

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: Hypertrophic cardiomyopathy in 2013 Revision R1).

Title: Hypertrophic Cardiomyopathy in 2013: Current Speculations and Future Perspectives

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Name of Journal: *World Journal of Cardiology*

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The manuscript has been improved according to the suggestions of reviewers and editors:
1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer 1:

(1) "However, I would suggest the authors to dedicate a couple of sections to the clinical relevance, diagnosis and management of two additional important issues in HCM 1) Myocardial ischemia and 2) atrial fibrillation. Myocardial ischemia is considered as part of the pathophysiology process in HCM, moreover there seems to be an interesting inter-relationship between ischemia and fibrosis. Management of ischemia is complex, often ungratifying, and in a minority of patients with intractable chest pain, orthotropic heart transplantation is the only option. Please see review article by Maron et al, The Case for Myocardial Ischemia in Hypertrophic Cardiomyopathy, JACC 2009. Atrial fibrillation is related to significant morbidity and probably mortality in HCM. Rate/rhythm control and anticoagulation in atrial fibrillation are important clinical topics that deserve discussion, especially since its management is controversial. Please see 2011 HCM guidelines in Circulation."

Two novel sections have been added to our review: one entitled "HCM and blunted myocardial perfusion" dealing with myocardial ischemia in HCM and a second entitled "atrial fibrillation" dealing with the controversies of risk stratification and management of AF in HCM.

(2) "Finally, the author should also discuss current and future management perspectives for patients with non-obstructive HCM (1/3 of patients)."

Based on your comment a paragraph has been added in the "Novel treatment potentials" section.

(3) "Page 5, second paragraph: Suggest the sentence should read as: "Preclinical diagnosis of HCM has many medical and social implications.""

The sentence has been corrected accordingly.

(4) "Page 8, first paragraph: Please describe incidence of complete heart block with both procedures; also address the fact that patients with LBBB and RBBB are more likely to develop complete heart block with surgery and alcohol septal ablation, respectively."

Incidence of complete heart block following both procedures has been incorporated in the revised text. Your comment about LBBB and RBBB and complete heart block after surgery and alcohol septal ablation has also been included: "However... septal ablation" first paragraph, page 9.

(5) "Page 10, first paragraph: NSVT is considered a risk factor for SCD, primarily in patients under the age of 30. Please see Monserrat et al. Non-Sustained Ventricular Tachycardia in Hypertrophic Cardiomyopathy: An Independent Marker of Sudden Death Risk in Young Patients. JACC 2003."

The sentence concerning NSVT has been modified according to your suggestion also citing the above mentioned reference: Page 10, second paragraph, last line

(6) "Page 10, second paragraph: The author describes "Extensive late gadolinium enhancement on MRI" as a potential risk-modifier or new risk factor in SCD. However, the authors should be acquainted or discuss as an issue of controversy that to date, there is no compelling published evidence that the extent is more important than just the presence of LGE for risk-prediction. Moreover, the 2011 current guidelines emphasize that is the presence and not the extent of LGE relates to adverse CV events. But again, this is an interesting, controversial topic, and it is my understanding that there is an ongoing multicenter trial with over 1000 HCM patients, which will show that the extent of LGE is also relevant, however this is unpublished data (Martin Maron, ACC 2013)."

Your comment about the extent of LGE has been incorporated in the revised version of our manuscript: "To date... ACC 2013" page 11, second paragraph.

(7) "Page 13: Please spell out "HMG-CoA reductase inhibitors""

It has been spelled out in the revised version

2 Revision has been made according to the suggestions of the reviewer 2:

(1) All suggested language corrections have been made while run on sentences have been simplified through out the text.

(2) Concerning pharmacological treatment of obstruction: "This information needs to be expanded or reorganized. What is the rationale of this treatment protocol? What are the outcomes, the strength and shortfalls, and the potential improvement based on research and clinical trials?"

Following your suggestion we have reorganized this chapter providing more information for pharmacological treatment: page 7, last paragraph

3 References and typesetting were corrected

4 Images 2 and 3 have been provided in an editable format

Thank you again for publishing our manuscript in the *World Journal of Cardiology*.

Sincerely yours,



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