

MARTÍN DONATO ^{MTSAC}**Do Diabetes Mellitus and the Metabolic Syndrome Interfere with the Cardioprotective Effect of Ischemic Postconditioning?**

Oosterlinck W, Dresselaers T, Geldhof V, Nevelsteen I, Janssens S, Himmelreich U, et al. Diabetes mellitus and the metabolic syndrome do not abolish, but might reduce, the cardioprotective effect of ischemic postconditioning. *J Thorac Cardiovasc Surg* 2013;145:1595-602. <http://doi.org/ptw>

Ischemic preconditioning is a myocardial protection mechanism whereby brief periods of ischemia-reperfusion turn the heart more resistant to an ensuing prolonged ischemic insult. Although this protective mechanism has been demonstrated in different species, including humans, its clinical extrapolation is limited since there is need to know when the coronary artery is going to be occluded to perform the preconditioning intervention, and in addition, some studies strongly suggest that its effect is limited in animal models with diabetes mellitus. Consequently, ischemic postconditioning arises as a strategy which can be more easily extrapolated to the clinical setting. This mechanism, which was described in 2003, consists of ischemia-reperfusion cycles at the onset of reperfusion after a prolonged ischemic insult. On this respect, Oosterlinck et al. assessed the cardioprotective effect of postconditioning in two mice models, one with type 2 diabetes (obob) and another with metabolic syndrome (DKO).

Mice were submitted to 30 minutes coronary occlusion and at the onset of reperfusion they underwent an ischemic postconditioning protocol (3 cycles of 10 seconds ischemia-reperfusion). Infarct size was significantly reduced (40%) in normal mice, and contractility recovered after postconditioning. In obob

and DKO mice, postconditioning reduced infarct size by 24%. Ten weeks after the postconditioning protocol, ejection fraction and survival were higher in DKO mice and collagen content was lower both in control and DKO animals.

The cardioprotective effect of postconditioning was preserved in control mice reducing adverse left ventricular remodeling. In type 2 diabetes mice, protection against reperfusion injury was present, leading to increased survival after ischemia and reperfusion.

A great number of experimental studies evaluating different mechanisms of myocardial protection are performed in normal animals. However, ischemic heart disease in humans is a complex disorder which is accompanied by numerous risk factors, including hypertension, hyperlipidemia, diabetes and insulin resistance, among others. All these conditions are associated with molecular alterations that could potentially affect the protective mechanism of some interventions (ischemic preconditioning or postconditioning). The mechanism by which diabetes inhibits cardioprotection is not clearly defined, but one cause could be hyperglycemia per se. Still, other mechanisms might be involved. One of them could be the presence of mitochondrial dysfunction as a consequence of the increased production of reactive oxygen species. Moreover, other intracellular signals participating in the pre- or postconditioning mechanism could also be altered, including mitochondrial K⁺ channels. Therefore, the work of Oosterlinck et al. is important, as it studies a protective mechanism in a scenario which resembles more closely the clinical setting and shows the persistence of protection, though reduced, in two highly prevalent conditions as type 2 diabetes and metabolic syndrome.