BRIEF MYOCARDIAL ISCHEMIA FOLLOWED BY REPERFUSION INITIATES MICROVASCULAR CELL DEATH THAT CAN CONTRIBUTE TO THE “NO-REFLOW” PHENOMENON AND POTENTIALLY BE AMELIORATED

ACC Poster Contributions
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Introduction: The “no-reflow” phenomenon refers to diminution of perfusion in the microcirculation despite restitution of perfusion in the macrovascular supply by relief of epicardial coronary artery occlusion. We have previously described death of vascular cells (vascular rhexis) following persistent coronary occlusion. The present study was designed to determine whether transitory ischemia can initiate vascular rhexis in the coronary microcirculation that can contribute to “no-reflow” and late negative left ventricular (LV) remodeling.

Methods: C57Bl6 mice were subjected to coronary ligation (3-4) hours followed by reperfusion. Soluble fractions of LV homogenates were obtained 48 hours after the onset of transitory coronary occlusion. They were assayed by Western blotting for quantification of increased α-smooth muscle actin (α-SMA) and smooth muscle myosin heavy chain (SM-MHC) that we have shown reflects vascular rhexis delineated immunohistochemically. Angiopoietin 2 in serum, elevations of which reflect vascular injury, were measured by Western blotting as well.

Results: Transitory coronary occlusion initiated vascular rhexis evident 48 hours later (n = 11). α-SMA increased by 2.12 ± 0.22 fold compared with that in normal hearts, 1.00 ± 0.07, n = 10, p ≤ 0.05. SM-MHC increased also by 1.94 ± 0.15 compared with that in normal hearts, 1.00 ± 0.07, n = 9, p ≤ 0.05. After 48 hours the number of small and medium sized vessels in the previously ischemic zones was reduced, 6.3 ± 0.62 vessels per high powered field, n = 4 hearts, compared with 23 ± 4.0, n = 3 in normal hearts. Capillary degradation was evident also as judged from immunohistochemically detected CD31 and TUNEL that co-localized. Angiopoietin 2 was significantly increased in serum 48 hours after the onset of ischemia (226% ± 26% over baseline, n = 16, p ≤ 0.05).

Conclusion: Vascular rhexis occurs after ischemia as brief as 3 hours. Because it may be amenable to amelioration relatively soon after the onset of ischemia, it is an attractive therapeutic target for diminution of “no-reflow” and preservation of LV function in patients with acute coronary syndromes undergoing early coronary intervention or thrombolysis.