

Meeting abstract

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1042 Multi-modality magnetic resonance demonstrates factors critical to functional capacity in peripheral arterial disease

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Introduction

The primary pathophysiology of peripheral arterial disease (PAD) is hypoperfusion of the lower extremities. Alterations in microcirculatory function and muscle metabolism may play a significant role in ischemic symptoms and functional limitation but are not measured by standard diagnostic techniques. Assessment of therapies is limited to functional testing. More robust diagnostic techniques are needed to enhance understanding of PAD pathophysiology and to improve testing of novel therapeutics.

Purpose

We sought to use multi-modality magnetic resonance to further characterize the relationship between macrovascular obstruction, tissue perfusion and cellular metabolism and to correlate these measures with functional capacity in patients with PAD.

Methods

Sixty-two patients with mild-to-moderate PAD (35 males, mean age \pm S.D. 65 ± 11 years) had their most symptomatic leg studied (ankle-brachial index (ABI) 0.68 ± 0.13).

Calf muscle perfusion was measured at peak exercise on a MR-compatible ergometer using first pass contrast-enhanced imaging with gadolinium-DTPA 0.1 mM/kg. A GRE pulse sequence simultaneously acquired muscle per-

fusion (inversion recovery, TI 320 ms) and arterial input in the mid-calf (saturation recovery, TI 10 ms) with FOV 180×180 , matrix = 64×64 , flip 15° , TR 900, TE 1.8. A perfusion index (PI), defined by tissue perfusion/arterial input, was obtained from the slope of time intensity curves from the muscle/artery.

Phosphocreatine recovery (PCr) time following peak exercise, used to assess muscle metabolism, was measured by ^{31}P MR spectroscopy using a single-pulse, surface coil localized, 512 ms free induction decay acquisition centered on the mid-calf. PCr recovery time was calculated using a monoexponential fit of the PCr integral versus time.

Plaque volume (PV) in the superficial femoral artery was assessed using a thigh surface coil and a fat suppressed multi-slice TSE pulse sequence with blood suppression and spatial presaturation (TR 1100 ms, TE 7.6 ms, echo spacing 7.5 ms, voxel size $0.5 \times 0.5 \times 3$ mm, interleaved image sets, 4 signal averages). PV was defined as ((total vessel area-lumen area) \times slice thickness) and %PV as the ratio of plaque volume to total vessel volume.

Macrovascular disease was assessed with gadolinium-DTPA (0.2 mM/kg) enhanced MR angiography from the abdominal aorta to the foot with a moving table/bolus chase technique in 3 stations (64 – 104 slices, FOV 500, TR 2.5 – 3.0 , TE 1.0 – 1.1 , flip 20 – 25° , voxel size 1.6 – 2.0×1.0 –

1.3 × 1.0–1.5 mm). For analysis, a 16 arterial segment model and five point ordinal scale was used to grade severity of disease by segment and then indexed to the total number of segments to generate an MRA index score (MRAi).

A Skinner-Gardner exercise treadmill test was done and total treadmill time (TTT), time to claudication (TTC) and VO_2 max were measured. In addition, six minute walk distance (6 WD) was recorded.

Correlations between ABI, MRAi, PI, PCr, and functional parameters were examined by Pearson's correlation coefficient. The bivariate relationship between the variables were tested using F-tests and stepwise linear regression models.

Results

Mean MRAi was 0.97 ± 0.74 , PI was 0.45 ± 0.15 , and PCr was 73.1 ± 30.0 sec. For reference, values in normal subjects are $0, 0.69 \pm 0.17$ and 34.7 ± 16.6 sec, respectively. See Table 1.

Mean TTT was 517 ± 362 s, TTC 130 ± 50 s, VO_2 max 12.6 ± 4.2 , 6 WD 1028 ± 391 ft. See Table 2. By stepwise linear regression, independent predictors of TTT were ABI ($r^2 = 0.12, p < 0.01$) and PCr ($r^2 = 0.09, p < 0.03$). Independent predictors of VO_2 max were %PV ($r^2 = 0.24, p = 0.0001$), MRAi ($r^2 = 0.20, p < 0.001$), and ABI ($r^2 = 0.11, p < 0.02$).

Conclusion

Using multi-modality magnetic resonance, we have demonstrated that functional capacity in PAD is determined in part by macrovascular blood flow, but muscle metabolism and plaque burden play an important role. Calf muscle microvascular perfusion and metabolism are uncoupled, suggesting factors independent of blood flow and intrinsic to skeletal muscle are critical in PAD. Multi-modality magnetic resonance provides a window into the pathophysiology of PAD and a foundation to monitor disease progression and novel therapies.

Table 1: Correlation between imaging parameters.

	%PV	PI	PCR	MRAi	ABI
%PV					
PI	$r = -0.09, p = \text{NS}$				
PCR	$r = 0.25, p = 0.07$	$r = 0.03, p = \text{NS}$			
MRAi	$r = 0.44, p = 0.0005$	$r = -0.27, p = 0.06$	$r = 0.15, p = \text{NS}$		
ABI	$r = -0.34, p = 0.009$	$r = 0.46, p < 0.001$	$r = -0.27, p = 0.05$	$r = -0.39, p < 0.005$	

Table 2: Correlation between imaging and functional parameters.

	TTT	TTC	VO2 max	6 WD
ABI	r = 0.37, p < 0.01	p = NS	r = 0.33, p < 0.02	p = NS
MRAi	r = -0.34, p = 0.01	p = NS	p = -0.44, p < 0.001	p = NS
%PV	r = -0.33, p < 0.02	r = -0.34, p < 0.03	r = -0.49, p = 0.0001	p = NS
PI	p = NS	p = NS	p = NS	p = NS
PCR	r = -0.31, p < 0.03	p = NS	p = NS	p = NS

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