Peer Review File

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Reviewer A:

1) This study applied both CMR-FT and LGE to evaluate the relationship between regional/global myocardial strains and the transmural extent of myocardial infarction at different segment. This will be very helpful for more comprehensive evaluation of cardiac function of MI patients.

Reply 1: Thank you very much for your positive comments.

Changes in the text: As for this comment, we have not made required revisions.

2) The author found that more than 2 transmural segments in apical-mid part was related to an increased risk of cardiac events. This indicated that transmural exceeded mid part of the ventricle would significant influence the prognosis. It was like to be a simple and useful quantified index in the future.

Reply 2: Thank you very much for your attention to our study.

Changes in the text: As for this comment, we have not made required revisions.

3) I suggested that the CMR should considered during follow up.

Reply 3: Thanks for your kindest comments. As you mentioned, the lack of CMR evaluation during follow-up was one of the limitations of our study. Future studies are needed to investigate myocardial changes by comprehensive follow- up CMR examinations. We have added this point in the last second paragraph of the discussion section (see Page 16, lines 321-323).

Changes in the text: We have added the description in the last second paragraph of the discussion section as follows: "Third, this study did not include CMR evaluation during follow-up. Future studies are needed to investigate myocardial changes by comprehensive follow- up CMR examinations.".

Reviewer B:

Authors analyzed the relationship between left ventricular myocardial strain and transmurality of myocardial infarction at three circular sections (basal, mid-ventricular, apical) by using cardiac magnetic resonance feature tracking (CMR-FT) and late gadolinium enhancement (LGE) information in ST-elevation acute myocardial infarction (STEMI) patients after primary percutaneous coronary intervention (PPCI). It is an interesting research, the main commons as follows.

1. "Merged" in the topic is misunderstood, it was only combined two methods to assess myocardial infarction patients, please revise the topic.

Reply 1: Thank you for your kindest suggestions. We are sorry for the inappropriate words. Considering your suggestions, we have revised the title as "Impact of Apical and Mid-Ventricular Transmural Infarcts in Patients with Acute Myocardial Infarction Determined by Using Late Gadolinium Enhancement Combined with Feature Tracking Magnetic Resonance" (see Page 1, lines 1-3). In addition, we have revised the words throughout the manuscript.

Changes in the text: The title was changed to "Impact of Apical and Mid-Ventricular Transmural Infarcts in Patients with Acute Myocardial Infarction Determined by Using Late Gadolinium

Enhancement Combined with Feature Tracking Magnetic Resonance".

2. Page 6, study population, CMR was performed 5±2 days after STEMI. How to differentiate edema and infarction in acute stage?

Reply 2: Thank you for your kindest comments. T2-weighted imaging was used for the detection of myocardial edema and LGE imaging was used for the detection of infarction in acute stage.

Changes in the text: As for this comment, we have not made required revisions.

3. For the LGE quantification, which method did authors used? SD or FWHM?

Reply 3: Thank you for raising this issue. In this study, LGE quantification was based on the full-width at half- maximum (FWHM) technique. We have added the description in the revised manuscript and cited a reference (see Page 8, line 152).

Changes in the text: We have added the description as follows: "LGE quantification was based on the full- width at half- maximum (FWHM) technique (16).".

4. In the methods, authors described that they assessed cardiac functional indices such as EF, EDV, ESV, but did not show the results in the results section.

Reply 4: Thank you for your kindest comments. We focused on the analysis of the relationship between left ventricular myocardial strain and transmurality of myocardial infarction at three circular sections. Moreover, EF is calculated from EDV and ESV. Thus, the analysis of cardiac functional indices such as EDV and ESV was not needed. The descriptions of cardiac functional indices such as EDV and ESV in the methods section were deleted (see Page 9). However, we revised Table 5 and added EF in the univariate and multivariate analysis.

Changes in the text: The descriptions of cardiac functional indices such as EDV and ESV in the methods section were deleted. In addition, we revised Table 5 and added EF in the univariate and multivariate analysis.

5. Please do not interpret results in the results section, such as "Taken together, the results suggested that data obtained from CVI42 analysis of local cardiac function were reliable and reproducible" and "indicated that regional radial and circumferential strain decreased with increasing transmurality of myocardial infarction irrespective of basal, mid ventricular, or apical segments. The longitudinal strain was lower in segments with transmural infarction, especially in apical and mid-ventricular portions of LV". Please remove these interpretations to discussion section.

Reply 5: Thank you for your kindest suggestions. According to your comments, we have removed these interpretations to the discussion section (see Page 12, line 227). Additionally, we deleted some of the interpretations in the results section that already existed in the discussion section.

Changes in the text: The interpretations such as "Taken together, the results suggested that data obtained from CVI42 analysis of local cardiac function were reliable and reproducible" and "indicated that regional radial and circumferential strain decreased with increasing transmurality of myocardial infarction irrespective of basal, mid ventricular, or apical segments. The longitudinal strain was lower in segments with transmural infarction, especially in apical and mid-ventricular portions of LV" were removed.

6. In the "Segmental analysis of regional myocardial strain" section, did authors assessed the strain in

3 levels or 16-segmental? It is unclear.

Reply 6: Thank you for your kindest comments and we are sorry to mislead you. Indeed, regional myocardial strain values were obtained for 16 segments and for basal, mid and apical segments (segments 1-6 are basal, 7-12 mid-ventricular and 13-16 apical, according to the AHA segment model). We have changed the subtitle from "Segmental analysis of regional myocardial strain" to "Relationship between regional myocardial strain and transmurality of myocardial infarction" (see Page 11, line 204). In addition, we added a bull eye plot with strain curves showing strain calculation in nontransmural and transmural infarcts as "Figure 2-revised". If there is any other question, please feel free to contact us.

Changes in the text: We have changed the subtitle from "Segmental analysis of regional myocardial strain" to "Relationship between regional myocardial strain and transmurality of myocardial infarction". In addition, we added another figure as "Figure 2-revised".

7. "At the midventricular level, longitudinal strain values", why only chose midventricular level? Only longitudinal strain assessed?

Reply 7: Thank you for your kindest comments. We analyzed the relationship between regional myocardial strain and transmurality of myocardial infarction at three circular sections (basal, mid-ventricular, apical). The corresponding results were summarized in Table 3. Unlike the radial strain and circumferential strain, longitudinal strain did not show a consistent distribution pattern regarding to non-infarcted segments, segments with non-transmural infarction, and those with transmural infarction at the basal, mid-ventricular, and apical levels. Thus, we described the change of longitudinal strain separately for basal, mid-ventricular, and apical levels. The detailed information can be derived from the corresponding Table 3 and complete descriptions of the revised "Relationship between regional myocardial strain and transmurality of myocardial infarction" section.

Changes in the text: As for this comment, we have not made required revisions.

8. "Longitudinal strain was not different between non-infarcted segments, segments with non-transmural infarction, and those with transmural infarction at the basal level", why did not assess apex level?

Reply 8: Thank you for your kindest comments. As the response for the above comment, we analyzed the relationship between regional myocardial strain and transmurality of myocardial infarction at three circular sections (basal, mid-ventricular, apical). The corresponding results were summarized in Table 3. Unlike the radial strain and circumferential strain, longitudinal strain did not show a consistent distribution pattern regarding to non-infarcted segments, segments with non-transmural infarction, and those with transmural infarction at the basal, mid-ventricular, and apical levels. Thus, we described the change of longitudinal strain separately for basal, mid-ventricular, and apical levels. The detailed information can be derived from the corresponding Table 3 and complete descriptions of the revised "Relationship between regional myocardial strain and transmurality of myocardial infarction" section.

Changes in the text: As for this comment, we have not made required revisions.

9. "indicated that regional radial and circumferential strain decreased with increasing transmurality of myocardial infarction irrespective of basal, mid ventricular, or apical segments. The longitudinal strain was lower in segments with transmural infarction, especially in apical and mid-ventricular portions of LV", it is hard to deduce this conclusion since many data were not available as common #6-#8 indicated.

Reply 9: Thank you for your kindest comments. As the responses for the above comments #6-#8, we analyzed the relationship between regional myocardial strain and transmurality of myocardial infarction at three circular sections (basal, mid-ventricular, apical). The corresponding results were summarized in Table 3. Unlike the radial strain and circumferential strain, longitudinal strain did not show a consistent distribution pattern regarding to non-infarcted segments, segments with non-transmural infarction, and those with transmural infarction at the basal, mid-ventricular, and apical levels. Thus, we described the change of longitudinal strain separately for basal, mid-ventricular, and apical levels. The detailed information can be derived from the corresponding Table 3 and complete descriptions of the revised "Relationship between regional myocardial strain and transmurality of myocardial infarction" section. From the results, we can deduce this conclusion. We hope that the response can address problem that your posed; if not, please do not hesitate to contact us with additional questions or concerns.

Changes in the text: As for this comment, we have not made required revisions.

10. Page 14, "global strain parameters in the basal section of the LV", which global strain, GLS? GCS? GRS?

Reply 10: Thank you for raising this issue. Considering your comments, we have revised the description as "global strain parameters (GRS and GCS) in the basal section of the LV" (see Page 12, line 238).

Changes in the text: We have revised the description as "global strain parameters (GRS and GCS) in the basal section of the LV".

11. "The results indicated that infarct severity in the apical and mid-ventricular sections significantly affected cardiac function", it is hard to deduce this conclusion. How many transmurality and nontransmurality segments in the 3 levels respectively?

Reply 11: Thank you for your kindest comments. According to the AHA segment model, segments 1-6 are basal, 7-12 mid-ventricular and 13-16 apical. We have already shown the number of non-infarcted segments, non-transmural infarcted segments, and transmural infarcted segments in the 3 levels for the 136 patients in Table 3. For instance, at the apical level, the number of non-infarcted segments, non-transmural infarcted segments, and transmural infarcted segments were 148, 281, and 115, respectively.

Changes in the text: As for this comment, we have not made required revisions.

12. Page 16, "we found that segmental longitudinal strain was significantly decreased in the transmural infarcted segments only at the apical and mid-ventricular levels", I cannot agree with this conclusion. How many transmural segments in basal level, midventricular level and apex level?

Reply 12: Thank you for your kindest comments. As the responses for the above comments #6-#9, we deduce this conclusion by referring to Table 3. Additionally, the number of transmural segments in basal level, midventricular level and apex level were 89, 144, and 115 respectively, which were already shown in Table 3. We hope that the response can address problem that your posed; if not, please do not hesitate to contact us with additional questions or concerns.

Changes in the text: As for this comment, we have not made required revisions.

13. Table 5, how to choose these variables? GLS, GCS and GRS have interaction, how to resolve this issue in the multivariate Cox regression analysis?

Reply 13: Thank you for your professional questions. These variables in Table 5 were selected by a univariate analysis including the variables of demographic data, clinical variables, MI location. To make it clear, we added the results of univariate analysis in the revised Table 5. With regard to the interaction issue, we admitted that theoretically, GLS, GCS and GRS have interaction. However, previous published articles [1] usually included these 3 global strain parameters in the multivariate analysis. Thus, GLS, GCS and GRS were included in the stepwise multivariate Cox regression analysis in our study. Please do not hesitate to contact us with additional questions or concerns.

Reference cited in the response:

Backhaus SJ, Kowallick JT, Stiermaier T, et al. Atrioventricular mechanical coupling and major adverse cardiac events in female patients following acute ST elevation myocardial infarction. Int J Cardiol. 2020;299:31-36.

Changes in the text: Revised Table 5.

Reviewer C:

"Impact of Apical and Mid-Ventricular Transmural 1 Infarcts in Patients with Acute Myocardial Infarction Determined by Using Merged Late Gadolinium Enhancement and Feature Tracking Magnetic Resonance" is an interesting single-center study conducted by Junchao Li, MS et als. However, during your reading some minor comments emerge that I indicate below.

1. In line 68 it is indicated "Myocardial strain is a measure of myocardial deformation and represents a load-dependent estimation of cardiac function", when it is exactly the opposite. The study of myocardial deformity does not depend on the load conditions of the left ventricle, as if it occurs with other more classical methods of determining ventricular function such as volumetric methods. This aspect must be clarified.

Reply 1: Thank you for your professional comments and suggestions, which are helpful for improving the quality of our manuscript. Considering your comments, we have revised the corresponding sentence as follows "Myocardial strain is a measure of myocardial deformation and can represent cardiac function" (see Page 4, line 63)..

Changes in the text: The sentence has been revised as "Myocardial strain is a measure of myocardial deformation and can represent cardiac function".

2. In line 176 in the follow-up, it seems to be understood that the collection of cardiovascular events was left in the hands of the patients' relatives? I believe that this aspect should be clarified and indicated if the events recorded in the medical records were supervised by healthcare personnel, who seem a priori better trained to identify this one.

Reply 2: We thank the reviewer for the thoughtful review and comments on our study. We are sorry for the inappropriate descriptions. Considering your comments, we have revised this aspect as follows: "Information on the outcome was obtained and confirmed using medical record files uploaded by the patients or their family members. The events recorded in the medical records were supervised by healthcare personnel." (see Page 9, line 160). Thank you again.

Changes in the text: The descriptions were modified as follows: "Information on the outcome was obtained and confirmed using medical record files uploaded by the patients or their family members. The events recorded in the medical records were supervised by healthcare personnel.".

3. Line 197. It should be indicated in Spearman's r and according to its value how the correlation strength between variables was considered, similar to how it was done with the ICC and with Cronbach's alpha coefficient (excellent, reasonable, weak, etc.)

Reply 3: We acknowledge your comments and suggestions very much, which are valuable in improving the quality of our manuscript. The correlation was interpreted as negligible (r <0.10), weak (0.10-0.39), moderate (0.40-0.69), strong (0.70-0.89), or very strong (r ≥0.90). We also cited a reference. In the revised manuscript, we added the corresponding descriptions (see Page 10, line 182). The cited reference:

Schober P, Boer C, Schwarte LA. Correlation Coefficients: Appropriate Use and Interpretation. Anesthesia and analgesia 2018;126:1763-8.

Changes in the text: We added the descriptions as follows: "The correlation was interpreted as negligible (r <0.10), weak (0.10-0.39), moderate (0.40-0.69), strong (0.70-0.89), or very strong (r ≥0.90) (19).".

4. Lines 215 to 217 "As shown in Table 2, the ICCs for inter-observer and intra-observer agreement were 0.899 and 0.912 for radial strain, 0.854 and 0.910 for circumferential strain, and 0.742 and 0.761 for longitudinal strain". The sentence could be simplified because the data already appears in the corresponding table.

Reply 4: Thank you for raising this issue. The corresponding sentence was simplified in the revised manuscript (see Page 10, line 199).

Changes in the text: The sentence was revised as "As shown in Table 2, longitudinal strain, radial strain, and circumferential strain analysis showed good or excellent intraobserver and interobserver agreement (ICC>0.74).".

5. Lines 266 to 269 A table with demographic data, clinical variables, MI location, etc. is necessary to know what differences exist in the univariate analysis according to whether or not patients present an adverse cardiovascular event and to put it in supplementary material.

Reply 5: Thank you for your professional comments and suggestions. To make it clear, we added the results of univariate analysis in the revised Table 5.

Changes in the text: Revised Table 5.

6. Line 319: this interesting reference (25) does not mention postoperative patients and should indicate that GLS determined by speckle tracking echocardiography predicts events after STEMI treated with PPCI.

Reply 6: Thank you for raising this issue. We are sorry for citing inappropriate reference. In the revised text, we have removed the original reference (25) (see Page 14, line 289).

Changes in the text: In the revised text, we have removed the original reference (25).

7. Line 335 Something related to the no-reflow of the PPCI in STEMI should be commented here.

Reply 7: Thank you for your professional comments and suggestions. We added the description "Myocardial no-reflow may be more likely to occur in the distal segment" after the sentence "Therefore, the repair of the infarcted tissue in the apical segment is inferior to that of the infarcted

tissue in the basal segment." (see Page 15, line 306).

Changes in the text: We added the description "Myocardial no-reflow may be more likely to occur in the distal segment (29)".

8. Could the authors explain why the distribution of men and women is so different?

Reply 8: Thank you for your professional questions. Cardiovascular disease develops 7 to 10 years later in women than in men. In women aged more than 60, the coronary artery disease rate elevated and exceeded the level of CAD risk reported in men. The mean age of our study population was 55.9±11.6 years old. At this age, the prevalence of myocardial infarction is higher in men than in women.

Changes in the text: As for this comment, we have not made required revisions.

9. Table 3 indicates "All variables of non-normally or normally distributed in this table are described as mean ± standard deviation (SD)". Variables that do not follow a normal distribution should be indicated as median and IQR.

Reply 9: Thank you for your kindest suggestions. According to your comments, we made necessary changes. All variables of non-normally or normally distributed in the table 3 are described as median (interquartile range, IQR) or mean ± standard deviation (SD). The corresponding descriptions in the "Statistical analysis" were modified as follows: "Shapiro-Wilk test was applied to assess data normality. Results are expressed as mean ± standard deviation (SD) or median (interquartile range, IQR)." (see Page 9, line 165). In addition, we removed "Supplementary material: P value calculated by Shapiro-Wilk test for data normality".

Changes in the text: The descriptions in the "Statistical analysis" were modified as follows: "Shapiro-Wilk test was applied to assess data normality. Results are expressed as mean ± standard deviation (SD) or median (interquartile range, IQR)."

10. I think Table 3 of the supplementary material could be removed "Supplementary material: P value calculated by Shapiro-Wilk test for data normality".

Reply 10: Thank you for your kindest suggestions. We have removed the supplementary material in the revised manuscript.

Changes in the text: We have removed the supplementary material.

Reviewer D:

It is a well-written manuscript. The study design and data analysis are also appropriate. I would suggest adding two images showing strain calculation in nontransmural and transmural infarcts. A bull eye plot with strain curves will be useful especially for the readers who have not seen those images.

Reply 1: Thank you for your professional comments and suggestions. According to your suggestions, we have added a bull eye plot with strain curves as a new Figure 2.

Changes in the text: Revised Figure 2.