Reviewer’s report

Title: Low concentrations of serum testosterone predict acute myocardial infarction in men with type 2 diabetes mellitus

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Reviewer: Giovanni Corona

Reviewer’s report:

The authors investigated the associations between endogenous testosterone concentrations and the incidence of acute myocardial infarction (AMI) in men and women with and without type 2 diabetes. They found that low concentrations of testosterone predicted AMI in men with type 2 diabetes independent of other risk factors.

General comments
Overall the manuscript is well written but some important points should be addressed.

Abstract
The mean age of the patients enrolled as well as the immunometric nature of steroid method must be reported.

Introduction
This section must be improved. In particular it should be recognize the bidirectional relationship between low T and MetS as well as T2DM since both associated with reduced T but low T itself can predict the development of MetS and T2DM (Corona et al., J Sex Med 2010; Brand et al., PloS ONE 2014).

A correctly stated by the authors the contribution of T in the stratification of CV risk is conflicting. 3 independent meta-analyses have documented an association between low T and CV mortality but not CV morbidity (Araujo et al., JCEM 2011; Corona et al., Eur J Endocrinol 2011; Ruige et al., 2011). All these paper must be quoted and discussed.

Previous meta-analysis documented a positive outcome of TRT in subjects with type 2 diabetes (Corona et al., Best Pract Res Clin Endocrinol Metab. 2013). However, a more recent meta-analysis (Grossman et al., Clin Endocrinol 2015) reported no effect of TRT in patients with MetS or T2DM. These points must be recognized and discussed.

Results
Figure 1 is of poor quality and must be improved.
Table 3 is hard to follow and must be improved. In particular, I suggest to change the order putting the labels of men and women in the lines and the data deriving from the different adjusted models in the columns just labeling them as model 1-4. The confounding factors must be reported the table legend.

Discussion
A better analysis of the relationship between T and CV risk must be performed. In 2014 both FDA and EMA released warning concerning TRT safety. A recent meta-analyses (Corona et al., Expert Opin Drug Saf. 2014;13:1327-51.) suggested no risk of TRT and a possible protective role in subjects with metabolic syndrome.
All these points must be recognized and better discussed.

Level of interest: An article of importance in its field

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 that I have no competing interests