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INVITED REVIEW

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Limb-girdle muscular dystrophies: A scoping review and overview of currently available rehabilitation strategies

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Abstract

Limb-girdle muscular dystrophies (LGMDs) constitute a diverse group of inherited disorders primarily affecting skeletal muscle. Despite the absence of cures, rehabilitative treatments offer potential for preventing and mitigating loss of muscle strength. However, the role of exercise training in LGMD patients remains contentious. This review aims to provide an overview of the currently available motor rehabilitation strategies for the most common subtypes of LGMD. To identify relevant articles, we performed a systematic search in PubMed, Embase, Cochrane Library, and Web of Science, focusing on muscular and respiratory interventions. The search resulted in 560 potentially relevant articles, of which 16 were included in the review. Eight studies concentrated on neuromuscular functional rehabilitation therapy programs, seven combined both neuromuscular rehabilitation and interventions to maintain or enhance respiratory functionality and one focused on respiratory intervention only. Altogether, the papers examined offered a comprehensive view on the rehabilitative strategies available and provided an indication of the most valuable practices to deal with patients' health and needs. Upon analysis, we conclude that, when tailored to individual needs, muscle training can enhance strength and functional abilities, positively impacting psychological well-being. However, generic protocols may lead to limited benefits, fatigue, pain, and compliance issues. Moreover, early management of respiratory symptoms and personalized respiratory physiotherapy can enhance

Abbreviations: CK, creatine kinase; FVC, forced vital capacity; HIT, high-intensity training; IAPV, intermittent abdominal pressure ventilation; LGMD, limb-girdle muscular dystrophy; LOIT, low-intensity training; NIV, noninvasive ventilation; RMT, respiratory muscle training.

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The objectives of this activity are to: (1) Appreciate the heterogeneity of the limb-girdle muscular dystrophies and be able design individualized rehabilitative approaches to patients; (2) Understand and be able to implement appropriate aerobic and strength training as part of a comprehensive rehabilitative strategy for patients with limb-girdle muscle dystrophies; (3) Understand the symptoms and signs of respiratory involvement in the limb-girdle muscular dystrophies and implement appropriate respiratory interventions as part of comprehensive rehabilitative strategies.

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patients' well-being and their capability to participate in muscle training exercises. Future studies should not only refine rehabilitation approaches but also assess their impact on patients' quality of life, including psychological factors like depression and self-esteem.

KEYWORDS
fatigue, limb-girdle muscular dystrophy, physiotherapy, quality of life, rehabilitation

1 | INTRODUCTION

The limb-girdle muscular dystrophies (LGMDs) are a group of genetically diverse diseases affecting disparate proteins that alter muscle physiology and lead to a wide range of clinical manifestations.[1] These disorders are responsible for progressive muscle weakness and atrophy,[2] mainly impacting the proximal limb-girdle musculature. To date, more than 30 different subtypes of LGMDs have been identified, with an estimated prevalence for all forms of LGMD between 1/14,500 and 1/123,000.[3–5] LGMDs are autosomal disorders that can be transmitted with both dominant and recessive inheritance and originate from defects in proteins expressed in different compartments of the muscle fiber, such as the nucleus (e.g., transportin-3), sarcomere (e.g., titin), sarcolemma (e.g., sarcoglycans, dysferlin), and extracellular matrix (e.g., collagen, laminin). Consequently, LGMDs exhibit high clinical heterogeneity, with symptoms sometimes overlapping with other types of dystrophies. The phenotype can range from severe, with disease onset within the first decade of life ultimately leading to profound weakness and disability, to mild, with later onset and slower progression.[6,7] Notably, although the onset of weakness occurs in proximal muscles, the disease eventually affects most muscle groups. In the advanced stage, the diaphragm may become involved, resulting in reduced forced vital capacity (FVC) and respiratory insufficiency, which can lead to respiratory failure and premature death.[6,8] The continuous degeneration/regeneration process and muscle damage are usually associated with elevated serum creatine kinase (CK). The definitive subtype diagnosis is achieved by genetic testing.

There are currently no cures for muscular dystrophy and effective therapies are still lacking; therefore, symptomatic treatment is the mainstay of management. The main guidelines for LGMD include physical exercise, which contributes to the reduction of mortality and morbidity.[9,10] Individuals affected by neuromuscular diseases show weakness and fatigue as primary symptoms, and this reduces their ability to walk and perform daily living activity, leading to sedentary lifestyle and obesity.[11] Rehabilitative treatment plays a key role in prevention of, and compensation for, loss of muscle strength and therefore in preserving for as long as possible the patient's maximum autonomy. In the past, clinicians have been cautious about the use of muscle training when dealing with neuromuscular disorders, due to the fragility of patients' muscles typical of this group of diseases.[12] The disease makes it difficult for patients to sustain prolonged muscular effort and frequently causes fatigue, which occurs when the intended physical activity can no longer be continued or is perceived as excessive effort and discomfort.[13,14] It is thus necessary to balance muscle training to improve strength and quality of life of patients with the need to preserve the delicate muscle fibers that can easily be damaged with the wrong type of exercise.[15,16]

Neuromuscular functional rehabilitation occupies a central position in the ongoing debate concerning the benefits and risks of exercise training for patients with muscular dystrophies. Given that patients must rely mainly on symptomatic treatment, it is only natural that muscle training is taken into consideration in the management of LGMDs. Two main types of physical training are considered safe and potentially beneficial in the rehabilitation of patients with muscle disorders: strength training and aerobic training. Low-impact aerobic exercise (e.g., swimming, stationary cycling) has been shown to provide positive effects on muscle strength and cardiovascular functions in slowly progressive myopathies.[17] These regimens may be combined with body weight supported training and respiratory muscle training (RMT). In fact, many patients need assistive devices to help them breathe efficiently and intervention aiming to improve strength or endurance of inspiratory and/or expiratory muscles could be beneficial. To this purpose, RMT can be applied both with targeted exercise through respiratory techniques and indirectly via aerobic training.[18]

The most common LGMD subtypes are LGMDR1 calpain 3-related, LGMDR2 dysferlin-related, LGMDR3 to R6 sarcoglycan-related, and LGMDR12 anoctamin 5-related. This review aims to describe the currently available muscular and respiratory rehabilitation strategies for these subtypes and their reported outcomes, providing an overview of the current knowledge and gaps in LGMD management.

2 | METHODS

This work was undertaken following the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR).[19]

2.1 | Data sources, search, and selection criteria

We searched for articles written in English in PUBMED, EMBASE, WEB OF SCIENCE, and the Cochrane Library. The first search was performed in May 2023. An updated search was performed upon

revision, spanning from May 2023 to April 5, 2024. The search strategy and the search syntax used to search the databases are presented in the Supporting Information: Appendix A.

Selection criteria for inclusion comprised studies and reviews, which included adults (>18 years old) affected by LGMD, who underwent a motor rehabilitation program including one or more types of training: for example, strength, anti-gravity, resistance training, and/or RMT. Our primary outcomes were the following: (i) muscle strength, assessed through shoulder abductor and knee extensor muscle strength, isometric knee extension, and flexion muscle strength; (ii) respiratory function assessed through respiratory rate, inspiratory time, minute ventilation, tidal volume. Secondary outcomes of interest were: (i) muscle fatigue; (ii) quality of life levels assessed with questionnaires targeting physical self-worth, self-esteem, anxiety.

Exclusion selection criteria comprised articles in any language other than English, abstracts, posters, and any other article that did not fulfill any of the inclusion criteria listed above. Articles that considered types of muscular dystrophies other than LGMD were also excluded.

2.2 | Study selection

The identified articles obtained from the search of each database were imported into EndNote X7. Duplicate items were identified and removed. Records were then imported in Rayyan (https://www.rayyan.ai/), an online tool used to perform title and abstract screening. Two reviewers (M.S. and S.F. for the first search; G.D. and S.F. for the second search) independently screened records identified through the search strategy described above, based on the title and abstract. After the title and abstract screening process, the included full texts were examined for final inclusion by the same two authors, independently. Any disagreement was resolved after discussion with a third reviewer (L.C).

2.3 | Data synthesis and analysis

All relevant data of the included articles were extracted in a systematic way using a pre-developed synoptic table (included in Table S1) that presents the general characteristics of included studies, with the following information: (1) authors and year of publication; (2) study design; (3) aim of the study; (4) patient characteristics (i.e., age, LGMD subtype, sex, age, any relevant patient characteristics that were considered for the study's inclusion and exclusion criteria); (5) type of rehabilitation intervention; (6) intervention protocol; (7) outcome measures; (8) authors' conclusions.

3 | RESULTS

3.1 | Search results

Initially, 511 items were retrieved from the electronic databases while the updated search identified 49 additional elements. A total of 560 items were subjected to the selection procedure, as illustrated in Figure 1. Sixteen articles met all the criteria and were included in this review (Table S1).

3.2 | Characteristics of the included studies

Among the 16 included studies, 6 were clinical studies and 10 were reviews of scientific literature and clinical practice that have been used as references for this review. Among the chosen papers, eight focused on neuromuscular functional rehabilitation therapy programs,[20–27] seven combined both neuromuscular rehabilitation and interventions aimed at maintaining or improving respiratory functionality[28–34] and one included respiratory intervention only.[35]

The neuromuscular functional rehabilitation studies employed various types of physical exercises, including body weight exercises,[15,36–38] cycling,[16,39,40] and exoskeleton-assisted exercises.[38,39,41] Regarding rehabilitation interventions on respiratory functionality, the studies employed ventilators,[42] respiratory assistive devices, and physical therapy.[40] One study investigated the impact of resistance muscle training on the functional abilities and quality of life of patients with LGMD. The included studies were divided into two categories based on the type of intervention (respiratory intervention and neuromuscular rehabilitation, including conventional and novel approaches).

3.3 | Neuromuscular functional rehabilitation

Exercise training protocols can vary significantly in terms of duration, intensity, and frequency and these variations can lead to different outcomes, necessitating careful evaluation. The very first studies on the effects of strength training on LGMD patients were conducted in the 1980s: Ansved[43] analyzed those previous studies in which high-resistance training programs were tested in a heterogeneous group of LGMD patients.[20,44] The author reported limited positive effects, including an increase in strength among patients with mild to moderate muscle weakness and proposed further functional studies to assess the effects of muscle training exercises on the overall well-being of patients. Results indicate that high-resistance and eccentric training should be avoided in those forms of LGMD in which structural proteins are involved because this may lead to muscle injury. In contrast, moderate intensity training may be beneficial to patients, and that muscle training regimen should commence in the early stages of the disease, when a substantial amount of trainable muscle tissue is present.

In their review, Angelini et al.[15] examined in depth the causes and mechanism of adverse effects caused by prolonged muscular training, in particular in LGMD patients affected by sarcoglycanopathies. Their analysis of the molecular mechanisms underlying muscle fiber damage in disorders with impaired dystrophin complex protein function revealed that post-exercise fatigability is primarily attributed to a depletion of the neuronal nitric oxide synthase enzyme in the fibers.[28]

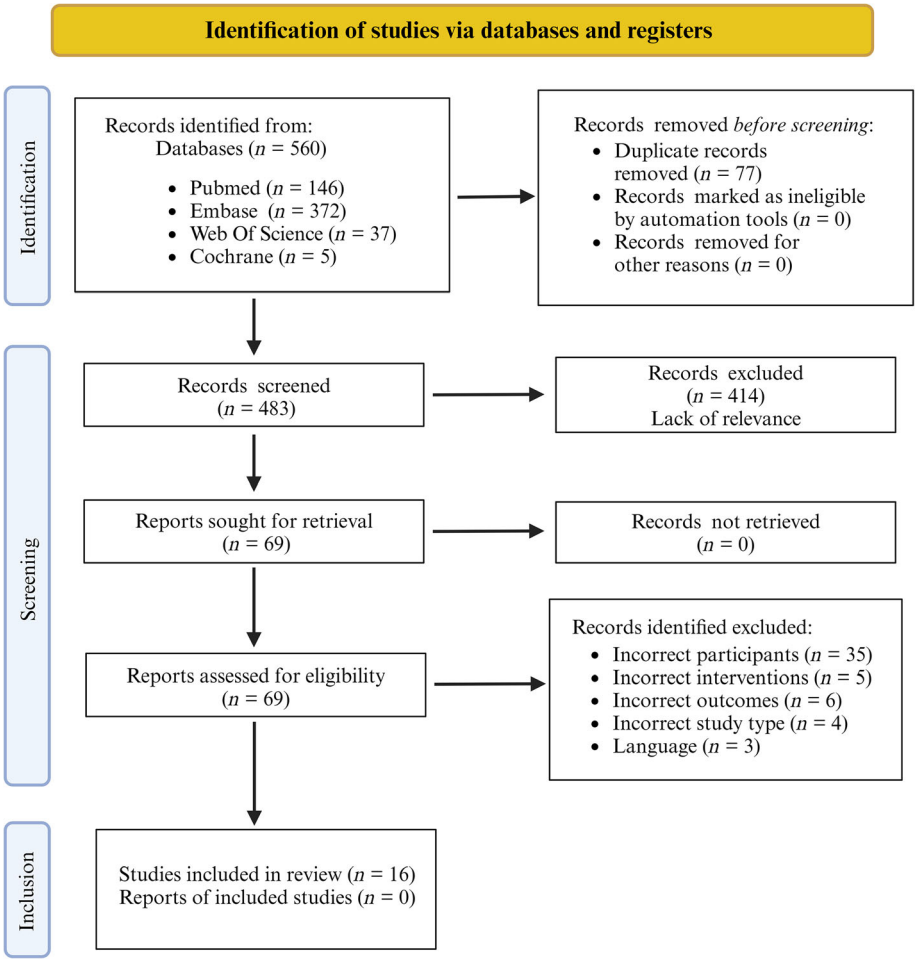

FIGURE 1 PRISMA study flow diagram.

Angelini emphasized the importance of assessing patients' nitric oxide levels during physiotherapy and correlating them with muscular strength, fitness, and therapy compliance, adjusting the required effort accordingly. Moreover, genetic defects in LGMDR1 and R12 patients may cause muscle fragility leading to detrimental results during training. Damage can be both metabolic and mechanical as a result of ischemia and muscle fiber overload[45]; therefore, eccentric exercise should be avoided, while supervised aerobic exercise is well tolerated. Siciliano et al.[16] in their review agree that muscle exercise has a positive role in reducing loss of muscle strength; however, specific protocols must be carefully evaluated and monitored by trained specialists.[17] The most feasible and safe solution remains aerobic exercise of moderate intensity (<70% of a patient's maximal aerobic capacity).[46]

Many studies involve specific protocols both for aerobic and strength training: Vissing et al.[37] proposed a 10-week aerobic moderate-intensity training program to treat six LGMDR12 patients. Participants were trained at home on a stationary bicycle ergometer for at least 3 days per week for 30-min sessions. The training program improved not only aerobic capacity but also muscle strength, as measured by the ability to rise and stand from sitting, without causing further increase in CK or muscle soreness. Sveen et al.[47] obtained a similar result on LGMDR9 patients: stationary cycle ergometer for 12 weeks improved work capacity without negatively affecting CK levels or muscle morphology. These results are quite important since aerobic exercise prevents cardiovascular diseases associated with a sedentary life and increases the strength of targeted muscle groups resulting in an increased long-term quality of life by easing everyday tasks. Sveen et al.[36] investigated the effect of strength training in patients with LGMD: the authors compared the effect of low-intensity training (LOIT; $n = 6$, 2 LGMDR1 and 4 LGMDR9) and high-intensity training (HIT; $n = 5$, 4 LGMD2A and 1 LGMD2I) in muscles of the upper and lower extremities in terms of strength and damage. Patients were tested for maximal strength and endurance. Over 6 months, LOIT increased biceps strength and endurance, while HIT improved wrist and elbow strength and endurance, though to a limited extent. LOIT was well tolerated; while HIT caused elevated CK levels, pain, and overload symptoms in two patients as determined by analysis of CK levels and questionnaire on reported daily functions. Altogether, these preliminary findings suggest that resistance training in the form of LOIT could be beneficial and safer for managing patients with LGMDR1 and LGMDR9, whereas HIT requires careful monitoring due to its potential adverse effects. Moreover, Nandanwar et al.,[40] reported that a complete program based both on low-intensity strength training and aerobic exercise was beneficial for one LGMDR1 patient. This case study report is particularly interesting since the

patient, a woman who was diagnosed at a young age when first symptoms appeared, was followed with a complete training protocol: she underwent physical therapy interventions aimed at improving muscle strength, joint mobility, balance, and gait obtaining valuable results. The authors discuss the importance of accurate diagnosis and tailored therapy in managing LGMD: the paper highlights the significance of an immediate multidisciplinary approach in managing LGMD to improve quality of life and functional outcomes.

Another problem that requires consideration is addressed by Preisler et al.[41] in their review: safety and long-term effect of exercise on disease progression are great concerns in patients with LGMDs. The authors included a clinical study[21] in which patients were grouped according to how much strenuous physical activity, in both aerobic and strength training, they had engaged in during their teenage years (10–20 years old) and compared this with self-reported age of first symptoms of muscle disease. Interestingly, teenagers with higher self-reported activity level and sport participation prior to onset of symptoms showed increased risk for earlier symptom onset and wheelchair use and displayed an increase in the rate of disease progression. In addition, Preisler noted that patients with specific types of LGMDs (including LGMDR9) did not show this correlation between childhood physical activity levels and symptoms onset, underlining the need to avoid extending conclusions based on studies of one LGMD subtype to other subtypes.

All these findings were supported and summarized by Sheikh and Vissing.[37,38] The authors analyzed a number of papers, including some of those discussed above, and concluded that moderate aerobic training seems to be generally better tolerated and safer, while strength training, although providing beneficial effects on muscle strength, should be performed in moderation and carefully monitored to avoid potential muscle damage. Extreme fatigue and muscle pain, during or after exercise, should prompt therapists to modify the intensity and frequency of training. In addition, the authors point out the need to consider a patient's motivation and compliance when designing exercise therapy trials.

Both Preisler[41] and Sheikh[38] also focused on assisted exercise such as body weight-supported physiotherapy approaches and antigravity training. Body weight supported treadmill training is a type of supported ambulation involving assistive devices that is usually performed on a specifically designed treadmill, surrounded by a pressure chamber, offering the opportunity to train individuals with reduced muscular strength, injuries or other conditions that could potentially limit physical exercise in a natural environment.[22] This type of training can be combined with the use of neurorobotic gears, including exoskeletons such as the hybrid assistive limb, a wearable mobile machine with a frame and actuators on hip and knee joints. The equipment uses surface electrodes to detect electromyographic signals coming from the muscles of the patient to exploit voluntary muscle activity to provide patients with the motion support needed.[23,24] This type of approach allows the treatment of patients with reduced muscular strength who are not able to perform traditional types of exercises. Sczesny-Kaiser et al.[39] investigated the effects on walking function of the hybrid-assisted limb on 1 patient with LGMDR1 and 2 patients with other LGMD subtypes treated for 30 min 3 days a week for 8 weeks. Other than the improvement of muscle strength, the protocol assessed safety, balance, and functional mobility. After training with the hybrid-assisted limb, patients improved on various tasks, such as distance training time and velocity on the treadmill.

Exercise produces beneficial effects on mood and psychological well-being[25]: O'Dowd et al.[26] studied the impact of 12 weeks of moderate-intensity resistance training on psychological parameters in 6 LGMD patients with various genotypes (R1, R2, R9, R12). Patients underwent a progressive, moderate-intensity resistance muscle training program that was tailored to each participant's needs and functional capability. Quality of life and general well-being were assessed with objective and subjective approaches such as psychological evaluations and self-reporting questionnaires. The study found that moderate-intensity resistance training improved the quality of life of participants, with a decreased severity of depressive symptoms and anxiety and increased self-esteem and physical self-worth.

3.4 | Respiratory intervention

Multidisciplinary management of muscular diseases must also focus on respiratory intervention. Pulmonary complications are often seen in patients with LGMD and respiratory muscle strength is commonly compromised. The early signs of respiratory insufficiency are snoring, apneic episodes, and daytime somnolence. These, if not treated promptly, degenerate into sleep hypoventilation, affecting daytime activities. The most commonly employed measurement of respiratory functionality is FVC. The majority of LGMD2 patients have both inspiratory and expiratory muscle involvement that typically occurs late in LGMDR1, while in LGMDR2 the respiratory function declines with the disease duration. Types R3–R6 (sarcoglycanopathy) exhibit high respiratory morbidity, often with FVC below 40% of predicted values resulting in the need for noninvasive ventilation (NIV) support in 1 out of 4 patients before the age of 30 years.[9,27,29–31,35] Therefore, respiratory intervention and management play a crucial role in the care of individuals with LGMD due to the potential impact of respiratory muscle weakness on both quality of life and overall health: the main aim is to optimize respiratory function, prevent complications, and improve overall well-being.

Guidelines for LGMD treatment include the monitoring of respiratory dysfunction via pulmonary function test to assess FVC,[32] while the main recommended interventions include respiratory therapy, aerobic exercise, and NIV devices; however, no clear consensus has been achieved, hence the need for further studies and tailored protocols, based on the needs of patients.[32] The study by Kakulas et al.[33] was one of the first to consider the decline in respiratory function in some forms of LGMD, specifically sarcoglycanopathies. They identified irritability, headache, and loss of concentration as the first, subclinical symptoms of hypoxia during sleep, and indicated NIV as beneficial. As the disease progresses, the need for ventilatory support may become permanent. Manzur et al.[34] and Angelini[48,49] focused independently on management options for respiratory insufficiency in patients with

LGMD. Both concluded that the best management approach is nocturnal ventilatory assistance with ventilator support. Monitoring of respiration during overnight sleep (when FVC falls below 50% of normal values) is important to determine when nocturnal NIV should be provided, without waiting for daytime ventilatory failure, allowing the patients to become accustomed to the ventilation support. Aoki and Takahashi[50] described the current diagnosis and management strategies for LGMDR2. The authors concluded that the use of NIV, together with mobility and stretching exercises, can prolong survival and improve quality of life, and suggested performing annual pulmonary function tests and spirometry as surveillance approaches to evaluate the effects of muscle weakness on respiratory function.

Regarding physical therapy for respiratory dysfunction, aerobic exercise was proven to positively impact respiratory capacity, as observed by Sveen et al.[47] and Vissing et al.[37]: the maximum oxygen capacity was increased as an effect of exercise on the cardiovascular system, providing indirect benefits to the respiratory system. Therefore, the positive impact of an aerobic training program for these patients may be of substantial importance on the overall well-being, affecting many physiological aspects. In addition, exercise that directly targets respiratory muscles may be carried out, as reported by Nandanwar et al.[40]: in that paper, rehabilitation intervention included deep breathing exercise as well as intercostal stretching with beneficial results.

Lastly, Volpi et al.[42] provided a comparison of noninvasive ventilatory support via nasal or oronasal masks and intermittent abdominal pressure ventilation (IAPV) via a new model of the abdominal corset and a home ventilator specifically designed to operate with IAPV through dedicated software. They achieved increased expiratory flow due to abdominal compression, eliminating facial or nasal interfaces. This retrospective study showed that IAPV use led to an amelioration in hypoxemia and the normalization of hypercapnia, resulting in an improvement in quality of life, resulting in a conclusion that alternative ventilation methods could become a key part of daytime support for muscle dystrophy, including LGMDs.

4 | DISCUSSION

The rehabilitative strategies described in this review are not intended as cures, but rather as ways to support patients' functional abilities, enabling them to maintain their daily activities throughout the progression of the disease.[51,52] Exercise therapy plays a crucial role in addressing muscle fiber weakening and sedentary behaviors, factors that contribute to the high prevalence of metabolic syndrome in patients with neuromuscular diseases.[10]

It generally appears that the outcome of the treatment is influenced by factors such as the initial strength and endurance parameters, the specific type of dystrophy, and the nature of the exercise regimen implemented. Researchers have reported mild to moderate muscle pain in patients undergoing muscle training, and in recent years, this aspect has increasingly gained consideration in designing physiotherapy exercises.[53,54] In recent studies examining muscle fatigue, various authors concur to some extent that aerobic endurance training designed to exert a moderate amount of strength from patients generally yields positive results in terms of patients' functional muscle strength and aerobic capacity.[33,37,39] These improvements are functionally significant, making daily activities easier for patients, with minimal signs of muscle damage or fatigue. Conversely, an approach centered on strength training, which pushes patients to the limits of their already reduced muscular strength, is associated with fatigue, muscle pain, and the accumulation of toxic byproducts in muscle fibers.[15,38,43] However, while aerobic endurance training is generally well tolerated, being a moderate stimulus, it often does not elicit a significant positive effect on trained muscles, leading to results that are only partially successful.[36,37] Furthermore, the recent emergence of innovative approaches, based on the use of body-weight support combined with neurorobotic devices such as active exoskeletons, provides accurate and reproducible ways of training that can be used as efficient tools for rehabilitation.[38,39,41] However, the accessibility of this kind of technology is limited due to the high costs and the difficulty in administering the therapy in a patient's usual environment.

In order to achieve the best possible rehabilitative results, future studies and clinical trials should aim to combine the most promising features of the approaches used thus far, creating more therapeutically effective aerobic endurance training without causing harm to patients. Exercises should be individualized as much as possible for each subject, assessing the maximal force their muscles can generate without causing fatigue, and frequently monitoring for signs of damage.[15] Insights from the investigation of the disease progression in Duchenne muscular dystrophy have informed the development of assessment tools adapted for LGMDs.[39] In addition, effective management of respiratory functionality is of great importance to allow patients to conduct a normal daily life as much as possible and maintain their aerobic capacity at a level that is compatible with the execution of physical rehabilitation protocols. Existing literature provides valuable information about how to identify early signals of reduced oxygen intake and the current available management options. The progressive weakening of the diaphragm muscle primarily affects the most severe, fast-progressing forms of LGMDs. Therefore, making a correct and early diagnosis is crucial in directing the appropriate management strategies to the right patients. Moreover, a physiotherapy program based on aerobic exercise and muscle training targeting the diaphragm and respiratory muscles has shown beneficial effects on patients.[37,40,47] Authors agree that it is important to monitor FVC using spirometry or pulse oximeters as a measure of ventilation efficiency, especially during the night. It is of maximum importance to start early with overnight ventilatory support without waiting for the development of dangerous daytime hypoventilation, taking advantage of noninvasive ventilatory support via masks or IAPV via specific corsets and ventilators.[42] However, one area of disagreement among studies, and a necessary focus for future studies, is the percentage of FVC reduction at which ventilatory support should be provided.

An important issue emerging from the literature is the heterogeneity of LGMD subtypes included in the studies. As reported by

Preisler et al.,[41] different levels of physical activity during childhood are associated with different times of onset of symptoms in different LGMD subtypes. In fact, even when considering two subtypes of disease under the same classification, one must be very careful in applying knowledge of one subtype to the management of the other, and future studies should try to enroll only clinically and genetically homogeneous participants. Therefore, it is becoming increasingly clear that for a rehabilitation protocol to be effective, it should be included within an integrated care system, a "total care system" as defined by Kakulas,[33] composed of physicians, physiotherapists, speech therapists, occupational therapists, psychologists, and educators. Providing social and emotional support also has a positive effect on the quality of life of patients. O'Dowd study demonstrated how physical and mental health are connected, with muscle training ameliorating quality of life, and how important is to consider the psychological side of care when developing a rehabilitation protocol for degenerative muscle disorders.[26]

Our review has some limitations that should be acknowledged. First, the number of patients enrolled in each study is low, due to the rarity of this group of diseases; therefore, it is difficult to derive robust results and considerations from the analysis of the published work. As a result, a quantitative meta-analysis to assess the overall effectiveness of the different rehabilitation strategies was not feasible. Furthermore, the absence of clinical studies providing long-term assessments of the efficacy of physiotherapy protocols makes it difficult to ascertain whether positive effects on muscle strength, well-being, and respiratory function play a role in the long run.

5 | CONCLUSIONS

Despite scientific advances in the cure and treatment of various degenerative neurological disorders, disease-specific therapy for LGMDs is not yet available. The challenge is enhanced by the broad heterogeneity of this group of disorders, which does not allow for a single approach. Rehabilitative intervention is valuable to maintain and ameliorate strength and quality of life. When carefully managed and tailored to individual patient needs, muscle training exercises can increase muscular strength and functional abilities, assisting patients in maintaining their daily living activities as the disease progresses. This, in turn, has a positive impact on their psychological well-being.[16,26,37,39] Some of the designed training protocols, including those that did not consider patients' individual genetic diagnoses and clinical presentations, showed limited positive effects on muscular strength and were associated with fatigue, muscle pain, and inconsistent compliance.[15,36,43] The early management of respiratory symptoms and tailored respiratory physiotherapy can significantly benefit patients' well-being and their ability to engage in muscle training exercises.[33,34,48–50] These findings highlight the importance of designing personalized muscle training in rehabilitation programs. Future studies should focus on elaborating the best rehabilitation approach taking into account the impact of therapy on the quality of life of patients by checking psychological parameters such as depressive symptoms, anxiety, and self-esteem.

AUTHOR CONTRIBUTIONS

Giorgia D'Este: Investigation; visualization; writing – review and editing. **Mattia Spagna:** Investigation; visualization; writing – original draft. **Sara Federico:** Data curation; formal analysis; validation; writing – review and editing. **Luisa Cacciante:** Data curation; formal analysis; investigation; methodology; validation; writing – review and editing. **Błażej Cieślik:** Writing – review and editing. **Pawel Kiper:** Supervision; writing – review and editing. **Rita Barresi:** Conceptualization; supervision; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

ETHICS STATEMENT

We confirm that we have read the journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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