Author's response to reviews

Title: Assessment of Left Ventricular Volumes and Primary Mitral Regurgitation Severity by 2D Echocardiography and Cardiovascular Magnetic Resonance.

Authors:

Caroline M Van de Heyning (carovdh@email.com)
Julien Magne (jul.magne@yahoo.fr)
Luc A Piérard (lpierard@chu.ulg.ac.be)
Pierre-Julien Bruyère (pj.bruyere@chu.ulg.ac.be)
Laurent Davin (ldavin@chu.ulg.ac.be)
Catherine De Maeyer (catherine.demaeyer@uza.be)
Bernard P Paelinck (bernard.paelinck@uza.be)
Christiaan J Vrints (chris.vrints@uza.be)
Patrizio Lancellotti (plancellotti@chu.ulg.ac.be)

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Author's response to reviews: see over
Dear Editor-in-Chief,

We are pleased to resubmit the enclosed manuscript entitled: “Assessment of left ventricular volumes and primary mitral regurgitation severity by 2D echocardiography and cardiovascular magnetic resonance” for possible publication in “Cardiovascular Ultrasound”.

We would like to thank the reviewers for their careful reading and comments. We believe the manuscript has been greatly improved after revision according to their suggestions. We will address the comments of the reviewers below.

Furthermore, we believe that this manuscript could merit publication priority because it provides more evidence for the implementation of cardiovascular magnetic resonance in the assessment of asymptomatic severe primary mitral regurgitation to improve clinical decision making.

We have no conflict of interest with regard to the content presented in this manuscript. We certify that each author has approved the final manuscript and we have taken great care to ensure the integrity of this work. Each author has generated a part of the intellectual content of the manuscript and agrees with all interpretations and conclusions. We also certify that this article is not under concurrent consideration by any other publication. In addition, none of the paper's contents have been previously published. We have no relationship with industry related to this paper.

We thank you in advance for your reconsideration of this manuscript and we look forward hearing from you.

Address for correspondence:
Professor Patrizio Lancellotti
Department of Cardiology
University Hospital Sart-Tilman
B-4000 Liège (BELGIUM)
Tel: + 32.4.366.71.94
Fax: + 32.4.366.71.95
E-mail: plancellotti@chu.ulg.ac.be
Reviewer’s Report 1

Comment 1. Have all patients CMR ? Sometimes patients are claustrophobic.

Authors’ reply: As stated in the section ‘Methods’ we excluded patients in whom CMR was contra-indicated (CMR incompatible devices), but indeed, we did neither schedule patients with severe claustrophobia for CMR. We added ‘claustrophobia’ as an exclusion criterion in the section ‘Methods’. All patients who were scheduled for CMR, underwent CMR.

Comment 2. Do you have problems with image quality?

Authors’ reply: Initially 41 patients who met clinical and echocardiographic criteria for inclusion were scheduled for CMR. 3 patients had limited image quality on CMR and were excluded from further analysis. In the first version of this manuscript we only used the data of the remaining 38 patients. We agree that this information must be included in the ‘Methods’ and ‘Results’ section. The manuscript has been revised accordingly.

Comment 3. The authors should present distribution of eccentric jets and how this was handled with the PISA method.

Authors’ reply: 19 out of 38 patients (50%) had eccentric jets, mostly due to P2 prolapse. ERO and regurgitant volume were obtainable by the PISA method in all of the patients with an eccentric jet included in the present study. Measurements were performed in line of current EACVI recommendations (Lancellotti et al. Recommendations for the echocardiographic assessment of native valvular regurgitation. Eur Heart J Cardiovasc Imaging 2013). The PISA radius was measured at mid-systole using the first aliasing with a reduced Nyquist limit (15-40 m/s). In figure 2 we have provided an example of a patient with an eccentric jet with illustration of the PISA method. However, we recognise that the PISA method may be challenging in some patients with eccentric jets, we therefore presented the distribution of eccentric jets in table 1 in the revised manuscript.

Comment 4. Could you perform the ARO measurements by CMR in all patients?

Authors’ reply: As described in the section ‘Methods’ ARO was measured in 21 patients of the study group, dependent on whether the CMR operator had acquired the adequate slice parallel to the valvular plane. These images were not acquired in the first patients from CHU Sart Tilman Liège and the patients from University of Antwerp Hospital because we only decided to measure the ARO after the study had already been started. We did not mention the only patient in whom the appropriate slice was obtained but in whom measurement of ARO failed. We agree that this information must be included in the ‘Methods’ and ‘Results’ section. The manuscript has been revised accordingly.

Comment 5. At which time points the measurements of TTE and CMR were performed?

Authors’ reply: All enrolled patients underwent CMR within a period of 1 month after 2DTTE, in 2 patients CMR followed 2DTTE within 2 months but follow-up 2DTTE confirmed stable LV dimensions in these patients. The fact that 2DTTE and CMR were not performed on the same date in most patients might influence the measurement of load-dependent parameters, in particular end-diastolic dimensions and regurgitant volume. However, we did not include patients with clinical or echocardiographic signs of heart failure
and there were no patients with acute onset of symptoms during the study period. Furthermore, underestimation of LV volumes on 2DTTE was also seen in patients in whom both exams were performed on the same date. We added this limitation of the study in the ‘Discussion’ section.

Comment 6. In Table 2, the authors should present LV end-systolic diameter and LV end-systolic volume.

Authors’ reply: We agree that the end-systolic parameters must also be presented, so we analysed the end-systolic diameters and end-systolic volumes measured by 2D TTE and CMR. In the revised manuscript, these data are presented in Table 2 as well as in Figure 3. Overall, the results are in line with the findings concerning end-diastolic diameters and end-diastolic volumes. There was a good agreement between 2D TTE and CMR regarding the LV end-systolic diameter. In contrast there was general overestimation of the end-systolic volume by 2D TTE in comparison with CMR although there was a good correlation of the end-systolic volume by both imaging methods. In the revised ‘Discussion’ section, both end-diastolic and end-systolic LV volumes were discussed together, rather than emphasizing the end-diastolic LV volume.

Comment 7. The measurement of the regurgitation volume by PISA is very high with 69±38 which underline the PISA problematic regarding volumes. In routine 2D echocardiography you measure often high values which are not plausibly.

Authors’ reply: As mentioned in the authors’ reply of Comment 3, 50% of our patients had eccentric jets, which sometimes are difficult to assess and overestimation of the PISA radius may occur. However, these high values for the regurgitant volume are in line with ERO and ARO in our population of patients with moderate to very severe MR. As our study shows, RVol measured by PISA method and by CMR are not necessarily interchangeable.
Reviewer’s Report 2

Comment 1. The authors do not provide any data on the end systolic diameters or end systolic volumes for either echo or CMR, yet these values are more important and relevant compared to the end diastolic values when deciding on the timing of mitral valve surgery or reverse LV remodelling following surgery. This is also particularly relevant as the authors have reported a difference in the mitral regurgitant volume between CMR and echo, and the LVESV is used in the calculation of the regurgitant volume in CMR. I would suggest that the authors include both these parameters in their analysis and provide a comparison of LVESD and LVESV values between echo and CMR as they have done for LVEDD and LVEDV.

Authors’ reply (idem as comment 6, reviewer 1): We agree that the end-systolic parameters must also be presented, so we analysed the end-systolic diameters and end-systolic volumes measured by 2D TTE and CMR. In the revised manuscript, these data are presented in Table 2, as well as in Figure 3. Overall, the results are in line with the findings concerning end-diastolic diameters and end-diastolic volumes. There was a good agreement of the linear end-systolic dimension. In contrast there was general overestimation of the end-systolic volume by 2D TTE in comparison with CMR although there was a good correlation of the measurement of the end-systolic volume by both imaging methods. In the revised ‘Discussion’ section, both end-diastolic and end-systolic LV volumes were discussed together, rather than emphasizing the end-diastolic LV volume.

Comment 2. I would suggest that the title be more appropriately changed to “Assessment of LV volumes…” in place of “Assessment of LV dimensions…” as CMR is the gold standard in LV volume assessment rather than LV dimensions, and the authors also make no reference to LV dimensions in their abstract or conclusions but instead refer to LV volumes.

Authors’ reply: We agree on this matter with the reviewer and changed the title accordingly.