

Tracking muscle degeneration and disease activity in FSHD using longitudinal MR imaging

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Supplementary Table 1. Clinical characteristics of patients with FSHD collected by questionnaire, including mobility assessment at baseline and at 1-year follow-up. Data are presented as mean $\pm$ standard deviation [minimum–maximum].

Clinical Data	FSHD cohort at baseline (n = 31)	FSHD cohort at follow-up (n = 27)
Age (y)	44.4 $\pm$ 17 [14.7 – 79.2] years	45.3 $\pm$ 17 [16 – 80.2] years
Sex	21 male, 10 female	18 male, 9 female
Initial diagnosis	12.6 $\pm$ 9.8 [2 – 42] years ago	
More severely affected leg	7 left, 11 right, 13 both or no symptoms so far	
Regular physiotherapy	21 yes, 9 no	17 yes, 8 no
BMI (kg/m ²)	24.9 $\pm$ 5.2 [19.2 – 39.3]	25.3 $\pm$ 4.9 [18.7 – 41.1]
Myalgia	13 yes, 18 no	13 yes, 14 no
Composite MRC score (less affected leg)	27.5 $\pm$ 3.5 [16.5 – 30]	26.7 $\pm$ 3.7 [16.5 – 30]
Able to walk freely	27 yes, 4 only a few meters or with a rollator	21 yes, 6 only a few meters or with a rollator
Difficulty walking on tiptoes	15 yes, 16 no	18 yes, 9 no
Stepping gait	14 yes, 17 no	13 yes, 14 no
Able to rise from floor	19 yes, 12 no	17 yes, 10 no
Able to climbing stairs	16 yes, 12 with banister, 2 with help, 1 no	13 yes, 12 with banister, 1 with help, 1 no
Able to rise from chair	22 yes, 9 with help	17 yes, 10 with help
Mobility score (0 -12)*	9.1 $\pm$ 2.8 [4 – 12]	8.5 $\pm$ 3.1 [4 – 12]

* The sum of mobility score was calculated based on six functional items: ability to walk freely, ability to walk on tiptoes, presence of steppage gait, ability to rise from the floor, ability to climb stairs, and ability to rise from a chair. Each item was scored as follows. For difficulties walking on tiptoes, rising from the floor, and for the presence of steppage gait and Gowers' sign, 0 points were assigned; otherwise, 1 point was given. For the ability to rise from a chair, 2 points were assigned for "yes," 1 point for "with help," and 0 points for "not possible." For the ability to walk freely, 3 points were assigned for "yes," 2 points for "only a few meters," 1 point for "with rollator," and 0 points for "no." For stair climbing, 3 points were assigned for "yes," 2 points for "with banister," 1 point for "with help," and 0 points for "no." The resulting total mobility score ranged from 0 to 12, with higher scores indicating better mobility.

Supplementary Table 2. Baseline patient demographics and muscle strength

assessments. Composite MRC scores for the upper limbs were calculated separately for each side by summing arm elevation, shoulder abduction, shoulder adduction, elbow flexion, and elbow extension (maximum 25 points per side). Composite MRC scores for the lower limbs were calculated separately for each side by summing knee flexion, knee extension, ankle dorsiflexion, ankle plantarflexion, foot inversion, and foot eversion (maximum 30 points per side).

Patient nr.	Sex	Age [years]	BMI	Myalgia	Composite MRC upper limbs right/left		Composite MRC lower limbs right/left		Sum of mobility score	Disease duration [years]
1	m	52.5	39.0	yes	22	23	26	30	11	33
2	m	43.6	26.9	no	25	25	30	30	12	5
3	m	21.7	23.8	yes	22	24	30	30	12	12
4	m	53.8	29.4	no	23	22	20.5	21	5	7
5	m	45.8	20.6	no	22.5	22.5	27	27	12	5
6	m	54.3	21.3	yes	16	20	23	25	8	13
7	f	57.5	20.8	yes	18.5	18.5	21.5	25	5	9
8	f	23.4	19.2	no	23	25	24	25.5	11	4
9	f	79.2	25.0	yes	25	25	30	26	7	2
10	m	58.5	25.3	no	22.5	21	28	25	12	2
11	m	47.5	19.6	no	16.5	18	15.5	15.5	6	28
12	m	63.4	22.7	no	23	23	30	30	11	13
13	m	66.1	30.5	yes	16.5	17	21	20	4	9
14	f	43.9	20.3	yes	19	22	25.5	28.5	5	5
15	m	14.7	19.7	no	23	25	30	30	12	3
16	m	34.6	22.3	no	25	25	30	30	11	19
17	m	41.7	25.0	yes	23	21	30	30	9	19
18	f	36.7	19.2	no	18	24.5	30	30	8	12
19	m	40.2	23.3	no	25	22	30	30	10	16
20	m	23.5	25.0	no	22	24	30	30	12	1
21	m	76.0	26.5	no	20.5	17	25	27	4	22
22	f	43.8	30.3	yes	20.5	21	23.5	26	9	10
23	m	59.4	26.0	yes	20.5	20.5	26.5	25.5	9	41
24	f	37.4	22.0	no	20.5	20.5	30	30	11	24
25	m	37.2	19.9	no	16	15.5	29.5	20.5	6	18
26	m	25.8	28.4	no	25	25	30	30	12	1
27	f	38.5	39.3	yes	22.5	22.5	30	30	10	21
28	f	64.3	30.9	yes	19	18.5	23	22.5	7	15
29	m	17.2	23.6	no	22	21	29.5	30	12	2
30	m	54.0	25.4	yes	17	17	28	30	8	1
31	f	20.7	21.6	no	21	21	30	30	12	5
Mean		44.4	24.9		21.1	21.5	27	27.1	9.1	
SD		17.0	5.2		2.8	2.8	3.8	3.8	2.8	
Min		14.7	19.2		16	15.5	15.5	15.5	4	
Max		79.2	39.3		25	25	30	30	12	

Supplementary Table 3. Descriptive statistics of control and patient cohorts. Values are presented as mean $\pm$ standard deviation. Group comparisons were performed using the Mann–Whitney U test (Control vs FSHD v1) and the Wilcoxon signed-rank test (FSHD v1 vs FSHD v2). Standardized response means (SRM) compare the sensitivity to annualized change for each metric. P-values were adjusted for multiple comparisons using the Benjamini–Hochberg false discovery rate (FDR) method.

Muscle	Metric	Control		FSHD v1		Difference CTL vs FSHD v1	FSHD v2		Difference FSHD v1 vs v2	
		Mean	SD	Mean	SD	p-value	Mean	SD	p-value	SRM
EDL	FF	0.05	0.03	0.17	0.18	<0.001	0.22	0.21	0.012	0.542
	FF IQR	0.04	0.03	0.17	0.20	0.003	0.20	0.20	0.053	0.497
	T2 (ms)	35.4	2.3	37.1	4.0	0.203	37.2	4.1	0.979	0.028
	T2 CV	0.13	0.03	0.19	0.06	<0.001	0.20	0.07	0.125	0.448
	STIR			0.43	0.49		0.44	0.49		
	T1w			1.74	1.81		1.74	1.81		0.192
GL	FF	0.06	0.03	0.16	0.19	0.001	0.20	0.22	0.002	0.504
	FF IQR	0.04	0.02	0.10	0.11	0.007	0.15	0.16	0.023	0.459
	T2 (ms)	34.4	2.8	35.9	4.2	0.203	35.6	5.7	0.856	-0.144
	T2 CV	0.16	0.03	0.16	0.04	0.623	0.18	0.06	0.281	0.311
	STIR			0.52	0.49		0.52	0.49		0.278
	T1w			1.11	1.31		1.22	1.48		0.000
GM	FF	0.06	0.04	0.36	0.32	<0.001	0.45	0.34	<0.001	0.631
	FF IQR	0.05	0.04	0.15	0.16	<0.001	0.15	0.15	0.424	-0.300
	T2 (ms)	35.3	3.0	37.3	4.1	0.203	35.7	5.5	0.856	-0.296
	T2 CV	0.13	0.03	0.19	0.08	<0.001	0.16	0.05	0.940	-0.014
	STIR			0.65	0.48		0.63	0.47		0.262
	T1w			2.22	1.80		2.22	1.83		-0.192
PER	FF	0.08	0.04	0.12	0.13	0.121	0.13	0.13	0.107	0.388
	FF IQR	0.06	0.04	0.09	0.07	0.349	0.10	0.07	0.158	0.429
	T2 (ms)	35.8	2.6	35.7	1.9	0.994	36.0	3.7	0.856	0.102
	T2 CV	0.11	0.03	0.12	0.02	0.079	0.13	0.03	0.125	0.486
	STIR			0.09	0.28		0.13	0.33		
	T1w			1.15	1.70		1.15	1.70		0.192

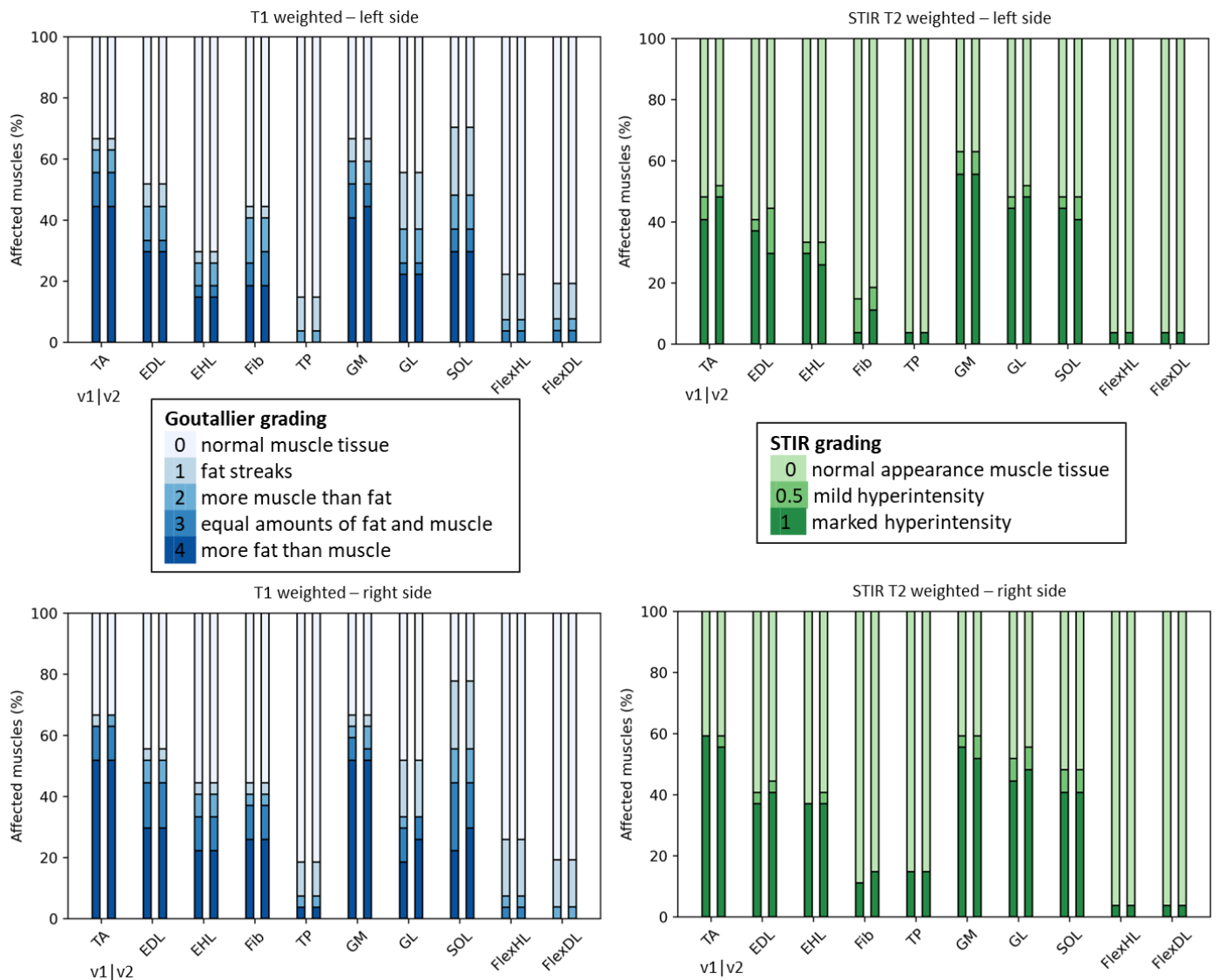
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SOL	FF	0.06	0.04	0.15	0.16	0.001	0.18	0.18	<0.001	0.811
	FF IQR	0.05	0.04	0.12	0.10	0.003	0.16	0.14	0.023	0.439
	T2 (ms)	35.5	1.7	37.8	4.7	0.203	38.3	5.6	0.856	0.178
	T2 CV	0.10	0.03	0.14	0.06	<0.001	0.14	0.05	0.158	0.222
	STIR			0.52	0.49		0.54	0.50		0.192
	T1w			2.00	1.54		2.04	1.58		0.085
TA	FF	0.03	0.02	0.19	0.23	<0.001	0.29	0.27	<0.001	0.538
	FF IQR	0.03	0.02	0.13	0.14	0.003	0.18	0.17	0.030	0.418
	T2 (ms)	35.1	2.0	36.7	3.8	0.203	37.2	4.3	0.856	0.105
	T2 CV	0.10	0.02	0.17	0.09	<0.001	0.17	0.09	0.267	0.394
	STIR			0.56	0.51		0.57	0.49		0.192
	T1w			2.33	1.88		2.33	1.88		0.085
TP	FF	0.05	0.03	0.05	0.03	0.359	0.06	0.03	0.222	0.113
	FF IQR	0.04	0.02	0.04	0.04	0.640	0.05	0.04	0.171	0.128
	T2 (ms)	34.8	2.0	35.4	3.0	0.658	35.4	2.9	0.856	0.025
	T2 CV	0.14	0.03	0.15	0.02	0.082	0.16	0.02	0.158	0.386
	STIR			0.11	0.32		0.11	0.32		
	T1w			0.19	0.48		0.19	0.48		
Average of all muscles	FF	0.06	0.03	0.17	0.13	<0.001	0.22	0.15	0.001	0.874
	FF IQR	0.04	0.03	0.11	0.08	<0.001	0.14	0.09	0.001	0.784
	T2 (ms)	35.2	2.0	36.7	2.8	<0.001	36.8	3.6	0.327	0.078
	T2 CV	0.12	0.02	0.16	0.04	<0.001	0.17	0.04	0.025	0.119
	STIR			0.41	0.29		0.42	0.28		0.364
	T1w			1.53	1.16		1.56	1.19		0.173

Supplementary Table 4. Annual change in fat fraction (Δ FF) in patients in comparison with normative fat fraction values in healthy controls (HC). For each muscle, the mean $\pm$ SD fat fraction (FF) and 5th–95th percentile range in healthy controls are shown alongside the mean $\pm$ SD annual change in FF (Δ FF/year) observed in patients with FSHD. The annual change is additionally expressed as a percentage of the mean FF in healthy controls. The proportion of patients with baseline FF values above the 95th percentile of the healthy control distribution is also reported.

Muscle	Healthy control FF	Healthy control 5th–95th percentile	FSHD Δ FF/year	Δ FF/year relative to HC mean	FSHD above HC 95th percentile
GM	0.063 $\pm$ 0.036	0.028–0.143	0.024 $\pm$ 0.039	38.4%	63.0%
GL	0.058 $\pm$ 0.026	0.029–0.113	0.033 $\pm$ 0.066	57.8%	37.0%
SOL	0.06 $\pm$ 0.04	0.029–0.138	0.019 $\pm$ 0.024	31.6%	22.2%
TP	0.048 $\pm$ 0.025	0.023–0.098	0.001 $\pm$ 0.008	1.7%	7.4%
PER	0.078 $\pm$ 0.041	0.031–0.151	0.004 $\pm$ 0.011	5.6%	18.5%
EDL	0.052 $\pm$ 0.027	0.023–0.098	0.018 $\pm$ 0.033	34.2%	44.4%
TA	0.034 $\pm$ 0.019	0.017–0.075	0.031 $\pm$ 0.057	91.7%	48.1%

Supplemental Material



Supplementary Figure 1. Bar plots showing the percentage of affected muscles in FSHD patients at baseline (v1) and follow-up (v2), displayed separately for the left and right lower legs. Affected muscles were defined based on visual grading of T1-weighted and STIR images. Side-to-side differences in the proportion of muscles with fatty replacement (T1w) and STIR hyperintensities are illustrated.