Significant early progression in the first 15 years of life was noticed. Age at acquisition of independent ambulation and its loss were significantly linked to the age at initiation of pulmonary and cardiac interventions. The detailed analysis of this well-characterized cohort of early-onset SML patients expands our understanding of its phenotypic spectrum, will aid in the anticipatory care of pulmonary and cardiac manifestations, and establishes a basis for the development of outcome measures and appropriate trial cohorts for future prospective natural history studies and therapeutic clinical trials.

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Random forest approach to assess relationships of subjective muscle fatty infiltration with age at clinical onset and time of disease evolution in *LMNA*-related muscle disorders

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Muscle MRI is a popular approach to orientate genetic studies in clinical practice. Systematic description of muscle infiltration with semiquantitative scores is important to define specific MRI profiles in the different muscle disorders. Recently, two studies have described fatty infiltration patterns in patients with LMNA mutations. One has described whole body MRI in congenital muscular dystrophy (Gómez-Andrés et al. 2016); the other has assessed fatty infiltration of lower limbs by CT or MRI in Emery-Dreifuss and LGMD phenotypes (Díaz-Manera et al. 2016). We aim to combine data from both groups to evaluate which muscles are related with age at clinical onset and time of disease evolution. We collected data from both studies selecting those muscles that were represented in both. In those cases that one study represented data for muscle groups, a median score was calculated. Random forests were trained to predict both age at onset and disease evolution based on imaging data. We calculated the importance of each muscle in the prediction to point out which muscle fatty infiltration is related with onset or evolution. Fatty infiltration patterns discriminates age at onset (rho = 0.71). The relevant infiltrations were those of tibialis posterior, semitendinosus, iliopsoas, soleus and rectus femoris. Fatty infiltration patterns are also related to disease evolution but the prediction capacity is lower (rho = 0.53). Infiltration of semitendinosus, medial and lateral gastrocnemii, long head of biceps femoris and semimembranosus are the potential indicators of disease evolution. These results may be helpful in the design of longitudinal studies with quantitative assessment of fat fraction. Based on this result, rational designs would include muscles whose semiquantitative fatty infiltration is related with significant events in the disease course. Moreover, this study may represent a proof of concept that supports the use of systematic evaluation of fatty infiltration and descriptive techniques such as heatmaps that allow meta-analytical approaches.

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Corticosteroid treatment in early-onset lamin A/C related muscular dystrophies

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Corticosteroid therapy has shown a benefit in Duchenne muscular dystrophy especially on delaying loss of ambulation, reducing the incidence and severity of scoliosis and the age at respiratory insufficiency. It is also beneficial in myositis. As the muscle biopsies of patients with lamin A/C mutations can have prominent inflammatory component, corticosteroids have been empirically used in several patients in the past. We present a series of 27 patients with early-onset muscular dystrophy associated with lamin A/C mutations, 21 of them are part of an international multicenter retrospective natural history study. Seventeen patients showed improvement with treatment duration ranging from 6 months to 26 years. Ten patients were non-responders. The corticosteroids administered were: prednisone, prednisolone, deflazacort, and budesonide. There is a male predominance (M:F = 18:7) in the series. The muscle biopsy was inflammatory in 16, and non-inflammatory in 9 patients. Of note, patients who responded to treatment did not always had inflammatory abnormalities on the muscle biopsy. The positive effect of corticosteroids was seen in the first month in several patients: improved function of maximum motor function, axial tone, motor measurement (MFM), 6-minute walk test, vital capacity and weight gain. In non-responders, treatment was discontinued after 2 months of initiation. A prospective study is needed to determine the responders and the degree of benefit at the motor, respiratory, cardiac and orthopedic levels.

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Two novel mutations in the *FHL1* gene extending the phenotypic spectrum

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The *FHL1* gene is located on chromosome Xq26.3. Mutations in this gene have been linked to several X-linked recessive and dominant inherited myopathies and muscular dystrophies. *FHL1* encodes the four-and-a-half LIM domains 1 protein (OMIM 300163) which contains a double zinc finger motif and plays a role in protein-protein interaction and cytoskeletal organisation. Here we report 2 patients with mutations in the *FHL1* gene that to our knowledge have not been described before. Whole exome sequencing (WES) and data processing were performed by genomics platform at the broad institute of Harvard and MIT. Patient DNA samples (>250 ng) were processed with Illumina exome capture and sequencing technology (human exome target 38 Mb), and data were analysed with the genome analysis tool kit (GATK). Variant calls were uploaded on to the seqr platform. Patient 1 is a 33-year-old female who presented in early adulthood with scapular and proximal upper limb atrophy, joint contractures of the lower limbs, and progressive weakness. Her muscle biopsy shows myopathic and dystrophic features. She has a pathogenic mutation in the *FHL1* gene (chrX:135290658, T > A) causing an amino acid change (p.His182Gln). Patient 2 is a 79-year-old male of Black Indian origin with a raised CK (>10x) and a myopathic and dystrophic picture on muscle biopsy. He has scapular winging, contractures, a heart conduction defect, respiratory dysfunction requiring artificial ventilation, and proximal upper and