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Aged rat heart: Modulation of age-related respiratory defects decreases ischemic-reflow injury

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ABSTRACT

Myocardial injury increases in the elderly heart during ischemia and reperfusion. Mitochondria, the key targets and sources of injury during ischemia and reperfusion, sustain ischemic damage to the electron transport chain that is superimposed upon age-related defects. In the adult heart, interventions to activate endogenous cytoprotective signaling systems meet in mitochondria to decrease cardiac injury. Unfortunately, these systems are largely ineffective in the aged heart. Thus, new treatment concepts are needed to reduce injury in the aged heart. Our group chose a strategy to directly treat the effector of cardiac injury in the aged heart, the mitochondria. We further utilized a novel approach to ask if the reversal of aging defects in cardiac mitochondria before ischemia could decrease ischemia-reperfusion injury in the heart. Three hours following treatment with the small molecule, nutriceutical acetylcarnitine (AcCN), oxidative phosphorylation as well as age-induced defects in electron transport chain complexes III and IV was corrected in the heart. When such hearts were then exposed to ischemia and reperfusion, cardiac injury was markedly reduced. Contraction during reperfusion improved and recovery became similar to that in adult hearts. Cardiac cell death was substantially reduced. Thus, age-related defects in electron transport are a key mechanism of the increased myocardial injury in the elderly heart during ischemia and reperfusion. Modulation of aging-induced defects in mitochondrial metabolism reduces cardiac injury from ischemia and reperfusion, and is a novel strategy to protect myocardium in the elderly patient at risk for an acute myocardial infarction.

KEYWORDS

Mitochondria; Cytochrome Oxidase; Complex III; Myocardial Infarction; Aging

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