the paper and it is not clear enough, then readers will discard the paper even without haven’t started reading it.
Reply 4: We have carefully edited the abstract, thank you for your comments.
Changes in the text: Details can be seen in the ABSTRACT section.

Comment 5: Since this paper is focused on totally endoscopic surgery, selection criteria for this technique must be mentioned in more detail. How is the ideal patient for totally endoscopic surgery? Those patients being operated conventionally or through other surgical approaches in the authors institution, why weren’t they candidates for totally endoscopic surgery?
Reply 5: All enrolled patients were diagnosed with mitral valve disease and FTR, which can be treated under totally thoracoscopic guidance, and minimally invasive approach was chosen by all the participants during presurgical visit.
Changes in the text: we have modified our text as advised (see Page 5, line 15-18).

Comment 6: As I understand all the patients presented secondary TR, but did all of them have an indication for surgery? Or did the attending surgeon just decided at his/her discretion wether or not to operate the TV? I suggest mentioning this. If all the patients did not have an indication for TV surgery, then the current comparison is not feasible. This problem was tried to be solved by matching both groups but it only matches the degree of TR but it doesn't necessarily mean that indications for TV surgery are now equally present in both groups after matching.
Reply 6: In retrospective studies, whether patients received MIMVS or MIMVS+TAP was influenced by baseline characteristics, e.g. surgeons were more likely to consider performing MIMVS+TAP in patients with more severe tricuspid valve closure insufficiency. In additional, the severity of TR was carried out in integrative approach as current guidelines recommend. The decision to perform tricuspid annuloplasty was depended on the severity of TR, the diameter of tricuspid annular, cardiac function, intra-operative saline testing, and the existence of atrial fibrillation, but the final decision was determined with the attending surgeon.

Because the decision to perform surgery is influenced by the surgeon, there may be cases where mild to moderate tricuspid insufficiency is not repaired intraoperatively, as there is a belief that tricuspid regurgitation will improve with treatment of left heart disease, while some surgeons believe that if tricuspid repair is not performed intraoperatively at the same time, it will affect right heart function in the long term or even aggravate tricuspid regurgitation, so there are various degrees of tricuspid insufficiency with and without surgery. However, in patients with severe tricuspid valve insufficiency, most surgeons prefer surgery; in patients with mild tricuspid valve insufficiency, some surgeons will perform surgery, so we have performed a propensity score matching to allow for a comparative study.

Comment 7: Since one of the most important and frequently mentioned complications is “cerebral dysfunction”, it should be explained more specifically what the definition of cerebral dysfunction is? How was the stroke rate? How often presented the patients Delirium? Cerebral dysfunction is a very wide term and this could be divided into 3 or 4 different outcomes, all of them with different burdens for the life quality of patients. It’s different to have a stroke than to have a transitory delirium.
Reply 7: Stroke was defined as an acute episode of focal dysfunction of the brain, retina, or spinal cord lasting longer than 24 h, or of any duration if imaging (CT or MRI) or autopsy show focal infarction or haemorrhage relevant to the symptoms. We have no stroke or TIE. According to your advice we have modified the Cerebral dysfunction changes as Stroke.
Changes in the text: we have modified our text as advised (cerebral dysfunction change as stroke).

Comment 8: Table 1 can show many other baseline characteristics:
Dialysis? Smoker? COPD? Liver disease? Previous myocardial infarction? Previous operation? Timing of the surgery? Cause of the MR: degenerative? Ischemic? Etc…
Reply 8: In retrospective studies, whether patients received MIMVS or MIMVS+TAP was influenced by baseline characteristics, e.g. surgeons were more likely to consider performing MIMVS+TAP in patients with more severe tricuspid valve closure insufficiency.

Propensity score matching does just that. It is scientifically described as matching

the propensity (i.e. odds, purpose) of two groups of patients to undergo TAP surgery, thus reaching a balance between groups of confounding factors as in the RCT study.

The basic rationale behind this approach is that the factors that determine a particular patient's propensity to undergo TAP surgery can only be something that existed before the surgery.

Some may say no. The surgeon's decision to perform MIMVS or MIMVS + TAP also takes into account what may happen during and after the procedure, such as the amount of CPB time.

Yes, but the surgeon anticipates what might happen during and after surgery, not by guessing, but by speculating based on the pre-surgical situation, i.e. the baseline characteristics.

Therefore, the inclusion of a propensity score must be something that is available prior to surgery, specifically including demographic and baseline characteristics.

Therefore, if something other than baseline characteristics, such as the inclusion of CPB time, are included in the propensity score, then the study is fundamentally untenable.

In addition, it has also been noted in the literature that there are no clear selection criteria for choosing control variables in PSM, so how do you determine which variables qualify? To be based on previous literature and your own scientific understanding of the reality of the situation.

Comment 9: Why is NYHA reported as median?? If median is reported, then IQR should also be reported. NYHA is normally reported as absolute frequency (i.e. how many patients had each NYHA category)

Reply 9: Thank you for your comments, we have used IQR and we apologise for our oversight, thank you.

Changes in the text: we have modified our text as advised (see Table3).

Comment 10:

- Bleeding event: exact definition required.
- Reintervention: does the author mean early reintervention because of bleeding or reoperation because of recurrent MR/TR?
- What are valve related events? This also needs a more detailed explanation.

- Early mortality is being reported: what's the exact definition of early mortality?Normally 30-day mortality or In-hospital mortality are reported. I personally recommend reporting in-hospital mortality.

Reply 10: Valve-related events were defined according to the guidelines published by Akins. Severe adverse events were defined as cerebrovascular accident, re-intubation or tracheostomy, acute renal insufficiency, heart block, re-exploration surgery, bleeding and thromboembolic events and sepsis.

Bleeding Event: A bleeding event is any episode of major internal or external bleeding that causes death, hospitalization, or permanent or necessitates transfusion.

Reintervention: Reintervention is any surgical or percutaneous interventional catheter procedure that repairs, otherwise alters or adjusts, or replaces a previously implanted prosthesis or repaired valve.

Changes in the text: Seen in the reference: Akins CW, Miller DC, Turina MI, Kouchoukos NT, Blackstone EH, Grunkemeier GL, Takkenberg JJ, David TE, Butchart EG, Adams DH, Shahian DM, Hagl S, Mayer JE, Lytle BW; STS; AATS; EACTS. Guidelines for reporting mortality and morbidity after cardiac valve interventions. Ann Thorac Surg. 2008 Apr;85(4):1490-5.