

Vascular smooth muscle reactivity in old spontaneously hypertensive stroke-prone rats – effects of prolonged cold ischemia followed by warm reperfusion in an in vitro model

Sevil Korkmaz-Icöz¹, Shiliang Li¹, Tamás Radovits², Sandra Schubach¹, Patricia Kraft¹, Tobias Mayer¹, Mihály Ruppert^{1,2}, Matthias Karck¹, Gábor Szabó¹

¹Department of Cardiac Surgery, University of Heidelberg, 69120 Heidelberg, Germany

²Heart and Vascular Center, Semmelweis University, 1122 Budapest, Hungary

Objectives Vascular grafts are essential therapeutic materials for bypass surgery. However, age and arterial hypertension are risk factors for cardiovascular complications after artery bypass graft surgery. We investigated the effects of both hypertension and ageing on vascular graft responsiveness in normoxic and prolonged cold ischemia/warm reperfusion (IR) conditions.

Methods In 18-month-old spontaneously hypertensive stroke-prone (shrsp, n=7) and age-matched normotensive Wistar (n=8) rats systolic (SBP), diastolic (DBP), and mean arterial pressure (MAP) values were recorded. Whereas thoracic aortic rings in the control and shrsp groups were immediately mounted in an organ bath (normoxia group), aortic segments in the control-IR and shrsp-IR groups underwent 24h cold ischemic preservation in physiological saline, followed by reperfusion injury simulated by hypochlorite exposure. Changes in isometric force were recorded.

Results SBP, DBP, and MAP were significantly higher in shrsp than in control (control SBP 134±7; DBP 108±6; MAP 117±6 vs. shrsp SBP 201±18; DBP 162±10; MAP 175±13mmHg). Even though aortic rings from shrsp group showed significantly greater maximal contraction to phenylephrine an α_1 -adrenergic agonist compared to control, shrsp-IR group showed further impaired contraction (control 2.2±0.1 vs. shrsp 2.9±0.1 vs. control-IR 2.6±0.2 vs. shrsp-IR 0.9±0.1g). In contrast to phenylephrine, all groups showed significantly reduced vasoconstriction responses to high K⁺-induced depolarization when compared to control. Additionally, both IR-groups showed significantly weaker tension compared to shrsp-group, and IR in shrsp rat further impaired high K⁺-induced contraction (control 4.7±0.1 vs. shrsp 3.6±0.1 vs. control-IR 2.6±0.2 vs. shrsp-IR 0.7±0.1g). Maximal endothelium-dependent relaxation (R_{max}) to acetylcholine was significantly weaker in rings from both IR-groups compared to control-group (control 57±2 vs. shrsp 48±3 vs. control-IR 44±3 vs. shrsp-IR 44±3%), and IR significantly decreased the sensitivity of aortic rings to acetylcholine in shrsp rats compared to normoxia shrsp-group. Maximal endothelium-independent relaxation to sodium nitroprusside was not significantly impaired in both IR-groups compared to control.

Conclusions Cold ischemia/warm reperfusion, in senescent shrsp rats with established hypertension, increases the susceptibility of aortic rings to smooth muscle contraction impairment.