Author's response to reviews

Title: The Relationship between Mitral annular systolic velocity and Ejection Fraction in Patients with Preserved Global Systolic Function of the Left Ventricle

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 Konstantinos Farsalinos:

Thank you for the critical review of our study. I am very glad that your general impression is positive. You qualify the article as important to those with closely related research interests. Your main suggestions, as I understand them, are directed at the extensive English editing and rewriting of the manuscript in some places.

Let me introduce, point by point how the manuscript was edited according to your recommendations.

**MAJOR COMPULSORY REVISIONS** which were made:

1. Past tense was used throughout the text wherever possible;
2. All data about the preserved EF and intentions with Sm cut-offs were removed from the results portion of the abstract;
3. In the abstract conclusion, the sentence that you specify was edited according to your comments;
4. The keywords were exchanged with the ones that you recommend;
5. Main text: In the hole manuscript all statements about setting an Sm(avg) cut-off point, as well as ROC analysis and figure 4 were removed;
6. Statistical analysis: ANOVA results were reported;
7. Results: this section was partially rewritten. The sequence of the paragraphs and the tables follows your recommendations, except table 2, which I kept in the same place as in the original body of the manuscript. I think that this layout clearly relays the statistical results to the reader.
8. The corresponding EF values of all subgroups were reported in tables 3, 4 and 5, as you recommended.
9. The abbreviations were corrected in the whole manuscript and in the tables.
10. Discussion: Everything about Sm(avg) cut-offs and preserved EF was removed.
11. It was highlighted that the reported results were only for subjects with normal EF.
12. Everything about Sm(avg) cut-offs was removed from the conclusion.

**MINOR COMPULSORY REVISIONS** which were made according to your suggestions:

1. In main text body;
In the first sentence of the first paragraph we removed all the “the”.

In the sentence "This parameter measured by pwTDI correlates more strongly with plasma BNP levels than those measured by M-mode." were added commas as you suggested me "This parameter, measured by pwTDI, correlates more strongly with plasma BNP levels than those measured by M-mode."

On the Second paragraph: “Even though the Sm of the MA”, was removed the “of the MA”.

2. Methods:
First paragraph: “All participants were agreed and signed...” was corrected as: “All participants agreed and signed...”
Second paragraph was rephrased as: “Physical examination, which included blood pressure and anthropometric measurements, and an electrocardiogram was performed.”
“The” was removed from “The standard laboratory blood tests were...”
The phrase “After that, eligible subjects were invited...” was corrected to: “Subsequently, eligible subjects were invited...”

Third Paragraph:
The “The” was removed from the sentence “The longitudinal contraction of the LV was investigated...”
The phrase “cardiac cycles” was used instead of the word “complexes” in the sentence “In accordance with the study protocol, 3 consecutive complexes were analyzed, and the mean value was calculated.”

3. Results:
Sixth paragraph:
The sentence “The data demonstrate that gender and age influence Sm(avg) such that the highest velocities are observed in men and they decrease, with aging and in women.” was rephrased according your suggestion as follow: “The data demonstrate that gender and age influence Sm(avg) in a way that higher velocities are observed in men, while they decrease linearly with age.”
The sentence “According to Sm(avg), there is a significant decrease of velocity.” was removed.
Seventh paragraph:
This paragraph was rewritten fully.

Response to reviewer Frank FL Dini:

Thank you for the critical review of our study. Let me comment on your major and minor notes/recommendations.

MAJOR COMPULSORY REVISIONS which were made:

1. I completely agree with you that TDI-derived mitral annulus systolic velocity only reflects LV long-axis function. I do not, however, agree that it is a major limitation for assessment of the
global LV function. Several studies demonstrated a strong correlation between Sm of the mitral annulus and LV EF estimated using different methods, such as MRI, CT, contrast echocardiography, radioisotope, contrast ventriculography, etc. The type of correlation established in these studies was different – linear, S-type or logarithmic – depending on the EF of the patients enrolled in the trials. I cannot imagine how global LV function can be presented without estimation of EF. Following is a part of my PhD dissertation, wherein I outline the relationship between long-axis contraction of the LV and global LV performance.

The importance of long-axis motion of the ventricles to the overall cardiac pump function has been known since the time of Leonardo da Vinci. Many years later, that novel observation was confirmed by Feigenbaum et al. Their work described LV performance like a pump with a piston, the role of which is performed by the mitral annulus. The systolic motion involves shortening in the longitudinal axis with concomitant reduction in internal diameter, and slight rotational movement around its longitudinal axis. In diastole, early ventricular relaxation returns the mitral annulus back to its original position. This annular displacement, more specifically its velocity and timing in relation to blood flow, are altered by disease and by the normal ageing process. Imaging the MA, therefore, provides an approach by which non-invasive techniques can be used to evaluate both regional and global LV function. Later, many investigators confirmed this general conclusion. (Emilsson et al, Vinereanu et al., Wandt B et al, Nikitin N, et al, KK Witte, et al, Fraser AG, Alam M, et al Gulati VK, et al ...........more than 70 citations.)

2. Due to the fact that none of the subjects had reduced EF, all the intentions about Sm(avg) and their relation to preserved EF were removed from the manuscript.

3. First of all, I would like to thank you for the interesting article. As to your query about the relationship between longitudinal systolic contraction and diastolic dysfunction, I published an article last year, wherein I demonstrated the relationship between the grade of diastolic dysfunction and the severity of deceleration of Sm velocity. This study is not a part of yours, if I understand your question correctly.

4. Probably the main advantage of using TDI-derived annulus systolic velocity with respect to M-mode fractional shortening is independence of the poor image quality.

**MINOR COMPULSORY REVISIONS** were made according your recommendations:
Finally, I have attempted to edit the article in the places where the reviewers noted.

I would like to thank you once again for the 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. I am, of course, available for any further questions or comments that you might have.

Kindest Regards,

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