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Quantitative MRI evaluation of fatty infiltration and edema-like lesions in skeletal muscles of Myotonic Dystrophy type 1

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Purpose: Myotonic Dystrophy type 1 (DM1) is an inherited muscular dystrophy with a prevalence of approximately 10 per 100.000. On MR images of DM1 affected muscles fatty infiltration and edema-like processes can be identified1,2,3. These studies used only a semi-quantitative analysis1,2 or evaluated only a single muscle quantitatively3. In other muscular dystrophies the use of quantitative MRI to evaluate fatty infiltration and edema-like processes have been found to be extremely useful in the understanding of the disease4,5. Quantitative MRI is also essential in the proper evaluation of the natural progression of the disease and necessary to monitor the effect of therapeutic interventions. The aim of this study was to evaluate the extent of fatty infiltration and edema-like processes in muscles of DM1 patients by quantitative MR.

Methods: Patients: 10 genetically proven DM1 patients (7 male, age 50±8 years, MIRS score6 3.1±0.9)

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MR protocol: Patients were examined with a 3T Siemens ... the lower leg. To evaluate the extent of fatty infiltration, fat fractions (FF) were determined using ... ze: 1x1x5 mm, slices: 32) or a 3pt-DIXON (TE1/TE2/TE3: 2.31/3.68/5.07 ms). To quantify edema- ... TL: 17, ES: 8 ms, voxel size: 1.5x1.5x10 mm, slice gap: 20 mm, slices: 5).

Data analysis: Firstly, the T2 relaxation time of muscle ... is using a bi-component extended phase graph (EPG) model7: SI(TE) = A×FFEPG×EPG(T1fat,T2fat,E ...), with T1water=1400 ms, T1fat=365 ms and α the refocusing angle. T2fat was determined per patient ... ient water signal is needed to obtain a reliable T2water, voxels with a fitted FFEPG>50% were assume ... terest were drawn around the calf muscles on the 5 slices of the DIXON images that corresponded in ... muscle were determined per slice and as an average of all 5 sesximal slice (p<0.01)(Fig. 2). Finally, ... Muscles with a FF below 20% (blue dots) have a T2water comparable to that of healthy muscles (34.3 ... have a significantly elevated T2water (38.2 ms)(two-sided t-test p<0.0001). Muscles in which more t ... ead in T2water.

Discussion: We investigated disease signatures in muscles of DM1 patients by quantitative MR. The inverse relationship observed between FF and the prevalence of muscles with that FF (pyramid-like shape) indicates that fatty infiltration in DM1 occurs in an, apparently slow, gradual manner. This is in contrast with facioscapulohumeral dystrophy (FSHD), where healthy muscles can become completely fat infiltrated within about 3 years4. It was observed that the gastronemicus medialis and soleus are the most severely affected muscles, while the tibialis posterior is spared. This is in accordance with previous semi-quantitative studies1,2. Furthermore, we observed that fatty infiltration is higher in the distal part of the muscles compared to the proximal part. This suggests that the disease process with fatty infiltration starts distally in DM1, which is also observed in affected leg muscles of FSHD patients4. To prove this hypothesis longitudinal studies are required. At last, we showed that muscles who are in an apparent active state of fatty infiltration have an elevated T2water compared to muscles who are not in a fat infiltration process. This might indicate reactive edema, but the pathological mechanism causing this increased T2water requires further investigation.

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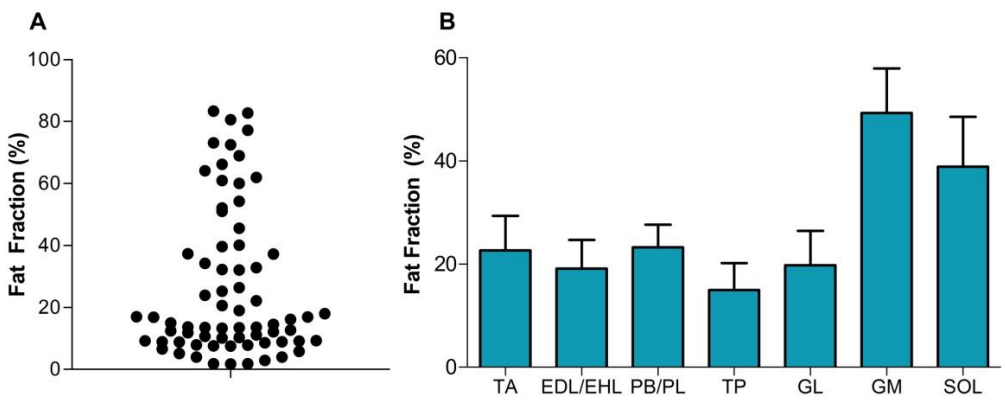

Figure 1: Distribution of average fatty infiltration in the calf muscles of DM1 patients. A: Fat fraction distribution of all muscles. B: Involvement of individual muscles (mean±SE). TA = Tibialis Anterior, EDL/EHL: Extensor digitorum and hallucis longus, PB/PL: Peroneus brevis and longus, TP: Tibialis posterior, GL/GM: Gastronemicus lateralis/medialis, SOL: Soleus.

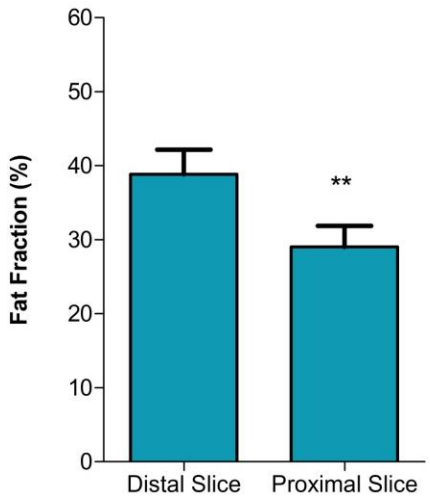

Figure 2: Comparison between the fat fraction (mean±SE) in the most distal slice compared to the most proximal slice. There is a significant decrease in fat fraction from distal to proximal. ** p<0.01

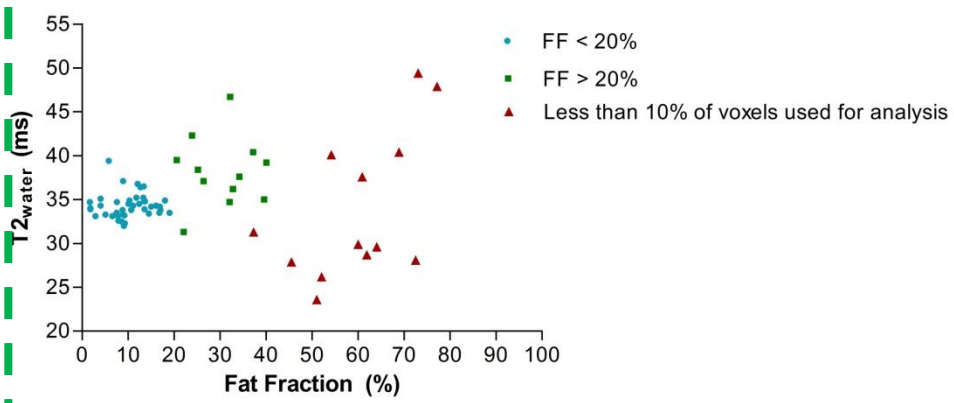

Figure 3: Relation between fat fraction and $T2_{water}$ of all calf muscles. Blue dots and green squares: The muscles with a fat fraction smaller or larger than 20% fat, respectively. Red triangles: Muscles in which less than 10% of all voxels within that muscle were used to calculate $T2_{water}$.