

Ketosis enhances vascular function, angiogenic signaling, and the erythropoietic response to exercise and hypoxia

By Nathan Vermaerke

Promoter: Prof. Dr. Chiel Poffé
Co-supervisor: Dr. Myrthe Stalmans



**Brain | Exercise | Muscle
Research Group**

Previous Research

Ketone supplementation – What we know

1

**3-weeks excessive endurance
exercise with ketone ester
supplementation**



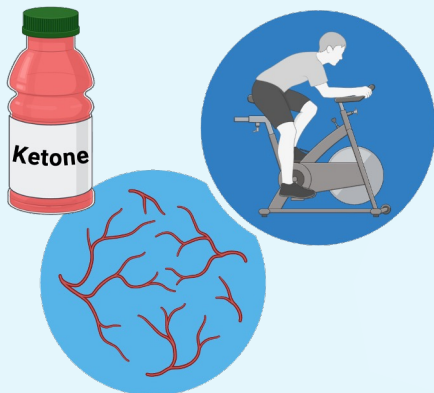
(Poffé. J Physiol. 2023)

Previous Research

Ketone supplementation – What we know

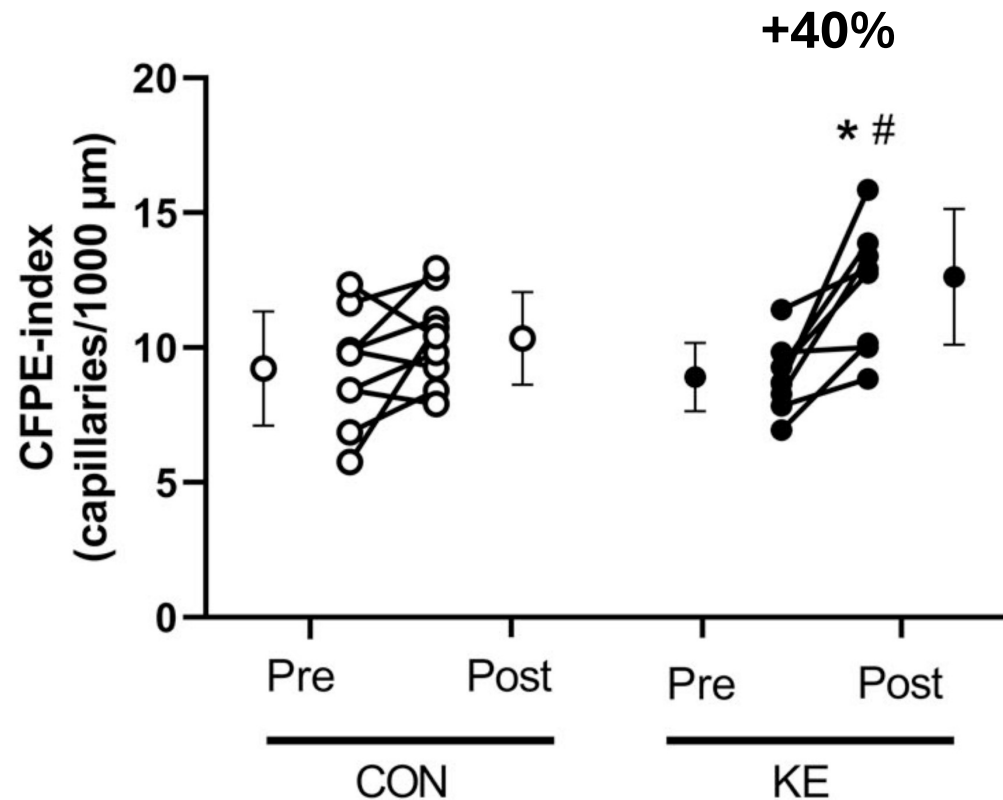
1

3-weeks excessive endurance exercise with ketone ester supplementation



**+40%
Capillarization**

(Poffé. J Physiol. 2023)



* $p < 0.05$ KE vs. CON; # $p < 0.05$ vs. Pre

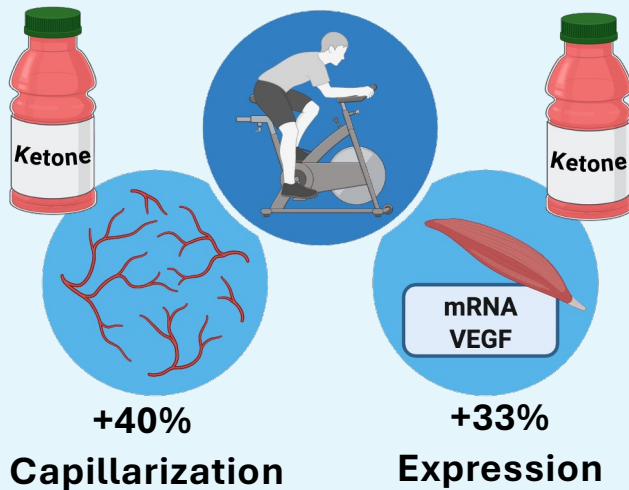
CON = control; KE = Ketone Ester

Previous Research

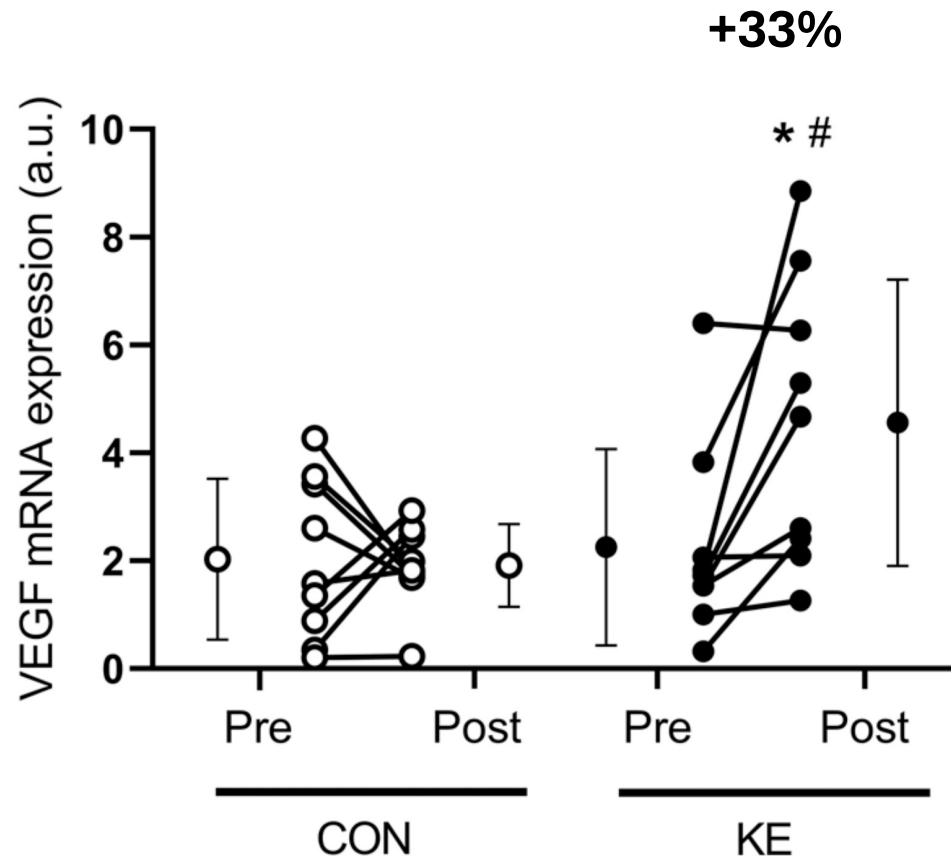
Ketone supplementation – What we know

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3-weeks excessive endurance exercise with ketone ester supplementation



(Poffé. J Physiol. 2023)



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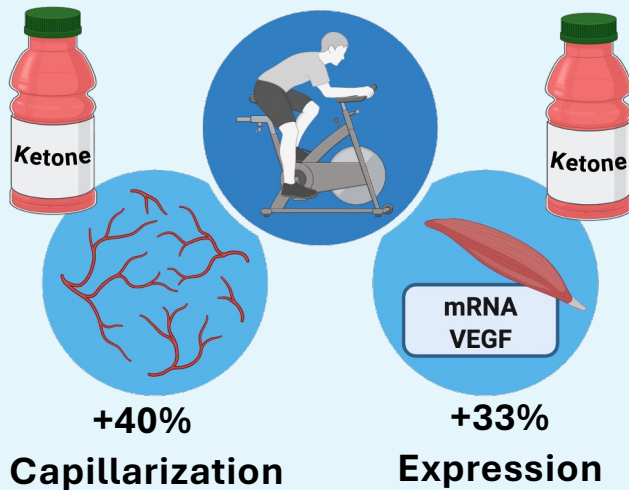
CON = control; KE = Ketone Ester; VEGF = Vascular Endothelial Growth Factor

Previous Research

Ketone supplementation – What we know

1

3-weeks excessive endurance
exercise with ketone ester
supplementation



(Poffé. J Physiol. 2023)

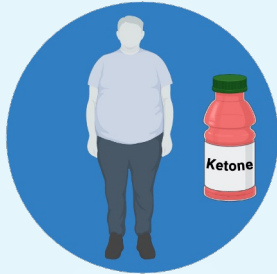
**Are ketone bodies an
acute regulator?**

Previous Research

Ketone supplementation – What we know

2

**2-weeks ketone ester
supplementation in obese**



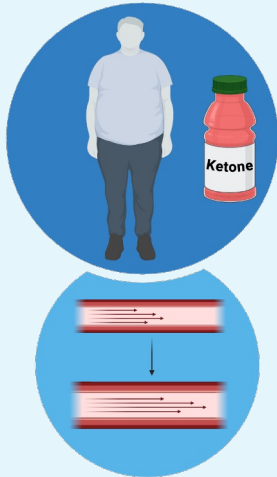
(Walsh. J Clin Endocrinol Metab. 2020)

Previous Research

Ketone supplementation – What we know

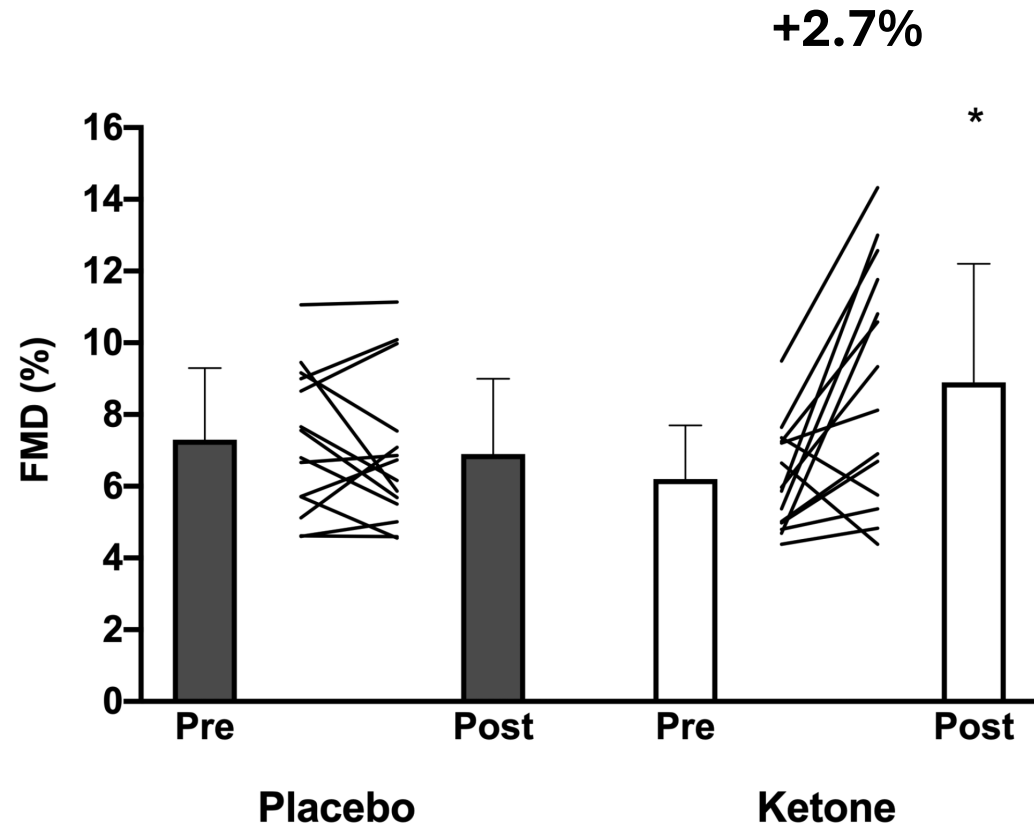
2

2-weeks ketone ester
supplementation in obese



+2.7% Flow Mediated Dilation (FMD)

(Walsh. J Clin Endocrinol Metab. 2020)



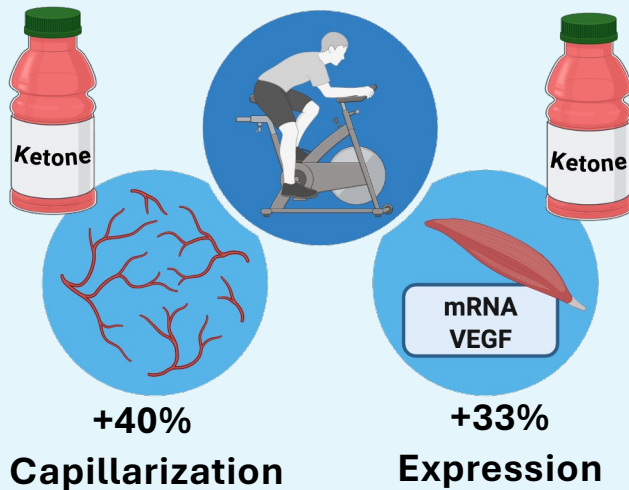
* $p < 0.05$

Previous Research

Ketone supplementation – What we know

1

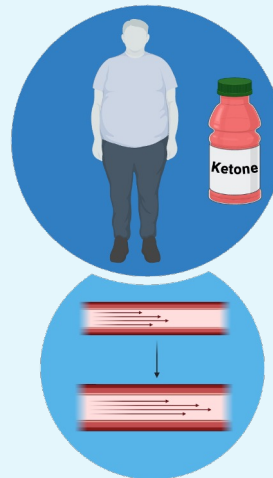
3-weeks excessive endurance exercise with ketone ester supplementation



(Poffé. J Physiol. 2023)

2

2-weeks ketone ester supplementation in obese



+2.7% Flow Mediated Dilation (FMD)

(Walsh. J Clin Endocrinol Metab. 2020)

Are ketone bodies an acute regulator?

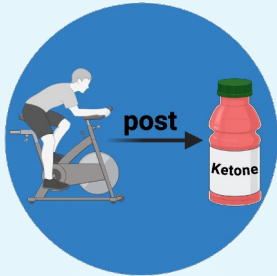
Can ketones acutely enhance FMD?

Previous Research

Ketone supplementation – What we know

3

**Post-exercise
ketone ester supplementation**



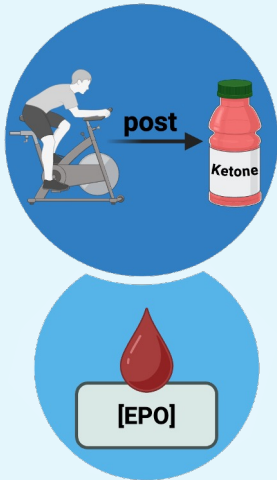
(Evans. Am J Physiol Endocrinol Metab. 2023)

Previous Research

Ketone supplementation – What we know

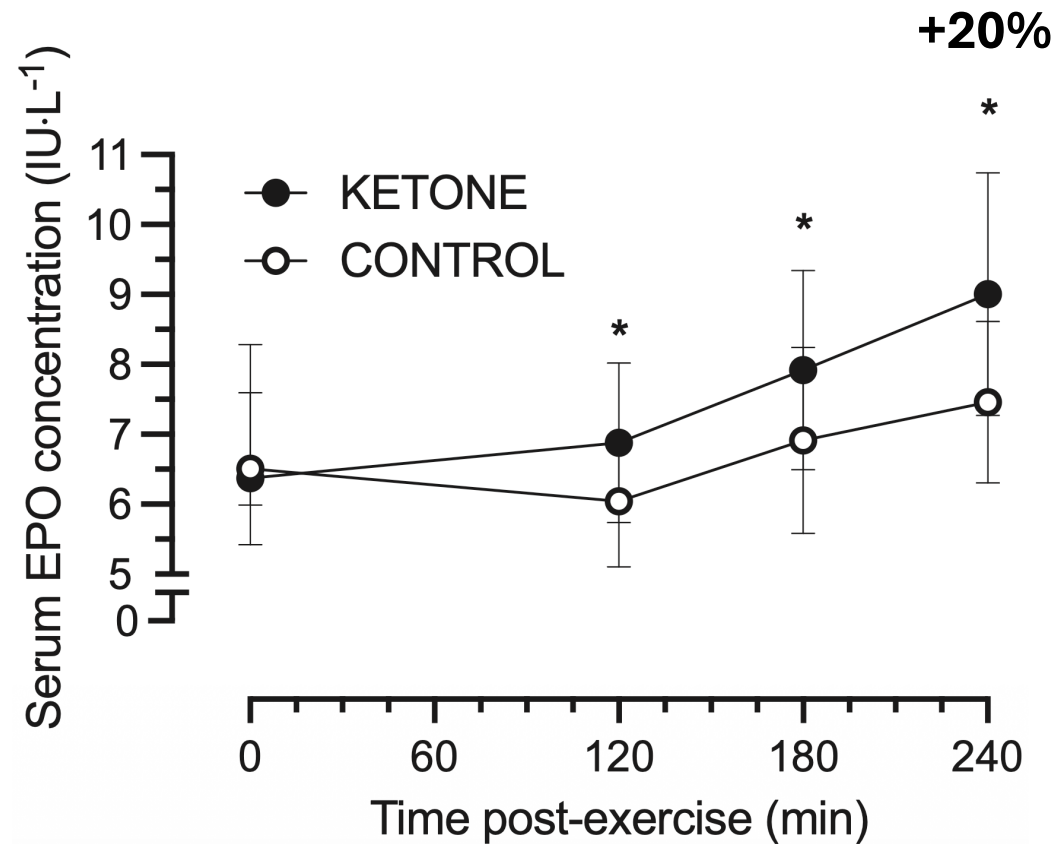
3

Post-exercise
ketone ester supplementation



+20% Concentration

(Evans. Am J Physiol Endocrinol Metab. 2023)



* $p < 0.05$ for KETONE vs. CONTROL

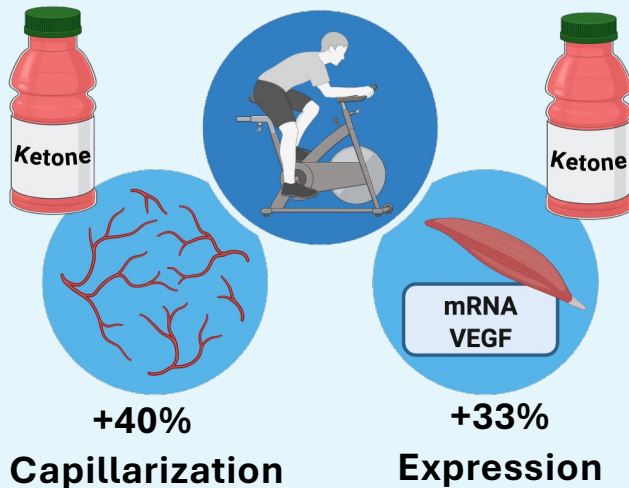
EPO = Erythropoëtime

Previous Research

Ketone supplementation – What we know

1

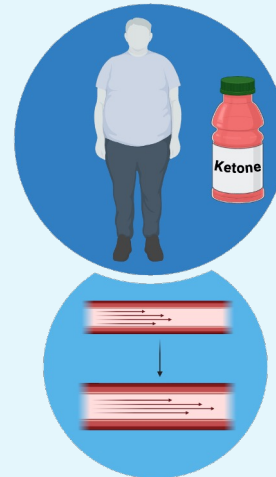
3-weeks excessive endurance exercise with ketone ester supplementation



(Poffé. J Physiol. 2023)

2

2-weeks ketone ester supplementation in obese

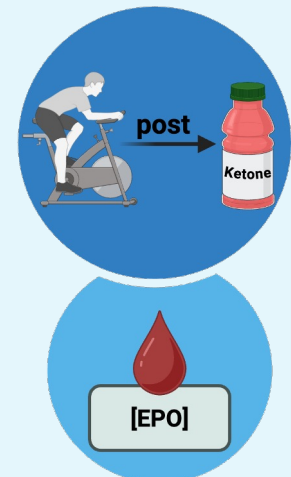


+2.7% Flow Mediated Dilation

(Walsh. J Clin Endocrinol Metab. 2020)

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Post-exercise ketone ester supplementation



+20% Concentration

(Evans. Am J Physiol Endocrinol Metab. 2023)

Are ketone bodies an acute regulator?

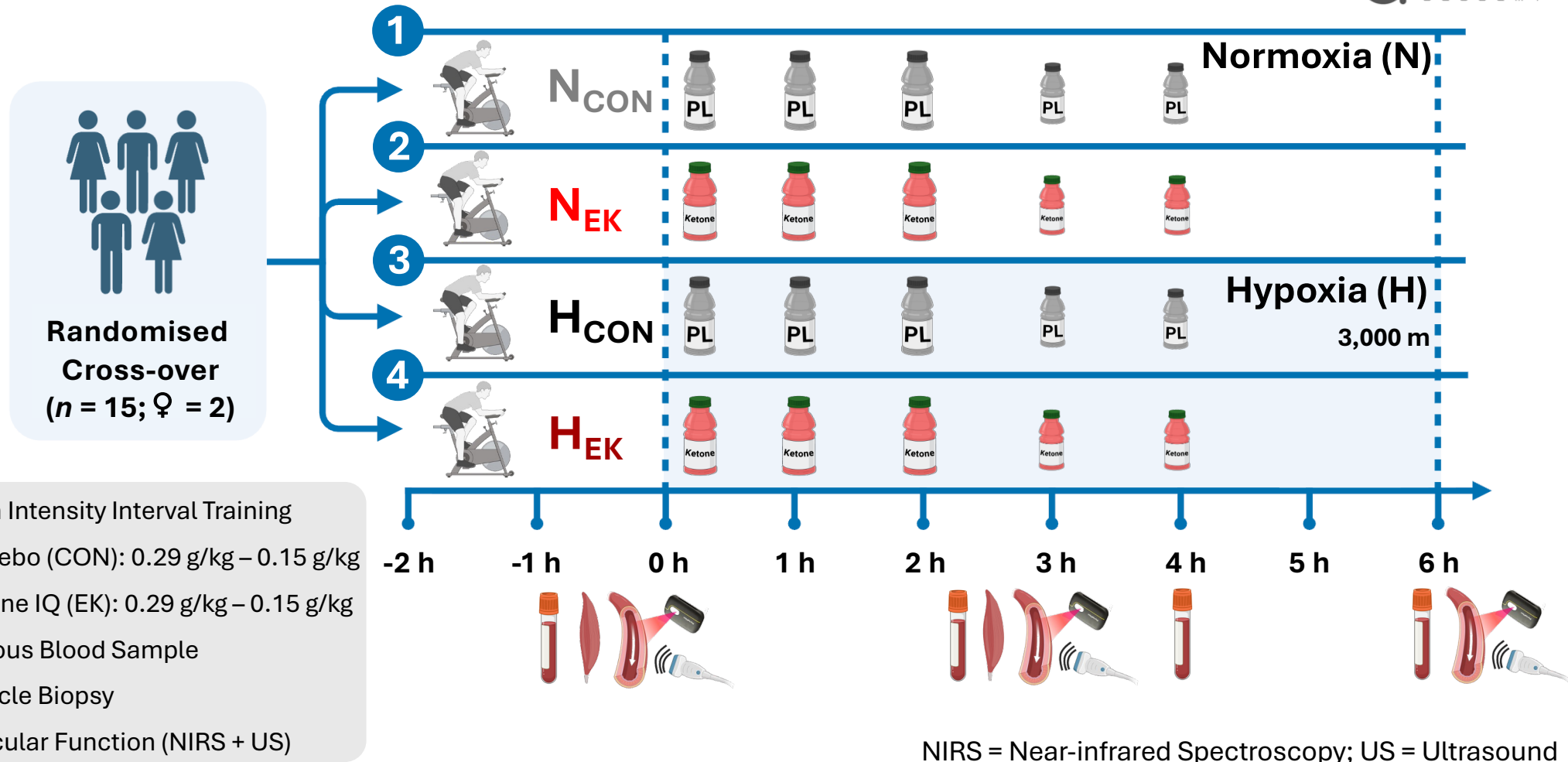
Can ketones acutely enhance FMD?

Is effect of EK additive to hypoxia?

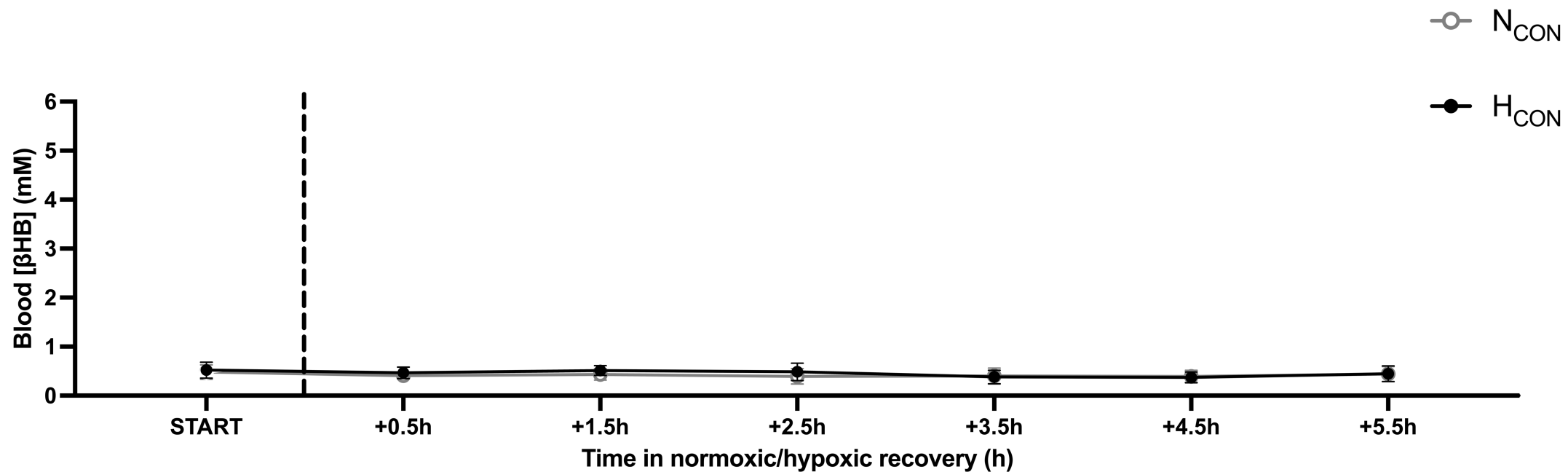
EK = Exogenous Ketosis

Methods

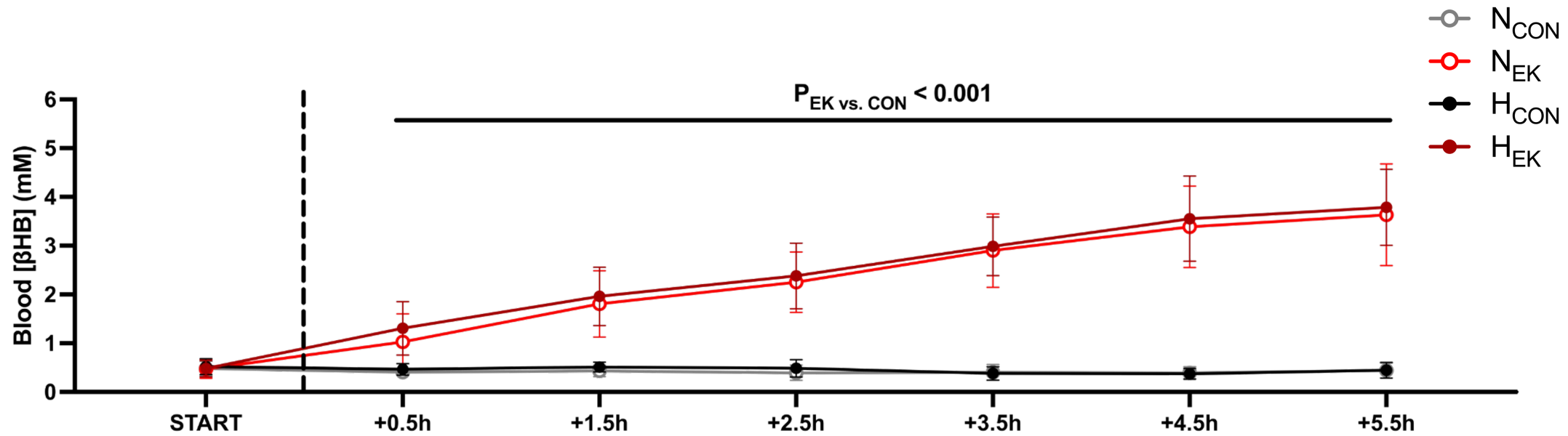
Randomized, placebo-controlled, cross-over design



Ketone precursor induced exogenous ketosis (EK)



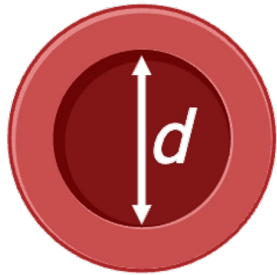
Ketone precursor induced exogenous ketosis (EK)



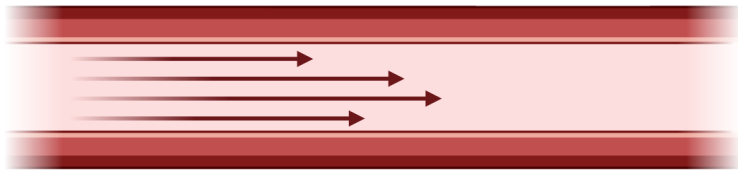
Macro- and microvascular function assessed via a vascular occlusion protocol



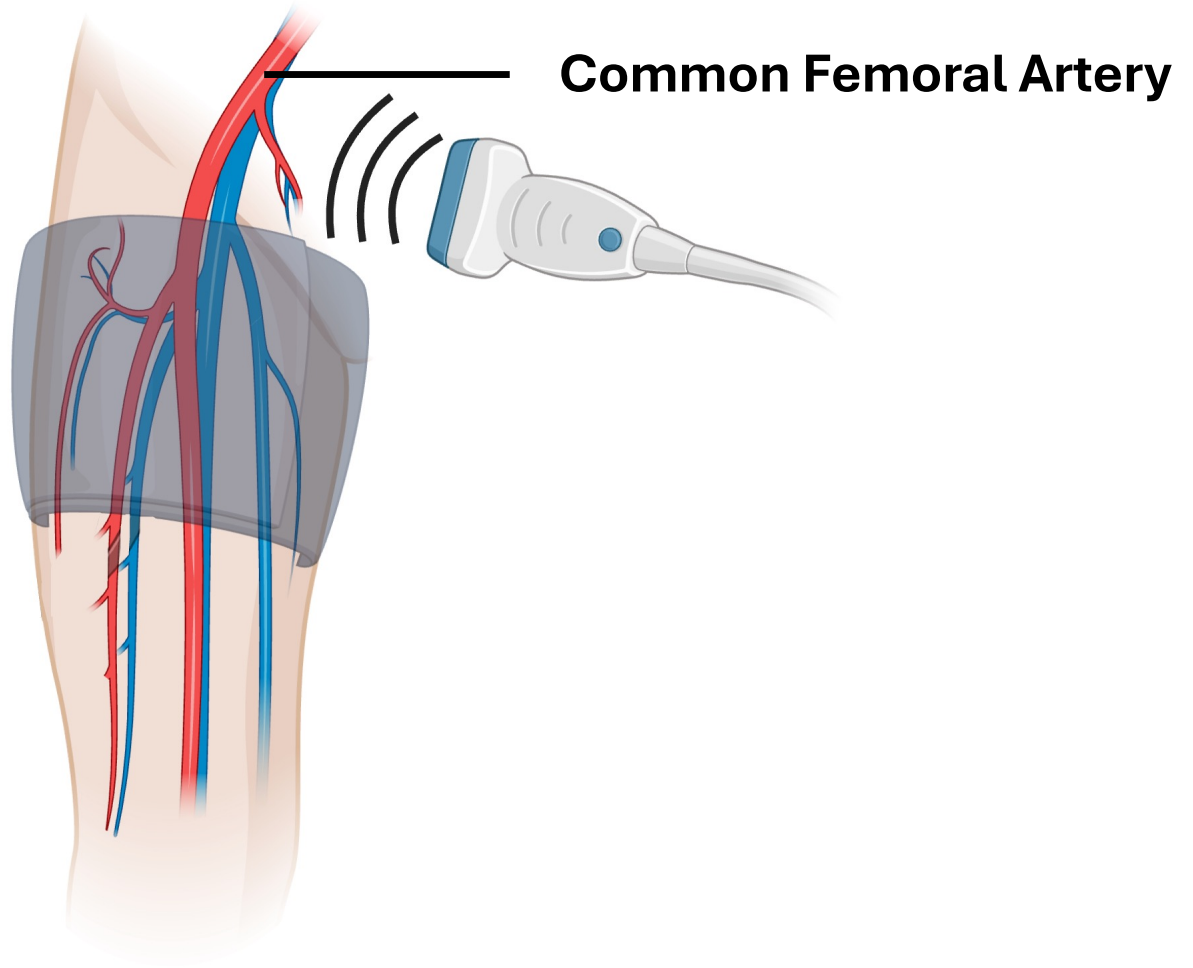
Macrovascular parameters



Artery Diameter

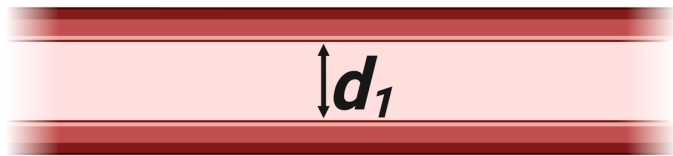


Blood Velocity & Blood Flow

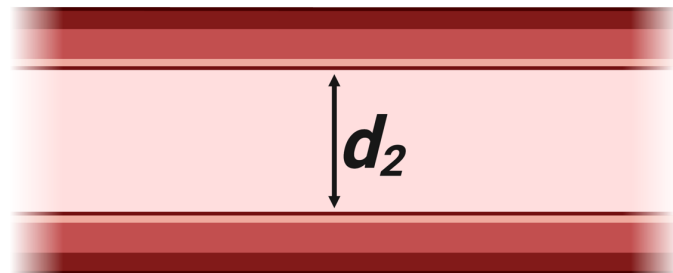
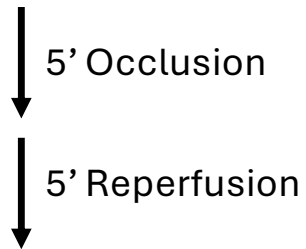


Macrovascular function

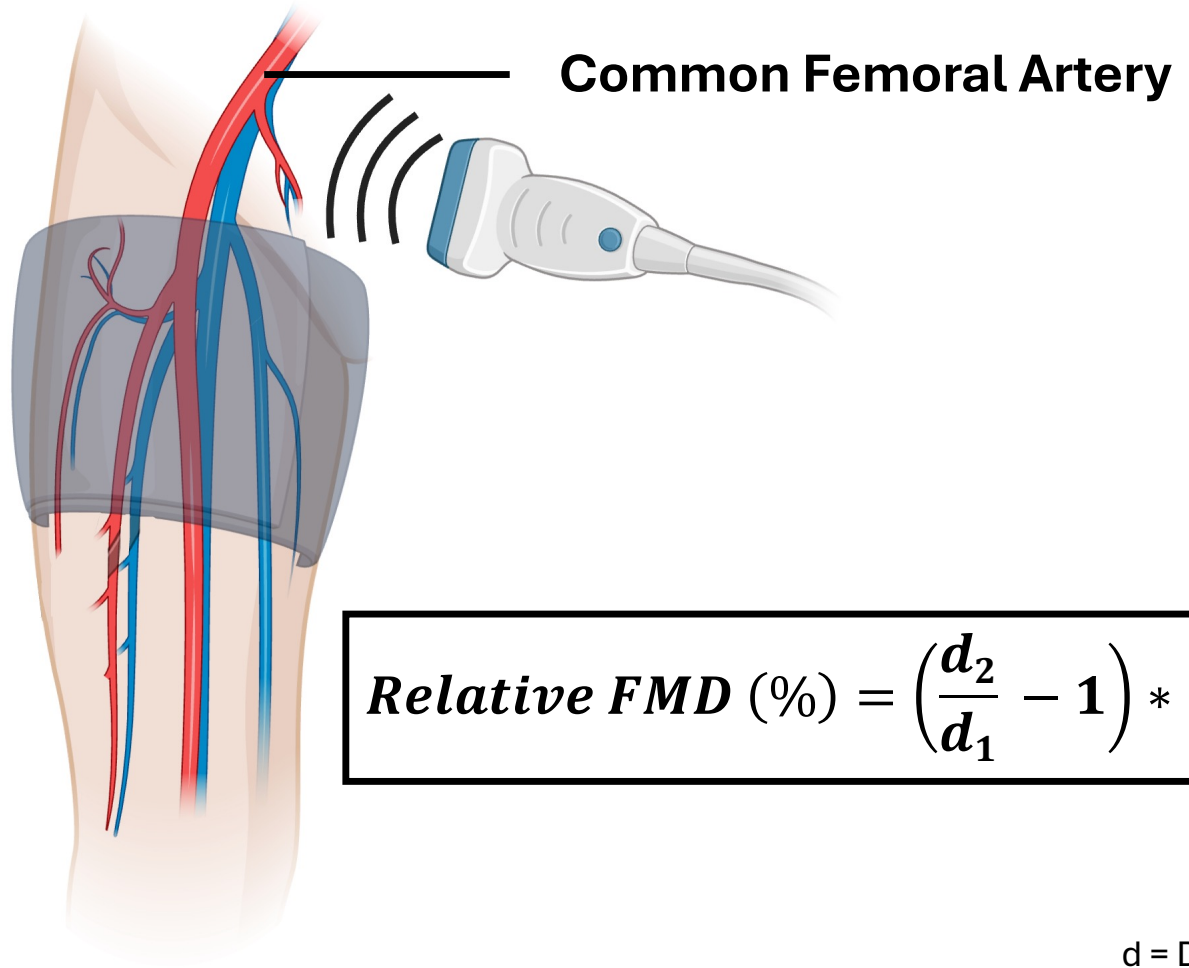
Flow Mediated Dilation (FMD)



Resting diameter = d_1



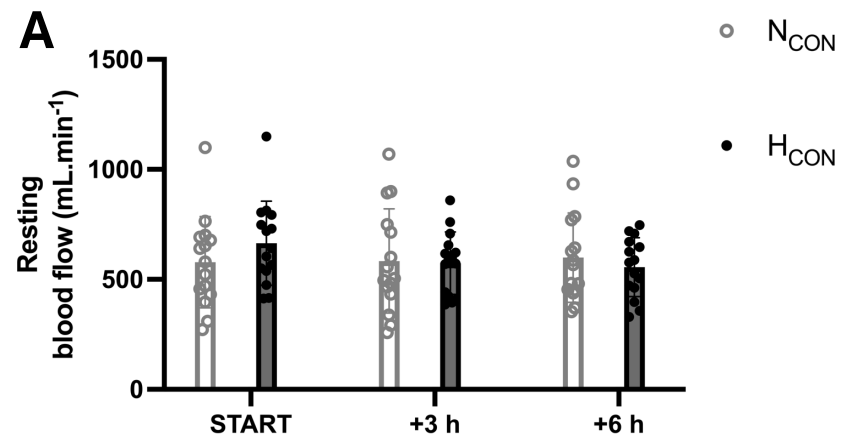
Peak diameter = d_2



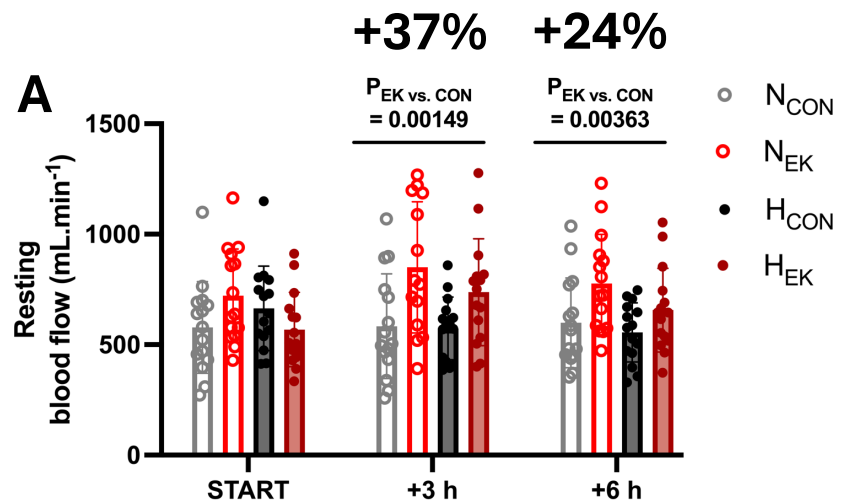
$$\text{Relative FMD (\%)} = \left(\frac{d_2}{d_1} - 1 \right) * 100$$

d = Diameter

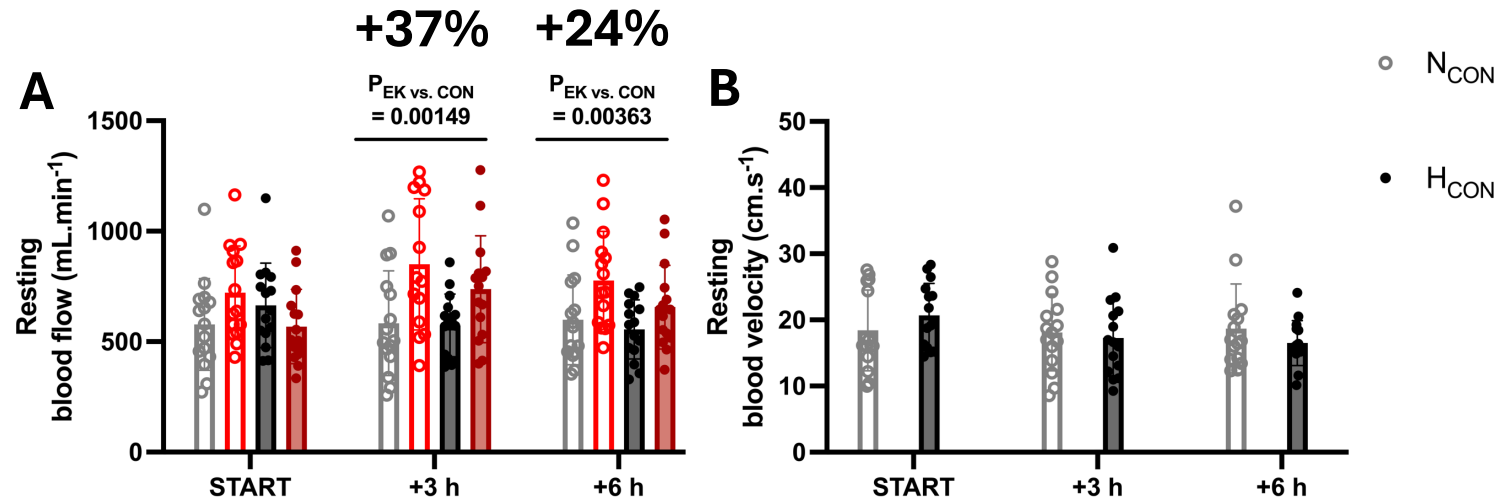
EK increased resting blood flow



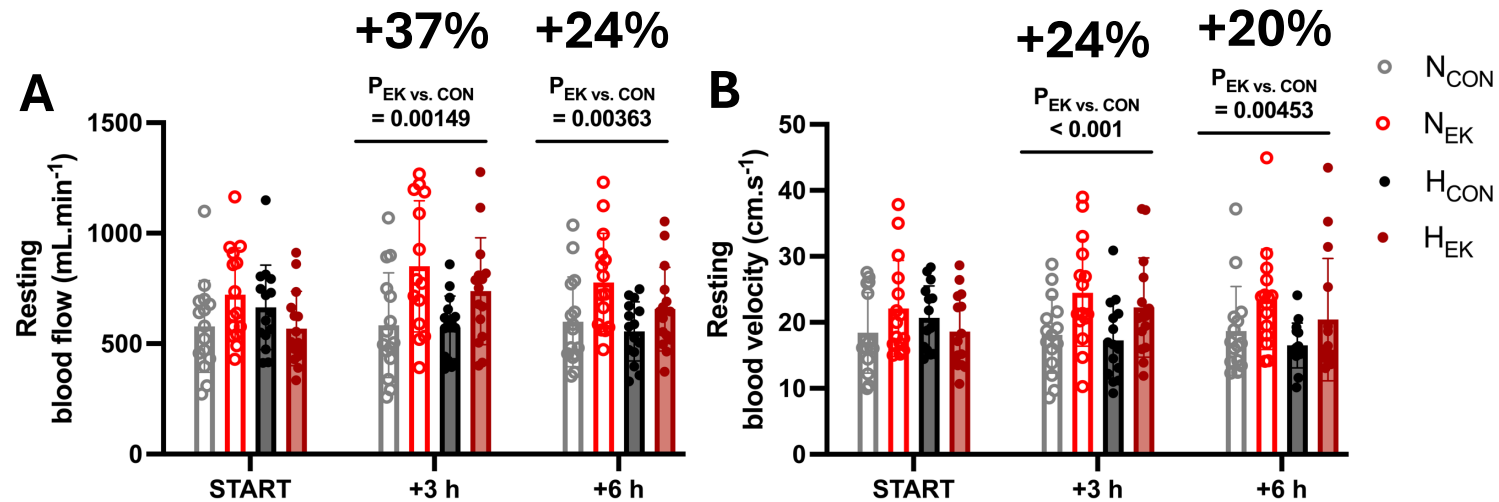
EK increased resting blood flow



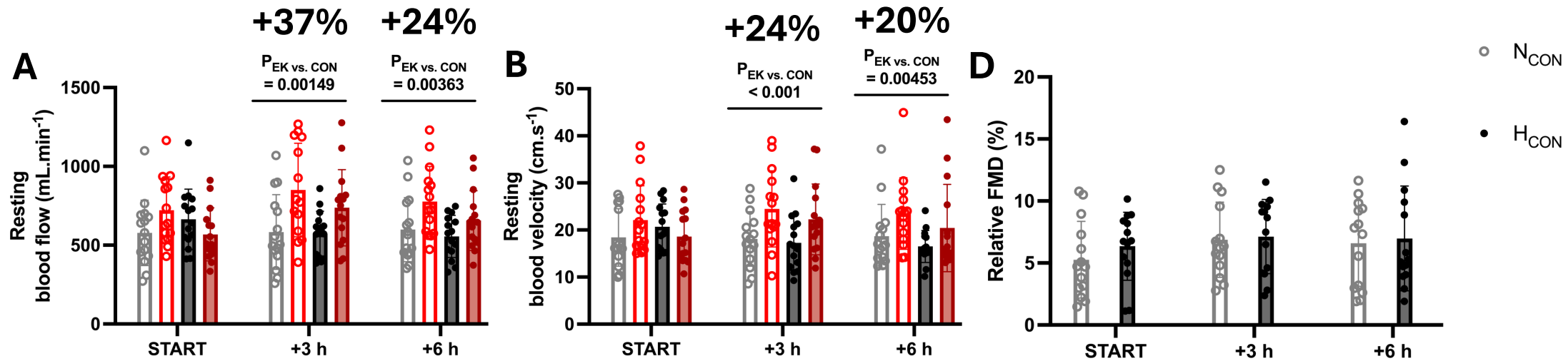
EK increased resting blood velocity



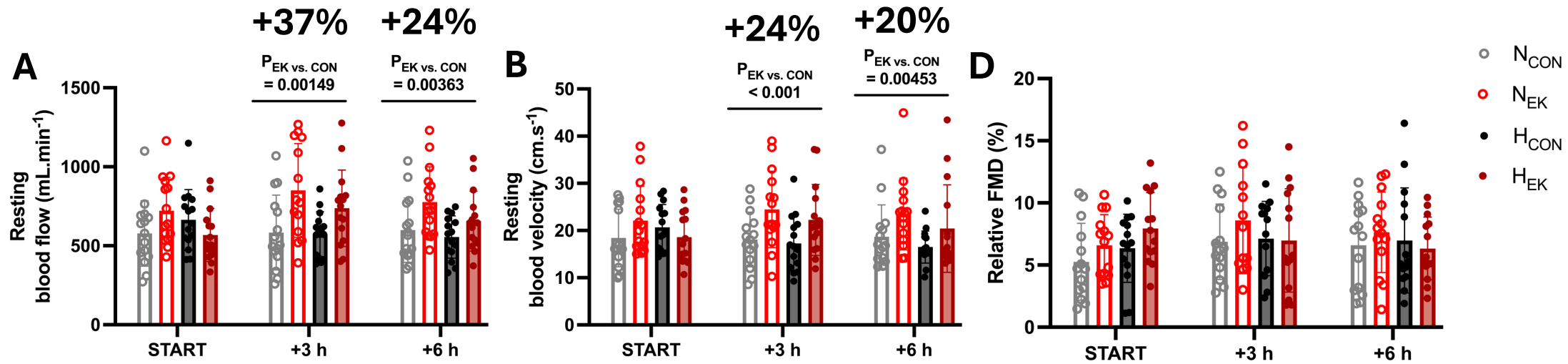
EK increased resting blood velocity



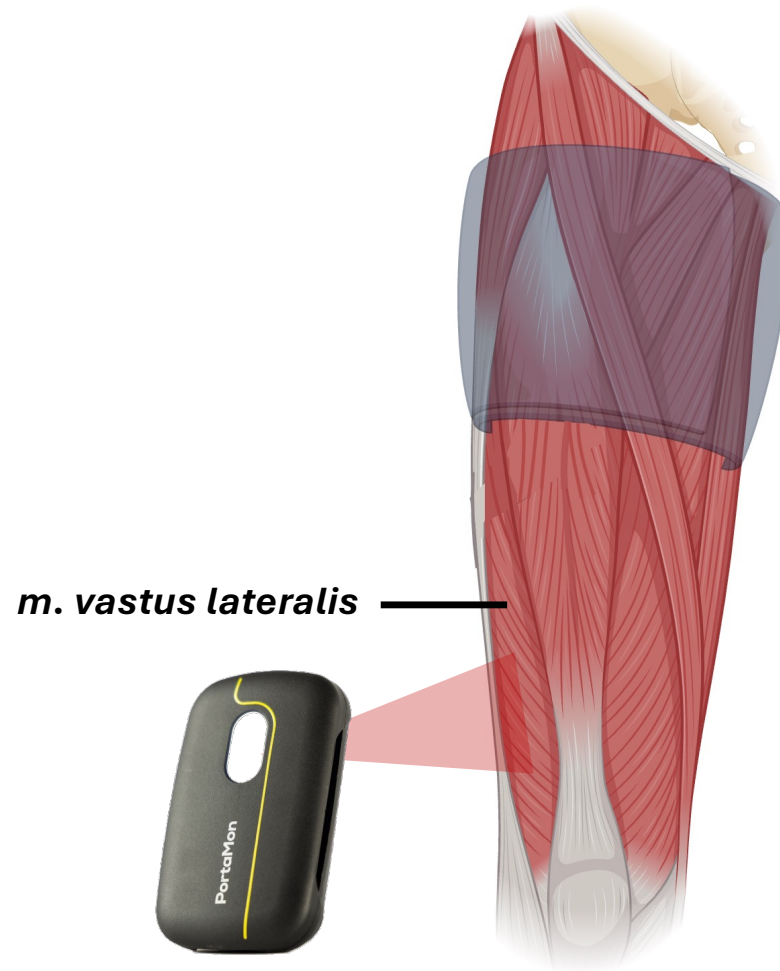
Relative FMD remained unchanged



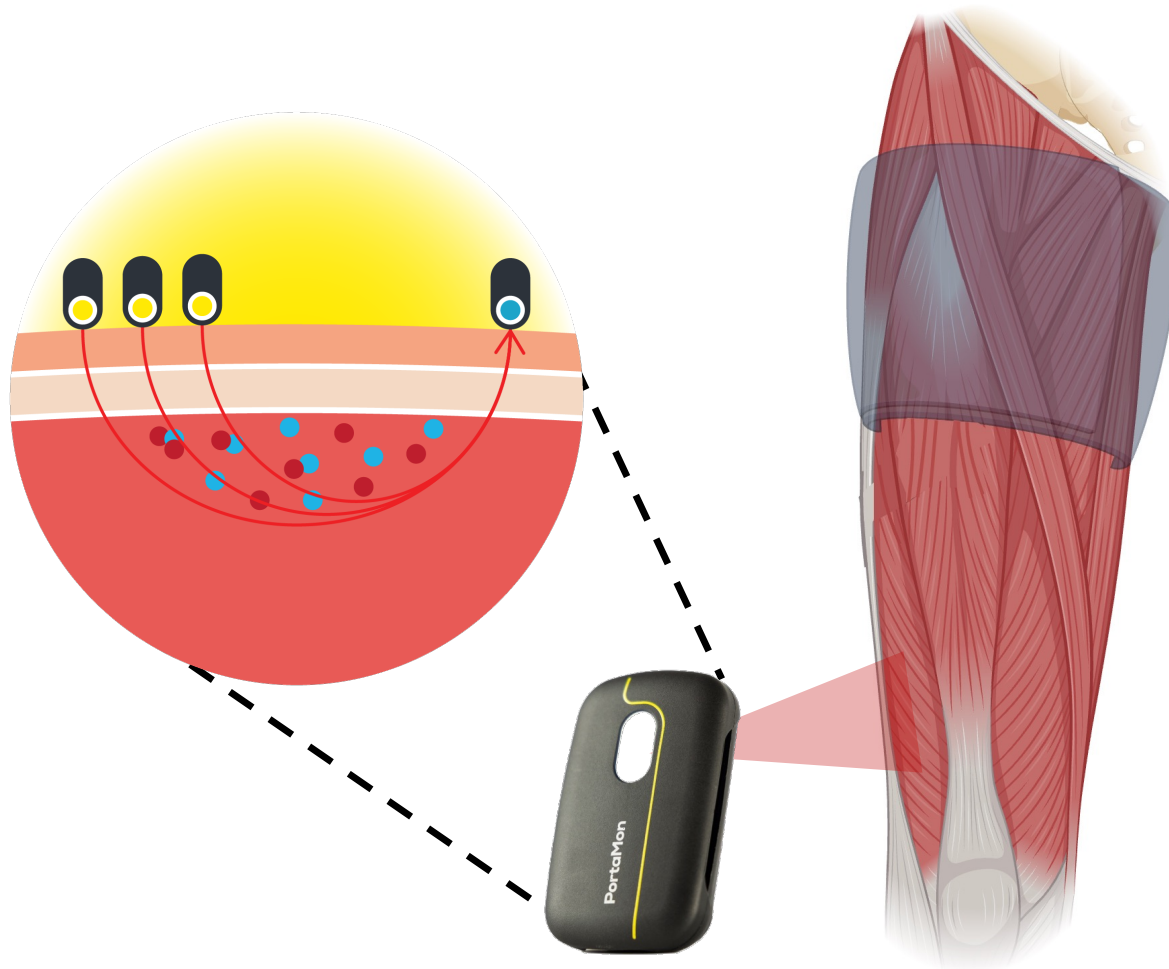
Relative FMD remained unchanged



Microvascular function



Microvascular function

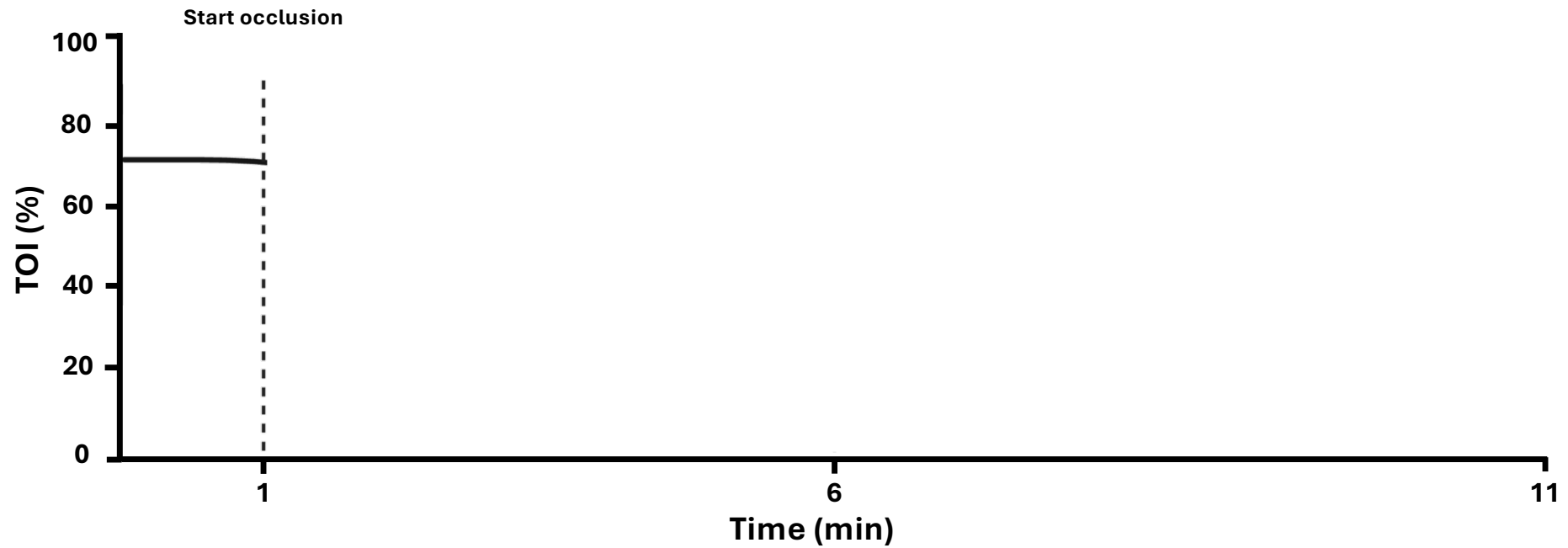


$$\text{TOI} = \frac{\text{O}_2\text{HB}}{\text{HHb} + \text{O}_2\text{HB}} * 100\%$$

TOI = Tissue Oxygenation Index; O₂HB = Oxyhemoglobin; HHb = Deoxyhemoglobin

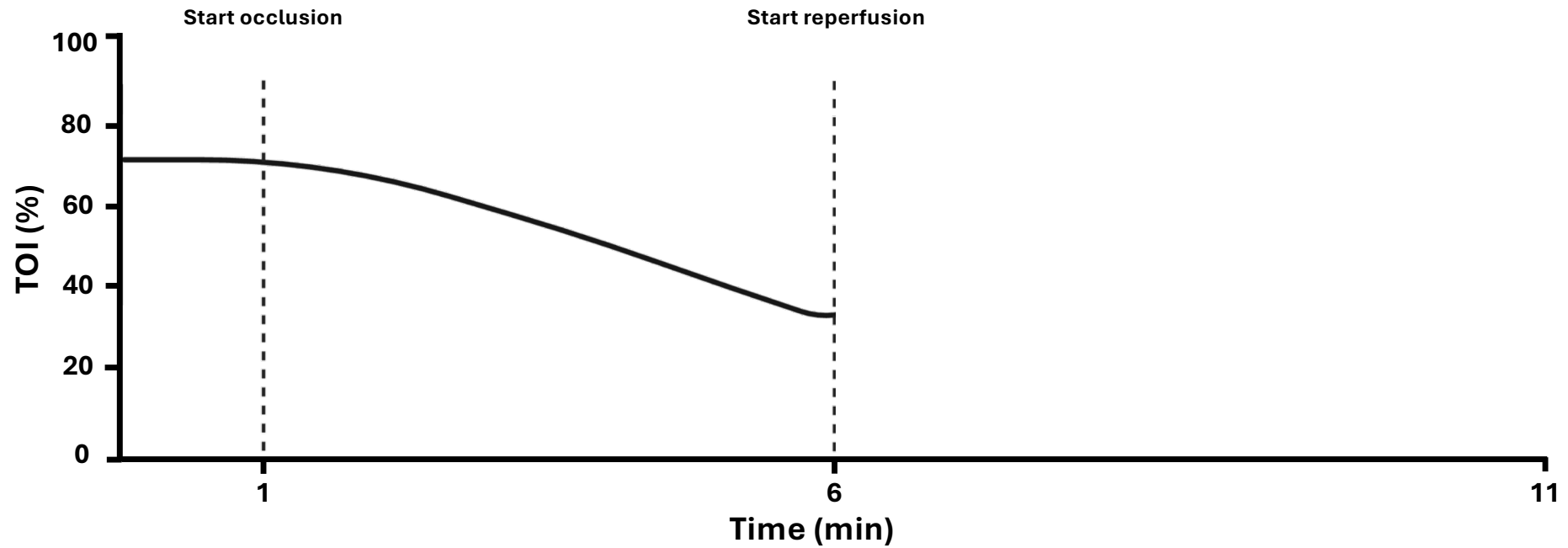
Microvascular function

Measured via a vascular occlusion test – Typical Curve below



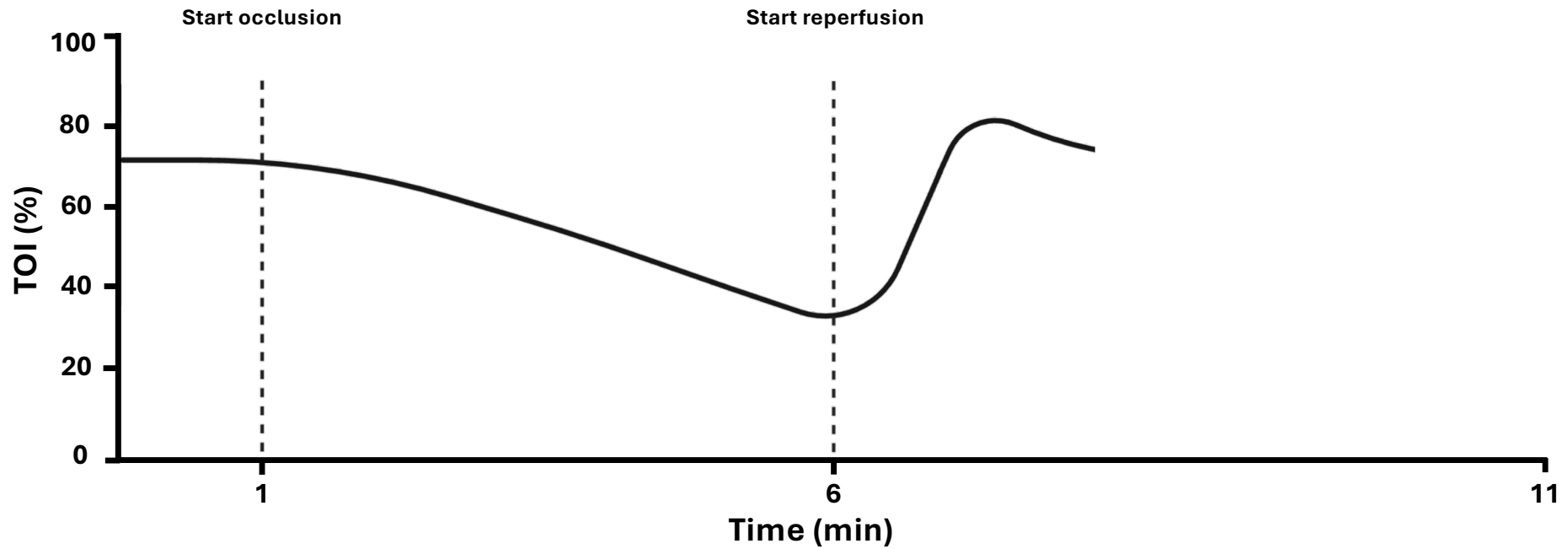
Microvascular function

Measured via a vascular occlusion test – Typical Curve below



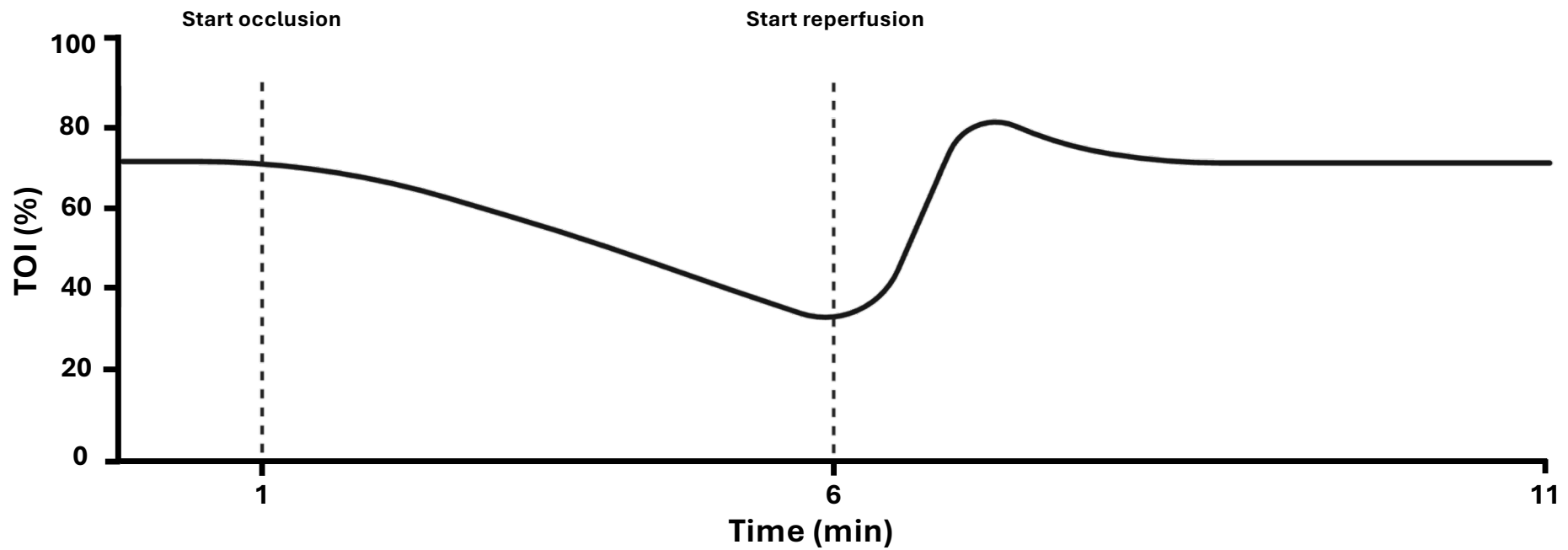
Microvascular function

Measured via a vascular occlusion test – Typical Curve below

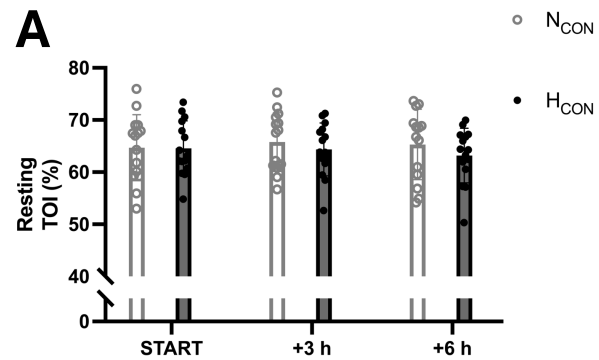
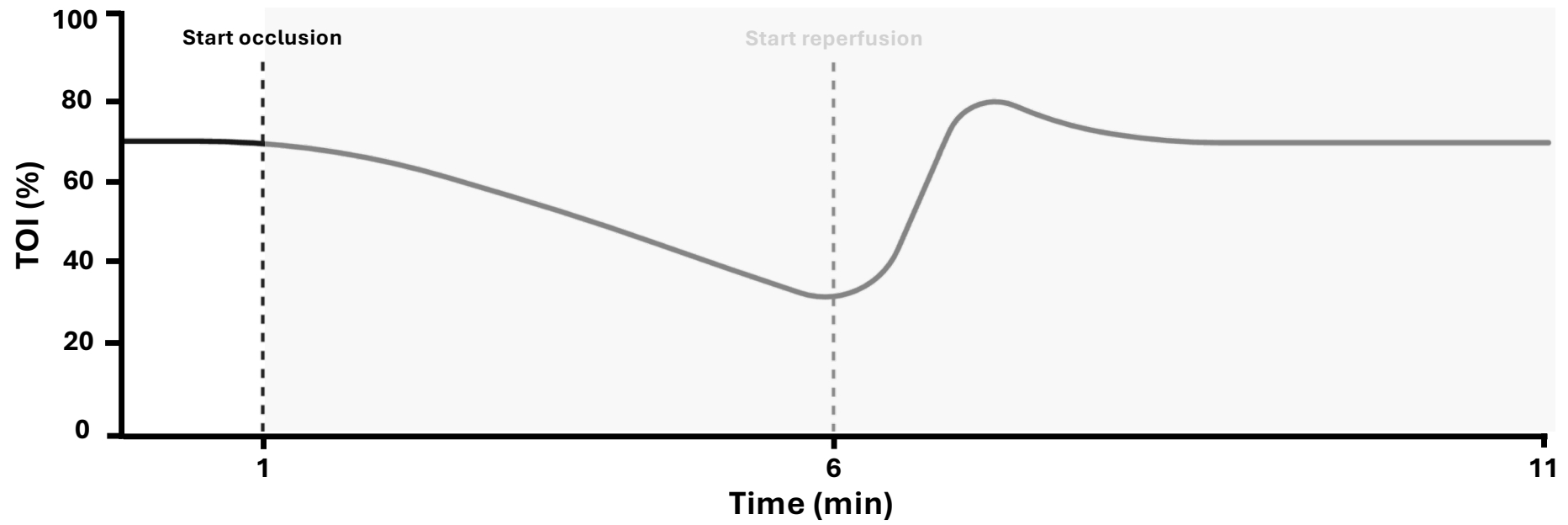


Microvascular function

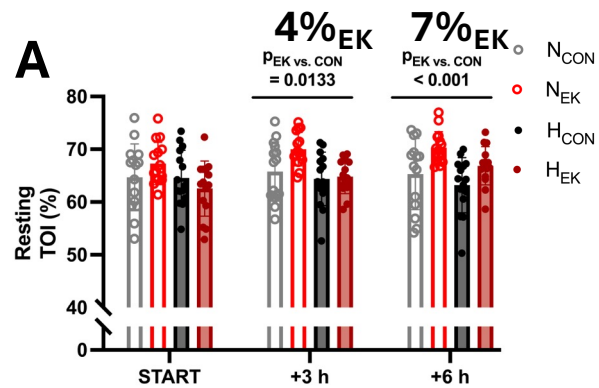
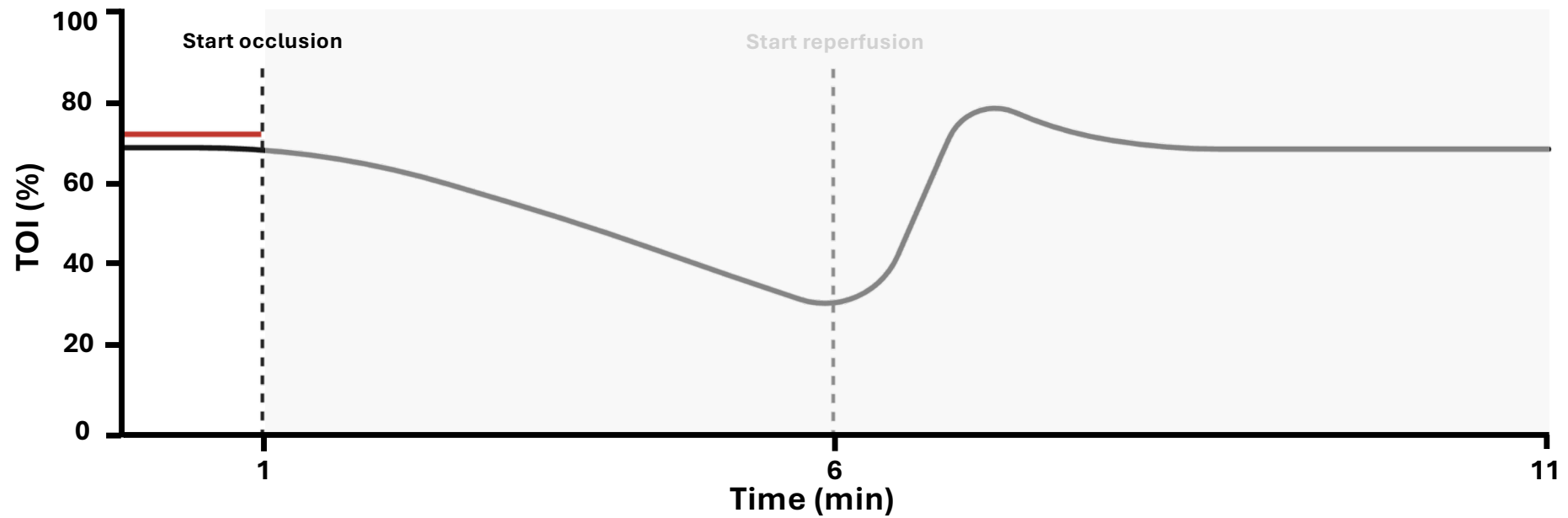
Measured via a vascular occlusion test – Typical Curve below



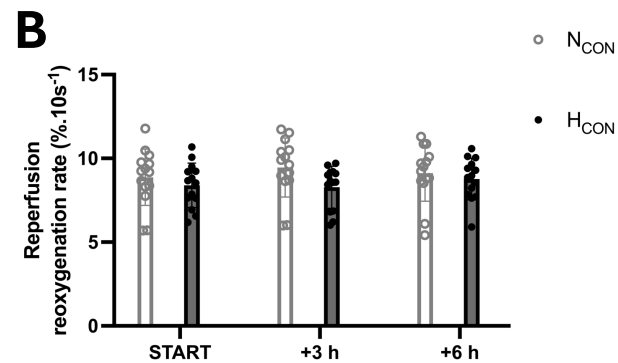
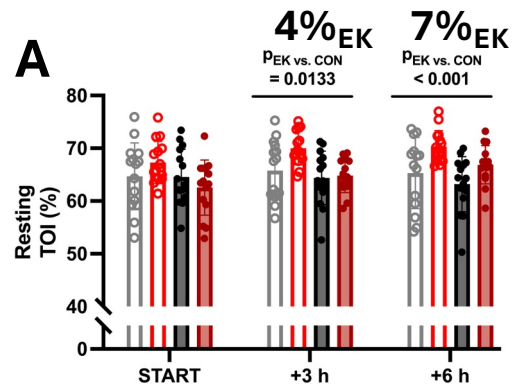
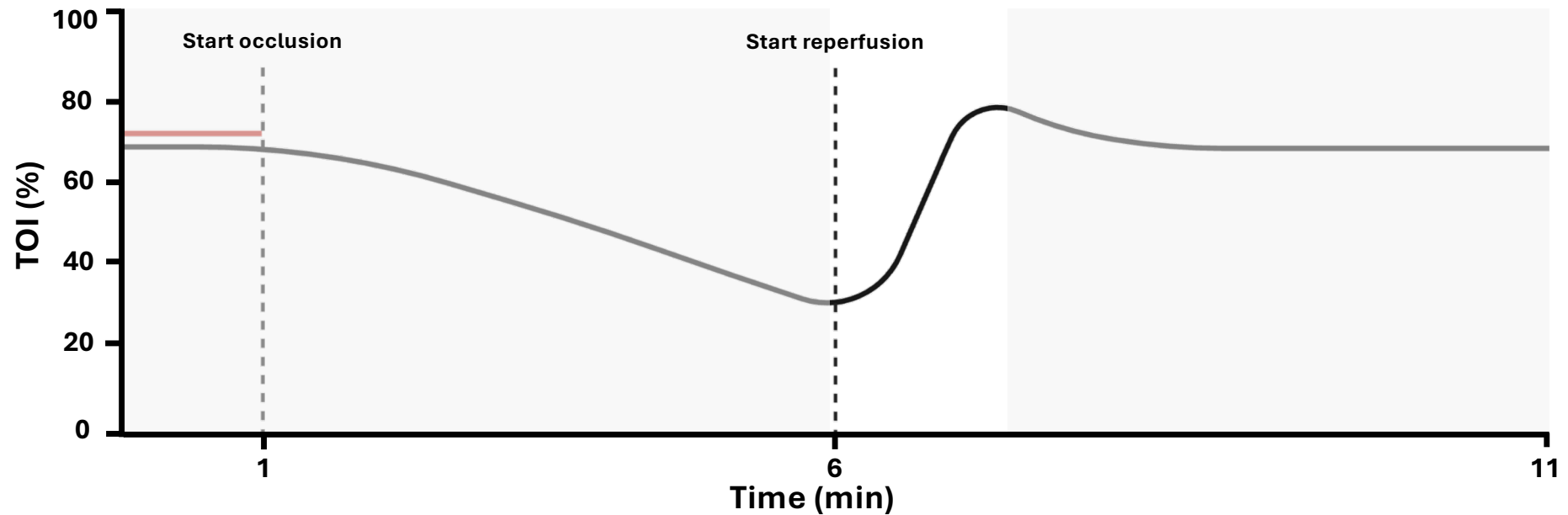
EK increased resting TOI



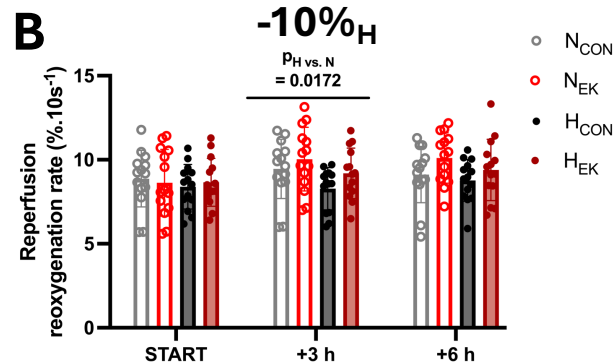
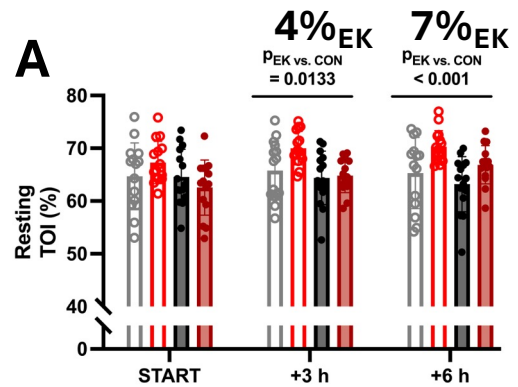
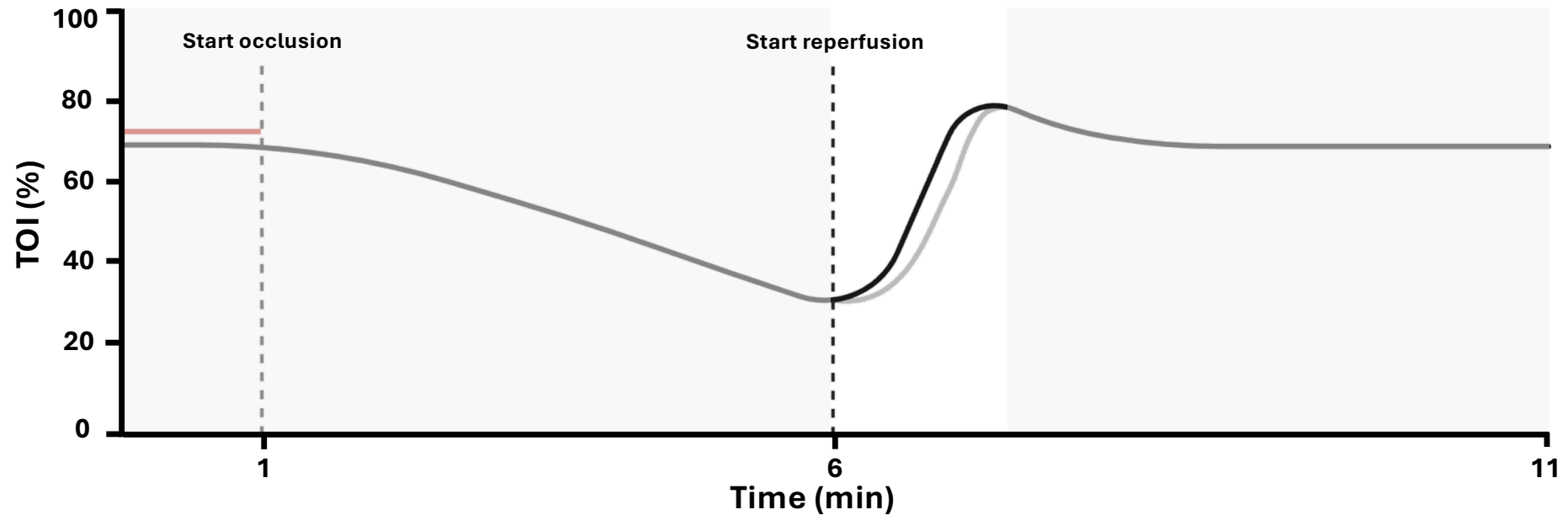
EK increased resting TOI



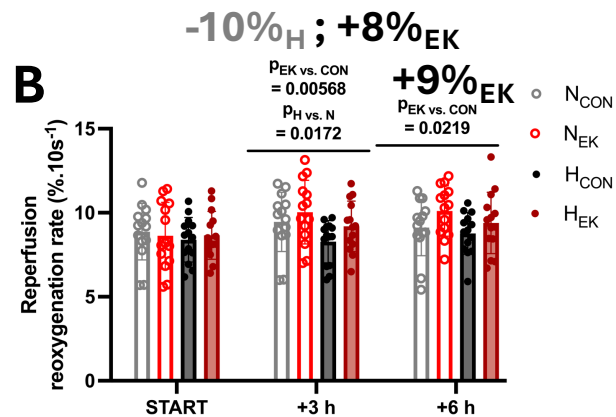
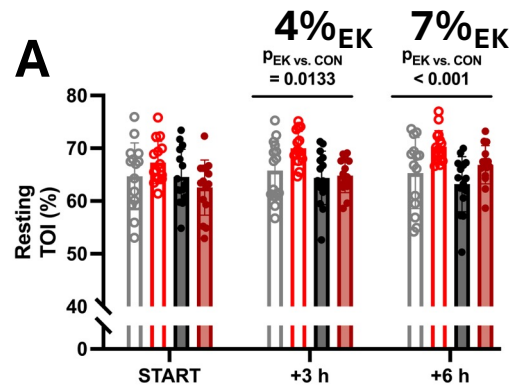
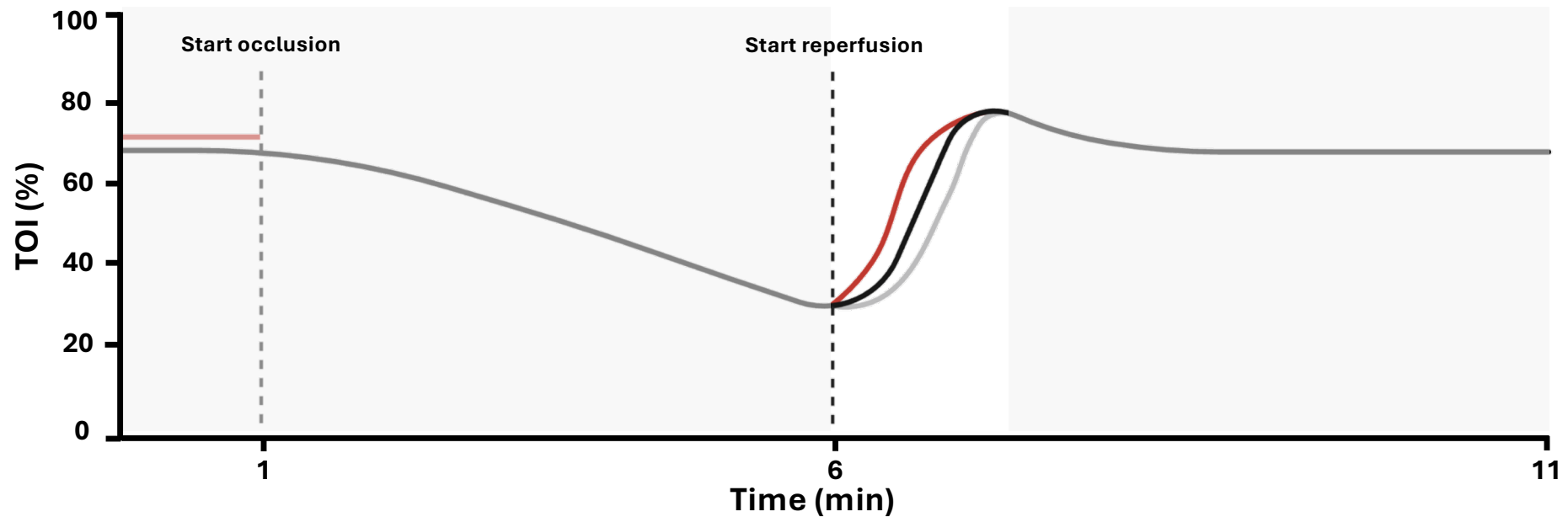
Hypoxia decreased reperfusion reoxygenation rate



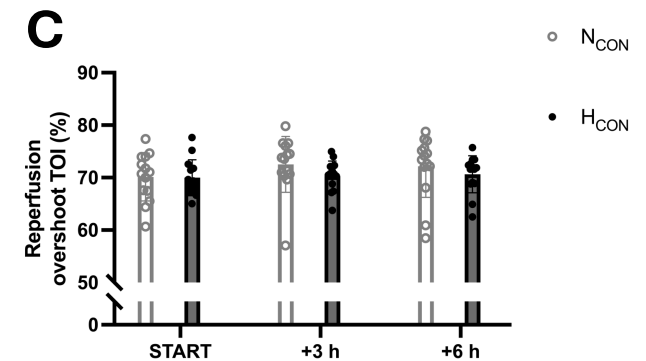
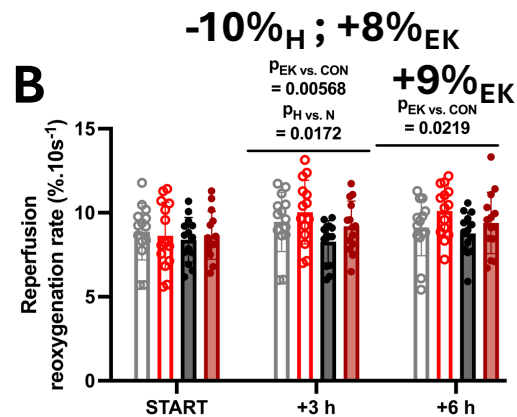
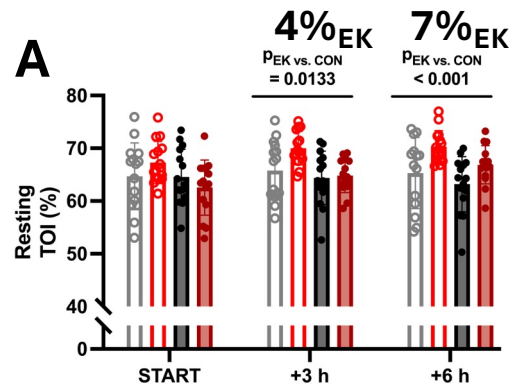
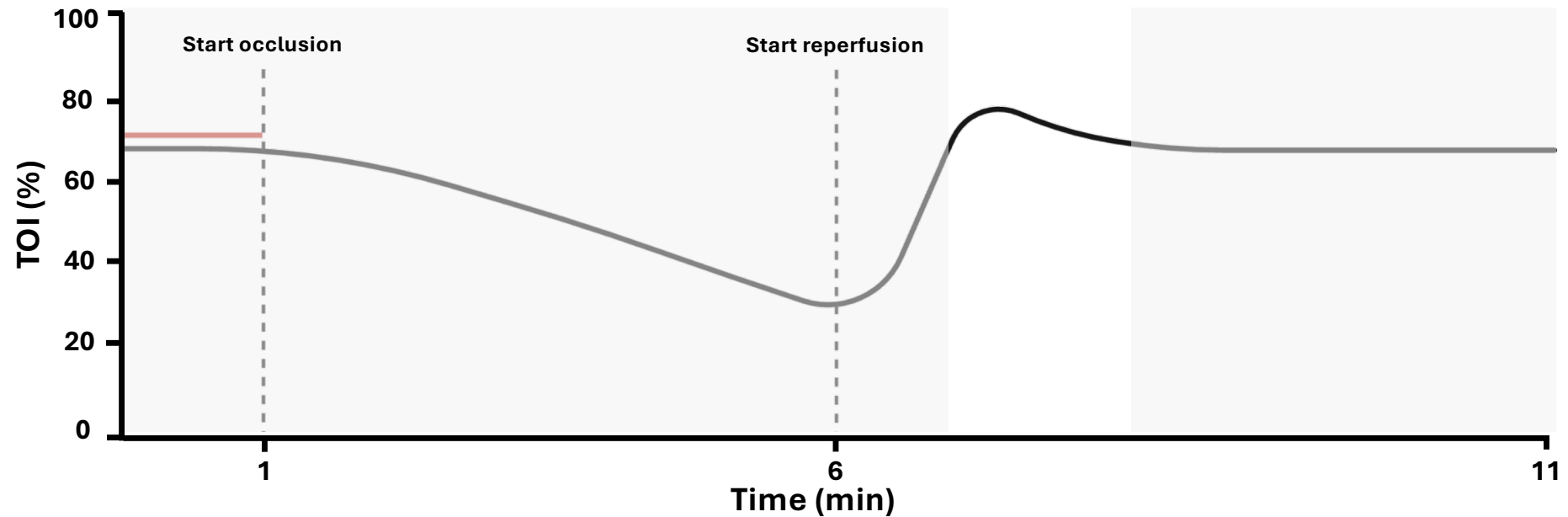
Hypoxia decreased reperfusion reoxygenation rate



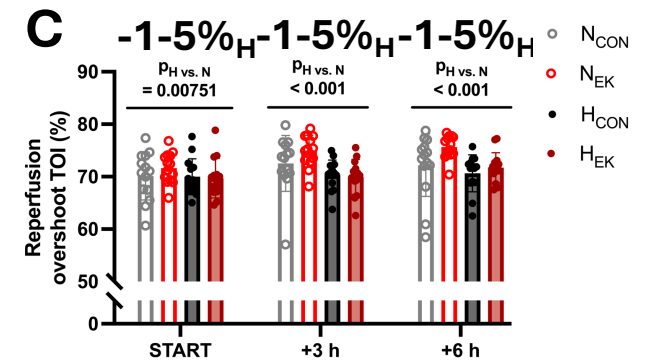
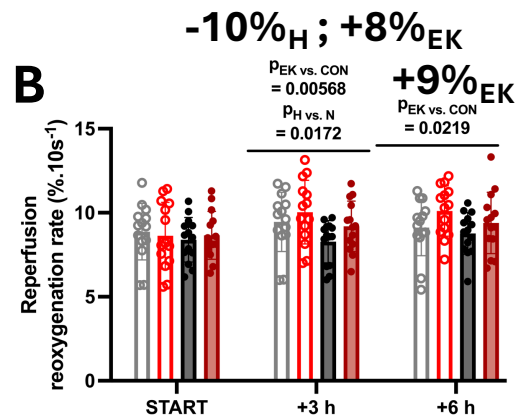
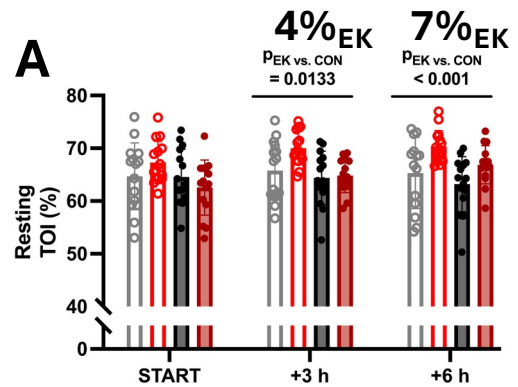
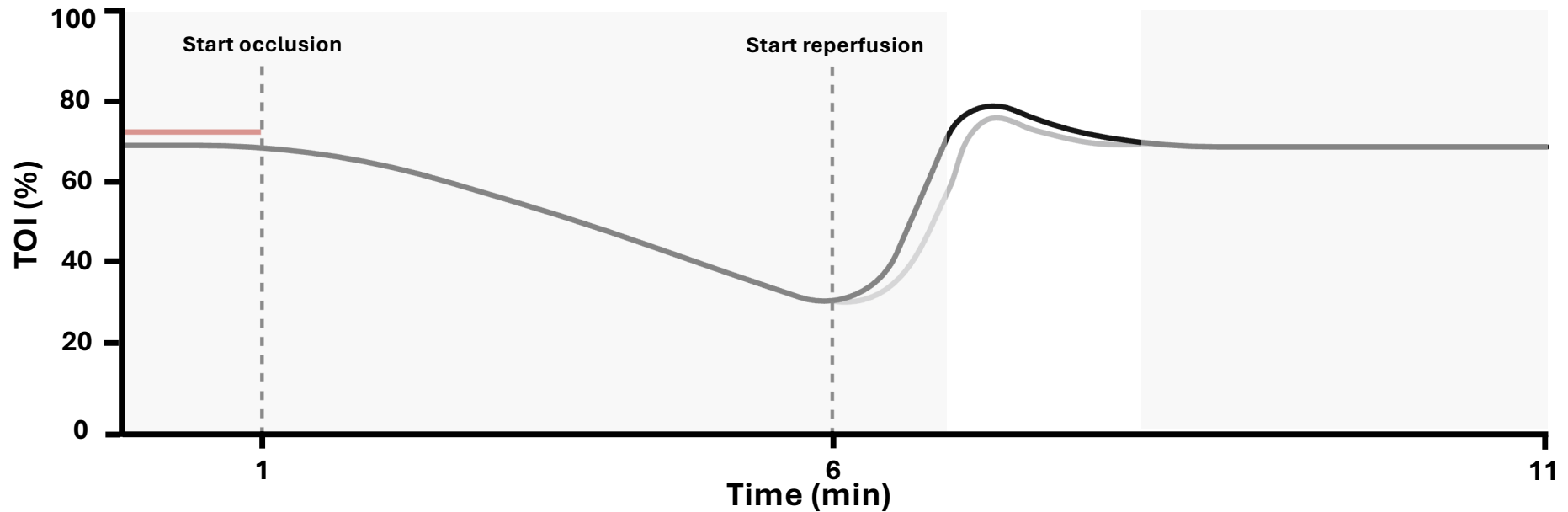
EK increased reperfusion reoxygenation



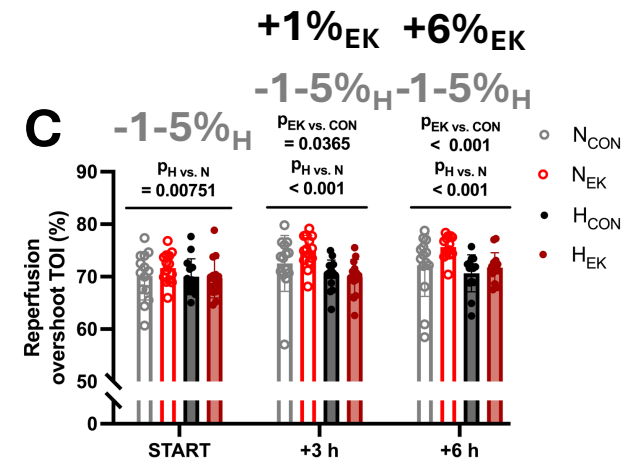
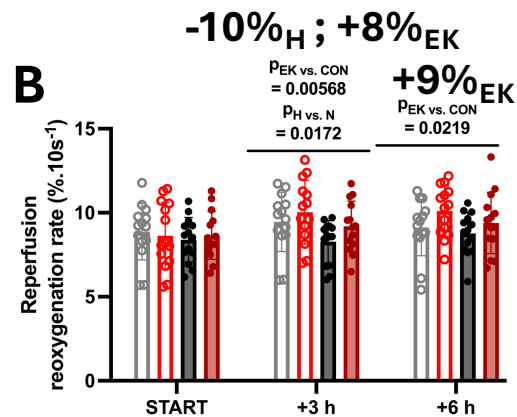
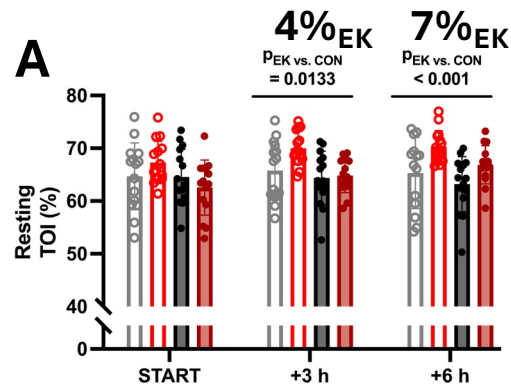
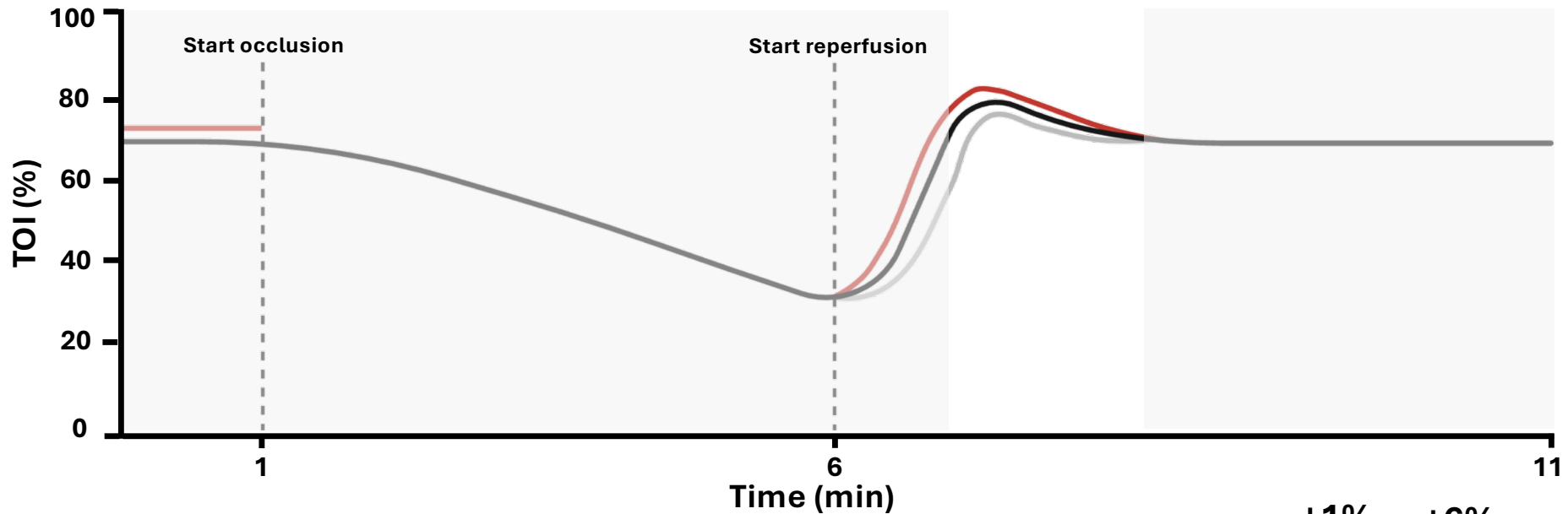
Hypoxia decreased maximal reperfusion overshoot



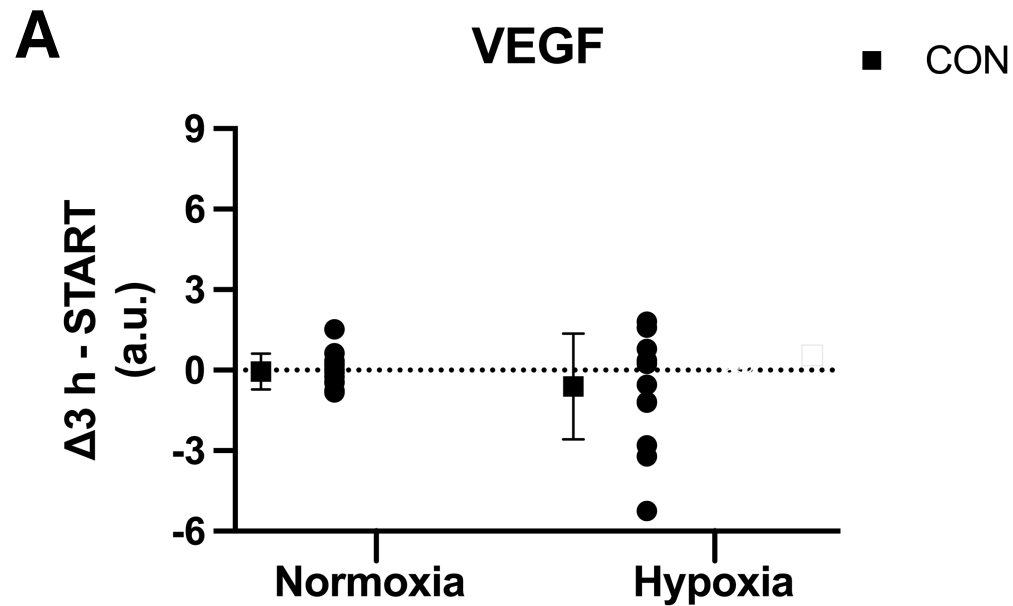
Hypoxia decreased maximal reperfusion overshoot



EK increased maximal reperfusion overshoot

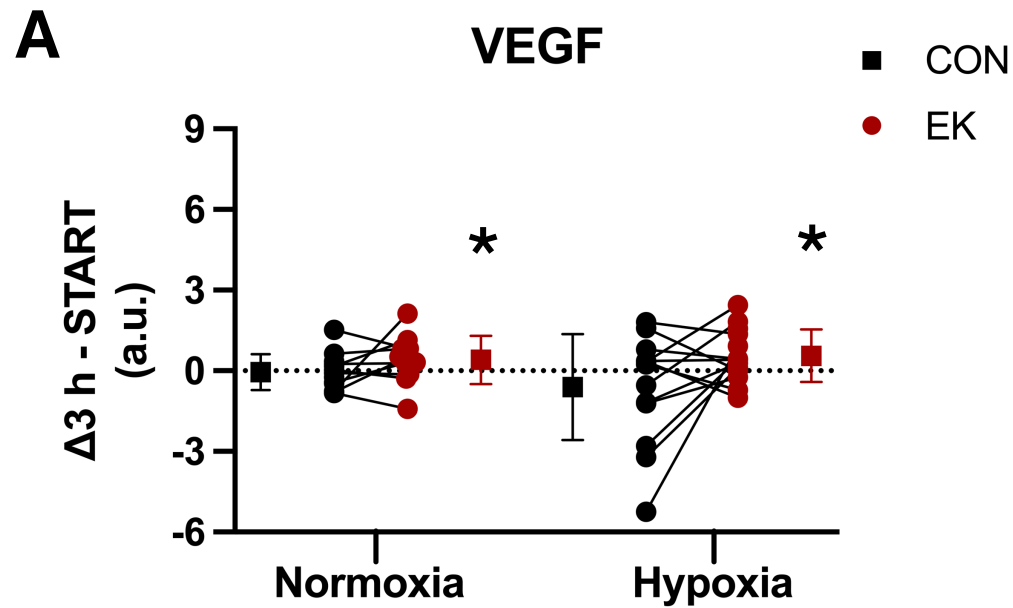


EK upregulated mRNA expression of angiogenic signaling



VEGF = Vascular Endothelial Growth Factor

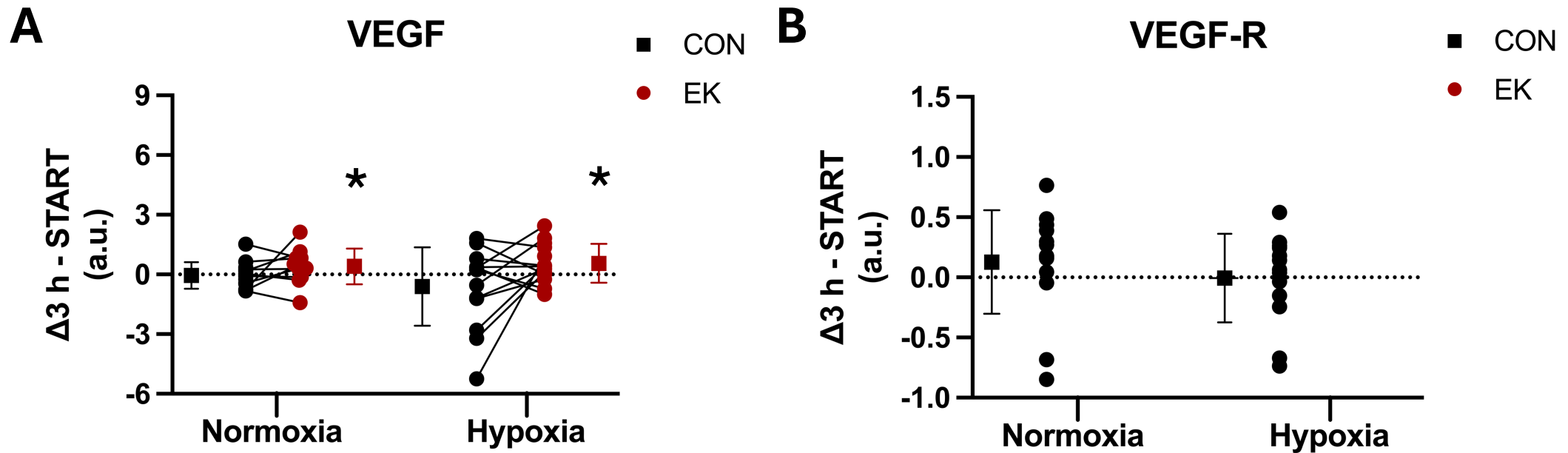
EK upregulated mRNA expression of angiogenic signaling



* $p < 0.05$

VEGF = Vascular Endothelial Growth Factor

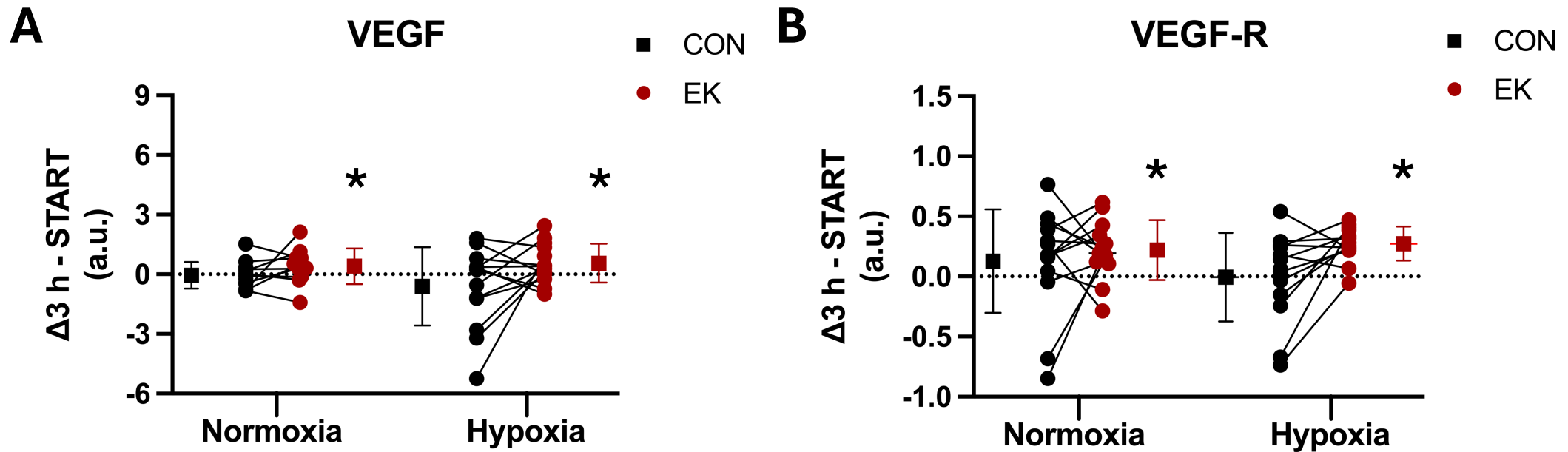
EK upregulated mRNA expression of angiogenic signaling



* p < 0.05

VEGF = Vascular Endothelial Growth Factor; VEGF-R = Vascular Endothelial Growth Factor Receptor

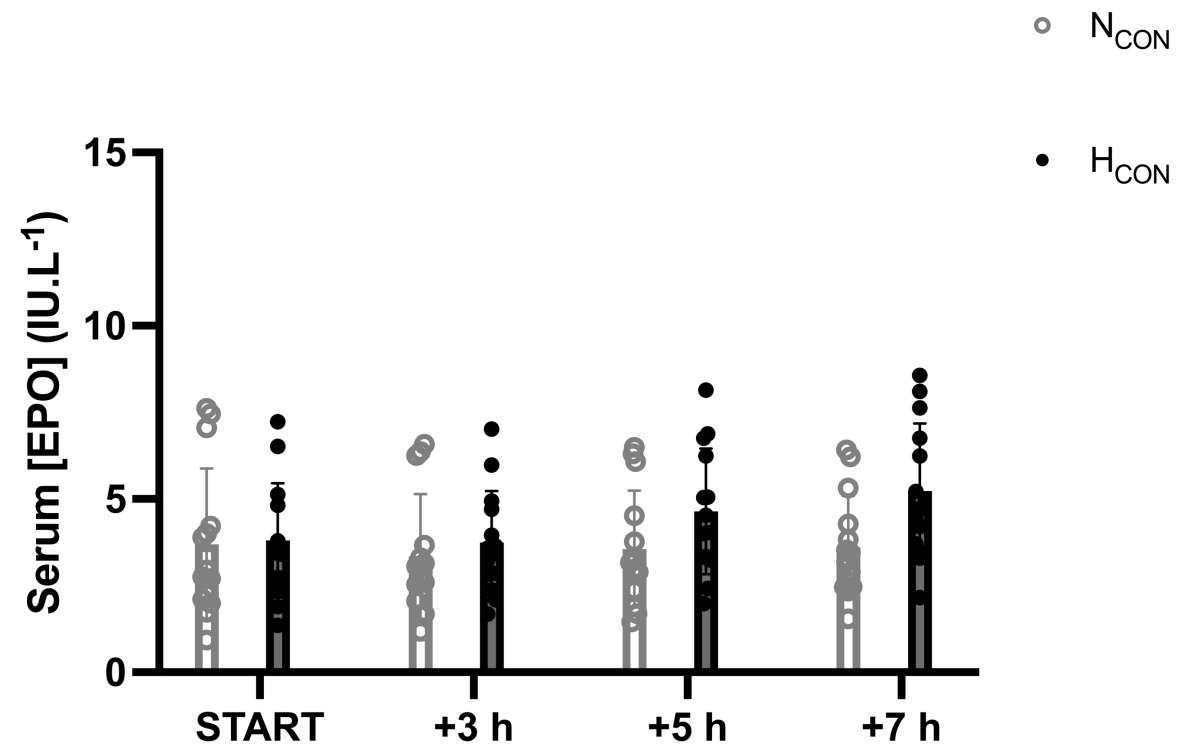
EK upregulated mRNA expression of angiogenic signaling



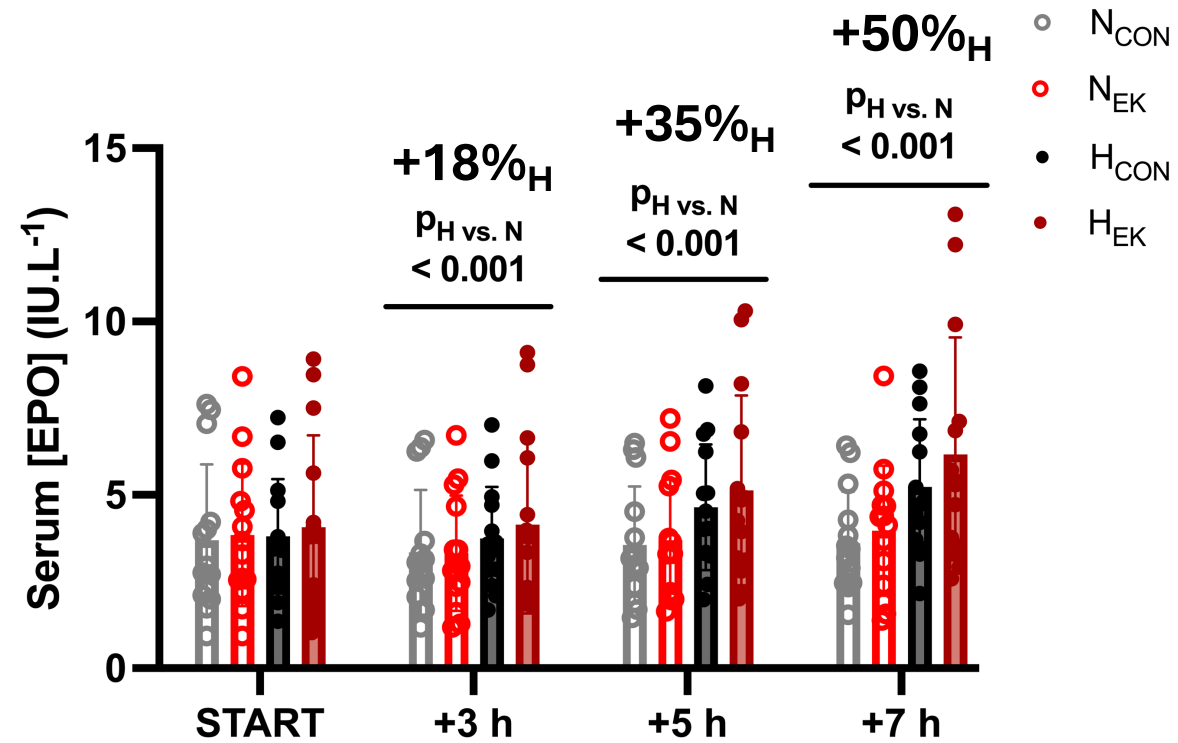
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VEGF = Vascular Endothelial Growth Factor; VEGF-R = Vascular Endothelial Growth Factor Receptor

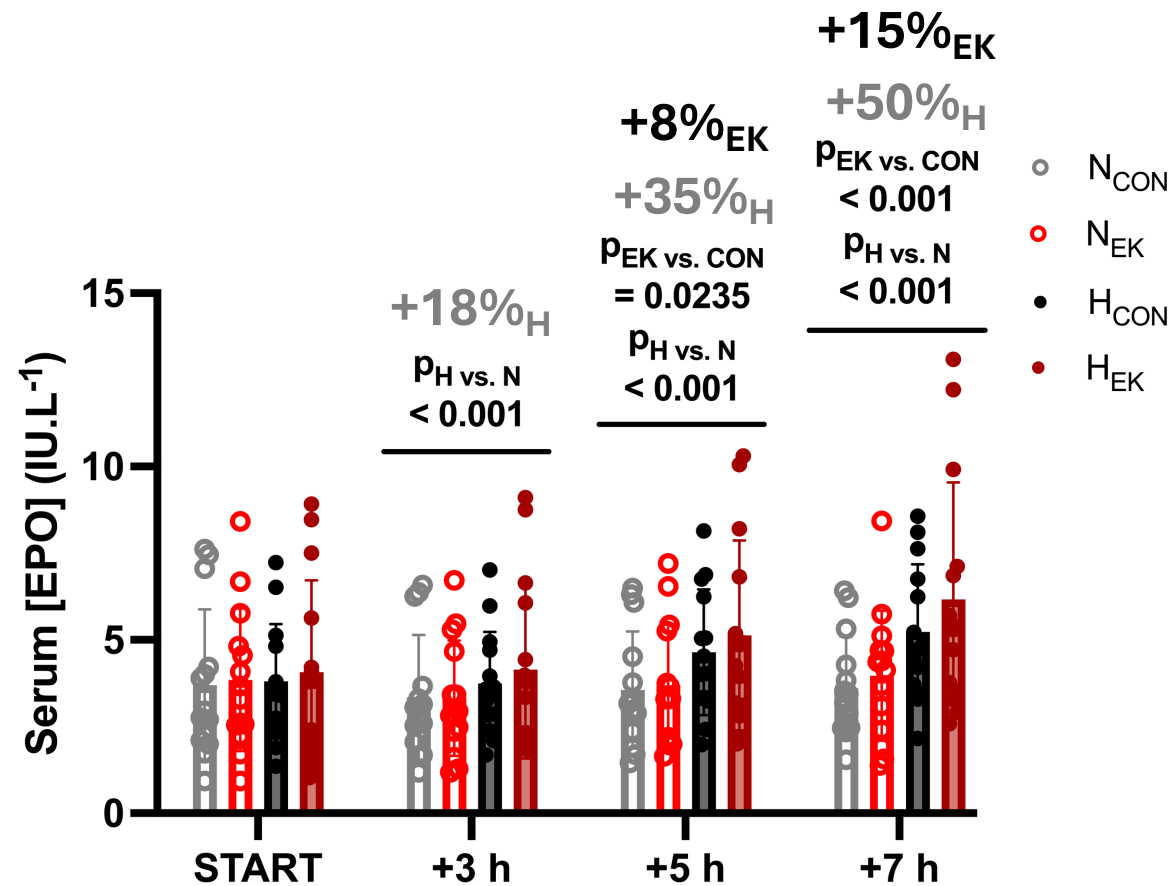
Hypoxia increased serum [EPO]



Hypoxia increased serum [EPO]



EK further increased serum [EPO]



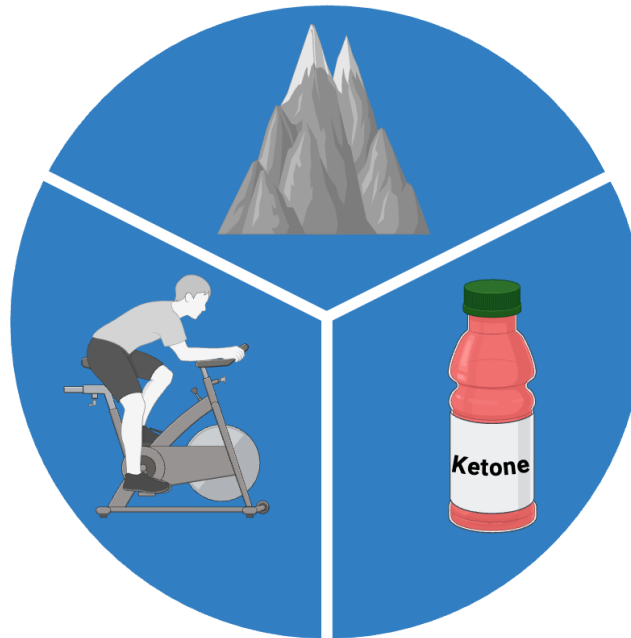
Conclusion



Conclusion

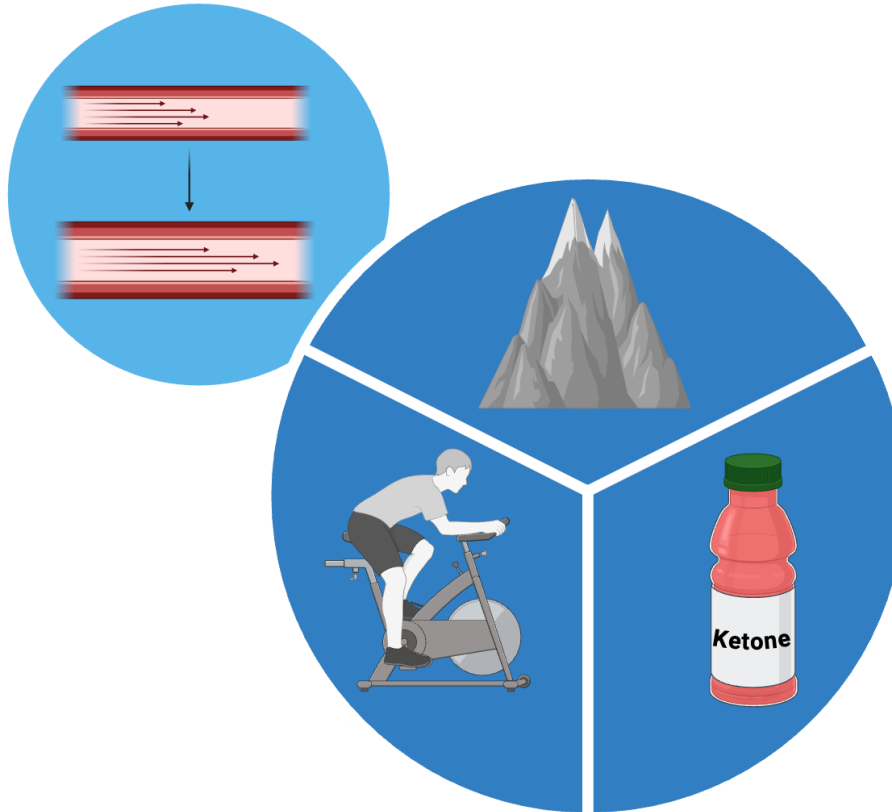


Conclusion



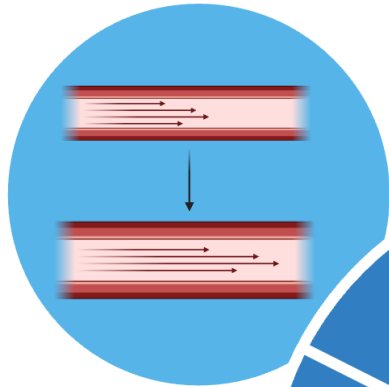
Conclusion

Macrovascular
function?

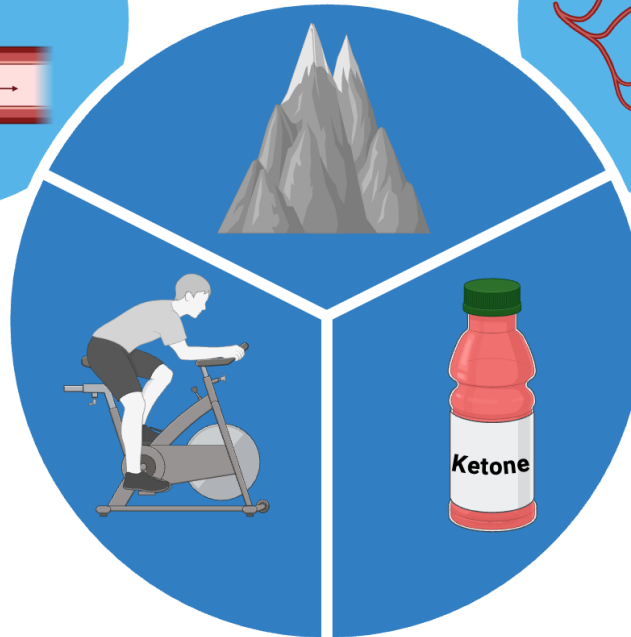
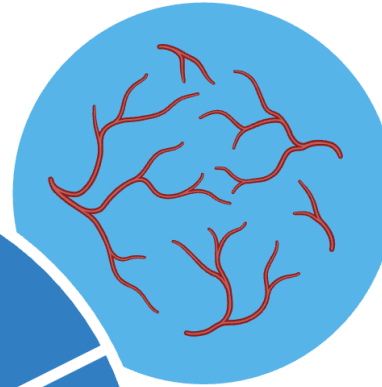


Conclusion

**Macrovascular
function?**

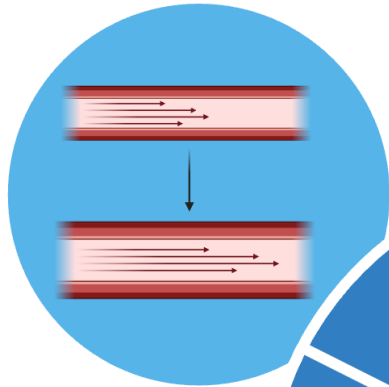


**↑ Microvascular
function**

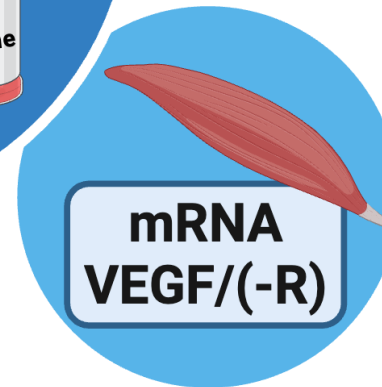
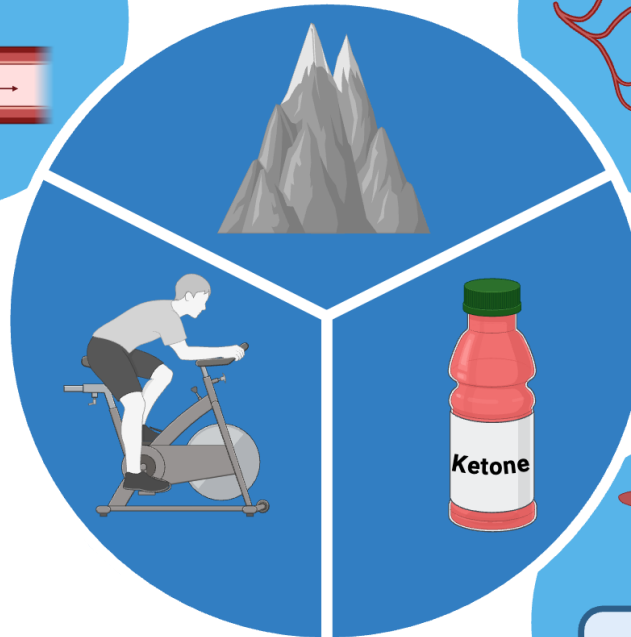
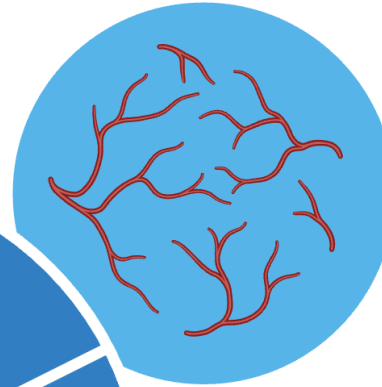


Conclusion

Macrovascular
function?



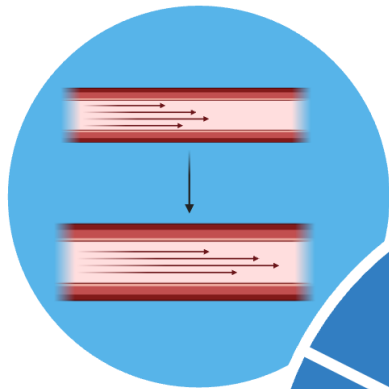
↑ Microvascular
function



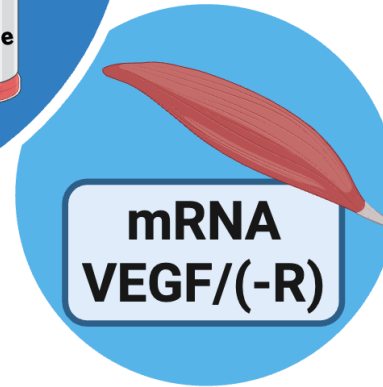
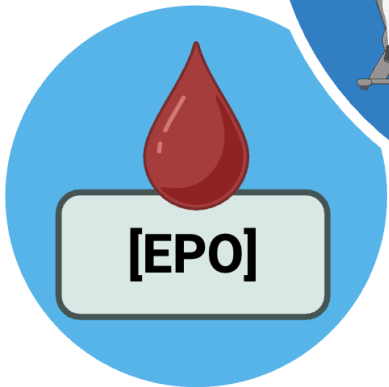
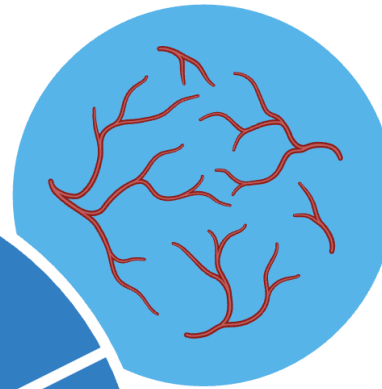
↑

Conclusion

Macrovascular
function?



↑ Microvascular
function



More information

The Journal of
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Ketosis enhances vascular function, angiogenic signalling and the erythropoietic response to exercise and hypoxia

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