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EDITORIAL

Translational research: Sounds intriguing, but can at times be a frustrating endeavor. How can we improve our methodology?

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If you do a search on *Pubmed* using the phrases "ischemic preconditioning, post conditioning, remote conditioning, or cardioprotection," the number of hits you find will be in the thousands, that is tens of thousands. If you go further and pull out some of the landmark experimental studies (for instance as reviewed by Heusch (1)), you will enter a fascinating field of likely and unlikely mechanisms and find signal substances demonstrating a very convincing cardioprotection from some odd stimuli applied in faraway organs.

However, despite almost 50 years of experimental research and a multitude of follow-up clinical studies and experiments, even the biggest enthusiasts point to a lack of convincing clinical data (2). Also, of some concern, "the pharmaceutical industry has largely left this field due to the lack of convincing clinical data" (3). What is really going on?

Looking at this field from the clinical perspective, it is understandable that a large number of small and exploring studies have been conducted. The mechanisms are intriguing and the techniques to induce cardioprotection are harmless and very easily applied even in complex clinical situations like acute myocardial infarction and cardiac surgery. However, are these studies serving their purpose, and are we as a scientific community, critical enough toward the research we want to present our fellow scientists?

In this issue of the *Scandinavian Cardiovascular Journal* we are presenting a small clinical study applying remote conditioning in coronary bypass patients (4). What could be potentially interesting for clinicians is the possibility that the applied technique of remote limb ischemia could reduce the incidence of postoperative atrial fibrillation. Such a potential effect was indicated in a back-to-back publication in *Circulation Research* (5), and this publication created enthusiasm also among the journal editors (6). However, our present SCJ publication could not confirm the protective effect on postoperative arrhythmias indicated in the first study. The disappointing history of yet another failed cardioprotective attempt seems to be evolving.

Are the two studies (4,5) substantially different, and are there differences that potentially can explain the disparate results? From a perspective on the patient populations and surgical techniques, such differences are not easy to see. Both studies are conducted by the same surgical team using the same basic pharmacological and surgical techniques. Also, the protocol for registering end-points (arrhythmias and enzyme release) is identical. That leaves us with the ever-revolving problem of power in small studies. It is in the Zeitgeist to call our studies "exploratory and demonstrating proof-of-principles," but for remote ischemic preconditioning, the time for do or do-not has come, and this defining question can only be answered in properly conducted large-scale clinical trials.

Are the experiences related to the huge number of failed cardioprotective attempts of general concern? Definitely; institutions like the National Institute of Health (7) and the European Society of Cardiology (8) both express the need to get out of the misleading path and onto a more meaningful

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use of resources and a more effective screening process for possible cardioprotective principles. Of interest, the NIH-sponsored CAESAR-consortium advocates a standardized experimental research protocol, a multiinstitutional common evaluation of data, and a strict concern on reproducibility and power calculations. The multiinstitutional randomized trial concept has come to experimental research.

Likewise, the working group on cellular biology from ESC has recently put up a defined series of requirements for clinical trials that should lead to meaningful studies, helping us to reach definite conclusions in cardioprotection trials (8).

What will the consequences be for the *Scandinavian Cardiovascular Journal,* its contributors, and editorial board? The logical step for all of us is to leave the "least publishable unit" and start an even broader collaboration with colleges nationally and internationally, and give priority to quality, resource consciousness, and critical assessment of what we want to communicate. It is logical and will be more meaningful to all of us!

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