Author’s response to reviews

Title: Rotation and torsion of the left ventricle with cardiovascular magnetic resonance tagging: comparison of two analysis methods

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Author’s response to reviews:

Reviewer #1 comments:

Comment: Small sample size is a major limitation of the study and should be addressed in a limitations section before the conclusions.

Response: We agree the reviewer that the sample size is unfortunately quite small to make definite conclusions. We have now revised our manuscript and better described the limitations of our study.

Comment: Data (esp rotation and torsion values) are probably not normally distributed so the choice of Kruskal Wallis test is appropriate. However, in the same manner, correlations should be calculated according to Spearman and not Pearson as noted.

Response: Thank you for this comment. We have revised our manuscript and calculated the correlations according to Spearman. The initial use of Pearson correlation was based on the sample size N=36, however, it is true that the data is not normally distributed.
Comment: What are the equations (Y = a + bX) of the linear regressions depicted in Figure 4 of the manuscript? Even with a small sample size, knowing the slope and coefficient of the equation could prove useful for future work or when comparing values between the two software.

Response: This is a good note, we have added the slopes of the equations in Figure 4 to our revision.

Comment: Define abbreviations in abstract, e.g. HPF

Response: We have revised our abstract accordingly.

Comment: The manuscript reads contains several grammatical errors. It should be thoroughly revised by a native English speaker.

Response: The revision has been reviewed by a native English speaker.

Comment: Is this the first study comparing CMR rotation/torsion data between the HPF and Segment software? If no, results should be compared to previous studies; if yes it should be stated in the discussion for the readers to know.

Response: This is the first study comparing CMR derived rotation and torsion data between the two software, we have elaborated on this in the discussion section.

Comment: Do the authors have some more demographics to show in Table 1? Also, was global longitudinal strain (GLS-LV) also measured in the population?

Response: We have added additional demographics to Table1. Unfortunately, strain was not measured in the present study.

Reviewer #2 comments:

Comment: The study has a number of important limitations. Firstly, the only report the peak systolic values for torsion and rotation rather than values through the cardiac cycle. Second, the sample size is very small. Third, the case definition of HCM is not given and it is not clear of HCM phenocopies were included (which would explain the lower LVEF in the HCM group) and the exact mutations identified in the mutation positive phenotype negative group are not identified. Fourth, the lack of matching for sex, age, BSA between controls and 2 patients groups is problematic because age and BSA may affect strain, torsion and rotation. Fifth, presence of comorbidity is not mentioned: the proportion of participants with hypertension,
dyslipidaemia, diabetes, smoking, etc in each group is important as all of these can affect the
parameters being compared.

Response: These are good points given by the reviewer. We have included only end-systolic
values as numerical data, but our Figures 1-3 show the entire systolic pattern. We have not
separately included numerical values throughout systole for the small additional value they
would bring. We have described our patient population in more detail in the methods section to
elaborate the nature of our study population. The study population involves HCM patients
carrying the Finnish founder mutation in the MYBPC gene (MYBPC3-Q1061X), the HCM
phenotype was based on the measurement of maximal left-ventricle wall thickness: &gt;13mm,
HCM and &lt;13mm, mutation carrier. We also have added more demographic information to
Table 1 and revised our discussion section to explain our study limitations more
comprehensively. Although we have employed a heterogenous study sample, we have analyzed
the data in the same way with both software. The main purpose of our study was to compare the
results between two analysis software. The message we want to express is that these post-
processing software yield very different results from each other, and that software-specific
references are a requirement for comparing absolute values of rotation and torsion.

Comment: In Table 1 and Table 2, it is not clear which comparison the p value is referring two as
there are three columns. Did the authors performs post-hoc Bonferroni correction and were
multiple comparisons undertaken at the same time?

Response: The comparisons in Tables 1 and 2 were done in all the groups at the same time.
Independent samples Kruskal-Wallis test is a non-parametric method for testing whether samples
originate from the same distribution. Similar approach was used in a previous study, which we
added as reference #8 (Tarkiainen et al. 2016). Bonferroni correction was not used in this study
as no pairwise comparisons (multiple tests) were made.

Comment: The average LVEF of 62% in HCM is unusual, as patients with HCM typically have a
high-normal or supranormal systolic function

Response: This is true. There were two patients in our HCM group who had EF &lt; 50%. As the
sample size is small, the decreasing effect on the group average is significant. Excluding the two
patients, the EF of the rest of the patients ranged from 61% to 70%.

Comment: Figures 1, 2 and 3 would have been aided by the presence of a p value on each graph

Response: We are not certain what the reviewer means by a p value on each curve as they show
many different time points throughout systole.
Comment: I am not certain how informative the Spearman correlations in Figure 4, as they are of two covariates measuring exactly the same phenomenon. What would have been more useful for me is a Bland-Altman analysis.

Response: We have used Spearman correlation to elaborate the fact that although the absolute values of rotation and torsion were significantly different between the two software packages, they are highly correlated to one another. We have also added a Bland-Altman analysis of both software to elaborate intraobserver variability.

Comment: It also would been helpful to have a clear statement on whether the readers of the CMR data were blinded to the diagnosis of the cases they were analysing.

Response: Readers were not blinded. We have added a statement on this in our revision.

Comment: What is the inter-user and intra-user variability of each of these analytic platforms?

Response: We have commented on this in the discussion section of our revision and added a Bland-Altman analysis of intraobserver variability with both software.

Editor comments:

Comment: In your submission, please clearly list all relevant limitations and elaborate on these in the discussion section.

Response: We have revised our manuscript and elaborated on our limitations in the discussion section.

Comment: In your data availability statement, you refer to all data being included in the article. Please note that the patient data that was utilized does not appear to have been added. Please consider depositing the data in a repository (more info here: https://www.springernature.com/gp/authors/research-data-policy/repositories/12327124) or clarify how readers can gain access to the analysed data.

Response: We have revised our data availability statement.