High-energy phosphate (HEP) metabolism during exhaustive calf exercise in patients with bilateral symptomatic peripheral arterial disease (PAD)

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Objectives:
Patients with peripheral arterial disease (PAD) and intermittent claudication suffer commonly from a limited walking range. However, degenerative spine disorders that belong to the typical disorders of the developed countries like PAD can also lead to leg pain induced by exercise. Clinical investigations revealed impaired muscle function as a characteristic for PAD, missing degenerative spine disorders. Previous studies using phosphorus 31 magnetic resonance spectroscopy (31P MRS) have shown that the phosphocreatine (PCr) on- and off-kinetics are prolonged in Patient with symptomatic PAD. The relation between atherosclerotic lesions load and PCr kinetcs, though, has been yet rarely studied.
Purpose:
The purpose of this study was to investigate the PCr kinetics in the calf muscle of patients with symptomatic, multisegmental PAD during incremental plantar flexion exercise in relation to the runoff resistance score with the help of time-resolved 31P MRS and MR angiography (MRA).
Methods:
Using a 1.5 Tesla whole body MR scanner (Magnetom Symphony and Avanto, Siemens, Germany), 23 patients with bilateral symptomatic PAD (66.7 ± 8.7 years), recruited in the outpatient clinic of the Division of Vascular Surgery at our University hospital, and 24 healthy controls (65.3 ± 8.6 years) underwent serial 31P MRS during exercise increments at 2, 3, 4 and 5 W. All patients received a MR angiography in three levels by using FLASH 3D sequences (field of view of 420 mm, matrix of 384 to 448, TR of 6.2 ms, TE of 2.3 ms, slice thickness of 0.8 to 1.2 mm, slab thickness of 96 to 128 mm and iPAT factor of 2) with moving bed technique and a three-phase gadobenate bolus (20 mL Multihance, Bracco, Italy). For 31P MRS, we used serial free induction decay sequences (TR of 1000 ms, TE of 0.13 ms, flip angle of 90°, 10-15 averages, acquisition time of 10-15 s) with NOE enhancement. The phosphocreatine (PCr) time constants were determined for each exercise increment and recovery. In the patient group, the runoff resistance (ROR) was determined on MR angiograms. Patients with exhaustion during our exercise protocol were included into this study.
Results:
All of the 46 patients' legs succeeded the 2 W increment, 44 legs the 3 W increment, and 18 legs the 4 W increment, whereas 7 legs reached but did not complete the 5 W increment. All normal controls succeeded the whole exercise protocol. The mean ROR of the patients was 10.7 ± 4.1 (Figure 1). Patients with bilateral, symptomatic PAD showed significantly increased PCr time constants during all exercise increments and recovery (Figure 2). Furthermore, the patients showed significantly lower PCr and pH level at the end of exercise (exhaustion) compared to the normal controls. The ROR showed a significant correlation with the PCr recovery times, but not with the PCr on-kinetics (Spearman correlation coefficient $r=0.39$; $p<0.001$).
Conclusion:
Our findings confirm that severe PAD is associated with impaired muscle metabolism during exercise and recovery. Interestingly, we did not observe a significant correlation between atherosclerotic lesion load and PCr time constants during exercise, but during recovery. This result might indicate that the atherosclerotic lesion load does not predict the hemodynamical impairment and therefore the metabolic impairment during exhaustive exercise, but during recovery in symptomatic PAD patients .

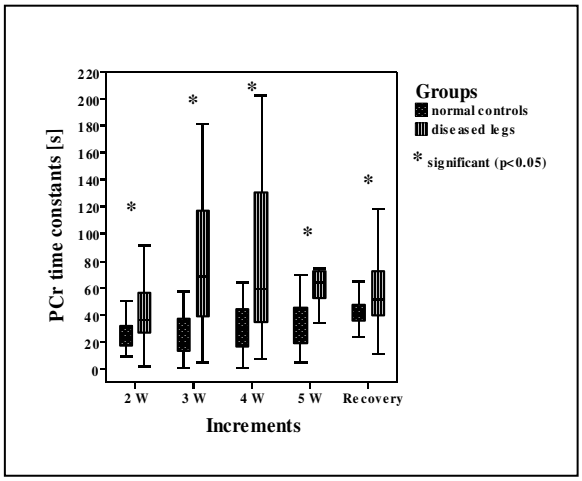

Figure 2: The PCr time constants are presented as boxplots, whereby the errorbars indicate the range, the box limits the quartiles and the white bars the medians.

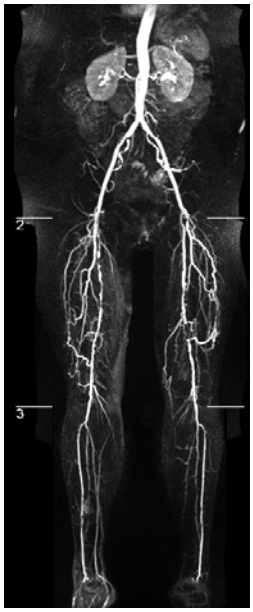

Figure 1: The MR angiogram shows bilateral, multisegmental PAD with several occlusive and non-occlusive athero-sclerotic lesions. Collaterals can be delineated on both upper legs.