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Letters

TO THE EDITOR

Intracoronary Delivery of Mitochondria to Prevent Ischemia–Reperfusion Injury

Challenging Pathway From Bench to Bedside

We have read with interest the paper by Shin et al. that demonstrates that intracoronary delivery of mitochondria affords protection against ischemia-reperfusion injury in pigs (1). This study is presented as a necessary step toward the assessment of a similar approach in human subjects who experience a myocardial infarction (MI), in whom intracoronary injection of mitochondria could prevent further myocardial necrosis following percutaneous revascularization of the culprit lesion (1). In this study, the reperfusion and intracoronary delivery of mitochondria occurred after a 30-min occlusion of the left anterior descending (LAD) artery. According to the ischemic cascade, cardiomyocyte necrosis will start after 30-min ischemia and only in the core of the hypoperfused area. Furthermore, a 30-min interval between first medical contact (FMC) and reperfusion is implausible in patients with ST-segment elevation MI (STEMI), in whom a much longer interval (<90 min between FMC and reperfusion) is deemed optimal (2). We add that intracoronary delivery of autologous mitochondria would require a tissue biopsy from the patient before coronary angiography, and the isolation and purification of mitochondria, with this last procedure lasting approximately 30 min (3).

Regarding the infarct area, the LAD is the culprit artery only in 39% of STEMI, and the risk of occlusion decreases by 30% for each 1-cm increase in distance from the ostium (4). Because the LAD measures 10 cm to 13 cm (5), the likelihood of an occlusion just after the second diagonal branch, which occurred in this study (1), is much lower than that in a more proximal location. The larger the ischemic area and the more prolonged the ischemic insult, the larger both the final infarct area and the border zone will be, with the latter being highly susceptible to ischemia-reperfusion injury and then potentially salvaged. In addition, mitochondrial uptake by cardiomyocytes is an energy-dependent process (1), which is crucially influenced by the severity of ischemic cardiomyocyte damage and the degree of impairment of energy metabolism associated with myocardial hypoperfusion.

In summary, we congratulate Shin et al. (1) on their interesting study, but their experiments could be usefully replicated in animals subjected to an ischemic insult with longer duration and involving a larger myocardial region, and taking into account the time needed for isolation and purification of mitochondria.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Basic to Translational Science* author instructions page.

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