

Format for ANSWERING REVIEWERS



29 June 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (File name: 16826-revised)

Title: Catheter-based intervention for severe mitral regurgitation and poor left ventricular systolic function.

Author: Poay Huan Loh, Christos Bourantas, Pak Hei Chan, Nikolaj Ihlemann, Fin Gustafsson, Andrew L Clark, Susanna Price, Carlo Di Mario, Neil Moat, Farqad Alamgir, Rodrigo Estevez-Loureiro, Lars Søndergaard, Olaf Franzen.

Name of journal: World Journal of Cardiology

ESPS manuscript NO: 16826

The manuscript has been improved according to the suggestions of reviewers:

1) Format has been updated

2) Revision has been made according to the suggestions of the reviewers as below:

Reviewer 571492

Case 1

Paragraph 1, line 4: We would like to confirmed that it is ' cerebrovascular accident.' and not 'incident'. It means that the patient had a previous stroke, more commonly known with the abbreviation 'CVA' or 'cerebrovascular accident'.

Paragraph 2, line 3: We have added in (LV ejection fraction < 10%) as suggested.

Discussion

Paragraph 1, line 1: 'suggested' changed to 'suggest' as recommended.

Paragraph 1, line 16: 'suggested' changed to 'suggests' as recommended.

Paragraph 2, line 6 – 9: 'The maximum LV performance presence of significant LVSD.' Changed to 'In the failing ventricles, the maximum LV performance is achieved at much larger LV volumes than that of the normal ventricles. This shows the importance of the Frank-Starling mechanism as a vital compensatory mechanism to maintain LV systolic contraction in the presence of significant LVSD.'

Paragraph 2, line 9: 'CHF' changed to 'chronic heart failure' as recommended.

Paragraph 4, line 1: 'common features' represents cardiovascular features as further alluded in the next sentence 'They had dilated LVsubstantial reduction following intervention.' Reference 7 was included as this recent study suggests that the cardiovascular features we observed were similar to some of the features found to be related to afterload mismatch following MitraClip treatment.

Paragraph 4, line 2: We can confirm that all the 3 patients had dilated LV and the LV end-diastolic diameters were illustrated in Table 1.

Reviewer 575423

No amendment was recommended.

Reviewer 1196819

1. Please show all testing parameters (including blood pressure, heart rate, LVSD, etc). This review guessed Table 1 only shows the data before treatment. Additionally, RV dilatation and RV systolic dysfunction should be shown

by actual data and not 'severe, moderate, or mild'.

- i. Blood pressure added to Case 1, paragraph 2, line 2 and Case 2, paragraph 2, line 3. Blood pressure of case 3 was already stated in the original manuscript.
 - ii. Table 1 only showed echocardiographic measurements before the treatment in order to highlight the common baseline features of these patients namely, dilated LV and severe LV systolic function, dilated RV and RV impairment and pulmonary hypertension. These features were recently identified to be associated with afterload mismatch following percutaneous MitraClip. As these patients had repeat echocardiographic study prior to discharge, it was too early to observe any change in the LV and RV dimensions. Some changes or measurements including LVEF following MitraClip have been mentioned in the text for individual case history.
 - iii. Assessment of RV systolic function is complex and based on measurements such as fractional area change, tricuspid annular plane systolic excursion (TAPSE) and in some cases, by visual interpretation of the overall function.¹ As this case series included cases from 3 different centres and it is not a study with any pre-specified protocol, the parameters measured and used for the assessment of RV function were not uniform across the three centres. Therefore, we would like to seek consideration of the reviewer and Editorial team to allow using the grade of RV dysfunction for our case series instead of a specific measurement or combination of measurements. Further, this would be more clinically relevant and make it more obvious to the broad range of audience of WJC who may not be familiar with the wide range of measurements to assess RV systolic function.
 - iv. Mid RV diameter added to Table 1.
2. Although the authors mentioned that "Treatment strategies and options in case of procedural failure should be discussed", the author should clearly conclude what patient should not be treated by percutaneous MitraClip based on the present study.
- i. The aim of our manuscript is to raise awareness and caution in all involved in the treatment of such patients that, although it may be a rare occurrence, some patients with severe LV systolic dysfunction may experience significant haemodynamic instability following acute reduction in their mitral regurgitation during MitraClip. Therefore we encourage active discussion and involvement of 'The Heart Team' or multi-disciplinary team in tailoring the appropriate treatment strategies for each patient. We feel that 'The Heart Team' approach should not be limited to the decision and planning of treatment but it should also involve active discussion on unforeseen events such as procedural failure. For example, whether surgical bail-out is an option for a patient and if so, should it be done in the same sitting should percutaneous MitraClip was unsuccessful. On the other hand, a patient may have multiple co-morbidities that there is no other treatment option is available should MitraClip was unsuccessful. Clinical team involved should have this clear in the mind such that appropriate steps or preparation could be made before putting a patient through the

procedure; whilst the patients and their family should be informed of such potential outcome before consenting for the procedure.

- ii. This is a case series and we don't feel that it is adequate and appropriate to make a definitive conclusion on the type of patients suitable or unsuitable for the treatment. However, based on the experience of our centres, we like to urge those who are involved in treating such patients to be cautious and extra-vigilant.

3. Please describe the methods (such as cardiac output, pulmonary arterial systolic pressure, etc) in the manuscript and give references.

- i. Our manuscript is unique as it is a case series based on the real-life clinical experience from 3 different centres, one case from each centre. It is not a pre-designed clinical study with a standard protocol. Therefore, there were differences in the methods and equipments used for certain measurements such as cardiac output. However, there is also similarity in some of the more standard measurements including invasive cardiac catheterisation for variables such as pulmonary arterial systolic pressure. We appreciate the importance of a well described materials and methods section as pointed out by the reviewer. However, we feel that it is beyond the context of this case report/series to describe the methods and equipments used in all the 3 different centres.

4. Please polish English.

- i. The grammatical and typographical errors pointed out by Reviewer 571492 have all been amended as recommended.

References

1. Rudski L, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K, Solomon SD, Louie EK, Schiller NB. Guidelines for the Echocardiographic Assessment of the Right Heart in Adults: A Report from the American Society of Echocardiography. *J Am Soc Echocardiogr*. 2010;23:685-713.

3) References and typesetting were corrected. The manuscript has been amended to the format similar to the sample manuscript provided.

Thank you again for publishing our manuscript in the World Journal of Cardiology.

Yours sincerely,

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