ANALYSIS OF FACIAL MUSCLE INVOLVEMENT IN ADULT FACIOSCAPULOHUMERAL MUSCULAR DYSTROPHY 1 PATIENTS THROUGH MAGNETIC RESONANCE AND ULTRASONOGRAPHIC ASSESSMENT

Elena Faedo 1, Federico Pistoia 2, Marta Macciò 3, Maria Elena Susi 3, Mehrnaz Hamedani 1, Veronica Caramellino 4, Sara Massucco 1, Andrea Francesco Maria Vollaro 1, Paola Mandich 1,2, Fabio Gotta 2, Carlo Martinoli 1,3, Federico Zaottini1,3 e Marina Grandis1,2.

1 Department of Neurosciences, Rehabilitation, Ophthalmology, Genetic and Maternal and Infantile Sciences (DINOGMI), University of Genoa, Genoa, Italy
2I RCCS Ospedale Policlinico San Martino, Genoa, Italy
3Department of Health Sciences (DISSAL), University of Genoa, Genoa, Italy
4 University of Genoa, Italy

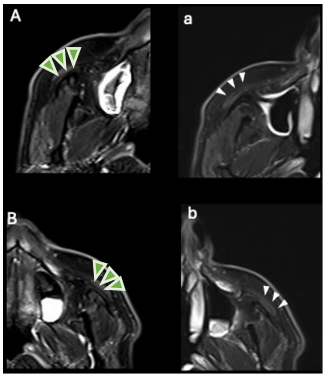
Introduction

Facioscapulohumeral muscular dystrophy type 1 (FSHD1) is an inherited myopathy, typically involving the facial muscles. While magnetic resonance imaging (MRI) is widely used for limb muscle evaluation, facial muscle imaging remains underutilized[1].

This single-center prospective study included adult patients with genetically confirmed FSHD, recruited between March 2024 and March 2025, to assess facial muscle involvement in FSHD1 through MRI and ultrasound (US), correlating these imaging findings with clinical severity.

CCEF Category	FSHD score	FWS	Closing eye gently	Closing eyes firmly	Raising eyebrow	Frowning	Pursing lips	Showing theeth	Puffing cheeks
B1	0	0	0	0	0	0	0	0	0
D1	2	1	0	0	0	0	1	0	0
D1	6	4	0	0	1	1	0	1	1
D1	7	2	0	1	0	1	0	0	0
D1	8	6	0	1	0	1	1	2	1
D1	12	7	0	0	1	1	2	2	1
A1	14	9	1	1	1	2	2	1	1
B2	15	9	0	0	2	1	2	2	2
D1	16	10	1	1	1	2	2	1	2
A2	17	10	1	0	1	2	2	2	2
A1	18	11	1	2	0	2	2	2	2
A2	21	12	3	2	0	1	2	2	2

Heat map of Clinical assessment of our cohort



***Hyperintensity of the ZMj** on T2-weighted fat-saturated sequences (green arrowhead) compared to normal (white arrowhead).*

Material and Methods

Clinical Assessment: application of the FSHD Clinical Comprehensive Evaluation Form (CCEF)[2]. Disease severity was assessed using the FSHD score, the age-corrected Clinical Composite Score (CCS)[2], and the Facial Weakness Score (FWS)[3].

Facial MRI Protocol: Zygomaticus major (ZMj), and orbicularis oris (OOr) were bilaterally evaluated for edema and atrophy using a standardized grading system (min 1= normal, max 3= severe atrophy). Images were independently assessed by one expert radiologist and two radiology residents.

Facial US Protocol: OOr and ZMj were assessed in standardized positions.

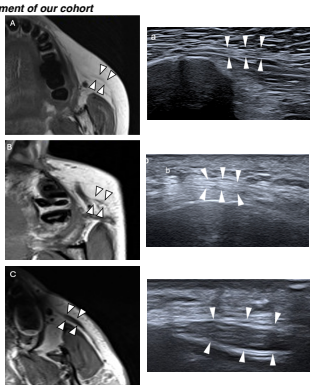


***Figure: ZMj grade of involvement in FSHD1 patients.** A and a) 26-year-old: advanced atrophy with near-complete fatty replacement. B and b) 59-year-old, moderate atrophic changes are present, with partial fatty infiltration. C and c) 61-year-old patient: preserved morphology and signal characteristics.*

Results

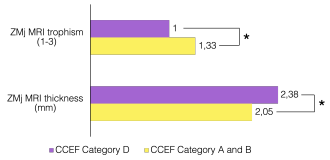
We studied 12 patients with FSHD1 (8 males and 4 females; mean age 57.8 years), predominantly Caucasian, with a mean disease duration of 23.8 years. Over half of the cohort (58.3%) reported a positive family history. Scapular weakness was the most frequent initial symptom, observed in 41.7% of patients, while facial and lower limb weakness were each reported in 25% of cases. More than half of the patients (58.3%) initially presented with asymmetric symptoms. Phenotypic classification according to CCEF[2] revealed a wide spectrum: four patients exhibited a complete typical FSHD phenotype (Category A), two showed incomplete presentations (Category B), and six were classified as Category D1, combining classical FSHD features with additional atypical findings. Assessment of disease severity showed that most patients (75%) had moderate involvement, with FSHD score[2] values ranging between 5 and 10 (mean: 7.58). The average FWS[3] was 6.8 to 21, indicating mild to moderate facial involvement. The OOr and ZMj muscles were most frequently affected, whereas forehead movement was relatively preserved.
Radiological assessment demonstrated no significant difference in facial muscle thickness between MRI and US.

***Heat map showing Spearman's correlation coefficients (ρ) between MRI muscle thickness (OOr and ZMj) and clinical scores.** Negative correlations are shown in blue, positive correlations in red.*

		FWS (0-21)	FSHD score: Scapular girdle (0–3)	Upper limbs (0–2)	Abdominal muscle (0–1)	Legs (0–2)
MRI thickness (mm)	OOr	1,05	1,8	-0,808	-0,43	-0,461
	ZMj	-0,489	-0,808	1,02	1,3	-0,598

***Median muscle thickness (mm) measured by MRI and US in patients with ("Yes") or without ("No") pathological FSHD score facial item.** Median thickness was lower in the "Yes" group compared to the "No" group.*

***Comparison of ZMj MRI thickness and trophism (medians) between CCEF categories A and B and D.** ZMj RM thickness: p = 0.045; ZMj RM trophism: p = 0.012 (Wilcoxon test).*



Reduced ZMj and OOr thickness correlated strongly with greater clinical weakness, as reflected by FWS and multiple domains of the FSHD score (scapular girdle, upper limbs, abdomen, and legs), as shown in the heat map.

Specific features, such as the presence of 'puckered lips', were significantly associated with decreased OOr thickness on US and reduced ZMj thickness on MRI. Similarly, the 'horizontal smile' item correlated with thinner ZMj measurements across both imaging modalities.

Interestingly, patients with atypical phenotypes (CCEF Category D) displayed significantly greater ZMj thickness and better muscle trophism compared to those with typical phenotypes (Categories A and B), as highlighted in the graph on the right.

Discussion and Conclusion

This is the first study to systematically evaluate facial muscle involvement in FSHD using both MRI and US, in parallel with detailed clinical and phenotypic assessment. Our findings support the use of facial imaging as a valuable tool for disease characterization, with significant correlations between muscle thickness and specific clinical signs, such as "puckered lips" and "horizontal smile". Patients with atypical FSHD1 phenotypes showed better preservation of facial muscle trophism, suggesting distinct disease trajectories within this subgroup. These findings highlight the potential of ZMj MRI parameters as imaging biomarkers to complement clinical evaluation, while also underscoring US's potential as a reliable and more accessible alternative for monitoring facial muscle involvement. This integrated approach may enhance phenotyping and outcome measurement in both clinical practice and future therapeutic trials.

References:

1. Vincenten SCC, Voermans NC, Cameron D, van Engelen BGM, van Alfen N, Mul K. The complementary use of muscle ultrasound and MRI in FSHD: Early versus later disease stage follow-up. Clin Neurophysiol. 2024 Mar 7:S1388-2457(24)00064-6. doi: 10.1016/j.clinph.2024.02.036. Epub ahead of print. PMID: 38521678
2. Ghasemi M, Emerson CP Jr, Hayward LJ. Outcome Measures in Facioscapulohumeral Muscular Dystrophy Clinical Trials. Cells. 2022 Feb 16;11(4):687. doi: 10.3390/cells11040687. PMID: 35203336; PMCID: PMC8870318
3. Loonen TGJ, Horlings CGC, Vincenten SCC, Beurskens CHG, Knuijt S, Padberg GWAM, Statland JM, Voermans NC, Maal TJJ, van Engelen BGM, Mul K. Characterizing the face in facioscapulohumeral muscular dystrophy. J Neurol. 2021 Apr;268(4):1342-1350. doi: 10.1007/s00415-020-10281-z. Epub 2020 Oct 28. PMID: 33113021; PMCID: PMC7990805

marina.grandis@unige.it

faedoelena@gmail.com