used in parts of Asia, and we certainly do not have all the answers there either.

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Commentary: The new kid in town: Pulsed ultrasound to prevent ischemia–reperfusion injury

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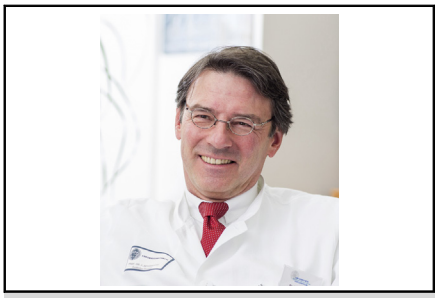

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CENTRAL MESSAGE

Pulsed ultrasound is a promising new approach to limit ischemia–reperfusion-injury.

Ischemia–reperfusion injury (IRI) is a major clinical problem in all fields of medicine, especially in cardiac surgery and cardiology. Major improvements in understanding the pathophysiology, the causes, and the consequences have been achieved over the last decades.[1-3] Charles and colleagues[4] from Irving Kron's group in Charlottesville are to be congratulated for drawing our attention to a new nonpharmacologic, noninvasive therapy option to reduce infarct size during acute myocardial infarction (MI). They provide promising data that pulsed ultrasound (pUS) is capable of attenuating the hyperglycemic exacerbation of myocardial IRI via the cholinergic anti-inflammatory pathway.[4]

Acute hyperglycemia in patients with MI (1) is independently associated with greater mortality and larger infarct size[5] and (2) leads to the stimulation of splenic leukocytes through activation of the nicotinamide adenine dinucleotide phosphate oxidase pathway, which plays an important role in leukocyte-mediated reperfusion injury.[6] Interestingly, reports show that pUS modulates splenic leukocytes into an anti-inflammatory phenotype.[7]

The strength of the study is that the authors not only report a significant reduction in infarct size in mice with acute hyperglycemia and 20 minutes of regional ischemia followed by 60 minutes of reperfusion, but that they provide insight into the molecular mechanisms of these beneficial effects. Splenic and neck pUS seem to reduce the splenic inflammatory response associated with hyperglycemic exacerbation of MI through vagus and acetylcholine signalling.[4]

The authors also point out 2 additional significant elements: (1) if neck pUS was applied 24 hours before IRI, it was as protective as if applied just before coronary occlusion; (2) when neck pUS was performed 10 minutes after reperfusion had started, no protective effect could be seen. In other words, the positive effects of modulation of splenic

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leukocytes via neck pUS into an anti-inflammatory phenotype lasts at least 24 hours. However, once reperfusion injury had occurred (for 10 minutes), neck pUS could not reverse the reperfusion injury. Reversal of reperfusion injury—the holy grail of research in IRI—is not possible even with this new approach to prevent IRI. The authors are to be commended on adding this important information to their study.

The limitations of the study are obvious, and the authors have summarized most of them in the Discussion. The short reperfusion phase of 20 minutes and no further follow-up prevents drawing conclusions in the clinical setting. Potential systemic effects of neck and splenic pUS could not be assessed in the current experimental small animal model.

Nevertheless, the authors are to be congratulated for exploring a new path in preventing IRI and adding basic research to shed some light on the pathophysiologic mechanisms to this nonintuitive, innovative approach. The reduced interest of surgeons in basic science and the detrimental effects of this development for the future of surgery has been clearly expressed in a recent editorial in *Nature*.[8] A transatlantic editorial about the same topic has described the reasons and possible solutions for this dilemma.[9] This paper by Charles and colleagues[4] is a very good example of merging research on clinically relevant problems with basic science tools.

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