Author's response to reviews

Title: Use of a highly-sensitive cardiac troponin I assay in a screening population for hypertrophic cardiomyopathy: a case-referent study

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Author's response to reviews: see over
Dear Sir or Madam,

Many thanks indeed for considering our manuscript for publication in BMC Cardiovascular Diseases and for your Reviewers’ very helpful comments. We have addressed these queries, and attach below a response to each one. We also attach an updated and revised manuscript for your attention.

We trust that this manuscript is now acceptable to BMC Cardiovascular Diseases

Yours sincerely

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Dr Catherine McGorrian, for the authors
Responses to Reviewer's report 1: Dr Gagliardi

Comment 1:
The article is interesting. However, there is some discrepancy between the results and the conclusion presented. Authors state that non significant increases in IDI and ROC were noted when the hsTnI assay was added to a clinic-based regression model to predict the finding of an abnormal echo consistent with a clinical diagnosis of borderline or definite HCM. But in conclusions affirm that hs-TnI may have better discrimination for HCM than the standard assay and that may add to ECG- and symptom-based prediction of HCM. The ROC curve categorization provides a moderate contribution. However it is not statistically different from the contribution of cTnI.

Response 1:
Thank you for this comment. Whilst the trend of the AUROC was greater for the hsTnI assay's discrimination, we agree that this did not achieve statistical significance. The key summary statements in the abstract, the first paragraph of the discussion, and the conclusion have all been amended to reflect this.

Discussion, Key findings, Page 9:
“While improvements in IDI and AUROC were noted when the hsTnI assay measure was added to a clinic-based regression model to predict the finding of an echo finding consistent with a clinical diagnosis of borderline or definite HCM, these improvements were not statistically significant.”

Conclusions, Page 11:
“This is the first study to examine a new hsTnI assay in persons at risk of HCM. Both cTnI and hsTnI are shown to have a graded, positive association with measures of muscle mass in persons with and at risk of HCM. There was a non-significant increase in AUROC with the addition of hsTnI to the clinic “screening” model. The cTnI and new hsTnI assay may add to ECG- and symptom-based identification of HCM in at-risk families, although further larger scale studies will be required to evaluate this.”
Responses to Reviewer’s report 2: Dr Donato

Comment 1.
The study is interesting and original. I make the following comments to assist the authors to hopefully a very strong work ... The authors evaluated the diastolic function through the transmitral doppler (E/A ratio). It would be helpful if the IVRT is measured in these patients and correlate it with the Tn assays ... It is known that strain rate imaging has been shown to be useful in differentiating nonobstructive HCM from hypertensive LV hypertrophy. However, tissue Doppler–derived strain imaging has technical limitations due to its angle dependence. Speckle-tracking echocardiography directly assesses myocardial motion from B-mode (2D) images and is independent of angulation between the ultrasound beam and the plane of motion. The authors should be considered used this technique.

Response 1.
Thank you for these comments. The comment regarding optimal measures of diastolic function, and in particular regarding Speckle tracking, are very useful. Unfortunately, the IVRT measures were not made during this study, and speckle tracing was not available on our echo system. We can however scope the inclusion of these measures in future recruitment and data collection, so this proposal is very valuable to our work. An acknowledgement of the limitations of the echo data included has now been added to the “Strengths and limitations” paragraph.

Discussion, page 10:
“Tissue and pulsed Doppler measures of diastolic dysfunction were used in this study, and were seen not to have a consistent relationship with cTnl or hsTnl. Use of a robust measure such as speckle-tracking echocardiography should however be considered for future studies.”

Comment 2:
Supplementary table 1: In the title the word “between” appears twice.

Response 2:
Thank you, this has been amended.