

# High intensive internal training induce cardioprotection against ischemic reperfusion injury

## Short communication

Cardiovascular diseases resulting in ischemic heart disease remain a major cause of morbidity and mortality all over the world and amongst the highest Non Communicable Disease (NCD) in Iran. The main attempts amongst researchers are to find out any appropriate ways to be practically able to prevent or treat the ischemic reperfusion injuries (IRI). Preconditioning (PC) is one of the main approaches to decrease the latter injuries.<sup>1-3</sup> Ischemic preconditioning is proved to be successive in reducing the myocardial infarction.<sup>4,5</sup> But as it has been mentioned, this and other techniques are not suitable in human life style. There should be applicable and non-invasive methods to achieved preconditioning treatment.

One of the most potent stimuli for eliciting such preconditioning is exercise.<sup>6,7</sup> In 2013, Other researchers showed that all different kind of exercises could ended to reduction of cardiac cells death by 4% to 75% and concluded that exercise training reduced infarcted size by average 34% in animal models.<sup>2</sup> In another study, continuous endurance training (CET) protects the heart against IR.<sup>8</sup>

Certainly, in Human epidemiological studies, it was shown that myocardial-IR induced cell death reduced following regular and continuous exercise (both short-term and long-term CET) confers cardioprotection against all level of IR-induced injuries.<sup>9</sup> Lennon et al.<sup>10</sup> concluded that both moderate and high-intensity continuous endurance training brings about same myocardial protection against IR injury. Therefore, it seems that both duration and intensity of exercise are significant factors in accomplishing exercise-induced cardioprotection also (EICP).<sup>8</sup> However, many investigators report that cardiovascular, muscle, and metabolic adaptations in healthy and patient populations are intensity-dependent and the beneficial effects of high intensity interval training (HIIT) rather than CET are better and more reliable for cardioprotection.<sup>11-16</sup> HIIT is characterized by repeated bouts of high-intensity exercise interspersed by periods of rest or low-intensity exercise for recovery.<sup>17</sup> According to the results of the previous studies, high-intensity exercise protects the heart against IR-induced diastolic dysfunction<sup>18</sup> and is recommended for patients with coronary heart disease.<sup>19</sup> Moreover, the existing evidence recommended that exercise intensity rather than duration and frequency is the most critical factor determining EICP.<sup>16,20-22</sup> Some of the studies have shown the advantages of the higher-intensity exercise over the moderate-intensity, in cardioprotection.<sup>22</sup> Whereas considerable evidence point out that CET leads to EICP, it is uncertain whether other forms of exercise bring about EICP against IR injury. The question remains to be answered is, what can the best type of exercise in order to achieve the optimal cardioprotection against IR injury? Doubtlessly, EICP vanishes after the termination of exercise training.<sup>23</sup> However, how long would it take for the EICP against IR to disappearance the exercise is terminated? In this context, Lennon et al.<sup>23</sup> reported that after 3 days of CET (60min, 30m/min, ~70 %VO<sub>2</sub>max), protection against myocardial stunning remains up to 9 days and is lost 18days after exercise termination. Calvert et al.<sup>4</sup>

reported that after 4 weeks of voluntary exercise (~7.4±0.2km/d), EICP against IR was only retained for a week after detraining. Therefore, we expected that HIIT induced cardioprotection to be more preserved to CET (9 days) and voluntary.

The purpose of the present writing was also to present that in our lab we have tried to examine whether short-term HIIT could reduce the incidence of ischemic-induced arrhythmias and infarct size; and if so, how long this protective effect is retained after exercise cessation.<sup>7,24</sup> Rats were randomly assigned into sedentary, sham, and exercise groups. Rats in the exercise groups performed 5 consecutive days of HIIT on treadmill: 5min warm up with 50% VO<sub>2</sub>max, 6×2min with 95-105% VO<sub>2</sub>max (about 40 to 45 m/min), 5×2 min recovery with 65-75% VO<sub>2</sub>max (about 28 to 32 m/min), and 3 min cool down with 50% VO<sub>2</sub>max, all at 0% grade. Animals exposed to an in vivo cardiac IR surgery, performed at days 1, 7, and 14 following the final exercise session. Ischemia-induced arrhythmias, myocardial infarct size (IS), plasma lactate dehydrogenase (LDH) and creatinekinase (CK) activities were measured in all animals and in some experiment nitric oxide metabolites were also measured. Compared to sedentary rats, exercised animals sustained less IR injury as evidenced by a lower size of infarction (Figure 1) and lower levels of LDH and CK at day one and day 7post exercise. In comparison of sedentary group, IS significantly decreased in EX-IR1 and EX-IR7 groups (50and 35 %, respectively), but not in EX-IR14 group (19%).<sup>25,26</sup> In Those experiments that nitric oxide was measured it seems that incremental changes in NO-NO<sub>3</sub><sup>-</sup>, NO<sub>2</sub><sup>-</sup> axis could be one of mechanisms through which HIIT program can protect the heart from I/R injury and decrease myocardial infarction. Exercise-induced cardioprotection disappeared 14 days following exercise cessation. There were no significant changes in ischemia-induced arrhythmia between exercised and sedentary rats.

The results clearly demonstrate that HIIT protects the heart against myocardial IR injury. This protective effect can be sustained for at least one week following the cessation of the training.

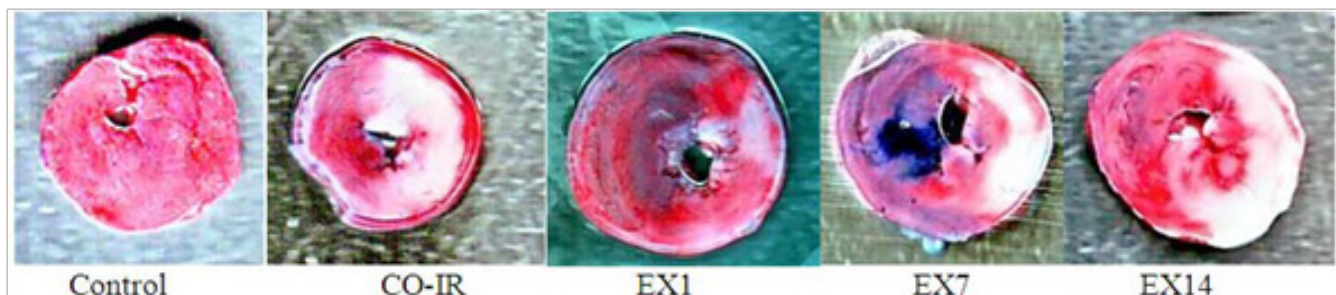
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**Figure 1** The ratio of myocardial area at risk to left ventricle area (AAR/LV%) and infarct size to area at risk (IS/AAR%) in rats subjected to 30min ischemia and 90min of reperfusion. Red areas indicate myocardium within the area at risk for infarction and whitish areas indicate infarcted tissue. CO-IR, control + ischemia-reperfusion; EX-IR1, exercise + IR performed after a day of rest; EX-IR7, exercise + IR performed after 7 days of rest; EX-IR14, exercise + IR performed after 14 days of rest.

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## Conflicts of interest

The author declares there is no conflicts of interest.

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