Author’s response to reviews

Title: The value of left ventricular strain–volume loops in predicting response to cardiac resynchronization therapy

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To: Cardiovascular Ultrasound

Dear Professor Rosa Sicari,

Thank you for your help in our manuscript, entitled: "The value of left ventricular strain–volume loops in predicting response to cardiac resynchronization therapy" (CARU-D-18-00081). Each of the reviewers' comments was carefully considered and the manuscript was revised as suggested. Below you will find the explanation to each of the reviewers' comments and the revision we made.

Reviewer #1:

Authors have partially responded to my concerns in their reply, although they found unnecessary to change anything in this respect in the manuscript. They did not tested different simple measures as suggested in point (1). In the reply to point (2) they extensively described other potential applications of GLS, with numerous references, but did not verify results with literature as suggested.
The reply to both points essentially states that the proposed parameters may not demonstrate a superiority in basic comparisons and in univariate analysis. However, the superiority is evident in multivariate analysis. Honestly, given the limited number of patients (40) for a reliable multivariate analysis, I am not sure that such small statistical difference is sufficient for a proof.

But I am not expert in clinical statistics; therefore, I suggest a quick statistical revision on this point (a check of the reply to review can verify if these are sufficient).

Thanks for your kind suggestions. We would like to accept your suggestions. On the one hand, we have listed the small sample size as a limitation. As you said, our study was performed in a single center, with a relatively small sample size. Therefore, we cannot draw definitive conclusions but only formulate a hypothesis that needs to be confirmed by future, larger, multi-center prospective trials. On the other hand, with regard to the sample size needed in performing multivariate logistic regression analysis in clinical trials, I have consulted a lot of relevant materials on the Internet or paper books in the library but found that there was no uniform standard. A lot of information indicates that there is really no good and authoritative estimation method for sample size calculation of logistic regression analysis, and more are based on experience and details in the analysis process. So, I consulted a colleague who work in Department of Epidemiology, School of Public Health, Fudan University and he is expert in clinical statistics. The advice he gave me was that the appropriate sample size was 5-10 times the number of variables included in the multivariate analysis. He reminded me that 40 was indeed the minimal standard of our sample size because a total of 8 variables significantly associated with CRT response in univariate analysis were involved in multivariate analysis. A two-sided p value < 0.05 could be accepted as indicating statistical significance of the independent predictor in multivariate analysis.

In addition, we added some related details of Figure 1 and Figure 3 in the corresponding Figure legends in order to give readers a better understanding of the figures, as you can see according the 'tracked changes'.

Above is the explanation and changes we have made. If you have more suggestions, we would like to accept. Thanks for all you have done for our manuscript. We hope this manuscript can be helpful in clinical practice.

Sincerely,

Xianhong Shu, MD