

# Muscle MRI early sign in presymptomatic patients with Late-Onset Pompe Disease (LOPD)



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## Background

Muscle MRI has an increasing role for diagnosing and monitoring disease progression in Late-Onset Pompe Disease (LOPD). T1-weighted sequences are used to detect fat substitution, which is a measure of muscle degeneration, while T2-STIR sequences are expression of oedema. Muscle MRI has also been incorporated as a supporting criterion for starting treatment, with a fat fraction >20% in at least two muscles considered abnormal. We retrospectively reviewed muscle MRI findings collected between 2009 and 2025 in a cohort of 31 patients with LOPD followed at the Neuromuscular Disorders Centre of Messina.

## Methods

T1-weighted and T2-STIR sequences of the paraspinal, thigh, and leg muscles were acquired in 31 patients. Complementary clinical assessments of motor and respiratory functions were performed.

## Results

Patients ranged from 7 to 72 years of age. 18/31 manifested axial and proximal muscle weakness, 17/31 had a respiratory involvement, 9/31 were paucisymptomatic. All symptomatic patients had a variable muscle fatty substitution observed in T1-weighted sequences. Interestingly, in 6/31 we identified a novel finding, characterized by hyperintensity on T1-weighted sequences in muscles of thighs, usually early affected.

These 6 patients (age range 20-26 years) were indeed at a presymptomatic disease stage with only hyperCKemia (700-2900 UI/L), normal muscle strength and no respiratory involvement. In these patients, hyperintensity on T1-weighted sequences matches perfectly with hyperintensity in T2-STIR, a common finding in LOPD, usually considered expression of oedema.

## Discussion

The coexistence of T2-STIR and T1 hyperintensities represents a radiological paradox, as STIR hyperintensity is typically attributed to increased water content, which should reduce T1 signal intensity. However, two classes of substances are known to shorten T1 relaxation time: paramagnetic substances and macromolecules. In our opinion, the hyperintensity observed on T1-weighted sequences may reflect the accumulation of macromolecules, such as glycogen, within affected muscle tissue. Notably, among the 9 presymptomatic patients, 6 exhibited both T2-STIR and T1 hyperintensities, whereas the remaining 3 (aged 7 to 15 years) showed no T1 signal abnormalities on muscle MRI. This pattern may reflect an early pathophysiological transition from the presymptomatic phase to overt disease and could carry both diagnostic and prognostic value.

## Conclusions

T1 muscle hyperintensities are easy to detect and may be a sign of glycogen accumulation, potentially preceding muscle fiber degeneration and fatty replacement and marking the onset of phenoconversion in presymptomatic patients.

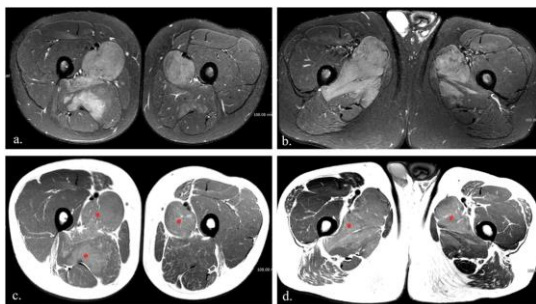


Fig. 1: 19-year-old patient axial fast-STIR (a,b) show an asymmetric involvement of the adductors and posterior compartment muscles of the thighs. In axial T1-weighted FSE (c,d) a mild hyperintensity (red asterisks) of non fat-infiltrated muscles, exactly matching to STIR MRI pattern, is detected.

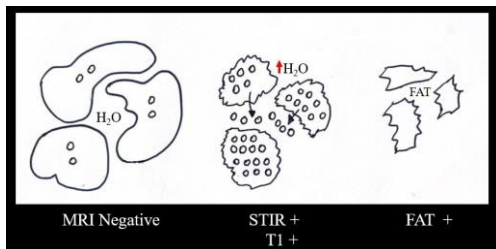


Fig. 2: Schematic explanation hypothesis of MRI coexistence of STIR/T2 and T1 hyperintensity in non fat-infiltrated LOPD muscles.



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