INTRODUCTION. Pulmonary arterial hypertension (PAH) is a vascular remodeling disease leading to right ventricular failure. Despite the most modern therapies, most patients display persistent and significant exercise intolerance. Many observations suggest that exercise limitation in PAH is not simply due to pulmonary hemodynamic impairment, but that other determinants intrinsic to the skeletal muscle are involved. We hypothesized that O₂ delivery to skeletal muscles during exercise is impaired in PAH independently of cardiac output.

METHODS AND RESULTS. Ten PAH patients performed a submaximal exercise at 70% of their peak workload (mean workload = 58 (15) W). Ten healthy controls performed the same exercise at the same workload as the PAH patients with whom they were paired. The increase in muscle deoxyhemoglobin concentration ([Mb-HHb]) (near-infrared spectroscopy, ISS) of the dominant quadriceps was significantly higher in PAH patients compared to healthy controls (20 (27) vs 30 (4) #cap/mm²; p<0.01) at the end of the submaximal exercise. This was not related to differences in cardiac output increases during exercise (+4.0 (0.7) vs +3.2 (0.4) L/min; p=0.29) in PAH patients with whom they were paired. The increase in muscle deoxyhemoglobin concentration ([Mb-HHb]) was mainly explained by a lower capillarity density compared to healthy controls (202 (7) vs 304 (23) #cap/mm²; p<0.01) that correlated with end-exercise muscle ([Mb-HHb]) (R²=0.37; p<0.01). Finally, muscle ([Mb-HHb]) during submaximal exercise correlated with VO₂ max (R²=0.65; p<0.01) and 6 minutes walk test distance (R²=0.54; p<0.01).

CONCLUSION. Our results demonstrate that PAH patients exhibit a lower capillarity density independently of cardiac output.

Hypothesis

We recently demonstrated that PAH is associated with a miR-126 dependent capillary rarefaction within the skeletal muscles. We thus hypothesized that:
1. PAH patients present a lower skeletal muscle oxygen supply during exercise
2. This lower oxygen supply is mainly explained by a lower capillarity density
3. Lower skeletal muscle oxygen supply is associated with poor exercise capacity

Conclusion

The present study documented reduced muscle oxygen supply during normoxic as well as during hyperoxic submaximal exercise protocol in PAH. This impairment is mostly related to muscle capillarity density. Because skeletal muscle oxygenation is associated with exercise capacity in PAH, our results lead to a better understanding of the implication of peripheral muscle dysfunction and impaired oxygen delivery on exercise tolerance in PAH.