Author's response to reviews

Title: The role in surgical and pathological classification of echocardiography in patients with ruptured mitral chordae tendineae: a large sample study

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Version: 2 Date: 10 July 2011

Author's response to reviews: see over
July 10, 2011

Dear Dr. Vipin Zamvar

The Journal of Cardiothoracic Surgery Editorial Team
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We are pleased to submit the manuscript entitled “The accuracy of echocardiography versus surgical and pathological classification of patients with ruptured mitral chordae tendineae: a large study in a Chinese cardiovascular center” in The Journal of Cardiothoracic Surgery.

Neither the manuscript in its entirety nor portions thereof have been published previously, nor is the manuscript under consideration for publication elsewhere. All authors have read the manuscript and approved of its submission to this journal. None of the authors of this manuscript have a financial interest related to this work.

Please see our response to the points raised in the Reviewer Reports in additional material submitted.

Thank you for your consideration.

Please don't hesitate to contact me if you have any problems or questions regarding our manuscript.

Sincerely,

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Answers for Reviewer Prof. Uri Gabbay

1. Along the entire manuscript the authors use of confusing definitions and unclear expressions such as “surgical results”, “surgical analysis” and “surgical outcome” which seem to refer in several occasions to the “surgical findings” during surgery rather than “results” in terms of post operative consequences.

Answer 1. We have changed “surgical results” “surgical analysis” and “surgical outcome” to the phrase “surgical findings” in our revised manuscript.

2. The aim was not clearly defined. I believe the main question the research targets is how accurate are the preoperative predicting tests (TTE and TEE) in comparison with the gold standards of surgical findings and histological examination. However, the authors should revise and clear the aim of the study.

Answer 2. We have revised our aim and clarified it in the Introduction as follows: ”Our study aimed to compare the accuracy of the preoperative predictive tests of thoracic echocardiography (TTE) and transesophageal echocardiography (TEE) with the gold standards of surgical findings and pathological examination.”

3. The title is confusing and the use of the term “sample” seems inappropriate.

Answer 3. We have changed the title to “The accuracy of echocardiography versus surgical and pathological classification of patients with ruptured mitral chordae tendineae: a large study in a Chinese cardiovascular center” in the revised manuscript.

4. There is no abstract although an abstract is clearly indicated by the Journal of Cardiothoracic Surgery instructions for authors.

Answer 4. We originally submitted the abstract and the main manuscript separately on request. However, it is unclear why the two reviewers did not receive it. Therefore, we have added the abstract to the revised manuscript.

5. As far as I understand the study is an observational study, however it was difficult to decide whether the study is an observational cohort study i.e. surveillance of several years or rather a retrospective cohort (historical prospective). If the study is not a
retrospective cohort the authors should clarify why so many cases were not examined (either TEE or histological). Please clarify and correct.

Answer 5. This was a retrospective cohort study. We attempted to collect all data during the previous 5 years, but we were unable to find some cases in our hospital records.

6. Missing patient information - how representative are the patients? There is some confusion regarding the said “sample” of patients in the title. Is it a sample or rather a complete surveillance of all consecutive patients as said elsewhere?
Answer 6. Our study was a complete surveillance of all consecutive patients. The word “sample” is incorrect in meaning and we have removed it.

7. Missing diagnosis data - how, where and when was the initial diagnosis made? Was the MR acute or chronic? How long was the time gap from diagnosis to surgery? How long was the time gap from symptoms to diagnosis? If this data is available please detail if not please notify.
Answer 7. According to our records, most of the patients had chronic MR (we have added it in Materials and Methods part) but there was no information on the time gap from diagnosis to surgery and the time gap from symptoms to diagnosis in our hospital records.

8. Data analysis and Statistical analysis: If the main aim was to compare the accuracy of preoperative predicting tests (TTE and TEE) with the gold standards of surgical findings and histological examination then the focus should have been on prediction accuracy (positive and negative predictive value, likelihood ratio etc’) for each leaflet, rupture severity and underlying cause. Please correct or clarify.
Answer 8. We have added positive and negative predictive values, and positive and negative likelihood ratios for each leaflet by TTE in accordance with the reviewer’s suggestion (see Table 1 for details).

9. If the main aim was to compare the accuracy of preoperative predicting tests (TTE and TEE) with the gold standards of surgical findings and histological examination what is
the relevance of surgery types. Please revise the result section accordingly.

Answer 9. I am very sorry that I could’t fully understand this question. The relevance of surgery type is that we wished to determine whether it affects the accuracy and classification of RMCT. Therefore, we have added the following sentences to the Results section on page 8: “The surgical types included mitral valve repair and replacement, and the methods of mitral valve repair included leaflet resection, chordal shortening, and chordal transfer. The methods of mitral valve replacement included a mechanical prosthetic valve and bioprosthetic valve.”

10. I’m bothered with the statement (page 6 under the title Echocardiography characteristics and role in classification of RMCT pathology) “mitral valve prolapse (n=242, 100%)” by which the entire research population was diagnosed with MVP. MVP is attributed to myxomatous degeneration. Are the authors suggesting in their population MVP is attributed to a different underlying cause such as being a consequence of the rupture itself (either of single leaflet or both). Is it still considered MVP? Anyhow, in that case MVP cannot be considered causative to RMCT. Please clarify and discuss this issue. 
Answer 10. We have removed the statement that “RMCT is a well-known cause of mitral prolapse” in the Discussion. We consider that MVP is a manifestation of RMCT, not a cause of RMCT. Furthermore, primary MVP is attributed to myxomatous degeneration, but secondary MVP is attributed to other reasons such as CRV and coronary heart disease.

11. The authors had notified a partial RMCT was more frequent than total (complete would be a better expression). These results are different from previous studies regarding surgical cases. It should have been discussed whether the predominance of partial rupture may be associated with poorer survival of complete rupture (survival bias) or a result of different indication for surgery.
Answer 11. We have changed the phrase “total RMCT” to “complete RMCT” in the revised manuscript. There are many studies regarding the long-term survival of mitral valve repair for anterior and posterior mitral valve prolapse, but to the best of our knowledge, there are no comparisons of partial and complete RMCT. Furthermore, in our study, we did not collect information on the patients’ survival, and therefore, we were
unable to calculate survival bias. However, we have added some discussion on the difference in survival regarding anterior and posterior valve repair in discussion part from page 11 to 12.

12. The low sensitivity in diagnosing complete rupture by TTE in comparison with TEE should be discussed regarding possible confounders as both tests were not performed simultaneously (the TTE preceded TEE which was only performed during the surgery), TEE was performed on a sedated patient (which may improve the accuracy of the results) and the examiner may be more experience. Please discuss.

Answer 12. We have added the following sentence to the Discussion part on page 11: “This finding is mainly because transesophageal echocardiography is close to the heart, the probe has a high frequency and is performed in a sedated patient, and the examiner may have more experience.”

13. Page 9 line 6; The authors discuss why RMCT of anterior leaflet is associated with higher rate of MVR while RMCT of posterior leaflet is associated with higher rate of mitral valve repair and suggest different leaflet chordae mechanical characteristics. It should be also analyzed by the underlying cause as CRV is highly associated with RMCT of the anterior leaflet and myxomatous degeneration with RMCT of the posterior leaflet. Thus the explanation for MVR predominance of anterior leaflet RMCT is the underlying cause of CRV which isn’t feasible for repair. Accordingly, in posterior leaflet RMCT the predominant underlying cause is MVP/myxomatous degeneration which feasible for repair. It should be mentioned that the overall outcomes in terms of mortality morbidity and quality of life are better for repair.

Answer 13. We have added the following sentences to the discussion section as follows: “Furthermore, posterior RMCT occurred more frequently with myxomatous degeneration and anterior RMCT was common in CRV and IE patients, which could be another possible reason. Additionally, the location of chordae tendineae rupture or prolapse may affect the survival of patients with MV repair, because Dania et al reported that reoperation was required after repair or replacement, but it was more frequent after repair of anterior MVP[14].”
14. Page 10 line 5 “according to Gabbay …they were still main cause of RMCT”. The cited reference suggested myxomatous degeneration is the leading underlying cause (as it is also MVP underlying cause) but both SBE and CRV remained considerable cause not the main causes.

Answer 14. We have changed the phrase “main cause” to “considerable cause” as suggested.

Minor Essential Revisions

15. Page 2 line 2: “… and of mitral regurgitation (MR)”. This is a confusing statement as mitral regurgitation is a consequence of the chordae tendinae rupture rather than its cause. Please correct or clarify. Similar statement appears along the manuscript.

Answer 15. Some studies have reported that RMCT is a cause of MR. Rupture of the chordae tendineae has been increasingly recognized as an important cause of mitral regurgitation and insufficiency according to the references below. Therefore, we do not consider that this statement needs to be changed.


16. Page 2 line 5: “Various surgery …”. It is not clear whether the author point toward a previous surgery the RMCT patient had undergone or rather to the present (RMCT) surgical findings (which seem to me the case). Please clarify.

Answer 16. We have changed the word “various” to “previous” to clarify this issue.

17. Page 2 line 9; “the role in surgical…” Again I believe the author had meant surgical findings. Please clarify.
Answer 17. We have added the word “findings” to read “surgical findings”.

18. Page 2 last line; “echocardiography, pathological and surgical analysis…”. Again the meaning is unclear (does surgical analysis refers to surgical findings?). Please correct or clarify.
Answer 18. We have clarified this sentence as suggested.

19. The TEE was performed during surgery while TTE sometime (how long?) earlier. This fact raises two problems. First, how similar are TEE results when it is performed in ambulated most probably anxious patient in comparison with sedated patient on the operating table? Second, the tests (TTE and TEE) were not performed simultaneously (TTE preceded TEE which was only performed during the surgery) which may raise possibility of deterioration with time.
Answer 19. The intervals of performing TTE and TEE in our hospital were not longer than 1 week. Our main goal was to observe the position and degree of rupture of the chordae tendineae, and therefore, we consider that this difference in time did not affect our results.

Discretionary Revisions

20. I strongly recommend the authors to seek the assistance of an English editor.
Answer 20. We have had the manuscript revised by a native English-speaking editor.
Answers for Reviewer Prof. João Carlos Leal

a. The authors haven’t used the ASE (American Society Echocardiography) classification to the evaluation of the degree of mitral valvular regurgitation in a complete way.

Answer A:

The degree of mitral regurgitation can be determined by many methods according to the ASE report. Therefore, we chose some easy and commonly used methods such as the MR jet area to classify the degree of mitral valvular regurgitation. The following is a contextual quotation “the qualitative and quantitative parameters useful in grading mitral regurgitation severity; mild small and center jet (usually < 4 cm2 < 20% of LA area); moderate: variable; severe: large center jet (usually > 10 cm2 > 40% of LA area)”.

b. The authors have used as a measure to the left atrium the diameter. I do recommend the volume as a more confident to measure the size and severity of the mitral valvular regurgitation.

Answer B: This was a retrospective cohort study. Therefore, we were only able to obtain information on left atrial diameter, but not volume.

Question: I suggest the authors to remove/extract the text part “Patients and clinical characteristics”, because I believe information and data here should be part of “Materials and methods” (Minor Essential Revisions)

Answer: We have removed the title “Patients and clinical characteristics” in Materials and Methods part. However, we have kept this content in the Results because it is important to report this data here.

Question: A correction of the paper is essential for its publication.

We have had the manuscript revised by a native English-speaking editor.