

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form ([see an example](#)) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

This paper was submitted to the Heart but declined for publication following peer review. The authors revised the paper and re-submitted to BMJ Open where it was re-reviewed and then accepted.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Two Dimensional Strain Profiles in Patients with Physiologic and Pathologic Hypertrophy and Preserved Left Ventricular Systolic Function: A Comparative Analysis
AUTHORS	Afonso, Luis ; Kondur, Ashok; Mengistu, Simegn; Niraj, Ashutosh; Hari, Pawan; Kaur, Ramanjit; Ramappa, Preeti; Pradhan, Jyoti; Bhandare, Deepti; Williams, Kim; Zalawadiya, Sandip; Pinheiro, Aurelio; Abraham, Theodore

VERSION 1 - REVIEW

REVIEWER	Ommen, Steve Mayo Clini0063
REVIEW RETURNED	20-Apr-2012

GENERAL COMMENTS	<p>heartjnl-2012-302116</p> <p>The manuscript by Afonso et al., describes echocardiographic variables among patients with LVH from hypertrophic cardiomyopathy, hypertension, or athletic training. From this study group of 129 patients, the authors found that several parameters (wall thickness, E', thickness dispersion, and strain) provided variable degrees of discrimination between the underlying etiologies. The authors concluded that longitudinal strain measures provided the best accuracy and, with confirmation from larger series, could readily implemented into clinical practice.</p> <p>Specific comments:</p> <ol style="list-style-type: none">1. Calculated LV mass and LV mass index are known to be inaccurate in HCM patients and this variable does not seem to add to this work.2. The strain dispersion index requires a more thorough definition. Is this some average of SD?3. Relative wall thickness has been previously utilized to help distinguish HCM from athletes. Inclusion of this variable would seem important in this sort of analysis.4. From the tabular data regarding distinction of HCM from athletes, it appears that septal thickness, with a perfect AUC=1, E', and ThDI all have better AUC than GLS. This should be discussed. Scatter plots and the ROC curves for each of these would provide the readers with more insight.
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	5. With respect to GLS, the scatter plot provided does show the difficulty, particularly when GLS is not at the extremes of the range observed in these subjects.
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REVIEWER	Spirito, Paolo Ospedali Galliera, Divisione di Cardiologia
REVIEW RETURNED	12-Apr-2012

GENERAL COMMENTS	<p>The authors have investigated the potential of 2-dimensional strain imaging to differentiate LV hypertrophy associated with hypertrophic cardiomyopathy, from that associated with systemic arterial hypertension or intense athletic training. The results are of interest and indicate that this new imaging technique can identify distinct functional differences amongst these forms of LV hypertrophy.</p> <p>I do not have major comments or suggestions. However, the authors should make it clear that their results identify differences amongst groups, not individual patients.</p>
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- The manuscript received a third review at JNNP but the reviewer did not give permission for their comments to be published

VERSION 1 – AUTHOR RESPONSE

Reviewer Comments:

Reviewer: 1

Comments to the Author

The authors have investigated the potential of 2-dimensional strain imaging to differentiate LV hypertrophy associated with hypertrophic cardiomyopathy, from that associated with systemic arterial hypertension or intense athletic training. The results are of interest and indicate that this new imaging technique can identify distinct functional differences amongst these forms of LV hypertrophy.

I do not have major comments or suggestions. However, the authors should make it clear that their results identify differences amongst groups, not individual patients.

We have strived to make this point clear in the opening paragraphs of the discussion

> Reviewer: 2

> Comments to the Author

> heartjnl-2012-302116

> The manuscript by Afonso et al., describes echocardiographic variables among patients with LVH from hypertrophic cardiomyopathy, hypertension, or athletic training. From this study group of 129 patients, the authors found that several parameters (wall thickness, E', thickness dispersion, and

strain) provided variable degrees of discrimination between the underlying etiologies. The authors concluded that longitudinal strain measures provided the best accuracy and, with confirmation from larger series, could readily be implemented into clinical practice.

Specific comments:

1. Calculated LV mass and LV mass index are known to be inaccurate in HCM patients and this variable does not seem to add to this work.

We concur with this comment and for this reason did not provide details of LV mass assessments in the original submission, explaining why these would be inaccurate. In the revised manuscript, we elected to delete any reference to LV mass altogether.

2. The strain dispersion index requires a more thorough definition. Is this some average of SD?

We have clarified the definition in the revised submission, the global strain dispersion index was calculated by averaging the individual SD of mean segmental strains in the basal, mid and apical segments. (highlighted in Pg7)

> 3. Relative wall thickness has been previously utilized to help distinguish HCM from athletes. Inclusion of this variable would seem important in this sort of analysis.

As suggested, relative wall thickness data has been incorporated into Table 1, and methods (Page 5); while helpful to differentiate athletes from HCM a significant overlap between hypertensives and HCM patients is apparent.

4. From the tabular data regarding distinction of HCM from athletes, it appears that septal thickness, with a perfect AUC=1, E', and ThDI all have better AUC than GLS. This should be discussed. Scatter plots and the ROC curves for each of these would provide the readers with more insight.

We do agree with this reviewer's comment and as indicated, GLS may not have a role in distinguishing HCM from athletes, in this situation morphologic (Septal thickness/RWT) or Tissue Doppler derived parameters may often suffice. This point has been made in the discussion (page 16, para 2). ROC analysis data were tabulated and not presented as curves to allow presentation of larger number of variables (Table 3)

> 5. With respect to GLS, the scatter plot provided does show the difficulty, particularly when GLS is not at the extremes of the range observed in these subjects.

This is true, nonetheless, our cutoffs for GLS do appear to segregate the large majority of HCM patients without the need to evaluate strain or thickness dispersion; the latter was examined to explore the functional correlates of the disorganized architecture prevalent in the HCM phenotype but as one might imagine, it is labor and time-intensive and thus cannot be recommended for routine use.

We would like to acknowledge and thank all the reviewers for their time and insightful suggestions. The changes incorporated in the revision as a result of their input have considerably strengthened our manuscript and we remain deeply indebted to them.

VERSION 2 - REVIEW

REVIEWER	Aaron L. Baggish, MD Cardiovascular Performance Program Massachusetts General Hospital Boston, MA, USA I have no competing interests relevant to this manuscript.
REVIEW RETURNED	05-Jul-2012

GENERAL COMMENTS	The authors have addressed my inquires and should be commended on completion of a nice study and corollary manuscript.
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