Remote Ischemic Preconditioning Is Redundant in Patients Undergoing Coronary Artery Bypass Graft Surgery Who Are Already Protected by Volatile Anesthetics

To the Editor:

We have read with interest the article by Heusch et al1 showing that troponin I levels of 12 coronary artery bypass patients treated with remote ischemic preconditioning (rIPC) performed under isoflurane anesthesia were reduced when compared with those of 12 untreated control patients. In that study, phosphorylation of the transcription factor STAT5 was also increased after reperfusion in left ventricular tissue samples of patients treated with rIPC. These findings are promising and the researchers should be commended for their analysis of human ventricular tissue samples. However, from the article, it is unclear whether data from these patients were also published in a report recently published by the same group,2 which was conducted under the same ClinicalTrials identifier number. A comparison of the perioperative cTnI levels between the two publications reveals that the peak cTnI levels are, on average, 5 ng/mL higher in the control patients in the study published in Circulation Research1 (15 ng/mL at 6 hours) compared to the peak cTnI levels of control patients in the study published in Acta Anaesthesiologica Scandinavica (10 ng/mL at 6 hours).2 Although this could be explained by biopsy-induced myocardial injury, it remains unclear why patients with rIPC in both publications, be it with or without biopsies, have similar peak cTnI levels because injury by biopsy is unlikely to be amenable to protection by rIPC. Another concern relates to the observation that phosphorylation levels of more than 20 kinases were determined, but no adjustment for multiple comparisons was performed. This is particularly disturbing with probability values as high as 0.05 for STAT5. At worst, the authors’ observation simply reflects a type I error. Finally, it appears that rIPC only may be of benefit in coronary artery bypass graft patients if cardioprotection is not optimal with respect to the choice of anesthetics or the type of cardioplegia. In support, Belhomme et al3 previously reported peak cTnI levels of approximately 4 ng/mL in patients undergoing coronary artery bypass graft surgery with isoflurane as a “preconditioning-mimicking” anesthetic. This is similar to the peak cTnI levels reported in the isoflurane plus rIPC group of the study by Kottenberg et al2 (5 ng/mL). Because Belhomme et al3 used cold blood cardioplegia but Kottenberg et al2 used crystalloid cardioplegia, it could well be that rIPC is only capable of providing protection under isoflurane anesthesia in cases in which cardiopreservation is suboptimal.

We have recently published a study showing that rIPC applied to the lower limb during isoflurane inhalation provided no additional protection to the myocardium in patients undergoing on-pump coronary artery bypass graft surgery.4 Using microarray analysis from atrial biopsies, we demonstrated that the release of NTpro-BNP, a marker of myocardial function/injury, clearly correlated with iso-flurane-induced transcriptional changes in fatty-acid metabolism and DNA damage signaling (previously established hallmarks of iso-flurane-induced transcriptional changes5), but not with rIPC-induced changes. This observation and other research suggest that volatile anesthetics6,7 and opioids7,8 potentially attenuate or even abolish signaling from ischemia-reperfusion damage. Hence, in the presence of efficacious cardioprotective pharmacological agents such as volatile anesthetics,9 rIPC may become redundant and may entirely lose its effectiveness, which is compatible with the recent results of the largest (so far) randomized double-blinded study.10

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References

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