Author's response to reviews

Title: Novel Association Patterns of Cardiac Remodeling Markers in Patients with Essential Hypertension and Atrial Fibrillation

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Editorial Board of the BMC Cardiovascular Disorders Journal

Manuscript title: Novel association patterns of cardiac remodeling markers in patients with essential hypertension and atrial fibrillation

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Dear Editorial Board,

On behalf of all the authors, I would like to ask you to consider our manuscript entitled “Novel association patterns of cardiac remodeling markers in patients with essential hypertension and atrial fibrillation” for publication in the BMC Cardiovascular Disorders Journal.

In the present study, we investigated the association of specific markers of the cardiac extracellular matrix remodeling, involving matrix metalloproteinases (MMPs) -2, -3, -9 and the tissue inhibitor of matrix metalloproteinases type-1
TIMP-1, with paroxysmal and permanent atrial fibrillation (AF). The authors, in an attempt to avoid as much confounding as possible, decided to enroll a specific population of patients with preserved cardiac function and a common cardiovascular disorder such as essential hypertension as the only factor responsible for triggering of AF. None of the patients had echocardiographic evidence of structural heart disease and study groups were matched for left ventricular mass index. Furthermore, all study participants were under constant anti-hypertensive treatment with angiotensin converting enzyme inhibitors or angiotensin receptor blockers for at least a year since the initial diagnosis of arterial hypertension and none had previous or ongoing treatment with aldosterone receptor antagonists.

We showed that AF, in individuals with essential hypertension, was associated with different patterns of these markers according to the type of the arrhythmia. In particular, when we compared AF patients to individuals with sinus rhythm (SR), matrix metalloproteinase-2 emerged as an acute reactant mediator that was up regulated in acute onset atrial fibrillation and in turn dropped off in patients with permanent AF. On the other hand, matrix metalloproteinase-9 demonstrated a totally inverse course, compared to MMP-2, by portraying a significant increase in patients with permanent AF, whereas remained roughly stable in those with paroxysmal atrial fibrillation. Regarding the tissue inhibitor of matrix metalloproteinases type-1 we demonstrated a gradual but significant decrease from sinus rhythm to paroxysmal and then to permanent atrial fibrillation and that lower levels of this marker were the only independent factor associated with atrial fibrillation incidence.

We believe that the findings of the submitted study are of great scientific importance and could attract the interest of the journal's readers, since they highlight a novel relation between extracellular matrix remodeling markers and the different phases of atrial fibrillation (paroxysmal and permanent). Furthermore, they may be of particular clinical interest as they suggest that in patients with hypertension, the measurement of the tissue inhibitor of matrix metalloproteinase type 1 could be utilized as a potent indicator for increased likelihood of AF incidence.

All authors have contributed significantly to this work and have seen and approved the submitted version of the manuscript.

The manuscript has not been previously published and is not under consideration for publication elsewhere. There is no conflict of interest for any of the participating authors.

Yours sincerely,

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