Smooth muscle-dependent vasodilation is impaired in immature arterialized collateral capillaries

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BACKGROUND

In Peripheral Arterial Occlusive Disease (PAOD), atherosclerotic plaques cause ischemia in limbs. Ischemic effects can be mitigated with collateral vessels, or natural bypasses to maintain perfusion. Not all patients may have robust collateral vessels.1

PREVIOUS WORK

Following an occlusion in vasculature lacking collateral vessels, capillaries will arteralize.2 Stimulating growth of arterialized capillaries may improve prognosis for patients lacking pre-existing collaterals.3 While fully functional at 21 days post-ligation, functional vasodilation is impaired at day 7.4 This impairment may be attributed to endothelial cell dysfunction.5

ENDOTHELIAL AND SMOOTH MUSCLE RESPONSES

Figure 1. Spincotrapezius feed artery ligation. A, Schematic of spinotorrapezius. B, BabyC vasculature lacking collaterals. C, Resulting arterialized capillaries. Figure adapted from MacGabhann.6

Figure 2. Functional vasodilation in arterialized capillaries. Percent change of vessel diameters after 90 s muscle contraction at 7 days (n=11) (A) and 21 days post ligation (n=11) (B). Terminal arterioles in sham operated animals, arterialized capillaries in ligated side (n=15); * indicates p < 0.05 using a paired students t-test.

Figure 3. Superfusion preparation with intravital microscope. A) Representative preparation with intravital microscope and heated syringes. B) Close-up of workspace and heat pad.

Figure 4. Reactivity of arterialized capillaries at day 7. Percent change in vessel diameter before and after exposure to 10^{-5} SNP (n=9), 10^{-4} papaverine (n=11), and 10^{-4} NaHS (n=11); * indicates p < 0.05 using a paired students t-test.

Figure 5: Reactivity of arterialized capillaries at day 7. Percent change in vessel diameter pre and post exposure to 10^{-5} SNP (n=8), 10^{-4} papaverine (n=11), and 10^{-4} NaHS (n=11); * indicates p < 0.05 using a homoscedastic t-test.

Figure 6: Functional stimulation of arterialized capillaries at day 21. Representative images of arterialized capillaries before (A) and after (B) functional stimulation, measured using intravital microscopy. C) Percent change of vessel diameter following stimulation and exposure to reagents via superfusion (n=3); * indicates p < 0.05 using a homoscedastic t-test.

Figure 7: Functional stimulation of pre-existing collaterals at day 21. Representative images of pre-existing collaterals before (A) and after (B) functional stimulation, measured using intravital microscopy. C) Percent change of vessel diameter following stimulation and exposure to reagents via superfusion in sham (n=2) and ligated: (n=3); * indicates p < 0.05 using a homoscedastic t-test.

REFERENCES


CONCLUSION

• Arterialized capillaries have impaired, but still significant, reactivity at 7 days post-ligation.
• This impairment can be attributed, at least in part, to smooth muscle cell dysfunction.
• Arterialized capillaries may depend on NOS-based pathways more as they mature.
• Pre-existing collaterals are present unexpectedly with tortuous structures and sporadic responses.

FUTURE WORK

• Evaluate molecular markers of smooth muscle cell immaturity.
• Evaluate conducted vasodilation stimuli arterialized capillaries.
• Determine arterialized capillary development and reactivity in animal models with co-morbidities.
• Determine reactivity of pre-existing collaterals.

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