The impact of outward remodeling on vasodilation in skeletal muscle resistance arteries

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Introduction

- Ischemic insult in patients with peripheral arterial occlusive disease (PAOD) is thought to be alleviated by collateral enlargement.

- Collateral dependent hyperemia is reduced in animal models following arterial occlusion, suggesting vasodilation is impaired.

- Project goal: determine the impact of arterial occlusion and subsequent outward vascular remodeling on vasodilation in collateral resistance arteries.

Surgical Model: Femoral Ligation

- The femoral artery was ligated distally to the profunda femoris (Figure 1) to induce ischemia in downstream tissues.

- Blood flow was redirected into the profunda femoris artery, inducing outward remodeling of the vessel and collateral circuit within the gracilis muscle (Figure 2).

Intravital Microscopy: Functional Vasodilation

- The gracilis muscle was electrically stimulated to cause endogenous vasodilation of the profunda femoris feed artery.

- An intravital microscope was used to measure the profunda femoris diameter before and after stimulation. The site of muscle stimulation is shown in Figure 3.

Functional Vasodilation is Impaired During Outward Vascular Remodeling

Endothelial- and Smooth Muscle-dependent Vasodilation is Impaired During Outward Vascular Remodeling

- To test the hypothesis that outward vascular remodeling results in a transient impairment in smooth muscle-dependent vasodilation, the diameter of the profunda femoris was measured at day -7 and -28 post-ligation before and after administration of endothelial- and smooth muscle-dependent vasodilators.

Intravital Microscopy: Vascular Reactivity

- To determine if impaired functional vasodilation is due to impaired endothelial- or smooth muscle-dependent responses during outward remodeling, cell-dependent vasodilators were superfused over the vessel.

- Increasing concentrations (10⁻⁴ - 10⁻⁵ M) of sodium nitroprusside (SNP, smooth muscle-dependent) and acetylcholine (Ach, endothelial-dependent) were applied to the tissue. Experimental set-up is shown in Figure 6.

Figure 1. Blood flow in the mouse hindlimb before (left) and after (right) femoral artery ligation.

Figure 2. Fluorescent images of the gracilis collateral circuit in a non-operated limb (top) and in a ligated limb 7 days after surgery (bottom).

Figure 3. Gracilis muscle stimulation.

Figure 4. Day 7: Images of the profunda femoris before (A) and after (B) gracilis stimulation. (C) Vessel diameter before and after simulation in sham-operated and ligated animals. (D) Percent change in vessel diameter. * p < 0.05. Scale bar is 0.1mm.

Figure 5. Day 28: Images of the profunda femoris before (A) and after (B) gracilis stimulation. (C) Vessel diameter before and after simulation in sham-operated and ligated animals. (D) Percent change in vessel diameter. Scale bar is 0.1mm.

Figure 6. Experimental set-up of vascular reactivity to endothelial- and smooth muscle-dependent vasodilation.

Figure 7. Day 7: Images of the profunda femoris at each concentration of Ach (A) and SNP (C). Percent change in vessel diameter in sham-operated and ligated animals in response to Ach and SNP is shown in (B) and (D), respectively. * p < 0.05. Scale bar is 0.1mm.

Figure 8. Day 28: Images of the profunda femoris at each concentration of Ach (A) and SNP (C). Percent change in vessel diameter in sham-operated and ligated animals in response to Ach and SNP is shown in (B) and (D), respectively. Scale bar is 0.1mm.