Dual gradient echo MRI method for the evaluation of muscle microvascular function

O. A. Sanchez[1], E. A. Copenhaver[1], M. A. Chance[1], M. J. Fowler[2], J. Kent-Braun[3], and B. M. Damon[1,4]

[1]Radiology and Radiological Sciences, Vanderbilt University, Nashville, TN, United States, [2]Diabetes, Endocrinology, & Metabolic Division, Vanderbilt University, Nashville, TN, United States, [3]Kinesiology, University of Massachusetts-Amherst, Amherst, MA, United States, [4]Biomedical Engineering, Vanderbilt University, Nashville, TN, United States

Introduction

Microvascular dysfunction is the underlying pathophysiological mechanism implicated in many of the long-term complications of diabetic patients and may be related to the onset and progression of insulin resistance (1,2). Unfortunately, methods to monitor microvascular function in skeletal muscles non-invasively are lacking and urgently needed. A recently described method uses a dual gradient-recalled echo (GRE) MRI sequence to evaluate muscle microvascular responses to physiological stimuli, such as brief isometric contraction. The time courses of the signal intensities at TE=6 ms (SI_6) and 46 ms (SI_{46}) reflect changes in blood volume and oxyhemoglobin saturation ($\%HbO_2$), respectively (3). Therefore, to assess the ability of this method to detect differences between healthy persons and those at high risk for dysfunctional muscle microvasculature, we compared the changes in SI_6 and SI_{46} following isometric contractions in healthy and diabetic subjects.

Methods

Protocol: 8 diabetic subjects (3 females) aged 36.7 ± 1.4 years and 4 apparently healthy subjects (3 females) aged 34.0 ± 1.6 years provided written informed consent to participate in this IRB-approved study. To control for factors that affect microvascular function, subjects were instructed to refrain from moderate to vigorous physical activities and alcohol for 24 hours before testing session and not to use caffeine or tobacco products for 6 hours before the testing sessions. Subjects wore a ActiLifestyle® Monitoring System for a week to track physical activity. Subjects reported to the clinical research center following an overnight fast and blood glucose and insulin, Hb_{A1c}, and urinary albumin-to-creatinine ratio (A/C) were measured. The subjects ate a breakfast containing 368 ± 14 kcal (mean ± SD) and 45% CHO, 23% protein and 29% fat. Then, each participant practiced the exercises and received a snack (130 ± 40 kcal; 59% CHO, 19% protein and 25% fat). A final blood glucose measurement was taken before the imaging session to ensure that blood glucose<180 mg/dl. Each subject performed 2 types of isometric dorsiflexion contractions: 1) maximal voluntary contraction (MVC) and 2) 50% MVC (50MVC), in random order. Each type of contraction was performed 4 times. For 20 s before, during, and for 150 s after each contraction, functional MRI data were obtained as described below.

MRI data acquisition and analysis: MRI data were obtained on a 3T Philips Intera Achieva MR Imager/Spectrometer. The dominant leg was placed in an 8 channel SENSE knee coil and the middle of the tibialis anterior (TA) muscle was aligned in the center of the coil. All imaging was performed at the maximum girth of the TA. A T_1-weighted anatomical image was obtained with TR/TE=500/16 ms, slice thickness=5 mm, FOV=18×18 cm, matrix size=256×256, N_{EX}=2. Dual GRE EPI dynamic scans were acquired with TR/TE= 1000/6, 46 ms, slice thickness=7.5 mm, FOV=18×18 cm, matrix=128×128, N_{EX}=1. Image analysis was performed in Matlab v. 7.0.1. Regions of interest (ROI's) were drawn around the superficial TA (STA), the deep TA (DTA) and the extensor digitorum longus (EDL) muscles. SI_6 and SI_{46} were expressed as percentage of pre-contraction intensity and plotted as a function of time. Each time course was characterized by its minimum and maximum post-contraction SI, the difference between them (ΔSI) and time to peak (TTP).

Statistical analysis: The average ΔSI_{avg} and TTP_{avg} of the two procedures were determined for each muscle and TE, for each of the 2 different experimental conditions (50MVC and MVC). A general linear model (GLM) repeated measures analysis was performed to test for differences in ΔSI_{avg} and TTP_{avg} between healthy controls and diabetic subjects by intensity and muscle, using body mass index (BMI) as a covariate. Data are given as mean ± SE.

Results

Diabetic subjects had a higher BMI, fasting glucose, blood glucose immediate to MRI testing and HbA_{1c} than healthy subjects ($p < 0.05$). ΔSI_6avg at 50%MVC is lower in the diabetics than in control subjects (* $p = 0.04$), but not at MVC ($p = 0.7$; Figure 1A-B). No differences were found between healthy subjects and diabetics for ΔSI_{46avg}. TTP was not significantly different between diabetic and healthy individuals by intensity ($p = 0.5$) or muscle ($p = 0.6$).

Conclusions

Changes in ΔSI_6, reflecting changes in blood volume, following isometric contractions of 50%MVC were lower in diabetic subjects than in healthy individuals. This method may be used to monitor microvascular function in skeletal muscles.

References

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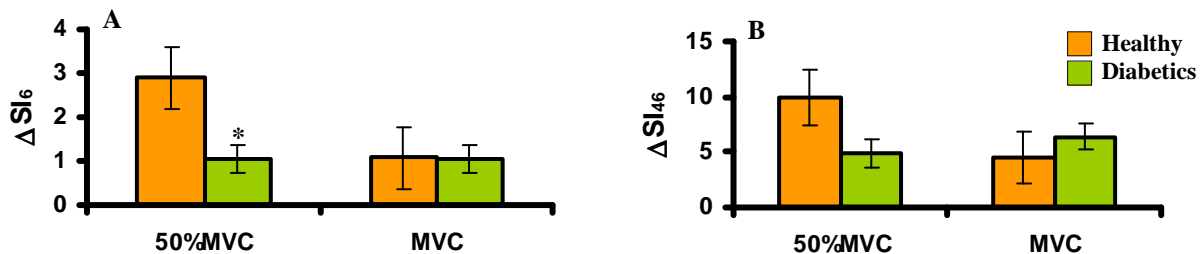3. Damon BM, et al. Magn Reson Med 2007;57(4):670-679.

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Figure 1. ΔSI_{6avg} (A) and ΔSI_{46avg} (B) between controls and diabetics by contraction intensity. Data are given as mean ± SE.