Efficacy of Different Physical Therapy Regimen for Amyotrophic Lateral Sclerosis: A Systematic Review

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ABSTRACT

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disorder characterised by the degeneration of upper and lower motor neurones, which results in progressive muscle weakness, functional decline, and ultimately respiratory failure. There is presently no cure for ALS; however, rehabilitation strategies have been investigated to enhance functional capacity and quality of life in affected individuals.

Objective: The objective of this narrative review is to evaluate the effectiveness of different exercise interventions and determine which forms of exercise are beneficial across the stages of amyotrophic lateral sclerosis.

Method: Articles were sourced from online databases including PubMed, Google Scholar, and Cochrane. The systematic review was conducted in accordance with the PRISMA 2020 Statement guidelines. All studies included in the review were randomised, controlled trials evaluating physiotherapy-based exercise programs, including aerobics, resistance, stretching, endurance, strengthening, and balance exercises. They were reviewed. Findings from the included studies were synthesised narratively to identify trends in exercise prescription and clinical outcomes.

Result: 30 articles were found; out of these, six randomised controlled trials examining interventions in individuals with ALS were included. The PEDro assessment indicated that the included studies demonstrated moderate methodological quality. Overall, moderate-intensity exercise programmes were reported as safe and beneficial for maintaining physical function, respiratory capacity, and quality of life in individuals with ALS.

Conclusion: Although ALS is a progressive neurodegenerative disease, evidence suggests that appropriately prescribed physiotherapy interventions may help maintain functional ability and improve quality of life. Moderate-intensity exercise appears to be beneficial across different stages of the disease when carefully monitored. However, larger randomized controlled trials are required to establish Standardised exercise guidelines should be established to determine the long-term safety and effectiveness of rehabilitation interventions in ALS.

Keywords: Amyotrophic lateral sclerosis, physiotherapy, exercise therapy, rehabilitation, and quality of life.

INTRODUCTION

Amyotrophic lateral sclerosis (ALS) has two related meanings in medical terminology. In a broad sense, ALS refers to a group of adult-onset neurodegenerative disorders characterised by progressive degeneration of motor neurons. In the United Kingdom, these disorders are collectively termed motor neuron disease (MND). In a more specific sense, ALS denotes a distinct form of motor neuron disease in which both upper motor neuron (UMN) and lower motor neuron (LMN) signs are present.[1]

The term “amyotrophic” describes the muscle atrophy, weakness, and fasciculations resulting from degeneration of lower motor neurons. Denervation of muscle fibers leads to progressive wasting and reduced muscle strength.

The term "lateral sclerosis" refers to the pathological hardening observed in the lateral columns of the spinal cord during autopsy. This hardening occurs due to gliosis following degeneration of the corticospinal tracts. Damage to these tracts produces classical upper motor neuron signs, including hyperactive deep tendon reflexes, positive Hoffmann sign, clonus, and Babinski sign.[1]

Riluzole, a glutamate antagonist, is the only FDA-approved drug for ALS, shown to slow muscle strength decline and extend survival by about 2-4 months, especially in early-stage patients. It is generally well tolerated, with mild, transient liver enzyme elevations being the most common side effect.

Other drugs under study include minocycline, which delayed disease onset in animal models, and antioxidant therapies like coenzyme Q10. Combination therapy (riluzole, minocycline, nimodipine) has shown promise in animal models but not yet in human trials.[2]

Most ALS patients ultimately die from progressive respiratory failure, making respiratory assessment vital. Forced vital capacity (FVC) is commonly used, but measures like nocturnal oximetry, maximal inspiratory pressure (MIP), and sniff nasal inspiratory force (SNIF) are more sensitive for early detection. Noninvasive positive pressure ventilation (NIPPV) helps manage symptoms but doesn't halt decline. Eventually, long-term survival may require tracheostomy and mechanical ventilation.[2]

Bulbar involvement in ALS combines upper and lower motor neuron damage, causing mixed spastic-flaccid dysarthria affecting the face, tongue, and throat. Early signs include slurred, hoarse, or nasal speech that worsens with fatigue. As tongue and lip movements slow, speech intelligibility declines, often leading to complete loss of speech. Communication remains crucial for maintaining social closeness between patients and their partners.[3]

Amyotrophic lateral sclerosis is a progressive and ultimately fatal disorder.[1] There is currently no cure, and the average life expectancy after symptom onset is approximately 2-5 years.

Despite the absence of curative treatment and the rapidly progressive nature of the disease, ALS is considered a "treatable disease" in terms of symptom management and supportive care. Comprehensive multidisciplinary rehabilitation is integral to optimizing functional independence and quality of life.[4]

Pain affects 24-73% of ALS patients, often due to spasticity, cramping, or immobility, and may appear even in early stages. Stretching, massage, and quinine sulfate can help relieve nocturnal cramps, while medications like baclofen, tizanidine, dantrolene, or diazepam are commonly used to reduce spasticity.

In severe cases, intrathecal baclofen or targeted botulinum toxin injections may provide additional relief. Proper cushions and frequent position changes help prevent joint stiffness and pressure-related pain. Nonsteroidal anti-inflammatory drugs or opioids are effective for pain control, with up to 74% of hospice patients achieving good relief.[2]

Physical and occupational therapy in ALS aim to maintain comfort, mobility, and independence through adaptive equipment and regular reevaluation. Moderate stretching and resistance exercises help preserve function and reduce spasticity, while overexertion should be avoided due to progressive weakness.[2]

Emerging evidence supports the role of structured therapeutic exercise in ALS management. Studies suggest that a combined moderate-intensity aerobic and resistance training program, individualized according to each patient's functional capacity, can improve aerobic fitness and help maintain physical function in individuals with ALS.[5]

These findings reinforce the importance of carefully prescribed and supervised physiotherapy interventions as part of comprehensive ALS care.

Although exercise is scientifically proven to improve aerobic fitness, physical function, and independence in many clinical conditions such as cancer, neurodegenerative, and cardiovascular diseases, its role in patients with ALS remains controversial and continues to be debated.[5]

LITERATURE REVIEW

Kalron et al. (2021) conducted a randomized controlled trial to compare combined aerobic-strength training with flexibility exercises in ambulatory patients with Amyotrophic Lateral Sclerosis. Thirty-two participants completed a 12-week program with two sessions per week.

The combined aerobic and strength training group showed significant improvements in ALSFRS-R scores, respiratory function, mobility, and quality of life compared with the flexibility group. The findings suggest that combined training is more effective than flexibility exercises alone in maintaining functional abilities in ALS patients.

Van Groenestijn et al. (2019) conducted a randomized controlled trial to evaluate the effect of aerobic exercise therapy (AET) with usual care in ambulatory Amyotrophic Lateral Sclerosis patients. Fifty-seven participants were assigned to AET plus usual care or usual care alone for 16 weeks.

The study found no significant differences in health-related quality of life between the groups. However, per-protocol analysis suggested that AET may help slow deterioration in disease-specific quality of life in some patients.

Clawson et al. (2017) conducted a randomized controlled trial to evaluate the safety and tolerability of resistance, endurance, and stretching/range of motion exercises in individuals with Amyotrophic Lateral Sclerosis.

The 24-week home-based exercise program showed that all three exercise regimens were safe and well tolerated without accelerating disease progression.

Compliance was highest in the resistance and stretching/ROM groups. No significant differences were observed in ALSFRS-R scores, pulmonary function, or other secondary outcomes among the groups.

Lunetta et al. (2015) conducted a randomised, controlled trial to evaluate strictly monitored exercise programmes (SMEP) in patients with amyotrophic lateral sclerosis. Sixty patients were randomised to SMEP (active exercise with cycloergometers, active exercise, or passive exercise) or usual care with passive and stretching exercises.

After six months and a follow-up, the SMEP group exhibited markedly elevated ALS Functional Rating Scale-Revised scores, signifying a decelerated motor decline. However, no significant improvements were observed in survival, respiratory function, or quality of life

Research Gap

Existing studies on exercise interventions in amyotrophic lateral sclerosis are limited by small sample sizes, heterogeneous exercise protocols, and lack of standardised guidelines. Consequently, there is insufficient evidence to determine the most effective type and intensity of exercise across different stages of ALS, which calls for further focused research.

Objective

This study aims to evaluate the effectiveness of different exercise interventions in individuals with amyotrophic lateral sclerosis and to identify which forms of exercise are beneficial for maintaining functional ability, respiratory capacity, and quality of life.

Methodology

- **Study Design:** Systematic Review
- **Data Source:** PubMed, Google Scholar, and Cochrane

- **Tools:**

1. The PRISMA 2020 Statement for conducting and reporting a systematic review.
2. The PEDro scale is used to assess the methodological quality of the included randomised controlled trials. (Table 2)

Inclusion criteria:

1. Randomized control trial
2. Limited to English language
3. Limited to humans
4. Limited to last 10 years (2013 – 2023)
5. Full-text articles
6. Studies are limited to only upper-limb and lower-limb exercise protocols.

Exclusion criteria:

1. Case studies or case series
2. Review articles
3. Editorials

Study selection:

1. 30 studies were considered, out of which 6 met the inclusion criteria.
2. All were experimental studies in which a total of 289 subjects had participated in the study.

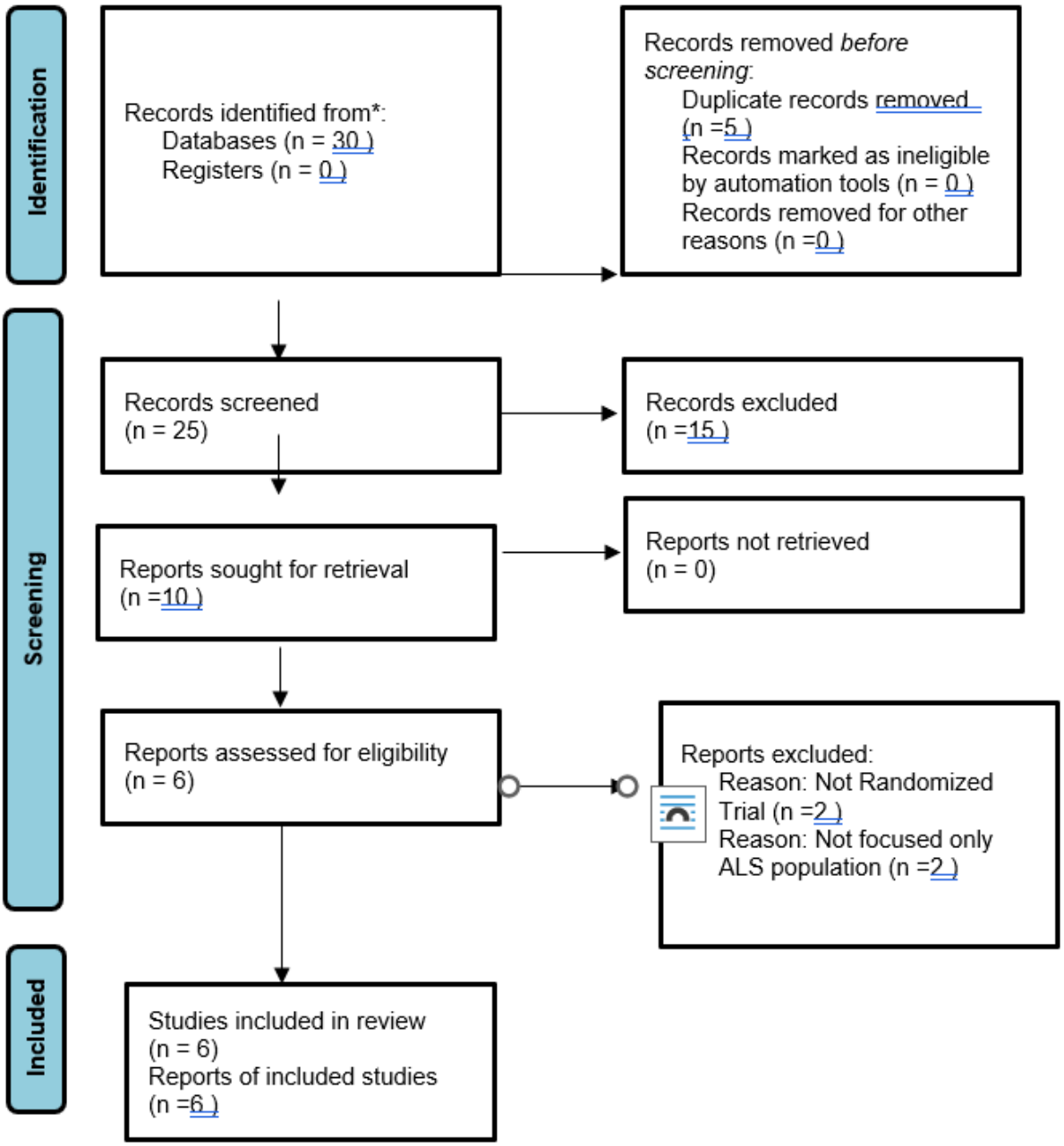
Study characteristics:

1. The characteristics of the included studies are represented in table 1.
2. Only randomised control trials were included.
3. All included studies provided exercise training for fatigue, functional mobility, aerobic fitness, strength, flexibility, and quality of life in ALS individuals through resistance training, stepping training, aerobic exercise, endurance exercise, flexibility training, and stretching exercise.

Selection criteria:

1. The authors independently assessed the title/abstract and identified records.
2. The full text of relevant papers was collected to assess them against selection criteria
3. Any disagreement among the authors was resolved by discussion and consensus.

PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only



Descriptive Analysis

A quantitative statistical analysis was not conducted in this review due to significant heterogeneity among the included studies on amyotrophic lateral sclerosis. The studies differed considerably in exercise protocols, intervention duration, frequency of training sessions, and outcome measures. Therefore, a descriptive narrative analysis was performed to summarise the findings of the included randomised controlled trials. The review included six randomised controlled trials, with a total of 289 participants diagnosed with amyotrophic lateral sclerosis, whose mean ages ranged approximately from 50 to 65 years. The interventions primarily involved aerobic exercise, resistance training, stretching or flexibility exercises, and combined exercise programmes. Overall, most studies reported that moderate-intensity and well-monitored exercise programmes are safe and beneficial for individuals with ALS, helping to maintain functional ability, mobility, and respiratory function. Several studies demonstrated improvements in functional outcomes measured by the ALS Functional Rating Scale-Revised and mobility assessments. However, some trials found no significant differences in disease progression, survival, or respiratory decline, suggesting variability in the effectiveness of different exercise interventions.

RESULTS

Table 1: Characteristics of Included Studies

Study	Type	Size	Age	Intervention	Outcome Measures	Result
Christian lunette et. al.(2015)	RCT	n= 60	G1=61.1± 10.1 G2 = 60.3 ± 9.9	G1= SMEP (subgroup 1 active exercise with cycloergometer) (subgroup 2 active exercise against gravity) (subgroup 3 passive exercise for 2 weeks/ month for 6 months for 20 min G2 = UC passive exercises 2 days/ week for 20 mins	ALSFRS-R, FVC, MGQoL, MRC, Borg perceived scale, HR	The subgroup of subjects with active exercise combined with cycloergometer showed the higher effect on motor functions measured with ALSFRS-R. Thus, Physical activity is not a risk factor for ALS and may eventually be protective against the disease.
Lora L. Clawson et. al. (2017)	RCT	n = 59	G1= 57.68 (9.72) G2= 63.65 (10.55) G3= 57.82 (11.88)	G1= Stretching and ROM G2= Resistance exercise G3= Endurance exercise For 24 weeks	ALSFRS-R, FVC, ALSSQoL-R, FSS, MAS, VO_2 MAX, VAS	All 3 forms of exercise were effective with resistance and SROM exercise showing the highest compliance
Alessandra Ferri et. al. (2019)	RCT	n = 16	TRAIN = 50.7 ± 3.3 UC= 55.5± 5.95	TRAIN= aerobic, resistance, balance and stretching exercise. (3 times/week for 12 weeks)	Peak power, peak oxygen uptake, GET, 1RM of knee extensor muscles, TUG, 6MWT, ALSFRS-R, ALS-SS, McGill QoL questionnaire	Combined moderate-intensity aerobic and strength training program improve aerobic fitness and maintain physical function in ALS individuals.
Elisabetta Zucchi et. al. (2019)	RCT	n = 65	G1= 65.14 (9.90) G2= 64.74 (10.10)	Aerobic training, endurance training, stretching or assisted active mobilisation. G1 = IER, 5 session/week for 10 weeks	ALSFRS-R, FVC, ALSAQ-40 and McGill QoL questionnaire, FSS, Beck	No significant changes in ALS progression as well as in survival and respiratory functions induced by high-frequency motor exercise.

				G2 = UER, 2 session/week for 10 weeks	depression inventory scale, caregiver burden scale,	
Annerieke C. van Groenestijn et. al. (2019)	RCT	n = 57	G1= 60.9± 10.0 G2= 59.9± 10.7	G1 = Aerobic exercise therapy (AET) + Usual care (UC) – 5min warm up, cycle ergometer, step board, treadmill, muscle strengthening exercise, 5min cool down 2 session/week for 16 weeks G2 = Usual care	ALSAQ-40 questionnaire, MCS, PCS, SF-36	AET + UC is not feasible for every ambulatory ALS subjects.
Alon Kalron et al. (2021)	RCT	n = 32	G1= 58.5 (13.2) G2= 60.4 (14.7)	G1= combined aerobic strengthening G2= flexibility training 2 sessions per week for 12 weeks	ALSFRS-R, FVC, 2MWT, 5STS, FSS, SF-36, SVC	Combine aerobic and strength training program is far superior to flexibility alone in improving respiratory functions and mobility with well-being in ambulatory ALS subjects.

Table 2: Methodological quality assessment of the included randomized controlled trials using the PEDro scale.

	1	2	3	4	5	6	7	8	9	10	11
Article	Specified Eligibility	Random allocation	Concealed allocation	Similar baseline	Subjects blinding	Therapist's blinding	Assessors blinding	Measure of key	Intention to treat	Statistical comparisons	Variability for at least
Alon Kalron et al., 2021	Y	Y	Y	Y	Y	N	Y	Y	N	Y	Y
Lora L. Clawson et al., 2017	N	Y	N	Y	N	N	Y	N	N	Y	Y
Annerieke C. van Groenestijn et al., 2019	Y	Y	Y	Y	N	N	Y	N	Y	Y	Y
Alessandra Ferri et al., 2022	Y	Y	N	Y	Y	N	N	Y	N	Y	Y
Christian Lunette et al., 2015	Y	Y	Y	N	Y	N	Y	Y	Y	Y	Y
Elisabetta Zucchi et al., 2019	Y	Y	Y	N	Y	N	Y	N	N	Y	Y

Note: Y=Yes, N=No

DISCUSSION

The findings of this systematic review indicate that structured physiotherapy interventions may help maintain functional capabilities and mobility in individuals with amyotrophic lateral sclerosis, particularly when moderate-intensity exercise programmes are used. The included randomised controlled trials showed that combined aerobics and resistance training produced favourable outcomes in terms of functional performance and mobility. For instance, the study by Cristina Lunetta et al. demonstrated that a strictly monitored exercise programme slowed motor decline The ALSFRS-R measurement compared with usual care suggests that controlled exercise may help preserve motor function without accelerating disease progression (Lunetta et al., 2016). Similarly, a trial conducted by Alon Kalron et al. reported that a 12-week combined aerobic and strengthening programme significantly improved mobility, respiratory function, and overall well-being compared with flexibility exercises alone (Kalron et al., 2021). Comparable safety findings were reported by Lora L. Clawson et al., who observed that resistance, endurance, and stretching programmes were well tolerated for up to 24 weeks without worsening disease progression, with the highest adherence observed in resistance and stretching groups . These findings are consistent with broader evidence from systematic reviews and meta-analyses indicating that exercise interventions can significantly improve functional scores and may also contribute to maintaining respiratory capacity in ALS patients.[12] Several randomised trials reported improved functional ability and forced vital capacity in patients performing exercise compared with usual care, but no increase in fatigue or adverse effects was observed. Another systematic review also concluded that resistance exercise appears particularly effective for improving functional performance, while aerobic exercise may contribute more to respiratory outcomes.[13] However, some studies included in the present review, such as those by Elisabetta Zucchi et al. and Annerieke C. van Groenestijn et al., reported limited improvements in survival, disease progression, or overall quality of life, indicating variability in outcomes depending on exercise type, frequency, and disease stage. Overall, these findings align with previous literature suggesting that moderate, individualised physiotherapy programmes are safe and potentially beneficial for maintaining function in ALS, although heterogeneity in protocols and small sample sizes indicate the need for larger, randomised trials to establish standard exercise guidelines for ALS rehabilitation.

CONCLUSION

This systematic review evaluated the effectiveness of physiotherapy-based exercise interventions in individuals with amyotrophic lateral sclerosis (ALS) with the aim of identifying exercise approaches that support functional ability, respiratory capacity, and quality of life. The findings from the included randomised controlled trials suggest that moderate-intensity, carefully supervised exercise programs are generally safe and beneficial for people living with ALS. In particular, combined aerobic and resistance training programmes appear to help maintain mobility, muscle strength, and overall functional performance without accelerating disease progression. Although exercise cannot stop the neurodegenerative process associated with ALS, structured physiotherapy interventions may help slow functional decline and promote independence in daily activities for as long as possible.

These findings highlight the important role of physiotherapy within the multidisciplinary management of ALS. Individualised exercise programmes that incorporate aerobic conditioning, strengthening, stretching, and mobility training can contribute to improved physical function and well-being when appropriately monitored. However, the current evidence remains limited due to small sample sizes and variations in exercise protocols across studies. Future research should therefore focus on larger randomised, controlled trials with standardised exercise guidelines and longer follow-up periods to better determine the most effective rehabilitation strategies for individuals with ALS.

Declarations

This research received no specific grant from any funding agency.

Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

Data available upon reasonable request.

AI Usage Statement

Generative AI tools were used for language editing only.

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