Reviewer's report

Title: ACE-Inhibition, but not weight reduction restores cardiomyocyte response to beta-adrenergic stimulation in the Metabolic Syndrome

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Reviewer: Constantinos Pantos

Reviewer's report:

The aim of this study was to investigate cardiomyocyte contractility and Ca2+ handling in a mouse model of metabolic syndrome and to study the effect of in vivo treatment with diet or ACE-I. The authors used a double knock out (DKO) mouse model using LDLR-/- and leptin-deficient ob/ob mice. This model resulted in diabetes type 2, obesity, dyslipidemia and hypertension. Cardiomyocytes from DKO showed impaired relaxation at baseline and reduced responsiveness to isoproterenol or increased Ca+2. Diet and ACE-I improved relaxation in DKO but only ACE-I improved responsiveness to isoproterenol. Calcium transient amplitude in DKO was significantly reduced and associated with slower kinetics, while diet reversed this response.

This is a well-written manuscript. The authors have considerable experience in the methodology used. The data provided give new insights about cardiomyopathy in metabolic syndrome.

Discretionary Revisions

1. It is not clear why the authors did not study Ca2+ handling in DKO mice with ACE-I treatment.

2. In the present manuscript, the authors did not investigate molecular changes (changes in calcium proteins or contractile proteins) in cardiac tissue in order to give more mechanistic insight. This issue should be added in limitations of the study

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare no competing interests