Reduced T2* values in Soleus Muscle of Type 2 Diabetes Mellitus

C. S. Zuo1, D. Simonson2, Y-H. Sung3, R. Villafuerte1, and P. F. Renshaw1

1McLean Hospital, Boston, MA, United States, 2Brigham and Women’s Hospital, Boston, MA, United States

Introduction

Type 2 diabetes mellitus (T2DM) affects skeletal muscles by impairing blood flow at the macrovascular and microvascular levels and promotes lipids to accumulate to abnormally high levels in diabetic skeletal muscles as the disease progresses (1). These changes are often gradual, and the onset of symptoms may be difficult to recognize until late in the disease process, which make MRI an attractive imaging modality in longitudinal monitoring of the disease progression. We hypothesized that T2* MRI is sensitive enough to differentiate physiological differences between disease and healthy skeletal muscles at resting state in the lower extremities. We conducted a cross-sectional study focusing on the soleus muscle because of its rich microvasculature supply, its essential role in lower limb function, as well as its high susceptibility to the pathophysiological effects of T2DM (2). This abstract summarizes our preliminary results.

Methods and Materials

Under protocol approved by institutional IRB, we recruited and measured values of T2* and T2 in 18 T2DM, 22 young healthy controls (YHC), and 7 older healthy controls (OHC) who had MR scans of the lower extremity using multi-TE spin echo and gradient echo sequences. Regional lipid level was also measured with MRI in a subset of the subjects (9 T2DM, 10 YHC, 7 OHC).

The MR images were acquired on a 3T scanner using a volume coil for transmission and reception. T2 and T2* values were measured at the same locations (slice thickness=8mm) with a multi-TE spin echo scheme (ETL = 12, TE1 = 15ms, TE step 15ms, TR3600) and a multi-TE gradient echo sequence (ETL = 12, TE1 = 9ms, TE step = 3ms, TR600). After assessing linearity of log(SI) vs TE plots, T2 and T2* maps were constructed from multi-TE spin echo images with least square fits based on the relationship ln(SI) = -TE/T2. The MR T2 and T2* maps were analyzed with ImageJ (http://rsweb.nih.gov/ij/). The T2 and T2* values of the healthy controls and DMs are presented as means ± standard errors of the mean (SEM).

Dixon’s two point water-fat separation method was applied to evaluate fat accumulation in the calf muscle region (3). To evaluate the influence of lipid in the region, images of water-fat in-phase and water-fat out-of-phase were acquired at TE of 2.46ms and 6.15ms respectively and at the same slice location and thickness of the T2 and T2* measurements. Fat and water maps were according to the following equations: fat = (in-phase - out-of-phase)/2 and water = (in-phase + out-of-phase)/2. The fat spatial ratio (FSR) = fat/(water+fat) was calculated and the value of FSR in the soleus was calculated for T2DMs and healthy controls.

Group differences in demographic variables involving continuous and categorical data were calculated using independent t-tests and Fisher's exact test for a 2xk table, respectively. For comparison of T2* values in soleus, anterior tibialis, and gastrocnemius (4), we used ANCOVA or a multiple linear-regression method was used, controlling for age, BMI, and FSR. As there was a high co-linearity between HbAlc and diabetes (DM)(r=0.83, p<0.0001), we used either DM or HbAlc in the regression modeling. The normality assumption was verified for each variable of interest using the Shapiro-Wilk test. Statistical significance was defined at an alpha level of p<0.05, two tailed.

Results

The images of calf muscles of the control subjects, especially in the soleus and gastrocnemius muscles. The T2* fit had a better linearity (R2≅0.998) compared to that of T2s (R2≅0.983). No significant difference in T2* values resulted from the fits of even or odd echoes, an indication that influence of fat can be negligible at the soleus region. Soleus T2* values of the healthy controls increased with age. Soleus T2* values of T2DM, however, were significantly lower than those of the OHC (22.9±0.5 vs 26.7±0.4 ms, p<0.01) (Fig 1) and were inversely correlated with the presence of diabetes (p<0.001) and with an increase in HbAlc, but not with BMI or regional lipid level. The latter was not only commonly found among the T2DM with a lowered T2* value but also encountered among the healthy controls. Soleus T2 values, however, increased (~10%) with age in healthy controls and dramatically increased in T2DM (Fig 2), consistent with a higher accumulation of body fluid measured independently with isotope dilution method (4). Soleus T2* had a weak relationship with BMI (PC=-0.41) among all subjects and a weak one with age (+0.058). FSR had a weak relationship with age in healthy controls (PC=0.32).

Conclusion

We have measured T2 and T2* values of calf muscles at rest and found that soleus T2* is significantly correlated with age and the presence of T2DM. Among factors that may contribute to T2* values, the lowered T2* value in the T2DM soleus muscle is most consistent with poor regional microvascular circulation which suggests that the T2DM soleus is likely under tissue oxygenation stress.

Acknowledgment

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Table 1 Summary of linear regression analysis between T2* and variables age, BMI, FSR, and DM

Figs 1-2  T2* (1) and T2 (2) of anterior tibialis (AT), soleus (S), and gastrocnemius (G) among DM, OHC, and YHC.

Reference
