Author's response to reviews

Title: Left Atrial Volume Predicts Adverse Cardiac and Cerebrovascular Events in Patients with Hypertrophic Cardiomyopathy

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Author's response to reviews:

Editor-in-Chief
Eugenio Picano, MD,
Cardiovascular Ultrasound

Dear, Dr. Eugenio Picano

I enclosed herewith the re-revised manuscript entitled "Left Atrial Volume Predicts Adverse Cardiac and Cerebrovascular Events in Patients with Hypertrophic Cardiomyopathy", which we would like to submit for publication in Cardiovascular Ultrasound.

We thank the reviewer’s comments.

We answered the comments and checked our paper again.

I provided a point-by-point response to the comments in this cover letter.

Sincerely yours,

Tomoko Tani, MD
Department of Cardiovascular Medicine
Response to reviewer’s comments.

Reviewer: Dr. Rosa Sicari Comments. (First)

1. We thank the Reviewer’s comments.
   We added the sentences about the diagnosis of HCM.
   The sentences which were added or eliminated were shown by highlights.
2. We studied within the specified period in this study.
3. We exchanged the description of events in this section in Methods.
4. We thank the Reviewer’s comments. We described the exclusion criteria in Methods. I exchanged the sentence that was described about final population.
5. We thank the Reviewer’s comments.
   We corrected Table. 1, 2 and 3. We added the total numbers.
6. We thank the Reviewer’s comments. I prepared a table with events as Table.3.
7. We thank the Reviewer’s comments. I added the sentence in Discussion.
8. We performed the analysis about all parameters.
9. By multivariate Cox regression analysis, LAV/BSA was an independent predictor for MACCE.
10. We used ROC curve to identify the optimal cutoff values of LA volume index.
11. We thank the Reviewer’s comments.
Nistri S et al. showed that in health individuals LV size, competitive sport, age, and LV mass are independent determinants of LAVI.
In our study, we investigated the patients with HCM.
So, we did not discuss the normality values.
12. I agree with your comment. I added the sentence in Discussion.
13. I added the sentences in Discussion.

Reviewer: Dr. Rosa Sicari Comments. (Second)

1. We thank the Reviewer’s comments.
   We changed “normal pump function” from “normal LV systolic function”.
   I already added the cut-off used for normality of EF.
2. I already described the exclusion criteria in Methods.
3. I described the median time.
4. I had already Table 1 and 2 remade.
5. We thank the Reviewer’s comments.
   Indeed, AF may be considered as an event.
But, in our study, the rhythm of 7 patients was atrial fibrillation at the time of complications in 18 patients presented with stroke. So, AF was not endpoint in this study.

6. We thank the Reviewer’s comments.
I added the table of multivariable analysis. (Table.5)

7. Nistri S et al. showed that in health individuals LV size, competitive sport, age, and LV mass are independent determinants of LAVI.
In our study, we investigated the patients with HCM.
So, we did not discuss the normality values.
I added the sentence in Limitations.

Reviewer: Dr. Denisa Muraru Comments.

Major Compulsory Revisions:
1. We thank the Reviewer’s comments.
When we investigated this study, Tsang TS et al. reported about left atrial volume (Mayo Clin Proc 2001; 76:467-75). They described that apical 4- and 2-chamber views or 4-chamber and apical long-axis views had to be of good quality in this paper.

2-chamber views of some patients were not good images. So, we measured left atrial volume in 4-chamber and apical long-axis views.
2. If we detect eccentric jets, we may underestimate the grade of MR.
So, we had better perform other method of measurements in these cases.

About MR, in our study, we could clearly detect MR jet.
3. We thank the Reviewer’s comments.
From previous papers, LVOT obstruction was an independent long-term determinant of heart failure progression and stroke death.
Otherwise, Losi MA et al. showed that there was no statistical differences between patients with and without obstruction on outcome (J Am Soc Echo 2009).

Clinically, HCM patients without obstruction were sometimes occurred complications.
So, we investigated the clinical significance of echocardiographic parameters in patients with nonobstructive hypertrophic cardiomyopathy.
I added the sentence in Study populations in Methods.
4. The presence of PAF was documented by either 12-lead resting electrocardiogram (ECG) or 24h ambulatory ECG. The patients with PAF had at least one symptomatic episode.
But, if the patients had no symptoms, we might miss these patients.
5. We exchanged the description of events in this section in Methods.
6. We thank the Reviewer’s comments.
I added the sentence in Statistical Methods.
7. We compared the groups with not only septal wall thickness, but also the type of HCM.
I agree with your comments.
We investigated the type of HCM and there were no significant differences between two groups.
Minor Essential Revisions:
1. I corrected the abstract.
2. We replaced “normal pump function” from “Normal LV systolic function”.
3. The cut-off used for normality of EF was 60%.
I described in paper.
4. In our hospital, two or three operators performed.
5. I removed the description.
6. In this study, we measured and examined LV diameters.
7. We used consistently abbreviations.
8. We thank the Reviewer’s comments. We removed the last sentence.