

Remote Ischemic Preconditioning for Noncardiac Surgeries: is the Final Word "Ready" Yet?

Ischemic preconditioning was described first by Murry et al in 1986 in patients with coronary artery disease and was described as a phenomenon which "could delay cell death through multiple anginal episodes after coronary occlusion" and hence, increase resistance of the myocardial tissues towards ischemia (1).

Ischemic preconditioning is defined as *a stumbled or halted perfusion of a specific organ after a pause in perfusion*; in other words, it is a reperfusion after a transient perfusion pause which goes up to a sub-lethal degree of insult and could improve the recruitment of the tissue at risk of ischemia; it is generally believed that mitochondria are the main target of chemical conditioning in ischemic preconditioning (2-4).

Though the first discovery included direct preconditioning, the next experiences demonstrated another effect later known as *remote ischemic preconditioning* which implies the effects of ischemic burden on one organ protecting another organ so called "remote organ" (5, 6).

A number of mechanisms have been implicated as the underlying mechanism for ischemic preconditioning (both local and remote preconditioning) in different organs, including but not limited to (2-4, 7):

- ATP-sensitive K+ (K(ATP)) channels
- mitogen-activated protein kinase (MAPK)
- protein kinase C (PKC)
- astrocytic Toll-like receptor 3
- adenosine
- and a number of other intracellular signaling pathways

Though a considerable bulk of research have been published in favor of ischemic preconditioning and remote conditioning, there are still main controversies, especially about patients undergoing

cardiac surgery (6, 8, 9). However, Deng et al performed a meta-analysis and demonstrated that limb remote ischemic preconditioning reduces the size of myocardial damage in patients undergoing cardiac surgery (10). These studies challenge some of the beliefs about ischemic preconditioning, including all namely remote its variants. and delayed preconditioning. In this volume of the Journal, Jamshidi et al, have studied the effects of remote ischemic preconditioning in lower extremity orthopedic surgeries on hemodynamic and respiratory and have shown that " remote ischemic preconditioning may reduce increases in systolic blood pressure and acidosis following tourniquet application" (11). The study by Jamshidi et al, though is not the final word about "the role of remote ischemic preconditioning in noncardiac surgeries" gives us a good clue for further studies assessing the possible merits of remote ischemic preconditioning. However, the final word is not uttered yet.

References

1. Murry CE, Jennings RB, Reimer KA. Preconditioning with ischemia: a delay of lethal cell injury in ischemic myocardium. Circulation. 1986;74(5):1124-36.

2. Zhao H. Ischemic postconditioning as a novel avenue to protect against brain injury after stroke. Journal of cerebral blood flow and metabolism : official journal of the International Society of Cerebral Blood Flow and Metabolism. 2009;29(5):873-85.

3. Zhao H, Ren C, Chen X, Shen J. From rapid to delayed and remote postconditioning: the evolving concept of ischemic postconditioning in brain ischemia. Current drug targets. 2012;13(2):173-87.

4. Jin Z, Wu J, Yan LJ. Chemical Conditioning as an Approach to Ischemic Stroke Tolerance: Mitochondria as the Target. International journal of molecular sciences. 2016;17(3).

5. Thielmann M, Kottenberg E, Kleinbongard P, Wendt D, Gedik N, Pasa S, et al. Cardioprotective and prognostic effects of remote ischaemic preconditioning in patients undergoing coronary artery bypass surgery: a single-centre randomised, double-blind, controlled trial. Lancet. 2013;382(9892):597-604.

6. Hausenloy DJ, Candilio L, Evans R, Ariti C, Jenkins DP, Kolvekar S, et al. Efficacy and Mechanism Evaluation. Effect of Remote

Ischaemic preconditioning on Clinical outcomes in patients undergoing Coronary Artery bypass graft surgery (ERICCA study): a multicentre double-blind randomised controlled clinical trial2016.

7. Randhawa PK, Jaggi AS. Unraveling the role of adenosine in remote ischemic preconditioning-induced cardioprotection. Life sciences. 2016;155:140-6.

8. Hausenloy DJ, Candilio L, Evans R, Ariti C, Jenkins DP, Kolvekar S, et al. Remote Ischemic Preconditioning and Outcomes of Cardiac Surgery. N Engl J Med. 2015;373(15):1408-17.

9. Heusch G, Gersh BJ. The pathophysiology of acute myocardial infarction and strategies of protection beyond reperfusion: a continual

Ali Dabbagh, MD Professor, Fellowship in Cardiac Anesthesiology Chairman and Editor in Chief, *Journal of Cellular & Molecular Anesthesia* Anesthesiology Research Center, Shahid Beheshti University of Medical Sciences Tehran Iran challenge. European heart journal. 2016.

10. Deng QW, Xia ZQ, Qiu YX, Wu Y, Liu JX, Li C, et al. Clinical benefits of aortic cross-clamping versus limb remote ischemic preconditioning in coronary artery bypass grafting with cardiopulmonary bypass: a meta-analysis of randomized controlled trials. The Journal of surgical research. 2015;193(1):52-68.

11. Jamshidi F ES, Alimian M, Siamdoust A, Koleini ZS, Mohseni M. . Remote Ischemic Preconditioning in Lower Limb Surgery; the Hemodynamic and Respiratory Effects. J Cell Mol Anesth. 2016;1(3):97-102.