Author’s response to reviews

**Title:** ECHOCARDIOGRAPHIC EVALUATION OF NON-SURGICALLY TREATED MILD-TO-MODERATE MITRAL DYSFUNCTION IN PATIENTS UNDERGOING AORTIC VALVE REPLACEMENT

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**Author’s response to reviews:**

Dear Editors-in-Chief:

Prof Vipin Zamvar, Royal Infirmary of Edinburgh, UK

Prof David Taggart, John Radcliffe Hospital, UK

Thank you very much for reviewing the manuscript, "ECHOCARDIOGRAPHIC EVALUATION OF NON-SURGICALLY TREATED MILD-TO-MODERATE MITRAL DYSFUNCTION IN PATIENTS UNDERGOING AORTIC VALVE REPLACEMENT (JCTS-D-19-00018R1)". We appreciate the editor and reviewers for their thoughtful review and comments on our manuscripts. We have carefully reviewed the comments and criticisms and constructed our reply accordingly as best we can. Thank you very much.

Details of our responses to the editor and reviewers are as follow.

Sung-Ho Jung, M.D
Point-to-Point Responses to the First Reviewer’s Comments

1. In the late outcomes section the following sentence is difficult to understand: "The causes of cardiovascular-related deaths were unknown in 12 patients and those of congestive heart failure were unknown in 2 patients. I do not understand the meaning of this sentence: How can it be that the authors do not know the cause for cardiovascular deaths or at least had a suspicion. If the determination of cause of death was done by phone-interview with relatives, how did the authors know that it was cardiovascular, but did not know whether it was a stroke, acute MI congestive heart failure or other. The second part of the sentence "those of congestive heart failure were unknown" does not make sense. The authors must explain this better.

Response: Thank you for the important comments. Follow-up data were obtained from hospital records, clinical visits, and telephone interviews. In cases where there is no hospital record or if the patient has not been followed up or taken to another hospital, the cause of death was estimated through telephone interviews with the patient's family. Through telephone interviews, if the cause of death is not accident, trauma, cancer, infection, cerebral hemorrhage, lung disease, kidney disease, but the family does not know the cause, the patient's death is classified as cardiovascular deaths. The second part of the sentence is incorrect. We have changed the comment in the revised manuscripts (highlighted with RED FONT)

-Changes

‘Results- Late outcomes’

congestive heart failure in 2 patients

2. Are the two patients with congestive heart failure the same as the patients who had redo mitral valve surgery? Could some of the patients who died from cardiovascular events possibly have died because of their mitral valve?

Response: Two patients who died of congestive heart failure and two patients who had redo mitral valve surgery were different. Two patients who died of congestive heart failure were
associated with prosthetic aortic valve failure. The causes of redo mitral valve surgery were severe MR and infective endocarditis, respectively.

3. Do we have echo data on the patients that died from "cardiovascular disease"? There ought to be some data on these patients that died; especially if they did not have coronary artery disease, valve disease could be suspected.

Response: Of 14 cardiovascular deaths, 2 died of prosthetic aortic valve dysfunction, and 12 deaths were unknown. These 12 patients are those who have failed to follow-up or have moved to another hospital. A mean echocardiography follow-up duration of the 12 patients was 8.7 ± 17.3 months. Most of them had only echocardiographic data at discharge. The mean EF of the echo data was 53.5± 13.9%, belonging to the mild mitral dysfunction, and the prosthetic aortic valve functioned well. However, unfortunately, we do not have echo data before the death of these patients. As in the first question, 12 patients were classified as cardiovascular death if the cause of death is not accident, trauma, cancer, infection, cerebral hemorrhage, lung disease, kidney disease in a telephone interview with a family member.

4. I have some concerns about the statistical analyses and the handling of numbers in general. In the text it says that 229 patients had ECHO after 6 months, but in Fig 2 a total of 229+ 58 patients are listed with mild and moderate mitral regurgitation respectively. This should mean that 287 patients had ECHO I would assume.

Response: Thank you for the comments. As you mentioned, there were 229 patients with an echocardiographic follow-up duration> 6 months. However, even if the follow-up duration was less than 6 months, 287 patients had echo data, and we analyzed the statistics using all of them.