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Introduction

- Peripheral arterial disease (PAD) is characterised by reduced leg blood flow capacity and decreased exercise tolerance.
- In healthy individuals, vessel dilation and blood flow during rest and passive exercise are highly dependent on nitric oxide.¹⁻³ Furthermore, blockade of nitric oxide synthase diminishes the normal dilation and hyperemic response following cuff occlusion.^{1,2}
- Reactive oxygen species directly inactivate nitric oxide,^{4,5} but it is not clear how much this mechanism contributes to the symptoms of PAD.
- Our study compared participants with and without PAD for:
 - Leg blood flow and vessel dilation during rest, passive movement, exercise, and following cuff occlusion (reactive hyperaemia)
 - Levels of key proteins in vasodilatory pathways

Methods

- Subjects: 10 PAD and 9 control (see Table 1)
- Measures:
 - Duplex ultrasound measures of femoral artery blood flow and vessel diameter (Fig 1):
 - at rest
 - following 5 minutes of thigh-cuff occlusion in a reactive hyperaemia test
 - during 5-min bouts of passive, active (10 W) and maximal seated leg-kicking exercise.
 - Resting biopsy samples from the vastus lateralis (Fig 2) to determine muscle protein content for:
 - phosphorylated endothelial nitric oxide synthase
 - cyclooxygenase 1 and 2
 - thromboxane synthase
 - prostacyclin synthase
 - endothelin B receptor
 - nicotinamide adenine dinucleotide phosphate (NADPH) oxidase

	Healthy	PAD
n	9	10
Age (years ± SD)	62 ± 12	69 ± 7
Height (cm ± SD)	173.9 ± 8.8	176.9 ± 4.7
Weight (kg ± SD)	83.8 ± 13.9	80.0 ± 16.0
% Smokers	0	20
% Past smokers	89	100
Study leg ABI ± SD	1.22 ± 0.15	0.81 ± 0.16

Table 1. Subject details. ABI = ankle brachial index.

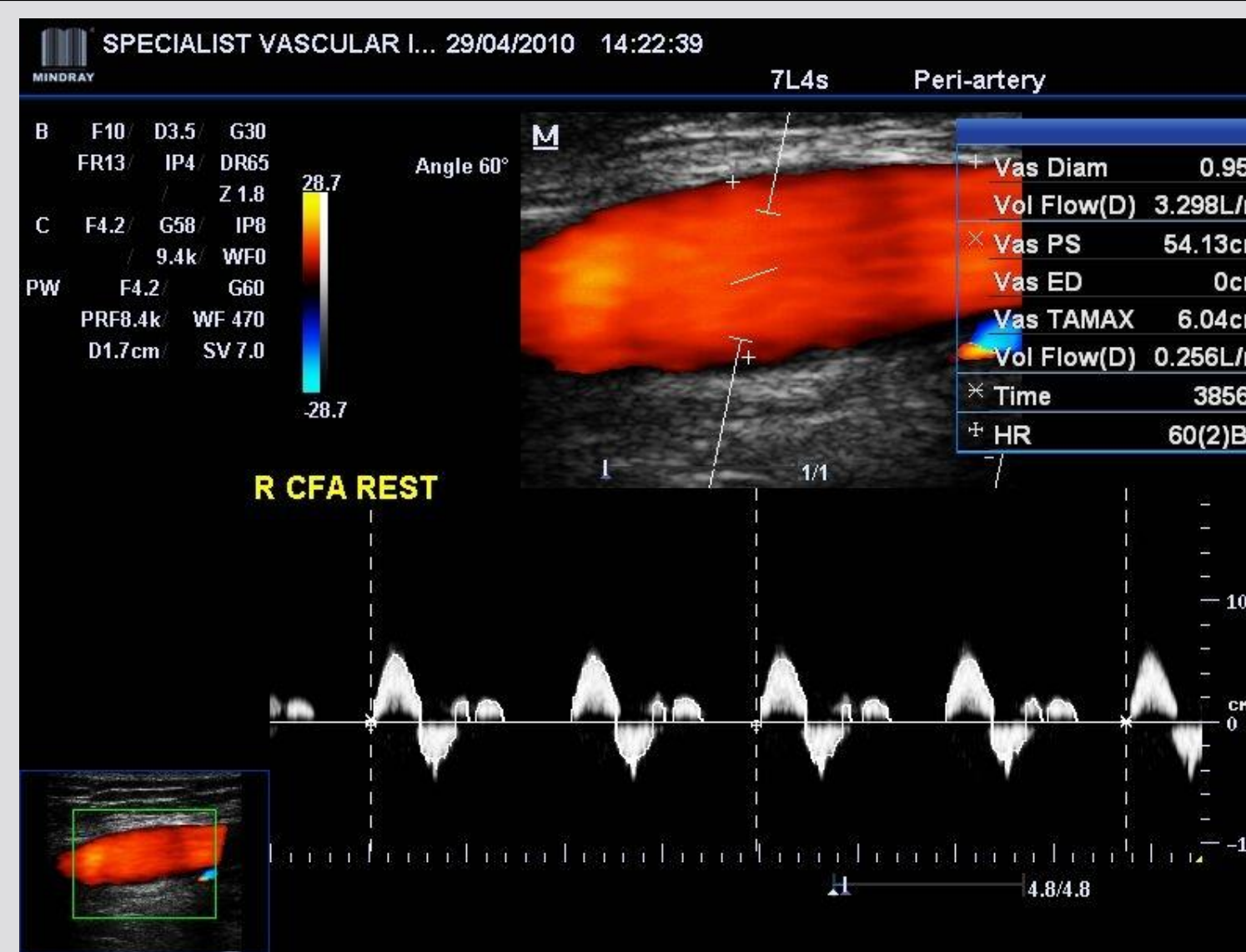


Figure 1. Duplex ultrasound image of femoral artery blood flow at rest



Figure 2. Muscle biopsy sample being taken for determination of protein content

Results

- Blood flow did not significantly differ between groups at rest or during exercise (see Fig 3).

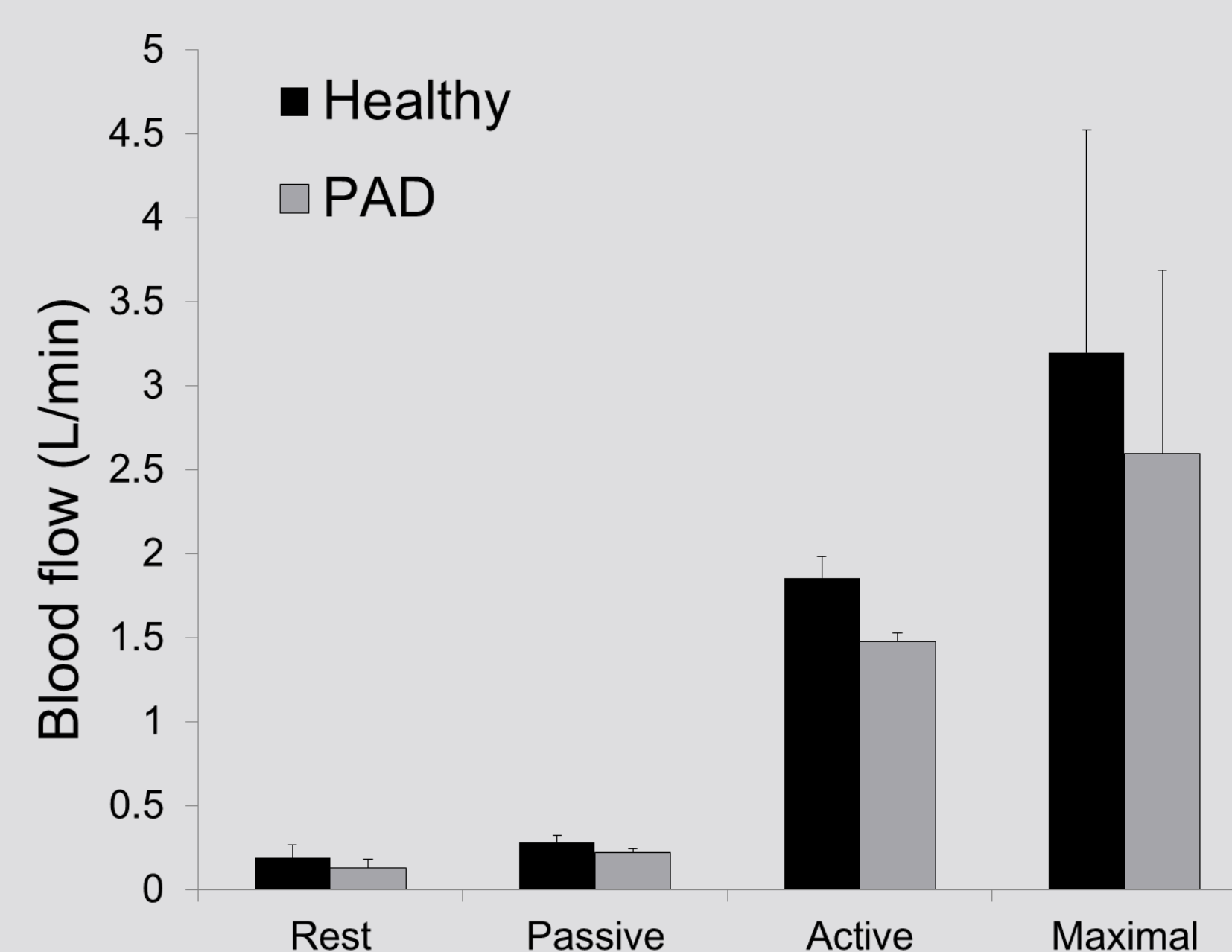


Figure 3. Blood flow at rest and during exercise for healthy participants and PAD patients. Mean (SD).

- During reactive hyperaemia, changes in blood flow and vessel diameter were blunted in PAD (see Figs 4 & 5).

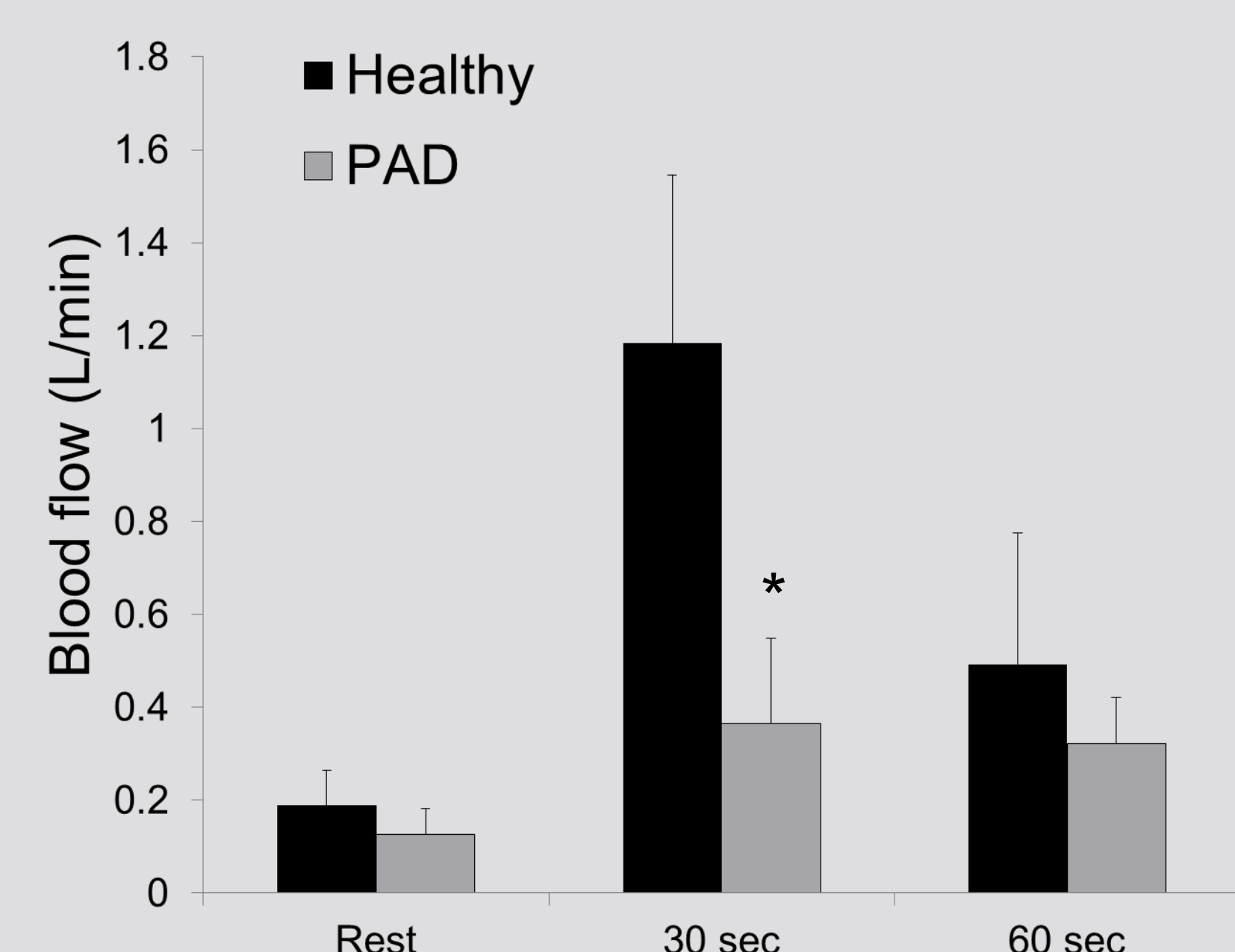


Figure 4. Blood flow at rest and 30 and 60 seconds after cuff occlusion for healthy participants and PAD patients. Mean (SD) * PAD less than healthy, p<0.001

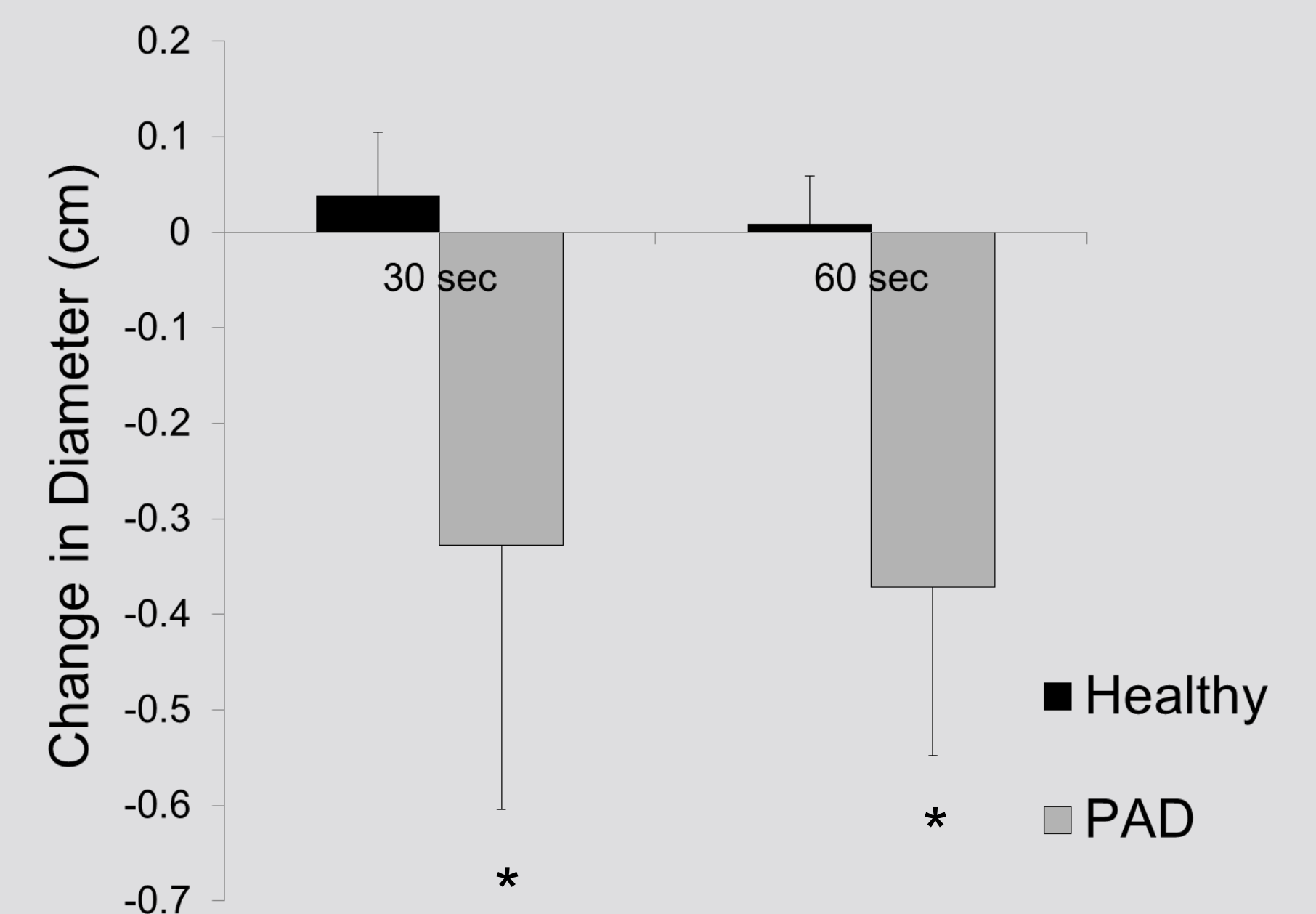


Figure 5. Change in femoral artery vessel diameter at 30 and 60 seconds after cuff occlusion for healthy participants and PAD patients. Mean (SD) * PAD change is greater than healthy, p<0.001.

- PAD subjects had significantly greater levels of NADPH oxidase (see Fig 6).

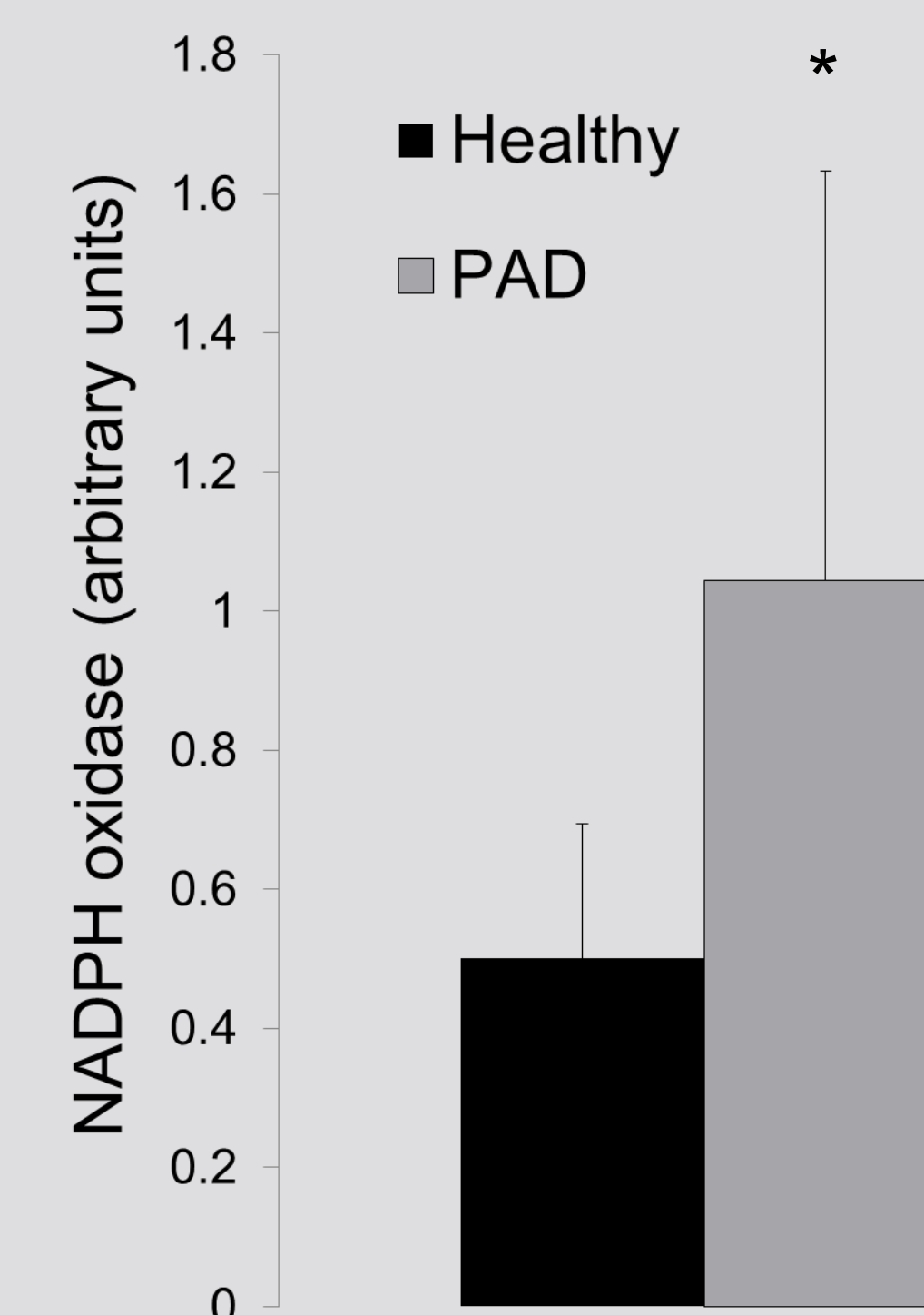


Figure 6. NADPH oxidase levels in healthy participants and PAD patients. Mean (SD) * PAD greater than healthy, p<0.05.

Discussion

- PAD participants demonstrated impaired vessel dilation and blood flow responses during reactive hyperemia.
- PAD participants have elevated levels of NADPH oxidase.
- It is established that NADPH oxidase plays an important role in the production of reactive oxygen species.^{6,7}
- It is plausible that our finding of elevated NADPH oxidase indicates an oversupply of reactive oxygen species, which would reduce the availability of nitric oxide,^{4,5} contributing to the impaired vasodilatory response of peripheral arterial disease patients during reactive hyperaemia.

References

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