Reviewer's report

**Title:** Left Atrial Volume Predicts Adverse Cardiac and Cerebrovascular Events in Patients with Hypertrophic Cardiomyopathy

**Version:** 1  **Date:** 7 October 2011

**Reviewer:** Denisa Muraru

**Reviewer's report:**

Major Compulsory Revisions:

In this paper, the Authors followed 102 patients with non-obstructive hypertrophic cardiomyopathy (HCM) for a mean period of 31 months and found that left atrial (LA) volume at baseline, unlike LA antero-posterior diameter, predicts the risk of adverse cardio- and cerebrovascular events during follow-up.

The novelty of the main study findings is questionable, since the prognostic value of indexed LA volume in patients with HCM has been previously documented in several studies (Losi - J Am Soc Echocardiogr 2009, Yang - J Am Soc Echocardiogr 2009, Moon - Am J Cardiol 2011 etc) and the superiority of LA volume measurement over LA diameter is widely accepted.

In addition, in its current format, the paper has several important limitations that deserve attention (besides the ones acknowledged by the Authors in the dedicated paragraph):

1. It is unclear to me the reason why the Authors have used the apical 4-chamber and long-axis view to compute biplane LA volume, instead of the apical 4- and 2-chamber (as commonly performed in LA studies and recommended by the guidelines - Lang et al - Eur J Echocardiogr 2006)

2. The way mitral regurgitation severity was assessed (i.e. jet area/LA area) is criticable and no longer recommended (Lancellotti et al - Eur J Echocardiogr 2010), representing a limitation particularly in HCM patients, in which mitral regurgitant jets are often eccentric

3. Why LVOT obstruction was an exclusion criteria? However, LVOT obstruction was not mentioned among the exclusion criteria at enrolment, but suddenly stated in the Results section. The definition of obstruction and whether latent dynamic obstruction was ruled out should be also specified.

4. The way data on PAF incidence was collected is quite questionable (especially under treatment with beta-blockers and calcium antagonists). In addition, it is ambiguous whether episodes of paroxysmal atrial fibrillation (PAF) were collected retrospectively (presumably and as stated in the paper published by the Authors in 2004 in JASE, that had a similar enrolment period) or prospectively. In case the former was accurate, specifying how many patients have developed PAF during follow-up would add value to the study findings, especially since 75% of MACCE were strokes.
5. Please clarify how major events were exactly defined (i.e. for heart failure: hospitalizations, self-reported worsened dyspnea etc).

6. Multivariate Cox model and Kaplan-Meyer analysis are missing from the Statistical methods description. Which parameters were actually included in the Cox regression model should be mentioned.

7. It is surprising that hypertrophy severity was not associated with a higher risk of MACCE. Since the pattern of hypertrophy was highly variable and 1 out of 5 patients had apical HCM, I believe that comparing the groups using only the septal wall thickness (Table 2) is insufficient and possibly misleading. The severity of hypertrophy should have been also assessed as maximal wall thickness, irrespective of localization (Nagueh et al. J Am Soc Echocardiogr 2011, 24:473-98) or by using quantitative scores that account for its extent on LV overall (Wigel, Spirito-Maron etc)

Minor Essential Revisions:
1. The abstract should be rephrased to reflect the study Methods and Results accurately
2. “Normal LV systolic function” to be replaced with “normal EF/pump function” throughout the manuscript, since it is well documented that patients with HCM have a reduced LV longitudinal systolic function despite a preserved overall EF.
3. The cut-off used for normality of EF should be mentioned.
4. How many operators performed the echo studies?
5. Redundant statements (follow-up duration, final patient population etc) in Methods and Results sections should be removed
6. LV volumes instead of diameters should be comparatively presented in Table 2
7. Abbreviations are used inconsistently throughout the manuscript
8. Last sentence in the Conclusion is not sound and should be removed/rephrased

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests