Limb-girdle muscular dystrophies: clinical characteristics of LGMD2A/R1 and LGMD2B/R2 patients from a single italian centre.

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Introduction: Limb-Girdle Muscular Dystrophies (LGMDs) are a heterogeneous group of inherited neuromuscular diseases characterized by progressive weakness of the proximal muscles, particularly of the pelvic and scapular girdle. The progression of disease can lead to loss of ambulation and respiratory or cardiac complications and the prevalence is estimated between 1.63 and 2.27 per 100,000 people, with significant regional variations [1]. In Italy, the most frequent subtypes are LGMD2A/R1 (calpainopathy) and LGMD2B/R2 (dysferlinopathy), together accounting for a significant proportion of diagnosed cases [2]. The current classification distinguishes between autosomal recessive (LGMD-R) and dominant (LGMD-D) forms, based on updated genetic and clinical criteria [3].

Objectives

To describe the clinical spectrum, disease progression and functional status of patients with genetically confirmed LGMD2A/R1 and LGMD2B/R2

Patients and methods

Study design: retrospective observational cohort from a single Italian tertiary centre.

Inclusion criteria: genetically confirmed LGMDR1 or LGMDR2; at least one year follow-up.

Data collected: demographic, genetic, clinical onset, motor milestones, functional assessments, CK levels, respiratory and cardiac function.

Results

Sample size: 30 patients: 14 LGMDR1 (green in table) and 16 LGMDR2 (blue in table). Mean age was respectively 42.5 (SD:13.8) and 49.3 years (SD:11.5).

Mean age at onset: LGMDR1: 25.7 years (SD:14.9); LGMDR2: 25.1 years (SD: 9.07).

Loss of ambulation: LGMDR1: 3/14 (21.4%); LGMDR2: 11/16 (68.7%)

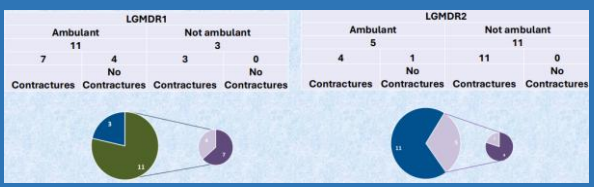
CK levels: elevated in both groups (mean: 2046 U/L and 2536 U/L respectively)

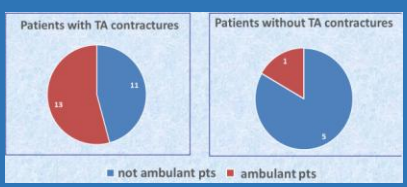
Cardiac and respiratory involvement: Rare in both groups

Achilles tendon contractures: high incidence (82%), but more involved in LGMDR2 The entity of pelvic girdle weakness was similar in both groups Among our cohort, only 61.5% of patients undergo physical therapy

Patients	Sex	Age (years)	Age at onset (years)	Ambulant	TA Contractures	Respiratory function (FCV, L)	Cardiac function
1	F	46	10	Yes	Yes	3.41	Normal
2	M	37	2	No	Yes	2.63	Bbdx
3	F	67	48	Yes	Yes	2.48	Normal
4	F	45	28	Yes	Yes	NA	Normal
5	F	35	15	Yes	Yes	4.67	Normal
6	F	83	47	Yes	No	NA	Normal
7	F	41	28	Yes	Yes	2.83	Bbdx
8	M	78	35	Yes	No	NA	Normal
9	F	64	33	No	Yes	2.17	Normal
10	F	50	17	Yes	No	NA	Normal
11	F	42	15	No	Yes	3.45	Normal
12	F	41	29	Yes	No	3.49	Normal
13	M	35	19	Yes	Yes	NA	Normal
14	M	24	13	Yes	Yes	4.64	Bbdx
15	F	56	27	No	Yes	4.40	Normal
16	F	61	38	Yes	No	3.42	Normal
17	M	69	32	Yes	Yes	3.02	Normal
18	F	65	38	No	Yes	3.07	Normal
19	F	70	28	No	Yes	3.18	Normal
20	M	38	24	Yes	Yes	6.04	Normal
21	M	56	32	No	Yes	3.96	Normal
22	F	37	10	Yes	Yes	3.57	Normal
23	F	75	31	No	Yes	2.41	Normal
24	F	71	37	No	Yes	3.01	Bifascicular block
25	M	45	19	No	Yes	2.27	Normal
26	F	47	15	No	Yes	1.58	Normal
27	M	36	22	Yes	Yes	5.26	Normal
28	M	41	15	No	Yes	3.16	Normal
29	M	35	19	No	Yes	NA	Normal
30	M	38	15	No	Yes	NA	Normal

Loss of ambulation does not correlate with mean of age (p=0.50 and p=0.18) either age of symptoms onset (p=0.052 and p=0.55) in both groups.





Conclusions: Despite mean age and age of onset were similar, 78.6% of LGMDR1 patients were ambulant whereas only 31,3% of LGMDR2 maintained this function. We identified a distinguishing feature between the two patient groups: Achilles tendon contractures occurred more frequently in ambulant LGMDR2 patients. We suggest that Achilles tendon contractures may play a significant role in the progressive loss of ambulation in LGMDR1/R2 patients, and our findings suggest that physical therapy is mandatory. Further natural history studies are needed to confirm our results and to better determine whether Achilles tendon contractures may act as an early marker or contributing factor in the transition from ambulant to non-ambulant status.

References

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