Author’s response to reviews

Title: Exercise Stress Echocardiography in the treadmill - upright evaluation During and after Exercise. Clinical Applications

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Author’s response to reviews: see over
Cover Letter

Dear Editor

We want to thank the reviewers the care that they had, reading and making what we sincerely believe are sound and clear suggestions that permitted to improve the article.

We have made almost all the alterations suggested:

Reviewer's report
Title: Exercise Stress Echocardiography in the treadmill - upright evaluation During and after Exercise. Clinical Applications
Version: 1 Date: 25 April 2013
Reviewer: Albert Varga
Reviewer's report:
This is an interesting review article written by Cotrim and coworkers about the usefulness of exercise echocardiography in upright position in various pathologies. The Authors used mostly their own data to bolster their conclusions.
The final conclusion of the Authors was that treadmill exercise stress echocardiography, performed in upright position could be a valuable tool for the diagnosis of several different pathologies.

I have the following comments and questions:
1. My first and major concern is the tone of the whole article. The conclusions of the Authors are based mostly on studies performed by the same group, sometimes with limited patient numbers. Therefore, I suggest the Authors to tone down somewhat the assertiveness of the phraseology and instead of declarative sentences (for instances, page 11, line 12: “… suggest that this methodology should be applied to the athletes that have symptoms…”; or page 16, last sentence, etc), a bit more cautious interpretation of the data is needed.

We made alterations to make the paper less declarative and more cautious

2. The paper is too long and sometimes difficult to follow (especially the part about pulmonary hypertension). It would be good to reduce the description of the studies already published.

We significantly reduce the chapter of pulmonary hypertension as suggested

3. The explanations of the findings are sometimes very speculative (especially the part about the pathophysiology of the appearance of the intraventricular or
outflow tract gradients).

The explanations of the findings that we present have been made by other authors that are referenced. We refer particularly to Yotti R: Qué significado tiene un gradiente de presión intraventricular sistólico durante el ejercicio? Rev Esp Cardiol 2004:57: 1139-42.

4. I very appreciate the efforts made by the Authors in the development of a new stress echo protocol, but to include it in a daily practice a multicentric validation is needed. It would be good also to know how difficult the protocol is, how long it takes to obtain a complete exam, how long the learning curve is. Please, provide a chapter dealing with this problems and with the limitations of the methodology.

5. It would be good to conduct head to head studies to prove the superiority of the new method in different pathologies.

We have create a new chapter (Limitations of the methodology) before the conclusions where we try to answer to point 4 and 5.

6. I was not convinced why treadmill stress echocardiography performs better than supine (or semi-supine) bicycle echo in patients with ischemic heart disease. The conclusion of the paper by Peteiro (ref 22) was: “Peak treadmill EE provides significant incremental information over post-EE for predicting outcome in patients with known or suspected CAD”.

We have explained in the article the advantages of treadmill (more heart rate and more VO2 so possibly more probability of inducing ischemia) however we accept that Dr Vargas is not convinced.

7. The chapter about aortic stenosis. On page 16, line 8, the Authors “disagree” with the current recommendations… I suggest the Authors to delete this statement and rephrase the whole part in a more cautious way.

We rephrase the whole part in a more cautious way.

8. The Authors proposed a new test for the evaluation of patients with symptomatic aortic stenosis, which is not in accordance with the current guidelines. Again, I suggest the Authors to be more cautious with the recommendations, since the experiences obtained are based on a limited patient population and case reports.

We rephrase the this part in a more cautious way.
9. I cannot accept the term: false symptomatic aortic stenosis.

**We excluded the term, as imposed by Dr Vargas however I truly believe that in the near future Picano or Lancelotti or other expert in aortic stenosis will use the term and it will be accepted**

10. The part about prosthetic valves is based on a case report and on an unpublished paper, therefore it should be excluded from the present manuscript.
**We eliminated this chapter as suggested**

11. The same problem with the congenital heart disease section.
**We eliminated this chapter as suggested**

12. The Authors suggest, that in patients with LBBB dobutamine echocardiography should be used instead of exercise stress echo. As a reference an abstract was given. Please, give an explanation and a stronger proof.

**We joined two new references about this issue**

13. There are many grammatical and typographical errors throughout the manuscript.

**We ask an expert in English to review the article**

**Reviewer:** Alberto Bouzas-Mosquera

**Reviewer's report:**
Cotrim and colleagues provide a comprehensive review of the methodology and applications of imaging acquisition during exercise in treadmill exercise echocardiography, not only for evaluation of myocardial ischemia but also for other indications beyond detection of coronary artery disease. The manuscript is well written and the subject is relevant. Nonetheless, some issues deserve comment.

**Major Compulsory Revisions**
- The authors claim in the abstract that “we use an original methodology, firstly published by us in 2000”. Then in page 4, lines 4-5, they state: “In 2001 we published this method [7] and most recently other groups also published the same methodology [8,9]”. Reference 7 refers to a paper published by Cotrim and colleagues in 2000. Reference 8 cites a paper by Peteiro et al published in 2010. Notwithstanding the unquestionable merit of Cotrim et al, it should be noted that Peteiro et al had already described echocardiographic imaging acquisition during exercise on treadmill in a paper published in 1999 (J Am Soc Echocardiography 1999;12:1073-9).
We correct the historical error and we make clear in the article that the first group that makes acquisition at peak exercise was the group of Peteiro. We introduce the reference presented by Dr Bouzas-Mosquera.

- Regarding the selection of the most appropriate stress echocardiography modality in patients with left bundle branch block (page 5), only an abstract published in 1993 is mentioned. Additional pertinent literature (e.g., Am J Cardiol.2000;85(7):890-3, Eur J Nucl Med Mol Imaging. 2006;33(12):1442-51) should also be taken into account.

We joined the two new references about this issue

Minor Essential Revisions
- Regarding the role of exercise echocardiography in patients with mitral stenosis, the authors report that 10 patients of their series were referred for valvuloplasty or valve replacement based on values of tricuspid regurgitation gradient obtained during exercise. The authors state that “These patients would have continued with medical therapy if the decision had been based on the values obtained during the recovery period”. Among other references they cite the European Society of Cardiology guidelines on valvular heart disease (reference 29, European Heart Journal 2012;33:2451-2496) for supporting the decision to refer patients with mitral stenosis for valvuloplasty or surgery if they develop a systolic pulmonary artery pressure >60 mmHg during exercise. Far from that, the ESC guidelines do not include any recommendations on exercise pulmonary artery pressure for guiding therapy in these patients.

We correct the reference error pointed by Dr Bouzas-Mosquera.

- Page 16: The authors state that “we routinely use exercise stress echocardiography in the evaluation of patients with asymptomatic aortic stenosis”. Do the authors mean all patients with “asymptomatic aortic stenosis” or just those with “asymptomatic severe aortic stenosis”?.

We make the text more clear as suggested

- There are a number of minor grammatical errors that should be carefully corrected.

We ask an expert in English to review the article

Discretionary Revisions

- When recommending aortic valve replacement if the aortic mean pressure gradient increases more than 20 mmHg (page 16), the authors might consider mentioning the degree of recommendation that current ESC guidelines have recently established for that indication.

We have mention the recommendation of ESC as suggested