PHYSICAL ACTIVITY

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PHYSICAL ACTIVITY AS ADJUNCT THERAPY IN PULMONARY HYPERTENSION: A NARRATIVE REVIEW OF RECENT EVIDENCE

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ABSTRACT

Background: Pulmonary hypertension (PH) is a chronic cardiovascular disorder marked by elevated pulmonary artery pressure and right ventricular dysfunction. It affects about 1% of adults and up to 10% of those over 65 years. Pulmonary arterial hypertension (PAH), its main subtype, occurs in 2–5 new cases per million annually, with a prevalence of 15–50 per million. Despite therapeutic advances, PH still carries high morbidity and mortality, with annual death rates up to 15% and a median untreated survival of 2–3 years. The condition severely limits exercise tolerance and quality of life. While patients were once discouraged from physical activity, recent trials show that structured, supervised exercise can safely enhance functional capacity and well-being in stable patients.

Aim: To critically evaluate contemporary evidence on structured physical activity as adjunct therapy in pulmonary hypertension and to address four questions: mechanisms of benefit, effectiveness of exercise modalities and intensities for functional capacity and quality of life, safety and tolerability profile, integration into personalized and telemonitored programs.

Methods: A literature search was performed in PubMed, Scopus and Web of Science for studies published between 2018 and 2024. Eligible randomized trials, cohort studies, systematic reviews and meta analyses in adult pulmonary hypertension populations were included. Thirty two publications were synthesized qualitatively. Main outcomes were six minute walk distance, peak oxygen uptake, pulmonary vascular resistance, right ventricular function and health related quality of life.

Results: Supervised physical activity improves six minute walk distance and peak oxygen uptake, reduces dyspnea and fatigue, and enhances quality of life in clinically stable patients. Aerobic training provides the core

benefit, resistance training supports functional independence, and inspiratory muscle training improves respiratory strength. Multimodal and home based telemonitored programs increase accessibility and adherence under clinical oversight. Safety was acceptable in stable patients with appropriate screening and monitoring. Hemodynamic improvements were inconsistent across studies and long term effects remain uncertain.

Conclusions: Evidence supports endothelial, metabolic, and anti-inflammatory adaptations with exercise in pulmonary hypertension. Individualized supervised programs combining aerobic, resistance, and inspiratory muscle training improve function and quality of life in stable patients. Safety is acceptable under medical supervision. Home-based and telemonitored approaches enhance accessibility. Larger standardized trials are needed to confirm effects on hospitalization and survival.

Keywords: pulmonary hypertension, physical activity, exercise training, pulmonary rehabilitation, six minute walk distance, quality of life

INTRODUCTION

Pulmonary hypertension is a progressive and life-threatening cardiovascular disease characterized by a sustained increase in pulmonary artery pressure, leading to right ventricular hypertrophy and failure. [1,2] According to recent reviews, the prevalence of pulmonary hypertension among adults is approximately 1%, rising to nearly 10% in individuals over 65 years of age. Pulmonary arterial hypertension (PAH), the principal subtype of the disease, occurs at a rate of 15–50 cases per million population, while the annual incidence is estimated at 2–5 new cases per million. [1,3] Without treatment, the median survival does not exceed 2–3 years; even with modern targeted therapies, mortality remains high, reaching up to 15% per year in patients with advanced disease. [1,2] The condition results in a marked reduction of physical capacity, quality of life, and work ability, making it a major medical and socio-economic health problem. According to the current classification, the leading subtype is pulmonary arterial hypertension, in which endothelial dysfunction, vasoconstriction, and vascular remodeling play a central pathogenic role. The main clinical manifestations include exertional dyspnea, fatigue, and signs of right ventricular failure. [3]

Historically, patients with pulmonary hypertension were advised to avoid physical activity due to fears of worsening symptoms and disease progression. Over recent years, however, a growing body of randomized controlled trials, prospective cohort studies, and analytical reviews has demonstrated that structured and supervised exercise programs can significantly improve functional capacity, cardiopulmonary performance, and quality of life in clinically stable patients. [4–8] Evidence has also expanded to include specific modalities, such as inspiratory muscle training, which have been shown to be effective and safe when appropriately monitored. [9–11]

The proposed mechanisms underlying these benefits include improvement in endothelial function, modulation of inflammatory and oxidative pathways, normalization of skeletal muscle metabolism, and attenuation of physical deconditioning. Nevertheless, the precise effects of exercise on pulmonary vascular resistance, right ventricular adaptation, and integrated hemodynamics remain incompletely understood, while study results vary considerably in design and outcomes. [7,12,13]

RATIONALE AND NOVELTY

Although numerous studies have explored rehabilitation in pulmonary hypertension, available data remain fragmented and heterogeneous in terms of exercise types, intensity, duration, and supervision. There is still no integrative synthesis combining clinical outcomes with mechanistic aspects across recent publications. This review aims to address this gap by focusing on studies published between 2018 and 2024 and by comparing the clinical efficacy and safety of various exercise modalities from a practical and translational perspective. [4,5,7,14]

AIM AND RESEARCH QUESTIONS

The aim of this review is to critically evaluate contemporary evidence on the role of structured physical activity as an adjunctive therapy in pulmonary hypertension. The following research questions are considered:

1. What are the physiological mechanisms underlying the beneficial effects of exercise training in pulmonary hypertension? [12,13]
2. Which exercise modalities and intensities yield the greatest improvements in functional capacity and quality of life while ensuring safety? [4,5,7]
3. What is the safety and tolerability profile of exercise interventions, including indications and contraindications in clinical practice? [7,9,10]
4. How can physical activity be integrated into personalized and telemonitored rehabilitation programs to enhance accessibility and adherence? [15,16]

RELEVANCE

Pulmonary hypertension remains a chronic and progressive disease with a profound impact on physical and psychosocial functioning. Identifying effective adjunctive interventions beyond pharmacotherapy is of high clinical importance. Synthesizing the current body of evidence may facilitate the implementation of individualized and supervised exercise programs into standard patient care, promote the optimization of training protocols, and encourage further research on long-term outcomes such as survival and hospitalization, as well as the development of tele-rehabilitation and digital monitoring strategies to improve accessibility and adherence. [4,7,15,16]

METHODS

This review was designed as a narrative evidence-based synthesis of current research addressing the role of structured physical activity as an adjunctive therapy in pulmonary hypertension (PH). The analysis was based entirely on published peer-reviewed studies available in international databases.

SEARCH STRATEGY

A literature search was conducted in **PubMed**, **Scopus**, and **Web of Science** databases for articles published between **January 2018 and May 2024**. Additional relevant references were identified through cross-citation from systematic reviews and meta-analyses. The search included combinations of the following keywords: *"pulmonary hypertension"*, *"pulmonary arterial hypertension"*, *"exercise"*, *"physical activity"*, *"rehabilitation"*, *"exercise training"*, *"aerobic exercise"*, *"resistance training"*, *"inspiratory muscle training"*, and *"tele-rehabilitation"*.

SELECTION PROCESS

All articles cited in this review were selected manually according to their relevance to the clinical and physiological effects of exercise in pulmonary hypertension. Both randomized controlled trials, observational studies, systematic reviews, and meta-analyses were included. Non-peer-reviewed papers, conference abstracts, and animal-only studies were excluded.

A total of 43 publications were included in the review, comprising randomized controlled trials, prospective cohort studies, systematic reviews, meta-analyses, and narrative reviews that provided mechanistic or clinical evidence relevant to physical activity in PH.

DATA EXTRACTION AND SYNTHESIS

Data from eligible studies were analyzed qualitatively. The key outcomes extracted from the literature included six-minute walk distance (6MWD), peak oxygen uptake (VO_2peak), pulmonary vascular resistance (PVR), right ventricular function, and quality of life indicators. Due to the heterogeneity of study designs and outcome measures, no quantitative meta-analysis was performed. Instead, findings were summarized narratively, with emphasis on clinical applicability and safety.

SCOPE OF EVIDENCE

The included studies covered a range of exercise modalities, including aerobic, resistance, inspiratory muscle, and multimodal training, as well as home-based and telemonitored rehabilitation programs. The synthesis also incorporated data from recent systematic reviews and meta-analyses that evaluated functional capacity, hemodynamic responses, and psychological well-being in patients with PH.

RESULTS

IMPACT OF PHYSICAL ACTIVITY ON PULMONARY HYPERTENSION

Effects on Exercise Tolerance and Daily Functioning. Several studies demonstrated that exercise intolerance is one of the key characteristics of PH manifested by early and progressive dyspnea, fatigue, and reduced functional capacity. [3] These factors include right ventricular (RV) dysfunction, reduced oxygen supply, and muscle disuse that are spelled out by the illness. Improving physical function is thus an important aspect in the treatment of PH especially through recommendations such as participation in walking. [17,18] Exercise training has been confirmed to have positive effects in exercise tolerance of PH patients by the current literature. Among the commonly administered outcome measures in this regard, the six-minute walk distance (6MWD) is the most popular. For example, in the meta-analysis by Yan et al., it was revealed that patient with diagnosed IHD (ischaemic heart disease) while being under the program of a supervised exercise-based rehabilitation, had

significantly increased the amount of 6MWD, which was consistently 33m above the minimum clinically important difference. [5] In the same way, Zeng et al. also demonstrated that aerobic training programs enhance both walking distance and oxygen partly in various forms of PH including group 1- PAH and group 4- CTEPH (Chronic Thromboembolic Pulmonary Hypertension). Apart from measuring their progress, patients also benefit from exercise interventions in terms of performing basic activities of daily living such as climbing up the stairs, walking a longer distance or doing basic chores in the house. [6] Previous studies support the notion that a fitted exercising schedule has multiple advantages. Furthermore, it is not only the hospital-based interventions which are effective in bringing about the benefits. In the systematic review of Grünig et al. a large multicenter RCT (Randomized Controlled Trial) was performed, investigating the effect of centre and home-based exercise training on physical capacity, and the improved values were maintained for several months. [7] This may imply that even low to moderate intensity programs, when supervised can help in improving functionality and independence daily functionality and independence in the case of PH patients. In conclusion, training and exercises are greatly significant in relation to enhanced functional capacity in pulmonary hypertension. The increase in mean distance walked and patient estimated activity level could also have been due to physiological change in the patients as well as increased confidence and a feeling of being independent when performing their daily activities. [7]

INFLUENCE ON PULMONARY HEMODYNAMICS AND VASCULAR FUNCTION

PH can be defined as pathological changes in the pulmonary vessels, which results in increase in PAP, PVR, and eventually right ventricular dysfunction. [2] Although antianginal drugs are thought to exert their effects through causing vasodilation and slowing disease progression, the current literature has paid special attention to the effects that physical training could offer in addition to medical approaches in ameliorating hemodynamic characteristics. [19] One of the largest bodies of literature evaluating user hemodynamic responses to exercise training in PH has been provided by Grünig et al. in their prospective RC trial. [7] The study used comprehensive pulsed wave Doppler echocardiography that showed that PAH and inoperable CTEPH patients who underwent supervised exercise training have marked increase in VO_2 peak and a significant change in body composition, mean PAP and PVR. Based on these changes, there are apparent increases in pulmonary vascular compliance and the matching of right ventricular and pulmonary artery function. From a physiological point of view, physical activity can reduce abnormal processes of pulmonary vascular remodeling by improving endothelial function, increasing NO production, and decreasing inflammatory signaling in the vessels. While it is more described in left sympathogenous heart failure, there is increasing investigative evidence of these pathways in PH. In clinical terms, these physiological adaptations will manifest into increased delivery of oxygen, less ventilatory efficiency and absence of right heart strain during submaximal and peak physical activities. [7] Tran et al. also found supporting evidence proving that inspiratory muscle train (IMT) can enhance the CP performance. They themselves proved that although IMT elevates inspiratory pressures, it is beneficial to the lungs and to the RV function. [10] The positive changes to the right ventricle imply better hemodynamic capacity during exercise. Similarly before, in 2016, Ehlken and others established that PAH patients who underwent structured exercise rehabilitation showed a decrease of RAP and an increase in the cardiac index, the indicators that have prognostic significance in PH. [20] Hence, while incorporating exercise into patient's daily regime, current evidence shows that pulmonary hemodynamic changes can be directly managed through disease progression, as well as increased functional in cardiac capacity. They confirm the growing value of physical exercise in the treatment of pulmonary hypertension, not only as a form of rehabilitation, but also as a physiological regulator. [20,21]

PSYCHOLOGICAL AND QUALITY OF LIFE BENEFITS

Pulmonary hypertension is a serious pathology which significantly affects physiological functions of human body and usually acquires a severe psychosocial impact. [22,23] Several studies of the last years confirm that structured exercise training is effective in enhancing general health and especially mental health, and quality of life of PH patients. In the study by Aslan et al. authors aimed to examine the potential of inspiratory muscle training for treating PH and found that not only there were physiological improvement, but also the patients' quality of life increased and was statistically significant. [11] The perceived dyspnea and fatigue of the participants in the intervention group also improved hence, were able to perform more tasks independently and had better psychological well-being. [11] In addition, study by Grünig et al. also highlighted that, center based and home setting exercise training have no psychosocial benefits which contributed to decrease social isolation and enhancement in self efficacy. [7] Several patients emphasized stating that they felt they had better control of their disease which is essential for patients' compliance to medication or regime as well as their quality of life. It is worth remembering that sometimes psychological improvement was associated with little or no physiological improvement, i.e., adding structure to days spent sedentary by walking and talking can serve as a social trigger for further conversation, setting achievable goals for completing meaningful tasks, and feeling empowered to decide your own destiny. [24] This is especially so to the patients suffering from PH who endure social exclusion or become reliant on careers. Therefore, the current evidence for exercise bears witness to the somatic benefits but also to the psychological well-being and quality of life. These are realistic changes in various domains of the quality of life in patients with PH and these improvements are clinically significant effects of physical activity interventions. [22]

ANTI-INFLAMMATORY AND METABOLIC EFFECTS

Abnormalities such as chronic low-grade systemic inflammation and metabolic dysfunction have also been reported to be involved in the development and progression of pulmonary hypertension. [1,25,26] Increased cytokines, raised markers of oxidative stress and endothelial dysfunction are frequently reported in PH patients if presented by concomitant comorbidities that include obesity, diabetes or the metabolic syndrome. [20] These inflammatory and metabolic changes accentuate the vascular changes of the PVH in the pulmonary circulation, as well as affecting right ventricular function, and exercise tolerance. [27] Exercise has been documented to have anti-inflammatory and metabolic properties in chronic diseases, and the same principle may apply to patients with PH. Directly speaking, research on these effects in patients with PH is sparse; however, research evidence from other cardiovascular/pulmonary diseases is helpful. [12] For instance, one of the straightforward forms of aerobic exercise has been proved to decrease circulating levels of C-reactive protein, interleukin-6, and tumor necrosis factor-alpha which are also in condition of PH patients. [20] Despite such biomarker-based evidence is relatively scarce in PH-specific research, Grünig et al. and Drummond et al. comment on other positive physiological changes that stem from the ET (Exercise Training), including the exercise training oxygen uptake and muscle metabolism improvements; that may plausibly be related to anti-inflammatory effects. [7,13] Furthermore, Drummond et al., found that aerobic training augment mitochondrial density and oxidative capacity in skeletal muscles that are likely to be compromised due to hypoxia and inactivity in PH. [13] Not only does this metabolic adaptation increase peripheral oxygen use, the ventilatory load during exercise which is a considerable problem for PH patients with respiratory impairment may be minimized. [20] While more work needs to be done to fine-tune the current understandings of these responses on molecular level, the current research does indicate that physical activity might help alter systemic inflammation in a positive way and support muscular and endothelial metabolism thereby indirectly assisting cardiopulmonary function. [22] Hence, though the anti-inflammatory and metabolic impacts of physical activity in lean seem to be still under investigation, the two tend to be a novel target through which exercise enhances clinical results apart from hemodynamic and functional indices in PH patients. [15]

TYPES OF EXERCISE INTERVENTIONS

Aerobic and Endurance Training

Enduring tasks such as walking, cycling or treadmill are some of the aerobic training methods which are considered fundamental in pulmonary rehabilitation. Several earlier trials have shown that supervised aerobic exercise also brings about a marked increase in exercise capacity that can be expressed in terms of the 6MWD and VO_2 peak. [28,29] For instance, Mereles et al. conducted a study and revealed that low dose aerobic exercise enhances both exercise tolerance and quality of life in patients with severe chronic PH. [30] In addition, Ehlken et al. conducted a randomized controlled trial to examine the effects of exercise training on change in peakVO2, and also hemodynamic parameters in PAH patients with inoperable CTEPH and findings of the study pointed out that patients undergoing aerobic training showed significant improvements in peak VO_2 and hemodynamic parameters. [20] This therefore supports the fact that aerobic training helped in the enhancement of functional capacity and general wellbeing of the PH patients.

Resistance and Strength Training

Resistance training [RT] aimed at improving muscle strength and working capacity that is spastic muscle volume, which is observed in patients with PH due to deconditioned state. RT, however, has been shown to have potential when performed alongside other types of exercises which are more closely explored. Drummond et al. stated that aerobic training lead to the amelioration of skeletal muscle function in patients with PH hence suggesting a possibility of undertaking resistance training. [13] Incorporating RT into rehabilitation programs may assist in increasing the muscle bulk, functional dependence, and metabolism in patients with PH. [31]

Inspiratory Muscle Training

Inspiratory Muscle Training (IMT) focuses on increasing the force of contraction of the respiratory muscles especially the diaphragm with the purpose of relieving dyspnea and increasing exercise capacity. [27] Recurrent researches have proved that IMT is effective among patients with PH. For instance, Tran et al., conducted a pilot, randomized controlled trial in patients with PAH and CTEPH, where they found that IMT increased inspiratory strength, as well as functional exercise tolerance. [10] Similarly, Aslan et al. studied that the IMT was effective in enhancing respiratory functions, functional exercise capacity, physical activity, and the quality of life of patients with PH. [11] Based on these results, the conclusion can be made that IMT has to be included in the set of rehabilitation measures for patients with PH. [32]

Combined and Multimodal Programs

Having a strength, cardio vascular and respiratory training approach to exercise, the pulmonary hypertension

enhances the training program in many aspects. [15] In one systematic review by Kourek et al., it was evident that the combined exercise training had a positive effect on the functional capacity and clinical health status of PH patients. [14] Also Grüning et. al. investigated on the effect of standardized exercise training incorporating combined modalities on patients with PAH and CTEPH where they affirmed the safety and effectiveness of exercise training. [7] These types of programs allow for comprehensive rehabilitation that encompasses cardiovascular, muscle, as well as respiratory systems in PH. [33]

Home-Based and Telemonitored Exercise Programs

Home as well as telemonitored exercise options can provide productive center based rehabilitation for the patients with limited possibilities to receive professional treatments. [16] Supervised home-based physical activity program is useful and effective as it advanced the functional capacity of life of the PH patients. Home and telemonitoring based programs should be utilized as viable approaches to address accessibility and engagement of rehabilitation in patients with PH. [34,35]

Table 1. Benefits of Different Exercise Training Types in Pulmonary Hypertension

Training Type	Key Benefits	Impact on Pulmonary Hemodynamics	Impact on QoL/ Psychological Well-being	Example Exercises
Aerobic/ Endurance Training	Increased exercise tolerance (6MWD, VO_2 peak). Improved overall fitness	Decreased Vascular Resistance (PVR), Improved right ventricular function	Improved QoL, Reduction in perceived dyspnea and fatigue	Walking, cycling, treadmill
Resistance/ Strength Training	Improved muscle strength and working capacity, increased muscle bulk, improved metabolism	May assist in skeletal muscle function (indirect impact on cardiac load)	Improved functional dependence	Dumbbell exercises, resistance bands, bodyweight exercises
Inspiratory Muscle Training (IMT)	Increased inspiratory muscle strength, reduced dyspnea, increased exercise capacity	Beneficial for lung and RV function, improved hemodynamic capacity during exercise	Improved QoL, enhanced physical activity, better psychological well-being	Exercises with inspiratory muscle training devices
Combined/ Multimodal Programs	Positive effect on functional capacity and clinical health status, safety and effectiveness, comprehensive rehabilitation encompassing cardiovascular, muscle, and respiratory systems	Impacts cardiovascular, muscle, and respiratory systems	Integrated psychological benefits and improved QoL	Combination of aerobic, resistance, and IMT

Home-Based and Telemonitored Programs	Useful and effective in advancing functional capacity, Address accessibility and engagement in rehabilitation	Maintains improved physical capacity	Decreased social isolation, enhanced self-efficacy	Remote-supervised exercises, using digital devices (e.g., pedometers, heart rate monitors, accelerometers)

CLINICAL EVIDENCE AND OUTCOMES

Patterns of Physical Activity in PH Populations

Studies by Kleinnibbelink et al. show that many patients with PH reduce the level of physical activity for a long time and stay at 50% of the healthy population levels, even after receiving medical treatment. [28] Although PAF is apparent, sedentary existence prevails especially in the elderly and patients with WHO functional class III or IV. Decreased physical activity is also evident in PH patients, mainly lower step count and higher sedentary time also, and these were associated with lower QoL and worse 6MWT. Registry data also support the notion that many PH patients do not have an access to structured program of rehabilitation, especially in the non-urban settings, or regions where resources are scarce. [36]

Use of Digital Monitoring Tools

One of the great trends in observational research area is the utilization of fitted devices like pedometers, heart rate monitors etc. In the pilot study, Ciara McCormack et al. implemented a style of remote monitoring with the help of accelerometers and showed that the patients who received the exact information from them about their level of activity was more effective in meeting the weekly activity goals and were more motivated and satisfied. Such results indicate that tele-rehabilitation and the e-health approach can enhance the levels of exercise in PH patients and those who may have difficulties with regard to the accessibility of specialized centers. [16]

BARRIERS TO PHYSICAL ACTIVITY IDENTIFIED IN SURVEYS

Surveys linked to the registry also asked about perceived and reported barriers to physical activity participation, such as: Panic experienced by patients about worsening their symptoms or, worse, fainting. Financial constraints, program availability, transpiration, and other constraints such as time and finances. This knowledge has guided several current pilot interventions aimed at ensuring that rehabilitation programs are personalized and provide conditions that are beneficial to the patient. [37]

Summary of Systematic Reviews and Meta-Analyses

Recently, several systematic reviews and meta-analyses have offered large evidence base for the utilization of exercise-based rehabilitation in managing PH especially PAH. These meta analyses review information from a number of RCTs in order to determine the effectiveness of diverse exercise regimes. [9,31]

Improvements in Exercise Capacity

Yan and other authors in their meta-analysis in 2021 examined the effect of exercise training in patients with PH. It was established that exercise-based rehabilitation programes led to enhancement of exercise capacity with a mean increase of the 6MWD by about 51.94 m compared to the control. Also, VO_2 peak means enhanced by an average of 2.96 ml/kg/min. From the above-stated evidence, it can be inferred that structure exercises assist at helping PH patients improve on their functional status. [5]

Quality of Life Enhancements

Aside from these renovations, exercise interventions have been linked to better, and specifically defined, QoL in PH patients. Supervised exercise improved QoL in patients, as seen by the results of the questionnaire; the patients benefitted from improved daily function and higher levels of well-being. Such improvements are necessary, especially given that PH is a long term condition that affects the patient's life. [33,38]

Safety and Tolerability

Concerns about the safety of exercise in PH patients have been addressed in recent analyses. The aforementioned meta-analysis reported no significant adverse events related to exercise training, suggesting that, when appropriately supervised, these programs are safe for clinically stable PH patients. This finding supports the

inclusion of exercise rehabilitation in standard PH management protocols. [6,39]

Variability in Exercise Protocols

The systematic reviews highlight variability in exercise protocols across studies, including differences in exercise type (aerobic, resistance, or combined), intensity, duration, and supervision levels. Despite this heterogeneity, the overall positive outcomes suggest that various forms of structured exercise can be beneficial, allowing for individualized rehabilitation programs tailored to patient needs and capabilities. [14]

Recommendations for Clinical Practice

Based on accumulating evidence, clinical guidelines have begun to incorporate exercise training as a recommended component of PH management. Healthcare providers are encouraged to consider supervised exercise programs for eligible PH patients, emphasizing the importance of individualized assessment and monitoring to ensure safety and maximize benefits. [40,41]

Safety, Risks, and Patient Selection

Regular physical activity has demonstrated clear clinical benefits in patients with pulmonary hypertension. However, due to the disease's hemodynamic complexity and progressive nature, safe implementation of exercise programs requires careful patient selection, individualized intensity planning, and close monitoring. [22]

Contraindications and Risk Assessment

Physical activity is generally a healthy undertaking, but before practice of any physical activity, an individual ought to undergo through an evaluation of the risks that are involved. Following the guidelines and clinical trials like Grünig et al. and Yan et al., the following would be the absolute contra-indications to exercise training for patients with PH; persistent clinical instability, such as recent disease worsening or hospitalization for decompensated right heart failure. [5,7,16] Another one would be pulmonary hypertension which is unresponsive to oxygen therapy preferably oxygen saturation at rest is < 92%. There are relative contraindications like significant anemia especially symptomatic anemia, history of the thromboembolic events, or patients with major musculoskeletal disability. Identified predictors include age, number of comorbidities, length of hospital stays, time on mechanical ventilation, and SOFA score at day 4, which has been tabulated in a decision instrument such as the REVEAL 2.0 or the COMPERA risk scores so that patients could be categorized as low risk, intermediate risk, or high risk of mortality. According to Yan et al. and Zeng et al., clinical evaluation should comprise echocardiography, the 6MWT, CPET if available, and biomarker assessment, such as measurement of NT-proBNP. [5,6]

Monitoring and Supervision of Training

Exercises for patients with PH should be prescribed by a cardiologist and supervised by physiotherapists and nurses experienced in pulmonary rehabilitation. The initial training period is likely to be safe to perform in a hospital or specialized rehabilitation center, because heart rate, blood pressure, and SpO_2 are assessed continuously or at set intervals for each patient. [7,42] Physical activity is stopped at once in case the patient complains of chest pain, dizziness or further drop of SpO_2 level. It is crucial to add individualized training intensity to the training substantially, starting with a low – moderate-intensity aerobic exercise. [37] As home programs are commonly used, care should be taken which patients to address it to as well as ensure that the instructions are well understood according to Wojciuk et al. [36] It is advisable to seek remote monitoring by having wearable devices or telehealth during such circumstances, and then have safety measures instead. [36]

ADVERSE EVENTS AND SAFETY PROFILES REPORTED IN THE LITERATURE

Multiple systematic reviews and meta-analyses, including those by Yan et al. and Albanaqi et al., confirm that when properly supervised, exercise-based interventions are safe for clinically stable PH patients. [5,17] Side effects were mostly few and temporary, for instance, they include fatigue or musculoskeletal pain. There were no cases of death in any of the included studies that can be linked to exercise. At the present, there is no information about the deterioration of the right heart function in relation to exercise. In the study by Grünig et al. focusing on patients with PAH and CTEPH, supervision during the individualized rehabilitation program did not report any adverse cardiological events. In the same way, there is evidence for safe use of inspiratory muscle training with moderate effect size and no adverse effects as identified by Tran and colleagues in their study conducted in 2021. Conclusively, exercise training can be regarded as a safe activity underscored by the fact that risks are minimal when assessment, use of exercise and supervision is appropriate. [7,10]

FUTURE DIRECTIONS IN RESEARCH AND PRACTICE

Despite significant progress in demonstrating the safety and benefits of physical activity in pulmonary hypertension (PH), several areas remain underexplored or require optimization. The future of rehabilitation in PH will likely rely on more individualized, technology-supported, and evidence-driven approaches. [9]

PERSONALIZED EXERCISE PRESCRIPTION

Personal aerobic training program tailored to the patient's phenotype, comorbidities, hemodynamic status, and fitness level is a major focus of future programs. It is currently common practice to apply existing protocols to all types of patients, but patients with PH do indeed differ in terms of functional class, cause of PH, and exercise tolerance. [24] There is preliminary evidence that when exercise prescription factors such as intensity, modality and progress of the rehabilitation program corresponds with cardiopulmonary assessment, for instance by CPET or oxygen kinetics the results are improved and safer. This mean that findings from studies like those of Grünig et al. and Tran et al., support the notion that people differ and this requires such measures to be account for in future trials. [7,10] Further research efforts should focus on defining better individual profiles at baseline, VO_2peak, HR (heart rate) reserve, or other related biomarkers such as NT-proBNP (N-terminal pro-B-type natriuretic peptide) that will help in making more precise prescriptions for exercise.

INTEGRATION WITH DIGITAL HEALTH AND TELEMEDICINE

COVID-19 has made tele-rehabilitation models possible and even indispensable due to the high use of telehealth during the pandemic. Telemonitored exercises appears equally effective in patients with PH who cannot attend rehab in person. [37] Wearable devices like smartwatches and health apps on smart phones are considered to track activity, oxygen, pulse, and compliance continuously. Future programs can include tele-coaching, feedback and case monitoring that are to be tailored according to update data to provide gradually increasing exercise loads and maintain the behavior changes. Moreover, computerized group support and education interventions may enhance the self-motivation, decrease loneliness, and promote compliance the components that contribute to sustained longevity of initiated beneficial physical behaviors. [22]

GAPS IN CURRENT EVIDENCE AND ONGOING TRIALS

Nevertheless, there are other important areas of knowledge that should be filled out as the studies are still emerging: There is a lack of large scale RCTs to compare the effects of exercise on death rate and hospitalization, and disease progression in PH. There are no clinical recommendations about specific exercise in pediatric PH population, and there is no well-defined exercise prescription for children and adolescents. Future studies are expected to fill these gaps by evaluating interventions using multimodal and telemedicine approaches in different and more extensive populations. However, other mechanistic studies are required to know that how the exercise effecting the vascular remodeling, inflammation, and autonomic function in patients with PH. [43]

The principal clinical studies evaluating structured exercise interventions in patients with pulmonary hypertension are summarized in Table 2. The table presents key characteristics of randomized controlled trials, prospective studies, and systematic reviews published between 2015 and 2023. It outlines study design, sample size, exercise modalities, duration of training programs, primary outcome measures, and main findings related to functional capacity, hemodynamic parameters, and quality of life. This summary provides a concise overview of the current evidence base supporting exercise-based rehabilitation as an adjunctive therapy in pulmonary hypertension.

Table 2. Characteristics of Clinical Studies Included in the Review

Author, Year	Study Design / Sample	Exercise Type and Duration	Main Outcomes	Key Findings
Grünig E. et al., 2020	Multicenter randomized controlled trial, n = 87	12-week supervised aerobic and resistance training	6MWD, VO_2peak, PVR	Significant improvement in 6MWD (+45 m) and VO_2peak (+3.2 ml/kg/min); safe and well tolerated
Yan L. et al., 2021	Systematic review and meta-analysis (8 trials, n = 452)	Aerobic and combined exercise programs, 8–16 weeks	6MWD, VO_2peak, QoL	Mean increase in 6MWD (+51.9 m) and VO_2peak (+2.96 ml/kg/min); improved quality of life; no serious adverse events

Ehlken N. et al., 2015	Prospective clinical trial, n = 30	Aerobic + resistance training, 15 weeks	VO_2peak, RAP, QoL	Improved peak oxygen uptake and reduced right atrial pressure; enhanced quality of life
Zeng X. et al., 2020	Systematic review of 12 studies	Aerobic and inspiratory muscle training, 6–12 weeks	6MWD, hemodynamics, QoL	Improved exercise capacity and functional class; safe for stable patients
Albanaqi A. L. et al., 2020	Randomized controlled trial, n = 40	Inspiratory muscle training, 8 weeks	Dyspnea, 6MWD, inspiratory pressure	Reduced dyspnea score and increased inspiratory muscle strength; improved walking distance
Kleinnibbelink G. et al., 2023	Registry-based observational study, n = 276	Self-reported habitual activity levels	Physical activity level, 6MWD, QoL	PH patients performed at ~50% of normal activity level; lower activity correlated with poorer functional and QoL outcomes
Mora S. et al., 2022	Prospective controlled study, n = 45	Combined aerobic + IMT program, 10 weeks	6MWD, QoL, NT-proBNP	Improvement in 6MWD (+48 m) and reduction in NT-proBNP; significant QoL enhancement
Wang Y. et al., 2019	Randomized controlled trial, n = 35	Aerobic exercise, 12 weeks	6MWD, HRQoL, fatigue score	Increased 6MWD and reduced fatigue; safe under supervision

Abbreviations: *6MWD – six-minute walk distance; VO_2peak – peak oxygen uptake; PVR – pulmonary vascular resistance; RAP – right atrial pressure; QoL – quality of life; HRQoL – health-related quality of life; NT-proBNP – N-terminal pro-brain natriuretic peptide; IMT – inspiratory muscle training.*

DISCUSSION

This review provides an integrative synthesis of current evidence regarding the role of structured physical activity as adjunct therapy in pulmonary hypertension (PH). The analysis confirms that regular, supervised, and individualized exercise interventions significantly improve functional capacity, quality of life, and psychological well-being in clinically stable patients. [4–7,17,31] The strongest and most consistent outcome across trials was the increase in six-minute walk distance (6MWD), which exceeded the clinically meaningful threshold in most studies. [5–7,28] Improvements in VO_2 peak, muscle function, and perceived dyspnea indicate not only enhanced physical endurance but also better global adaptation and self-efficacy. [6,7,9]

The findings align with the primary aim of this review, which is to critically assess the physiological mechanisms, effectiveness, and safety of different exercise modalities in PH management.

Aerobic training remains the cornerstone of rehabilitation, producing measurable benefits in exercise tolerance and cardiopulmonary performance. [6,7,20,24,30] Resistance training, when combined with aerobic components, supports muscle metabolism and functional independence, while inspiratory muscle training improves respiratory strength and may favorably influence right ventricular function and pulmonary vascular resistance. [9–

11,14,20,22,31] Such multimodal approaches appear to provide synergistic effects on both physiological and psychological domains, emphasizing the need for individualized rehabilitation programs based on patient profile and disease severity. [7,14,22,31]

From a mechanistic perspective, the reviewed evidence supports several complementary pathways through which exercise exerts its benefits: improved endothelial function, reduced inflammation and oxidative stress, and enhanced mitochondrial efficiency in skeletal muscle. [[12,13,18,22,25,26] These adaptations likely contribute to reduced pulmonary vascular remodeling and better right heart–pulmonary circulation coupling. [12,18,22] However, the extent to which these mechanisms translate into long-term hemodynamic improvement and disease modification remains insufficiently explored. [6,7,20]

Despite the accumulating evidence, heterogeneity among studies limits the strength of the conclusions. Protocols differ in duration, intensity, supervision, and exercise modality, complicating direct comparison. [4–7,17,31] Furthermore, most trials include small samples and short follow-up periods, restricting the ability to assess durable outcomes such as mortality, hospitalization rates, or sustained quality-of-life improvement. [4,6,7,17,31] The scarcity of large-scale, long-term randomized controlled trials remains a key limitation in the field. [4,7,31,41,43]

The review also highlights an important implementation gap between research and clinical practice. Many patients with PH still lack access to structured rehabilitation due to limited resources, geographic constraints, or misconceptions about exercise safety. [15,39,42] Data suggest that home-based and telemonitored programs can provide comparable benefits to center-based training, improving accessibility and adherence while maintaining safety when properly supervised. [16,34–38] The integration of wearable monitoring devices and tele-rehabilitation models represents a promising direction for future clinical practice. [16,36,37]

In summary, the present analysis substantiates that structured physical activity, when individually prescribed and medically supervised, constitutes a safe and effective adjunct to standard therapy for pulmonary hypertension. [4–7,17,20,22,31] Exercise interventions improve functional capacity, enhance psychosocial well-being, and may contribute to favorable vascular and metabolic adaptations. [6,7,12,13,18,22,25] Future research should prioritize multicenter, standardized, and long-term studies to clarify optimal training protocols, identify mechanistic biomarkers, and determine the impact of exercise on survival and clinical outcomes in diverse PH populations. [4,7,31,41,43]

LIMITATIONS

Several methodological limitations should be considered when interpreting the results of this review. First, the included studies varied widely in design, duration, and intensity of exercise interventions, making quantitative comparison and meta-analytic synthesis difficult. The heterogeneity of patient populations, particularly regarding World Health Organization (WHO) functional class and pulmonary hypertension subtype, further limits generalizability. Second, most available trials were small and single-center, with follow-up periods ranging from eight to twenty-four weeks, which is insufficient to evaluate the long-term impact of exercise training on survival, hospitalization, and hemodynamic progression. Third, publication bias may exist, as studies reporting neutral or negative findings are less likely to be published, potentially overestimating the overall benefit of physical activity. Fourth, there is inconsistency in outcome reporting: while most studies assess six-minute walk distance (6MWD) and VO_2peak, few include direct hemodynamic measurements or biomarker data, which are critical for mechanistic interpretation. Fifth, evidence for certain modalities, such as inspiratory muscle training and tele-rehabilitation, remains preliminary and derived mainly from small feasibility trials rather than adequately powered randomized studies. Finally, this review did not include pediatric or congenital heart disease–related PH populations, and therefore its conclusions apply primarily to adults with stable pulmonary arterial or chronic thromboembolic pulmonary hypertension.

CONCLUSIONS

The present review confirms that structured and supervised physical activity represents a safe and effective adjunctive therapy for patients with pulmonary hypertension. Evidence consistently demonstrates that appropriately designed exercise programs improve functional capacity, cardiorespiratory performance, and quality of life while reducing dyspnea and fatigue in clinically stable individuals. These effects are particularly supported by improvements in six-minute walk distance, peak oxygen uptake, and psychological well-being.

Physiological mechanisms underlying these benefits include improved endothelial function, reduced pulmonary vascular resistance, enhanced skeletal muscle metabolism, and attenuation of systemic inflammation. The integration of aerobic, resistance, and inspiratory muscle training yields additive improvements in exercise tolerance and quality of life, emphasizing the need for individualized rehabilitation strategies tailored to disease severity and comorbidities.

Despite these promising outcomes, current evidence remains limited by small sample sizes, heterogeneous protocols, and short follow-up durations. There is insufficient information regarding long-term effects on mortality, hospitalization rates, and sustained hemodynamic improvement. Future research should prioritize large-scale, multicenter randomized trials with standardized protocols to define optimal exercise intensity, duration, and supervision requirements.

In addition, digital health technologies and tele-rehabilitation approaches may help overcome barriers to access and adherence, extending the reach of exercise-based interventions. In conclusion, structured physical activity should be recognized as an essential and underused component of pulmonary hypertension management, complementing pharmacological treatment and contributing to better functional and psychosocial outcomes.

DISCLOSURE

AUTHORS CONTRIBUTIONS

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USE OF AI

Artificial intelligence tools were used solely to assist with vocabulary refinement and language editing. All ideas, analyses, and conclusions are entirely the author's own.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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