Lower extremity muscle pathology in myotonic dystrophy type 1 assessed by quantitative MRI

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Study objective and summary result
This study investigated the value of leg skeletal muscle MRI measures in patients with myotonic dystrophy type 1 (DM1). It identified muscle fat fraction (FF), muscle volume and contractile volume and muscle T2 water relaxation times (T2_water) as potential biomarkers to assess skeletal muscle disease states in patients with DM1.

What is known and what this paper adds
Clinical trials for DM1 will be aided by quantitative imaging biomarkers of disease within individual muscles. This study presents evidence that MRI of leg muscles can provide such biomarkers.

Participants and setting
This study included 33 patients with genetically and clinically characterized DM1 (55% male; mean age, 45 ± 12 years) and 10 healthy controls (HCs; 50% male; mean age, 45 ± 14 years). The patients were participants in a clinical trial (NCT02118779) and were invited to participate in this study through a center in the Netherlands or France.

Design, size, and duration
This study used MRI measurements, including one with a 3-dimensional Dixon sequence, to assess a single randomly selected leg in each participant. From the MR images the muscle FF, muscle volumes, contractile muscle volumes, and T2_water values were calculated for 20 leg muscles. By PCR and Southern blotting CTG repeat lengths in the patients’ DMPK genes were quantified, and somatic instability was estimated by subtracting the modal repeat length from the estimated progenitor repeat length (CTG_ePAL). Multivariate linear regression was used to identify factors contributing to between-patient variability in FF’s.

Primary outcome measures
The primary outcomes were comparisons of the DM1 and HC groups in terms of quantitative muscle biomarker values.

Main results and the role of chance
Compared to the HCs, the patients had greater muscle FF’s, smaller muscle volumes, smaller contractile muscle volumes, and greater T2_water values (p ≤ 0.028). The muscle FF’s were increased before clinical signs of muscle weakness appeared. Approximately 45% of the between-patient variability in FF’s was explained by age, and approximately 14% by somatic instability and CTG_ePAL values.

Bias, confounding, and other reasons for caution
This study had a relatively small sample size.

Generalizability to other populations
This study’s reliance on data from 2 European centers may require more data for international generalizability of the results.

Study funding/potential competing interests
This study was funded by the European Union. The authors report no competing interests. Go to Neurology.org/N for full disclosures.

Figure Comparisons of leg muscle biomarker values in the patients and HCs

A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The authors of the full-length article and the journal editors edited and approved the final version.
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