Reviewer's report

Title: Cardioprotection afforded by exercise training prior to myocardial infarction is associated with autonomic function improvement

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Reviewer: Giuseppe Rengo

Reviewer's report:

In the present manuscript, Rodrigues and collaborators have investigated the effects of a 4-week exercise training program (performed prior to MI induction) on LV remodeling/function, baroreflex sensitivity and cardiac autonomic modulation, in a rat model of surgically induced myocardial infarction. The manuscript is clear and well written, the method section and the paragraph on statistical analysis are well described.

I have few suggestions/concerns:

1) The authors state that their exercise program is able to decrease mortality rate. In the opinion of the present reviewer, it is not possible to draw conclusion on mortality from the present study. First of all, a higher number of animals is required for studies on survival; second, acute mortality (within few days after MI induction) is largely dependent on surgical procedures (i.e. bleeding, lung injury). Thus, I believe that the authors can describe this result but they have to remove from the text any conclusions on the effect of exercise training on mortality rates.

2) Capisco che gli autori hanno già dimostrato una correlazione tra la dimensione dell'infarto valutata mediante ecocardiografia con la dimensione infartuale misurata dal istologia; tuttavia, la mancanza di dati sulla dimensione dell'infarto misurati da istologia dovrebbe essere riconosciere in un paragrafo sui limiti dello studio.

3) The authors have mentioned several beneficial effects/mechanisms by which exercise training is known to influence cardiac structure and function. However, they did not mention the relevant effect of exercise training on MI-dependent neurohormonal hyperactivation. In particular after MI, it is well known that catecholamine production and release from adrenal glands and from cardiac SNS nerve endings are enhanced. Increased NE and Epi levels have relevant effects on cardiac beta-adrenergic receptor signaling/function influencing cardiac autonomic modulation. Can the authors measure cardiac or circulating catecholamine levels in their study groups? These results would be of great interest. In any case, SNS hyperactivity, its effects on cardiac beta-adrenergic receptor signaling and the effects of exercise training on SNS hyperactivity should be discussed in the text (quoting relevant recent literature on this argument).

4) Additional histological data on cardiac fibrosis and angiogenesis, as well as, biochemical analysis for molecular markers of hypertrophy/remodeling and beta...
adrenergic receptor signaling status would add significance to the present study. If the authors cannot produce these data they have to acknowledge the lack of these data.

**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 that I have no competing interests