

# Microvascular Dysfunction and Basal Membrane Thickening in Skeletal Muscle in ME/CFS and Post-COVID

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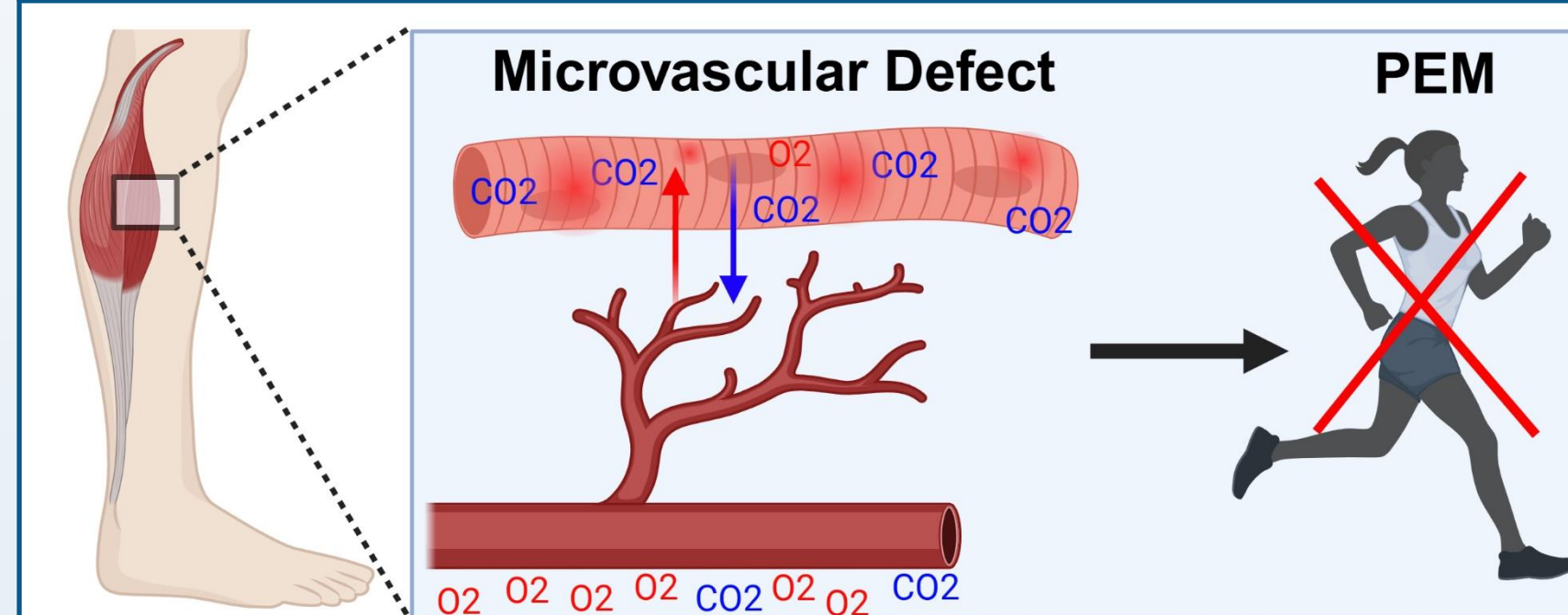
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## INTRODUCTION



### Hypothesis:

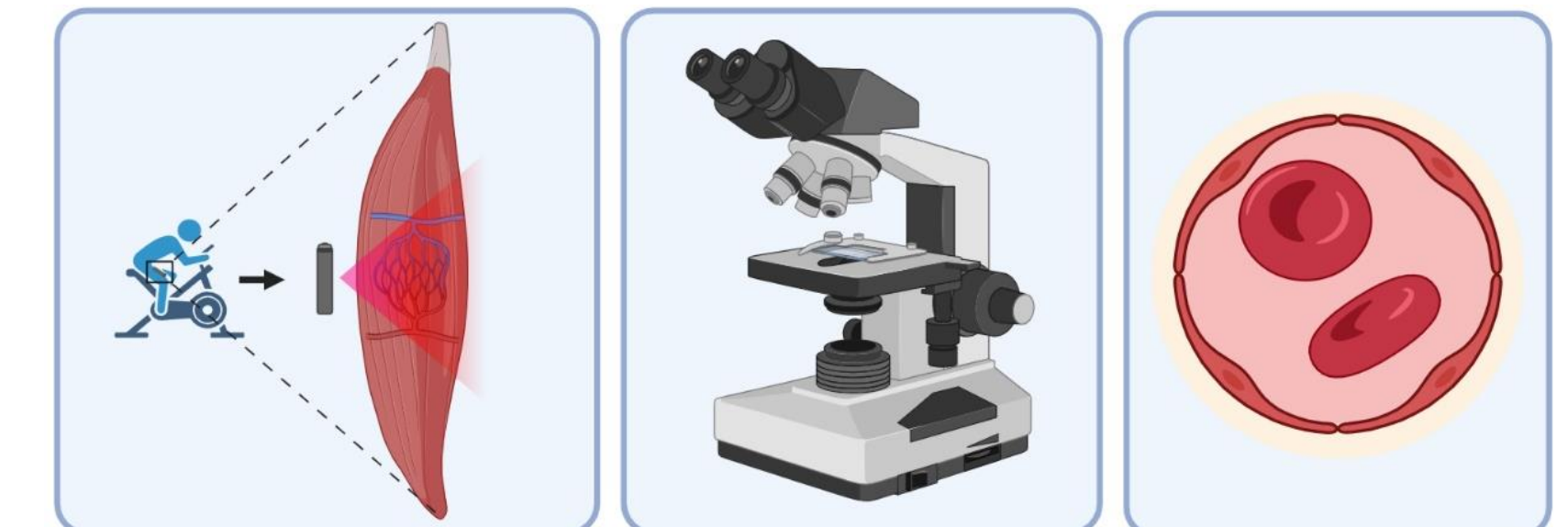
peripheral oxygenation deficit

ineffective matching of oxygen delivery ( $\dot{Q}O_2$ ) to consumption ( $\dot{V}O_2$ )

overexertion & muscle fatigue

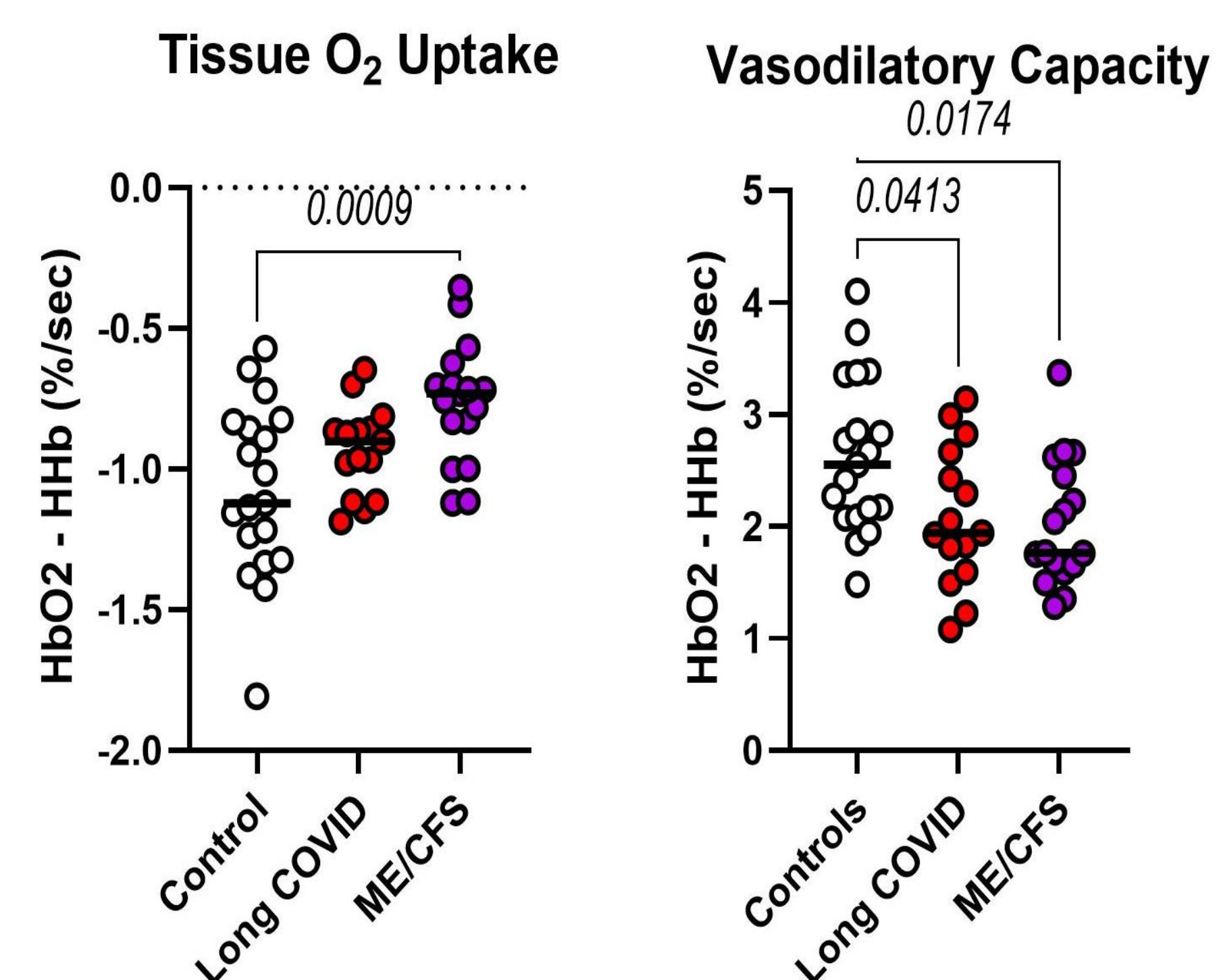
## METHODS

- Cardio-pulmonary function and **muscle oxygenation (NIRS)** were measured during and post-exercise.
- Vastus lateralis biopsies were obtained and assessed for **capillarization**, **collagen IV** content, and **capillary ultrastructure**



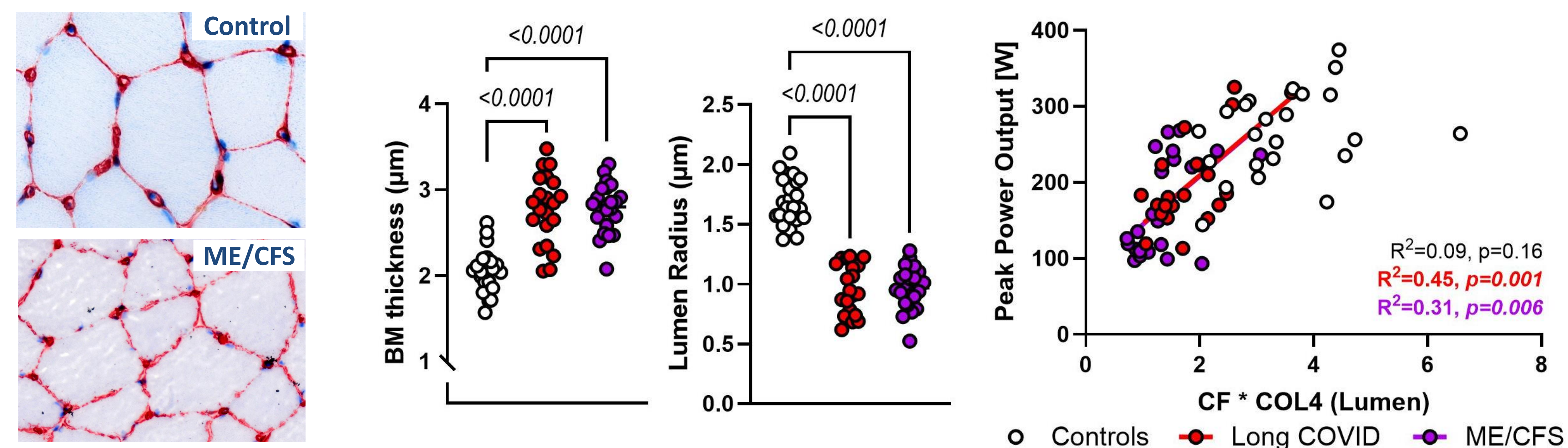
## RESULTS

### NIRS: Lower Oxygen Uptake and Vasodilatory Capacity in Patients



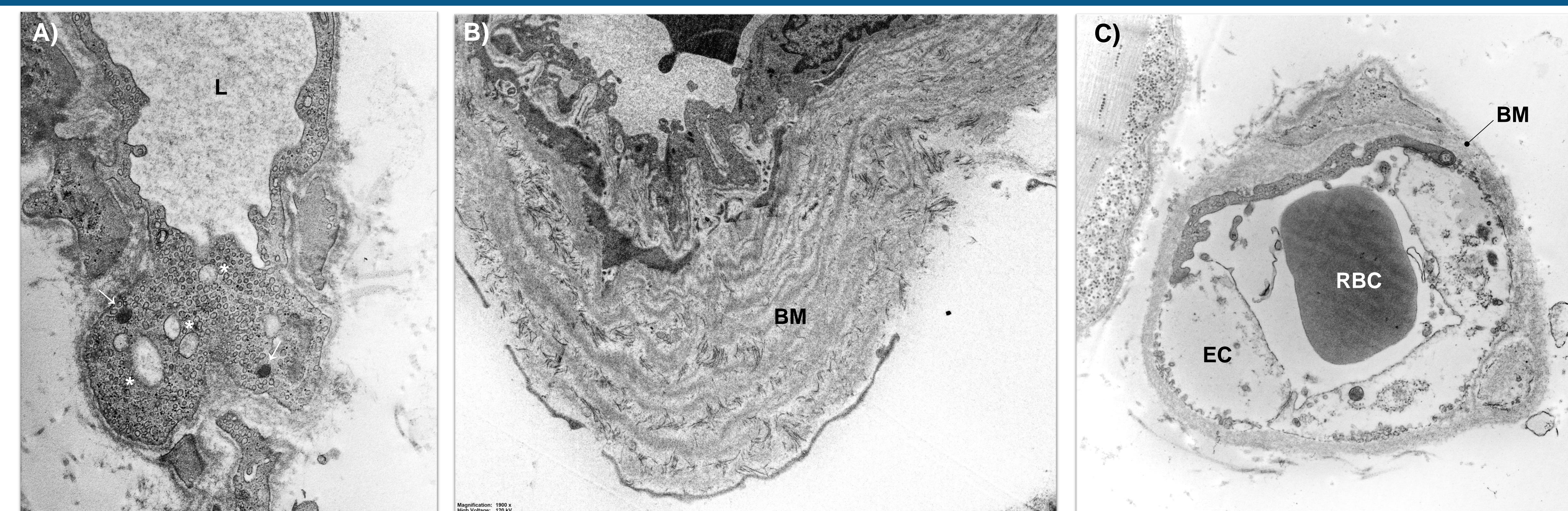
**Figure 1:** Even though no significant difference was observed in relative oxygenation kinetics during exercise, the **tissue oxygen uptake** ( $p=0.001$ ) and the **vasodilatory capacity** ( $p=0.011$ ) were significantly different between groups.

### Increased Collagen IV Deposition in the Capillary Basement Membrane of Patients



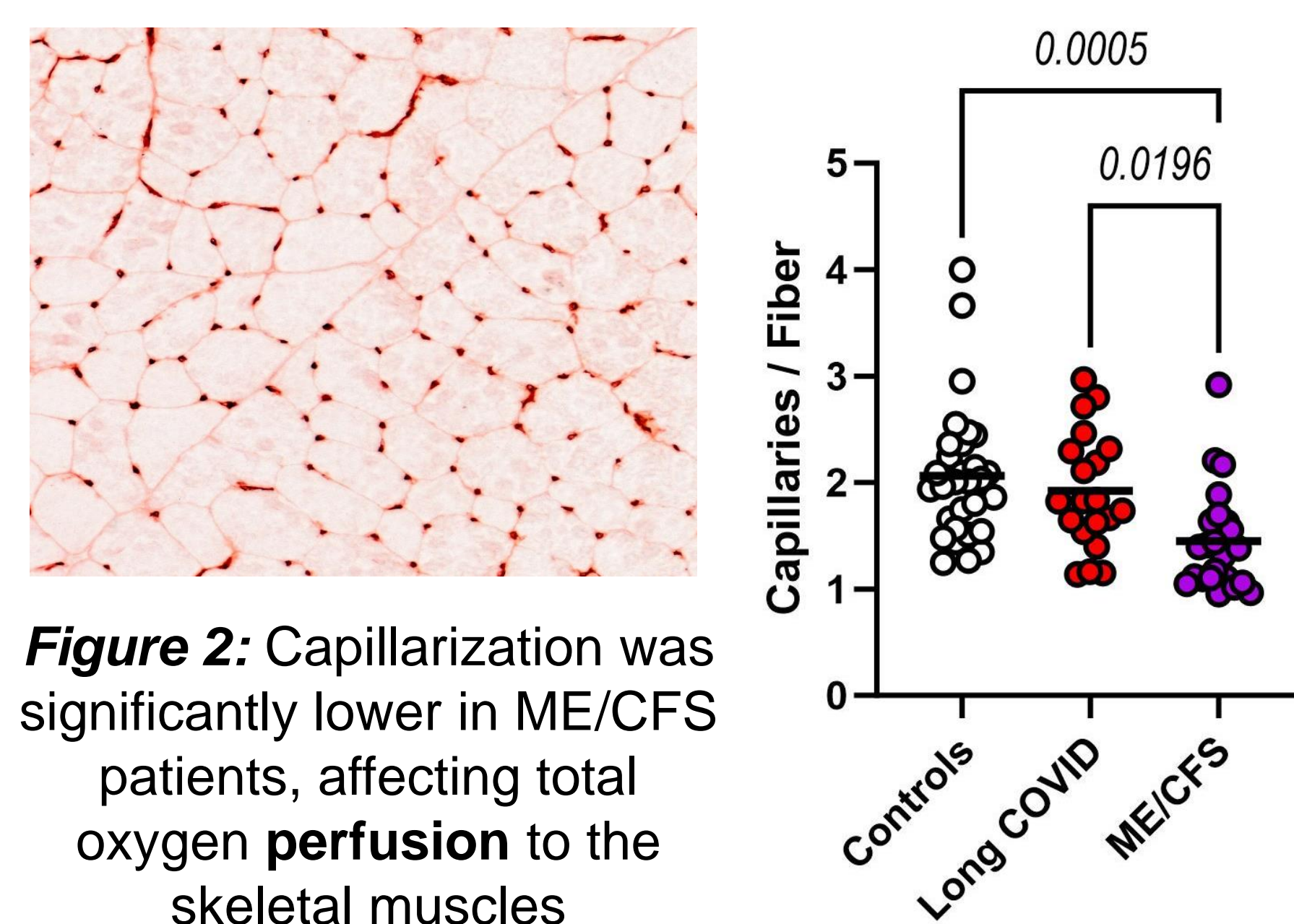
**Figure 3:** **A)** Collagen IV stain; **B)** Capillary basement membrane (BM) was significantly thicker in patients compared to controls ( $p<0.0001$ ); **C)** Also the lumen radius seemed to be affected by the collagen IV deposition; displaying a significantly lower cross-section in patients ( $p<0.0001$ ); **D)** A significant correlation was found between CF\*Lumen and CPET measurements in patients, suggesting that both perfusion and collagen IV deposition contribute to reduced exercise capacity.

### Microvascular Ultrastructural Abnormalities in Patients



**Figure 4:** Ultrastructural abnormalities observed in patients' capillaries, potentially affecting both **perfusion** and **diffusion**. **A)** The high nr. of pinocytic vesicles, microvacuoles (\*), Weibel Palade bodies (†), and endothelial thickening show signs of endothelial stress. **B)** Basal membrane duplications; **C)** Degenerating endothelial cells; as evident from the endothelial cell swelling and the lack of organelles.

### Lower Capillarization in ME/CFS

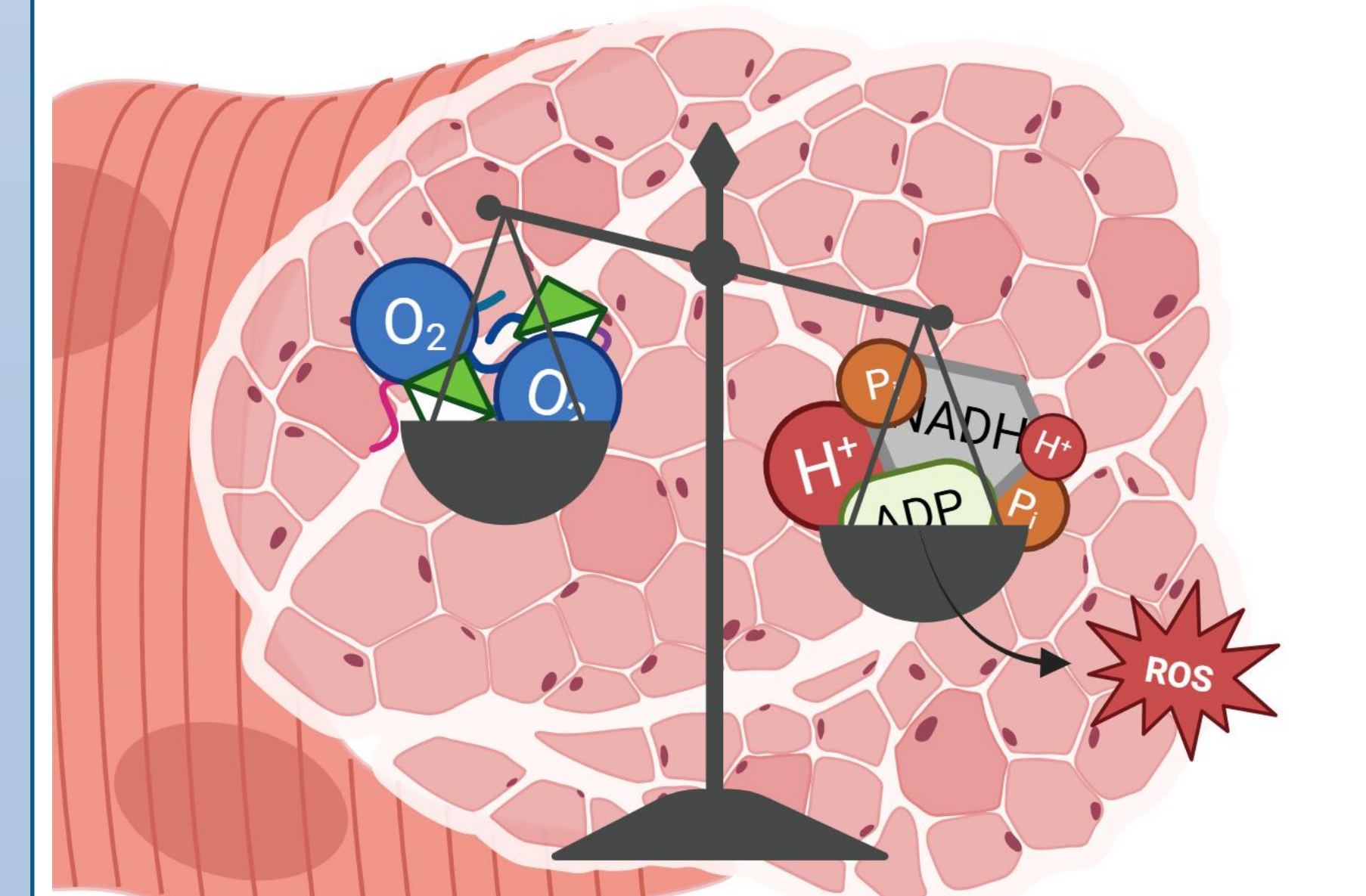
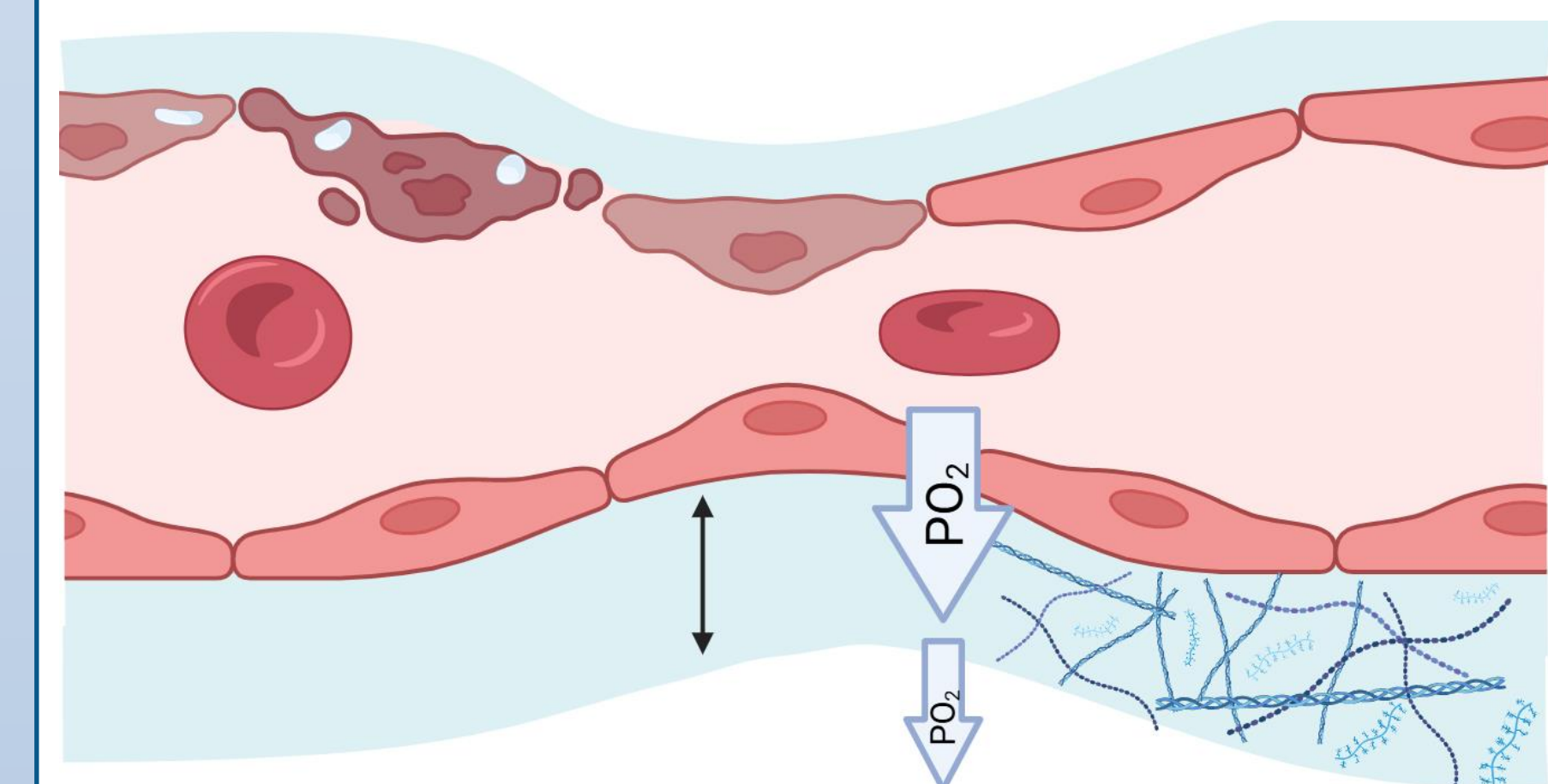


**Figure 2:** Capillarization was significantly lower in ME/CFS patients, affecting total oxygen **perfusion** to the skeletal muscles

## DISCUSSION

- Reduced lumen space
- Endothelial activation & dysfunction
- Basement membrane thickening

↓ metabolite removal & O<sub>2</sub> and nutrient delivery, predisposing to fatigue



↓ **lack of supply:** insufficient O<sub>2</sub> & nutrient supply | **lack of clearance:** built-up of waste-products ↑



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