**Integrative function of microcirculation and skeletal muscle function in peripheral artery disease**

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Peripheral artery disease (PAD) is an atherosclerotic disease that impairs lower-extremity circulatory function. Attenuated skeletal muscle mitochondrial function and oxygen utility capacity have been reported in the ischemic limbs; however, the underlying mechanisms are not well-understood. We investigated the impacts of chronic ischemia on skeletal muscle arteriole vasodilatory function and its contribution to skeletal muscle mitochondrial function and microvascular oxygen delivery and utilization capacity (TOI) in PAD. Skeletal muscle and arteriole samples from patients with PAD (n=18, 68.4±10.2 years) and age-matched controls (CON, n=11, 64.6±9.3 years) were harvested. Endothelial-dependent and endothelial-independent vasodilatory function was assessed by flow, acetylcholine (ACh), and sodium nitroprusside (SNP), and skeletal muscle mitochondrial function was measured by high-resolution respirometry. TOI was assessed by near-infrared spectroscopy *in-vivo*. Endothelial-dependent vasodilation was attenuated in PAD in response to ACh (10-3M, CON: 71.1±7%, PAD: 45.5±6%, *p*<0.01) and flow (CON: 46.6±6.8%, PAD: 29.2±4.5%, *p*<0.01), whereas endothelial-independent vasodilation was not different between groups (10-3M, CON: 101.5±4%, PAD: 91.6±5%, *p*=0.12). Complex I + II state 3 respiration was lower in PAD (CON: 26.1±2.1, PAD: 7.8±1.4 pmol∙s-1∙mg-1, *p*<0.01), and TOI was blunted in PAD (CON: 67.2±10.9, PAD: 26.6±7.0%∙min-1, *p*<0.01). Furthermore, flow-mediated dilation and ACh-mediated vasodilation were positively associated with complex I+II state 3 respiration (*r*=0.6 and *r*=0.5, respectively, *p*<0.05) and TOI (*r*=0.5 and *r*=0.6, respectively, *p*<0.05). These findings suggest that conduit artery atherosclerotic blockage-mediated chronic ischemia attenuates skeletal muscle microcirculatory endothelial function, which may be a key contributor to attenuated leg skeletal muscle mitochondrial function and oxygen delivery capacity in patients with PAD.