Author's response to reviews

Title: Mitral annular systolic velocity as a marker of preclinical systolic dysfunction among patients with arterial hypertension

Authors:

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Author's response to reviews: see over
Dear Editor-in-chief, editorial committee, and reviewers,

Thank you for the opportunity to edit the manuscript and resubmit it for possible publication. I will now attempt to address the issues you raise.

Response to reviewer Fabian Knebel:

Thank you for the positive review of our study. I am very glad that the main conclusion of the trial namely that the average peak systolic mitral annular velocity ($S_{\text{avg}}$) should be examined in patients with HTN because it is an early sign for preclinical systolic dysfunction has accepted successfully.

Such an approach could change the therapeutic strategy for patients being treated with different combinations of medications, although a well planned prospective study is needed to confirm that.

Regarding the methodology:

1. Patients with diabetes mellitus were excluded from participation by medical history and fasting blood glucose test.
2. Preserved EF of the LV was defined according to the ASE, EAE and BSE criteria as $>55\%$, as calculated by the Simpson method.
3. The protocol for this study included the use of coefficient of variances (CV), which is used in a number of other recognized studies. This coefficient enables quick calculation and assessment (clinical) of the differences in the calculated parameters. It is not software-based (SPSS, MedCalc), which makes it convenient. We will take your recommendation into account and present the intraclass correlation coefficient (ICC) results as well.
4. A figure, illustrating the technical execution will be included in the manuscript, as per your recommendation.
5. I cannot give a definitive answer to the question you pose regarding the differences between our reported mean values of peak systolic mitral annular velocity and the ones you have established in the past. The only thing I can assert is that the reason is not in the techniques we used. In the last 10 years several important studies on the topic were published (as cited in our manuscript). There is still no consensus, however, about what the norms should be for different age groups and gender, and what should be considered pathology. Regardless, there are tendencies, which direct clinical thinking. Regarding the parameter in question, more than just age and gender affect its value. Examples would include presence of HTN, DD, diabetes mellitus, coronary heart disease, myocarditis, cardiomyopathy, valve diseases, anemia, thyrotoxicosis, cardiotoxicity, etc. In short, in order to obtain “clean” results, the patient should exhibit none of the concomitant conditions. We have attempted to achieve this with the control group of healthy volunteers who served for the
calculation of mean values for the peak systolic velocity of mitral annulus. For greater clarity I am including some of the most important research utilizing pulse TDI and the published results.

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<td>27</td>
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<td>80</td>
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<tr>
<td>Age</td>
<td>31±13</td>
<td>44±16</td>
<td>24±10</td>
<td>33(16-68)</td>
<td>51(20-81)</td>
<td>45(&lt;50)</td>
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<td>45(&gt;50)</td>
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<tr>
<td>LV lat</td>
<td>10.3±1.8</td>
<td>11.7±2.5</td>
<td>10.3±1.9</td>
<td>10.2±2.1</td>
<td>9.9±2.9</td>
<td>7.9±1.9</td>
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<tr>
<td>Septum</td>
<td>8.7±1.4</td>
<td>10.9±2.2</td>
<td>8.1±0.8</td>
<td>7.8±1.1</td>
<td>7.7±1.4</td>
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<td>LV ant</td>
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<td>9.0±1.6</td>
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<td>LV inf</td>
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This table presents the peak systolic velocities of longitudinal motion for the basal LV myocardial segments (cm/s). Mitral annular velocities which we used in the study are usually slightly higher than the velocities recorded from the basal myocardium, and show a similar decrease with age.

Response to reviewer Maurizio Galderisi:

1. Thank you for the positive review. I would like to point out that the main conclusion of the study was that the mean annular peak systolic velocity in patients with HTN is reduced and diastolic dysfunction (DD) furthers this preclinical systolic dysfunction. It is of note that no patients with diabetes mellitus were included in this study. Its effect on myocardial annular systolic velocities was not evaluated. Such a topic is a good recommendation for a future, well planned prospective study. Hence, the recommendation for statistical analysis of patients with diabetes mellitus cannot be fulfilled at this time.

2. Regarding the recommendation to assess the reproducibility of S’(Sm), we have calculated the reproducibility of systolic velocities according to the approved protocol of this study, using the coefficient of variances (CV). We have complied with the recommendation of the other reviewer to make an assessment of the reliability of the results using intraclass correlation coefficient - ICC (relevant text and table added to the manuscript).

3. According to your recommendation, additional demographic parameters were included in the manuscript (height, weight, systolic blood pressure, diastolic blood pressure, heart rate, BMI, EF).

4. The list of authors has been edited as per your recommendation.

5. Regarding the recommendation to include a figure, demonstrating mean systolic velocities for the studied subgroups of patients I would like to draw attention to two figures in the original file that demonstrate the boundaries of the mean annular systolic velocities of the studied population.
I have attempted to edit the article in the places where the reviewers noted.

I would like to thank you once again for the presented opportunity to edit the article and resubmit it for publication. If there are any questions that I have not addressed clearly enough, I would like to apologize. It would be beneficial to clarify them soon.

Kindest Regards,

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