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Dubious effects by the choice of anesthetics in remote ischemic preconditioning

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Initial clinical studies of remote ischemic preconditioning (RIPC) led to encouraging proof-of-principle, while others did not. Possible explanations for the divergent results are that (I) most trials used only surrogate end points; (II) were conducted as single center studies; (III) used a single-blind design; (IV) and/or had a small sample size. The RIPHeart (1) and ERICCA (2) trials are encompassing more than 3,000 patients and provide now new evidence on this topic.

Cheung *et al.* (3) suggest that the use of propofol anesthesia inhibits organ protective properties and may increase complications. To our current knowledge we do not have evidence in form of clinical trials supporting or proving this hypothesis. We are neither aware of large prospective trials showing increased mortality with propofol anesthesia, nor of sufficient clinical evidence that propofol blocks potential protective effects. Indeed, a small study suggested RIPC in 14 patients to reduce the area under the troponin I time curve compared to 19 control patients undergoing propofol anesthesia (263±157 *vs.* 372±376 ng/mL × 72 h), although the effect was more pronounced in another subgroup of patients undergoing isoflurane anesthesia (4). This phase I trial is too small in sample size to allow any conclusion in general and the assumption of propofol's potential negative effects remains largely speculative. Notably, there is also a lack of data explaining such a mechanism of action of propofol.

Cheung *et al.* (3) have also accused us for not having adapt the RIPHeart study protocol during patient recruitment as these pilot data (4) were available in 2012 prior to the start of RIPHeart and ERICCA and that this effect was confirmed by a meta-analysis in 2015 (5). We strongly disagree with this criticism as the RIPHeart study was designed in 2010, and patients were recruited from January 2011 until May 2014. Again, we are still convinced that both cited studies (4,5) do not justify major protocol changes in a large-scale multicenter phase III trial. More importantly, the alternative use of volatile anesthetics has also been described to attenuate cardioprotection by RIPC in a recent meta-analysis of 15 randomized trials (6). As propofol is the standard drug for sedation worldwide, a 100% propofol-free regime for anesthesia in the OR and sedation at the intensive care unit would be a completely experimental and not clinical relevant regime for most of the participating centers, that otherwise would have a major impact on study performance, patient recruitment and study results.

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Footnote

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