Reviewer’s report

Title: The PGC1alpha Gly482Ser polymorphism is associated with left ventricular diastolic dysfunction in men

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Reviewer: Chao-Qiang Lai

Reviewer’s report:

The study examined the correlation between PGC-1A Gly482Ser polymorphism and ventricular diastolic dysfunction in 499 men and 533 women in South-Western Sweden, and found male carriers of the Ser allele have significantly lower risk of diastolic dysfunction. The manuscript was well written and clear. However, a few questions need to be addressed:

(1) Page 11, Results: Please check if the genotypes of PGC-1 Gly482/Ser are in Hardy-Weinberg equilibrium in the men, women, both, respectively. This should be clarified in the results.

(2) Page 9, 7th line from the bottom: Please list out the ABI assay ID and primer sequences if available, and rs # for the PGC-1 Gly482/Ser polymorphism.

(3) Page 11, line 3: Given that PGC-1a interacts with estrogen receptors, one should examine if interaction between Gly482/Ser genotype and menopause status in women influence on the risk of diastolic dysfunction.

(4) Table 3, females: Based on Table 2 –females, the Ser allele seems to act recessively on the risk of DD in females, i.e., G/S subjects have an increased risk whereas S/S have a decreased risk. For this reason, authors should compare SS vs GG+GS, instead of GG vs GS+SS as listed in Table 3 –females.

(5) Page 12, line 7: PGC-1a variants have been shown to be associated with CVD before, so this may not be the first finding.

(6) Page 15, Conclusions: Given that PGC-1A Ser allele is associated with increased risk of type 2 diabetes, and type 2 diabetes is an independent risk factor of cardiovascular disease, one would expect that the Ser allele should associate with increased risk of diastolic dysfunction. But the finding from this study is totally opposite to what we expected. Please check the data analysis. Switching in phenotype or genotype coding could lead to an opposite result. If indeed this observation is biological, sex-specific regulation of PGC-1a expression in cardiac myocytes could be the key.

Level of interest: An article of importance in its field

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