Evaluation of Tissue Perfusion in a Rat Model of Hindlimb Muscle Ischemia Using First-Pass Contrast Enhanced Magnetic Resonance Imaging (MRI)

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Introduction

In patients with peripheral vascular disease, skeletal muscle is inadequately perfused during exercise. Femoral artery ligation has been used as an animal model for peripheral vascular disease (1,2). First-pass dynamic contrast enhanced MRI has been used for assessment of tissue perfusion to study myocardial ischemia (3,4). Few studies have yet applied this technique to the study of skeletal muscle. The goal of this study was to evaluate the chronic changes in tissue perfusion by measuring the first-pass uptake of the contrast agent, Gd-DTPA, in rat hindlimb muscle after femoral artery ligation both at rest and during stimulation-induced hyperemia.

Methods

Adult Sprague-Dawley rats were prepared with unilateral femoral artery ligation. The non-ligated limb served as an internal control for normal perfusion. Both rat hindlimbs were exercised by sciatic nerve stimulation for 90 seconds. MRI measurements were performed at rest as well as immediately after the stimulation was stopped but while the hyperemia response persisted. This experiment was carried out at 30 min and 2,7,14,21,28 days post ligation on the resting group and up to 42 days on the group with stimulation (n=6).

MR images were acquired on a 4.7T Magnet using a volume coil. A 3 mm thick cross section of distal hindlimbs was imaged using a T_1-weighted spoiled gradient-recalled echo pulse sequence with parameters TR/TE=30/2 ms, flip angle=30°, 128×64 matrix zero filled to 128×128, FOV=6.4×6.4 cm^2. The first-pass dynamic signal enhancement was recorded with a time resolution of 1.9 second after a bolus injection of Gd-DTPA (0.2 mmol/kg, Magnevist) through a tail vein catheter.

The percentage signal enhancement vs. time curve was obtained for each limb by averaging the signal intensities over the cross sectional muscle area. The initial steepest slope of the enhancement curve was calculated and used as a perfusion index (3,5). It was then normalized to the non-ligated limb for characterizing the muscle ischemia relative to normal perfusion.

Results

Representative first-pass dynamic signal enhancement curves acquired 30 min post ligation with sciatic nerve stimulation are shown in Figure 1. A significant difference is observed in the first-pass enhancement pattern between ligated and non-ligated limbs.

At rest, a 51±6% reduction in perfusion index was observed in the ligated limb 30 min post ligation, while at later time points from 2 to 28 days after ligation, no significant differences were detected between the ligated and non-ligated limbs (Figure 2). During stimulation-induced hyperemia, the perfusion index reduced to 12±3% of the normal level 30 min post ligation and recovered with time from 29±8% on day 2 to 68±5% of the normal level on day 42, which was still significantly ($p<0.005$) lower than the perfusion to the non-ligated limb (Figure 2).

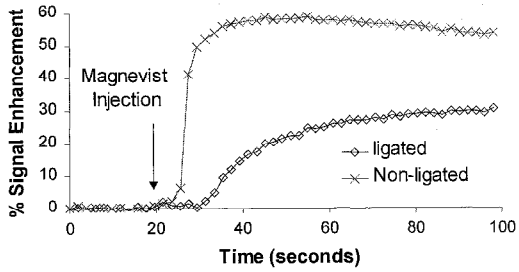

Figure 1

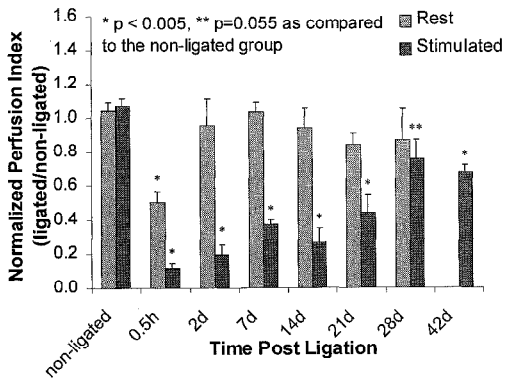

Figure 2

Discussion

By quantifying the first-pass dynamic MRI, we characterized the chronic changes in tissue ischemia of the rat hindlimb muscle induced by femoral artery ligation. This provided a rat model that can be used for studying collateral dependent tissue perfusion and evaluating the treatment response in improving collateral development (angiogenesis).

The first-pass uptake of Gd-DTPA is dependent on a number of physiological parameters such as blood flow, the intra- and extravascular distribution volumes, capillary permeability, diffusion, and interstitial compartments. It is important to note that these factors complicate the interpretation of the data. Therefore, the perfusion index used in this study provides a global assessment of tissue perfusion rather than an absolute quantitation.

References

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