Author's response to reviews

Title: Non invasive Evaluation of Cardiomechanics in patients undergoing Mitraclip procedure

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Author's response to reviews: see over
Reviewer 1
Title: Non invasive Evaluation of Cardiomechanics in patients undergoing Mitraclip procedure
Version: 1 Date: 26 February 2013
Reviewer: Gillian Whalley

This is a small retrospective study that seems to be suffering from the lack of prospective planning.

Major revisions:

Methods –
Selection of patients – were ALL patients who underwent the mitral clip procedure enrolled? It would seem unlikely, given the following statement; “…single expert operator using echocardiography the day before the procedure and at discharge from the hospital in all patients.” This suggests that only patients who had the same echo operator were included. If these are not all patients, then please explain how many procedures were completed and how many were excluded from this analysis. Adding the dates of study recruitment would be helpful.

In the manuscript we state in the results section that forty patients undergoing Mitraclip have been retrospectively screened, but we found complete echocardiographic data to assess non invasive ESSB in 18 patients. In our department only one cardiologist is dedicated to the evaluation of patients undergoing this procedure.

In general, the echo methods are scant. Please include more details, such as echo machine, whether measurements measured online or offline and all at the same time, how were they measured (eg LV volumes, and elastance).

Done.

Results – there are no data presented about timing of the post-procedure echoes, other than saying these were done at discharge. The timing is important. I imagine these echoes were done very close to the procedure, and although I understand the immediate reduction in the degree of MR, I find it surprising that other parameters have regressed so quickly, ie left atrial size has gone down, but the mitral gradient has not. The timing of these changes needs to be discussed in terms of mechanism and unloading of the heart.

In the methods section the timing of follow up echo was added and expressed as mean ±SD.

The reduction of left atrial volume seen in our study is similar to those seen in literature after 3 weeks from the intervention. Concerning the transvalvular gradient, we observed an increase, which was not significant as stated in results section.

Table 1 – I don’t understand how the EF has gone down, when the stroke volume has increased, in the presence of a reduced end-systolic LV volume, and a reduced (but not to the same extent) end-diastolic LV volume. This reduction in EF is seemingly then ignored throughout the remainder of the manuscript.
We agree with your first impression looking at table 1. But it must be considered that data are expressed as median and interquartile range and not means. If you consider the upper interquartile range the reduction of diastolic volume is higher than systolic volume. In substance, it is likely that most patients had a more pronounced reduction in diastolic volumes than systolic volumes with consequent effect on EF.

The authors should check the data in the last row of the table for possible duplication of numbers
Thanks. We corrected it.

The authors report no correlation between Ees and EF and since this is a major component in their discussion of why LV EF doesn’t matter, it would be good to see this graph.
We put scatter diagrams in the manuscript.

Were the measures of LV function related to any measures of severity of MR.
We agree with your point. However our aim was to investigate load independent indexes, such as elastances.

I am not sure the graphs add much more than could be addressed in the text or table.
We still feel these can help the reader, however we leave the final decision whether to maintain them or not to the Editor.

Discussion –
The authors assert “The observed reduction of the ejection fraction must not be considered as an index of decreased function and instead should be considered as a consequence of a lower preload, as evidenced by the reduction of the left atrial and ventricular volumes.” Without any evidence to support this, other than a lack of correlation between Ees and EF.

We agree with your point. We mitigated our statement as follows “We hypothesize that the observed reduction of the ejection fraction could not be an index of decreased function rather could be considered a consequence of a lower pre-load, as evidenced by the reduction of the left atrial and ventricular volumes”

The authors state:
“Furthermore our study suggests that data traditionally obtained invasively can be monitored at the bedside during and after the hospitalization of such challenging cases.” They have not correlated these data with invasive data so cannot conclude this.
Chen et al have validated the feasibility of monitoring ESPVR relationship in a non invasive manner and this method has been applied many times in literature. Moreover our goal was not to compare invasive and non invasive measurements, but monitoring midterm effect of Mitraclip positioning on Ea/Ees with non invasive echocardiography. In Limitation section we added that different results might be obtained with an invasive evaluation.

The discussion is not deep enough. The current study is mentioned briefly and other literature reported, but the mechanisms and challenges are not speculated upon enough. This is largely a confirmative study of others’ work and suffers form being small and retrospective.

We improved the Discussion by better underlying the main findings and expanding some other parts.

Reviewer 2

Reviewer’s report

Title: Non invasive Evaluation of Cardiomechanics in patients undergoing Mitraclip procedure
Version: 1 Date: 6 March 2013
Reviewer: Eustachio Agricola

Reviewers report:

General comments:
The findings reported by the authors, even though obtained in patients with a relatively new technique “MitraClip”, are not surprising because are data observed after MR correction with any surgical or percutaneous procedure able to correct MR. I have some remarks regarding the introduction, methods, results and data interpretation, that have to be considered by the authors in any revision.

Major comments:

Introduction

The introduction is very long and difficult to read, therefore initially it needs to be shortened and re-arranged.

Thanks for your comment. We changed it a little, however we feel it is necessary to summarise the non invasive evaluation of elastances.

The aim of the study should be relocated at the end of the introduction.

Done

The statement “This technique, mimicking Alfieri’s surgical approach, consists of
the approximation of the middle scallops of the mitral valve leaflets through the percutaneous delivery of a clip with the creation of a double orifice mitral valve" is not completely correct particularly in view of the new extended applications like paracommissural lesions treatment, zipping technique etc. Thus the concept of middle scallops approximation is quite reducing.

**Changed definition of the procedure in a more recent view.**

The concept that MitraClip reduces the risk of surgical mortality should be replaced with "the non inferiority of MitraClip device vs standard surgical approach", that is a different thing.

**Thanks. Corrected in the text**

**Methods**

All methods should be better specify in depth. The description of echocardiographic methods and patients selection is very superficial. In the methods, the authors state that only patients who met echocardiographic criteria were considered eligible for MitraClip procedure. The authors refer to reference n. 15 for the criteria. I believe these is an important point and today it is more appropriate to say that "only patients who met EVEREST II echocardiographic criteria were considered eligible for MitraClip procedures. Because the concepts of EVEREST II echocardiographic criteria are almost completely dismissed and more and more patients with defined as negative EVEREST II criteria were considered eligible for MitraClip. Thus, the authors should be provide the period of the enrollement and how many patients did not meet the criteria and how many were excluded.

**Thanks. Explained in the text**

Regarding the quantification of MR, the authors say that vena contracta and semiquantitative method were used for quantification. Vena contracta is not considered properly a quantitative method, so what semiquantitative methods were used? Please specify. Furthermore in case of contrasting results what method was used as reference one?

**Thanks. We added a dedicated table (table 1)**

**Results**

The increase in forward stroke volume independent of a decrease in ejection fraction is quite obvious and it is due to a direct consequence of the reduction of regurgitant volume after an effective MitraClip procedure.

The reduction of MV insufficiency associated with decreases in PAPS and the left ventricular and atrial volumes and amelioration of the NYHA class status are not innovative as stressed in the discussion. In fact, these results are already well described in the literature starting from EVEREST I and II trial.

**We agree with your consideration, but our intention is to analyze ventricular arterial coupling in a subset of patients that have clinical results similar to those shown in literature. We don’t think that maintained Ea/Ees after an interventional procedure is obvious and we feel it could be a point of interest to future studies. In clinical practice it is not rare to see a symptomatic patient after Mitraclip without MR.**
Discussion
In the first paragraph, what means primary MR?
Removed term primary. We had put it based on its meaning by the guidelines

I partially agree with conclusion of authors that the amelioration of symptoms is related to systolic cardiomechanic indices, since it is well known that the best results in terms of symptoms improvement are obtained through a significant reduction of wedge and pulmonary pressures that are obtained by a reduction of regurgitant volume. In this series the non-invasive evaluation of PCWP and its changes are lacking.

In this article we wanted to focus the attention on the non invasive evaluation of Ea/EsSB ratio after mitraclip. We agree with the reviewer that lowering of pcwp and unloading of the heart is the most important mechanism explaining the reduction of NYHA. We were unable to recover all data for estimation of pcwp (E/e'). However in this study we aimed to focus the attention on the possibility of using non invasive elastance and ventricular arterial coupling to monitor ventricular performance after Mitraclip procedure.