NONINVASIVE MONITORING OF MUSCLE DAMAGE DURING RELOADING FOLLOWING LIMB DISUSE

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Introduction

Reduced weight bearing, inactivity, and cast immobilization promote a progressive loss of skeletal muscle mass and function, a shift in fiber-type composition, and an increased vulnerability to muscle damage (1, 2). Several in vitro studies have shown that reloading or reambulation following hindlimb unloading results in ultrastructural alterations consistent with muscle damage. The objective of this study was to explore the utility of noninvasive magnetic resonance (MR) imaging to monitor muscle damage in the lower hindlimb muscles of the mouse during reloading following cast immobilization and to compare the findings in different muscles.

Experimental

A total of 16 female C57BL6 mice were studied prior to and following cast immobilization. The hindlimbs of C57BL6 mice were immobilized for 2 weeks in plantarflexion using a bilateral casting model. Following immobilization the mice were allowed to reambulate and muscle damage was monitored at different times. The mouse hindlimb muscles were MR imaged either in a 4.7-T horizontal bore Varian Inova or Bruker Avance spectrometer. The lower limb was inserted up to the knee into a five-turn, 1-cm inner diameter, single-tuned H solenoid coil (200 MHZ). Multiple-slice, single spin-echo images were acquired with the following parameters: pulse repetition time (TR), 2000 ms; echo time (TE), 14 and 40 ms; field-of-view (FOV), 10-20 mm; slice thickness, 0.5-1.0 mm; acquisition matrix size, 256 × 128; and 2 signal averages.

Results and Discussion

Cage-restricted reloading following cast immobilization induced a significant shift (P < 0.0001) in the transverse (T2) relaxation characteristics of the postural slow-twitch soleus muscle, but not in the neighboring gastrocnemius (Fig. 1A). A marked shift in the T2 relaxation properties was observed in the soleus muscle at 1-6 days of reloading. Peak T2 values were noted at 2 days' reloading when 35%-87% of the soleus showed EBD-positive fibers and massive macrophage infiltration (Fig. 1B). Muscle-specific changes in MR T2 relaxation properties correlated with uptake of Evans blue dye, a histological marker of muscle damage.

Conclusions

This study demonstrates that T2 MR imaging can be implemented to monitor noninvasively and sequentially muscle-specific damage during reloading following limb disuse.

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References