Open Journal of Therapy and Rehabilitation, 2026, 14(2), 86-100
https://www.scirp.org/journal/ojtr
ISSN Online: 2332-1830
ISSN Print: 2332-1822

Exercise-Based Rehabilitation for Patients with Pulmonary Embolism—A Narrative Review

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How to cite this paper: Nebel, R., Bjarnason-Wehrens, B. and Schmidt, T. (2026) Exercise-Based Rehabilitation for Patients with Pulmonary Embolism—A Narrative Review. *Open Journal of Therapy and Rehabilitation*, **14**, 86-100.
https://doi.org/10.4236/ojtr.2026.142008

Received: March 15, 2026
Accepted: May 22, 2026
Published: May 25, 2026

Abstract

Introduction: Pulmonary embolism (PE) is the third leading cause of cardiovascular death worldwide. If left untreated, the mortality rate is 25% to 30%. PE can have far-reaching long-term health consequences, like development of chronic thromboembolic pulmonary hypertension (CTEPH) or post-pulmonary embolism syndrome (PPES). PE is often associated with persistent symptoms or limitations in physical performance and affects quality-of-life, personal, family and professional circumstances. This review summarizes available evidence on feasibility, safety and effectiveness of exercise-based cardiac/pulmonary rehabilitation in PE-patients. **Methods:** A selective literature search was conducted in PubMed using predefined search terms. In addition, the bibliographies of all available studies and guidelines were consulted in order to identify any further sources. **Results:** Sixteen mostly small studies were identified. A considerable heterogeneity regarding study design, patient characteristics, intervention setting, duration, scope, and contents and outcome parameters was observed. Results demonstrate feasibility, safety, and/or efficacy of exercise-based interventions in PE patients. The intervention was well tolerated, and no serious events related to the exercise were documented. The interventions lead to a prolonged 6-minute walk distance, improved physical performance, quality of life, hemodynamic parameters, arterial oxygen saturation, oxygen uptake (peak VO_{2max}) and further respiratory parameters. Nevertheless, the evidence for benefit and efficiency remains mixed: the largest acute PE trial did not show superiority on its primary endpoint. **Discussion:** There is a significant need for structured follow-up-care, including rehabilitation for PE-patients. Despite frequent occurrence and potential physical and psychosocial consequences for those affected, there are no structured aftercare or rehabilitation programs in the first year after PE. Only a few studies have focused on the effects of a structured rehabilitation or aftercare program following PE. **Conclusions**: There is a considerable need for improved scientific evidence, targeted and structured care pathways, and interdisciplinary cardiac/pulmonary rehabilitation in PE-patients.

Keywords

Chronic Thromboembolic Pulmonary Hypertension, Post-Pulmonary Embolism Syndrome, Exercise Therapy, Cardiac Rehabilitation

1. Introduction

Pulmonary embolism (PE) is the third leading cause of cardiovascular death worldwide, with a high number of cases remaining undiagnosed [1]. PE is probably the most common clinically unrecognized cause of death in hospital. According to registry data, the annual incidence of PE is 60 - 200 per 100.000 inhabitants and increases significantly with age [2]. In over-70-year-olds, the incidence is above 500 per 100.000 inhabitants [3]. In Germany, PE leads to approximately 40.000 deaths annually [4]. New guidelines for the assessment and treatment of acute PE in adults were recently published [5].

1.1. Clinical Impact of Pulmonary Embolism (PE)

The scope of PE can range from a small, clinically undetectable subsegmental embolism, which occurs in over 50% of patients with proximal deep vein thrombosis (DVT), to bilateral high-grade vascular occlusion with circulatory instability [6].

Untreated, the mortality rate of PE is 25% to 30%. The 30-day mortality rate is 6.2% for central PE and 3.7% for distal, *i.e.* segmental or subsegmental, PE, amounting to 5.4% overall [7]. One-year mortality is 8.1%, with a wide variation between countries [8].

In addition to the acute thromboembolic event, PE can have serious long-term health consequences [9]. These include reduced physical performance, psychosocial effects, and significant limitations in health-related quality of life (HRQoL) [8] [10]. The risk of recurrence is significant, as is the risk of developing chronic consequences, including chronic thromboembolic pulmonary hypertension (CTEPH).

In CTEPH, a scarred remodelling of the embolic material leads to obstruction of part of the pulmonary circulation and to an increase in pulmonary vascular resistance. Around 3% of survivors of an acute pulmonary embolism develop this clinical condition which should definitely be diagnosed since targeted treatment options are now available [11] [12].

The current guidelines recommend diagnosing pulmonary hypertension after at least 3 months of effective anticoagulation [5] [13]-[15].

Post-pulmonary embolism syndrome (PPES) was defined around 10 years ago

[9] [16]. More than 50% of all patients who have survived a pulmonary embolism complain of persistent shortness of breath or symptoms of fatigue after at least 3 months of effective anticoagulation. This cannot be explained by signs of pulmonary hypertension or other lung changes. These symptoms are clear, but less pronounced than in CTEPH, and can persist for up to 10 years. A structured follow-up is necessary in order to identify the presence of PPES [17] [18].

In a prospective multicentre observational cohort study, 1,017 patients were followed up at 3, 12 and 24 months after acute symptomatic pulmonary embolism. CTEPH was diagnosed in 1.6% of patients after a median of 129 days (estimated cumulative 2-year incidence 2.3 (1.2 - 4.4)%). The cumulative incidence of PPES was 17% (12.8% - 20.8%). Patients with PPES had a higher risk of rehospitalization and death, and a poorer quality of life (QoL) than patients without PPES. Thus, every 6th patient or more was still symptomatic after two years [19].

A follow-up examination of all patients 3 - 6 months after the event clarifies whether dyspnea or other functional limitations that were not present before the event are still present. If this is the case, a (repeat) echocardiogram is recommended. In any case, it should be ascertained whether criteria for CTEPH are present [6] [20] [21].

1.2. Aftercare Following Pulmonary Embolism (PE)

Despite its frequent occurrence and potential physical and psychosocial consequences for those affected, there are no structured aftercare or rehabilitation programs in the first year after PE, apart from a few follow-up appointments. Moreover, there is a lack of detailed patient information, such as brochures or tutorials (exception: [22]). This is in contrast to global follow-up care, for example, post-myocardial infarction. The current ESC/ERS guidelines provide a class 1C recommendation for an "integrated patient care program" based on country-specific infrastructures [6]. The program should integrate interdisciplinary outpatient and inpatient care by physicians and nursing staff using standardized treatment protocols. Patient education, including a positive influence on persistent risk factors (especially smoking, obesity and a lack of exercise) should be part of the program. Personal preferences, the family, and the social and professional environment should all be taken into account. This concept was confirmed by the results of a study of 42 CTEPH patients [23].

The German guideline recommends cardiac rehabilitation (CR) after PE [24] [25]. Early, symptom-adapted mobilization and activating therapies reduce the likelihood of post-thrombotic syndrome in patients with PE and DVT [17]. The use of muscle pumps promotes venous decongestion of the affected extremity and effectuates (possibly complete) symptom relief [26]. Immobilization has a negative effect on the reduction of edema in the leg and patient symptoms [17].

Only a few studies have focused on the effects of a structured rehabilitation or aftercare program following PE. Studies on the safety and effectiveness of prevention and relief of post-thrombotic symptoms in patients with DVT are presented in a recent systematic review [27]. Specific rehabilitation programs for DVT and PE-patients are not yet available.

The aim of this review is to summarize and evaluate the available evidence on the feasibility, safety and effectiveness of exercise-based (CR) or pulmonary rehabilitation (PR) for these patients in order to gain insights for the establishment of such interventions.

2. Methods

A selective literature search was conducted in PubMed using the following search terms: cardiac rehabilitation, pulmonary rehabilitation, exercise training, pulmonary embolism, deep vein thrombosis, chronic thromboembolic pulmonary hypertension, and post-pulmonary embolism syndrome. Articles published in English or German were considered. Studies were included if they reported on exercise interventions or rehabilitation in patients with PE, DVT, CTEPH or PPES. Case reports, studies with very small sample sizes ($n < 10$), or those lacking sufficient methodological detail were excluded. Titles and abstracts were screened for relevance, and full texts of potentially eligible studies were reviewed. In addition, the bibliographies of all selected studies were screened to identify further relevant publications. However, given the narrative nature of this review, no formal systematic review protocol was followed, and selection bias cannot be excluded.

3. Results

The literature search identified 16 studies that met our search criteria [28]-[43]. These predominantly small studies evaluated the feasibility, safety and/or effectiveness of exercise-based rehabilitation or interventions in the target group. Seven studies were randomized controlled trials (RCTs) [29] [31] [34] [36] [38] [39] [43]. Nine studies were cohort studies [28] [30] [32] [33] [35] [37] [40]-[42], of which four were prospective [30] [33] [35] [42], three retrospective [28] [32] [40] and two observational [37] [41]. Two of the prospective studies were controlled [30] [31], another one evaluated the results of two different exercise programs [42].

The selected studies show considerable heterogeneity with regard to study design, characteristics of the included subjects, setting of the intervention, and the duration, volume and content of the exercise-based intervention/rehabilitation, as well as the outcome parameters evaluated. This heterogeneity makes it difficult to summarize the results and draw firm conclusions. DVT, CTEPH, pulmonary endarterectomy (PAE), and one mixed PAH/CTEPH study were included due to the fact that the involved patients typically enroll in CR programs as a clinical unity.

The intervention was well tolerated by all patients, and no serious events related to the exercise were documented. In summary, exercise-based interventions lead to a prolonged 6-minute walk distance (6MWD) [28] [35] [36], an increase in peak VO_2 [29] [30] [31] [35] [37] and physical performance [38], and an improvement in quality of life [28] [31] [35] [37]-[39]. The results show improved hemodynamic parameters [31] [40], arterial oxygen saturation 40 and respiratory parameters [28] [31] [36]. A summary of the study results is presented in **Table 1**.

Table 1. Summary of studies on cardiac and pulmonary rehabilitation in patients with DVT, PE and CTEPH.

Author and study-type	Diagnosis	Type of intervention	Main finding(s)
Lakoski *et al.* 2015 [29] mono-center prospective RCT, N = 19 (IG = 9, CG = 10)	VTE or PE	IG: 3-month out-patient supervised or home-based ET CG: usual care /no ET	significant increase in peak VO_2 (~10%, ~ 1 MET)
Noack *et al.* 2015 [32] mono-center retrospective cohort study, N = 422	consecutive PE, DVT known in 55.5%	3-week in-patient ET: cycle ergometer, respiratory therapy, water and resistance exercise	no influence of ET on occurrence of adverse events observed, no serious adverse events
Fukui *et al.* 2015 [30] prospective, controlled study N = 41 (IG = 17, CG = 24)	CTEPH following BPA with continuing exercise intolerance and symptoms on effort	IG: 12-week mainly out-patient program (home exercise, partly supervised). CG: no ET	peak work load (W), peak VO_2, muscle strength (quadriceps) significant in favour of IG
Amoury *et al.* 2018 [33] mono-center prospective cohort study, N = 70	PE, DVT known in 43%	3-week in-patient ET with range of exercise-based therapeutic activities, 12-month follow-up	during ET no serious adverse events, during follow-up in 4.2% cases serious adverse events
La Rovere *et al.* 2019 [40] retrospective data analysis, N = 110	CTEPH with Pulmonary Endarterectomy (PEA)	3-week in-patient CR: ET: aerobic and resistance exercise, 3 month follow up	6MWD significantly improved in both groups, improvements in hemodynamic data at rest
Nopp *et al.* 2020 [28] retrospective single-center cohort study, N = 22	PE with persistent dyspnea (NYHA class ≥ II)	6-week out-patient ET, endurance, strength, inspiratory muscle training, follow-up interview	follow up: 61% no significant functional limitations, 39% different degrees of limitations
Rolving *et al.* 2020 [34] multi-center RCT, N = 140 (IG = 70, CG = 70)	first-time acute PE	IG: 8-week home-based ET, CG: brief nurse consultation Follow-up at 8 and 26 weeks	non-significant improvements in primary outcome ISWT and secondary outcomes-QoL-scores
Nagel *et al.* 2020 [35] prospective cohort study, N = 45	CTEPH with PEA	19-week mainly home-based ET: cycle ergometer, walking, low weights and respiratory training	6MWD, peakVO_2, workload, HR_{rest}, $VECO_2$, SF-36 from 3 to 22 weeks after PEA significantly improved
Tran *et al.* 2021 [36] prospective single-center RCT N = 12 (IG = 6, CG = 6)	CTEPH or group 1 PAH (RHC), 10 PAH, 2 CTEPH)	IG: 8-week IMT using an electronic respiratory muscle training device CG: usual care	non-significant improvements in peak VO_2 ,6MWD, PI_{max}, decrease of NT-proBNP-levels

Continued

Ghram *et al.* 2021 [31] mono-center prospective RCT, N = 12 (IG = 12, CG = 12)	intermediate–high-risk acute PE	IG: 8-week supervised HIIT 3 times a week (24 training sessions) CG: no intervention, usual care	significantly improved VO_{2max}, FEV1, RV/LV ratio diameter and HRQoL. HIIT tolerated without serious adverse events. CG: no changes
Boon *et al.* 2021 [37] observational cohort study, N = 27	PPES	12-weeks ET. 2 90 min supervised units and 1 home-based unit/week (endurance, resistance)	significant increase of PPO (Watt) and improvements of Pemb-QoL-score, PVFS scale
Gleditsch *et al.* 2022 [41] mono-center cohort study, N = 26	persistent dyspnea following PE 6-72 months after diagnosis	8-week out-patient ET, 2 60 min supervised exercise sessions (IT, RT), 1 educational session/week	CMR: RV longitudinal and lateral strain, RV mass reduced, dyspnea significantly reduced (SOBQ)
Jervan *et al.* 2023 [38] two centre-RCT, N = 211 (IG = 108, CG = 103)	persistent dyspnea following PE 6-72 months after diagnosis	8-week out-patient ET, 2 60 min supervised exercise sessions (IT, RT), 1 educational session/week	IG: non-significant improvement in ISWT
Lachant *et al.* 2024 [39] mono-center, blinded pilot RCT, N = 21 (IG = 12, CG = 9)	acute, intermediate-risk PE	8-week home based ET with daily, electronically delivered instructions	IG: non-significant improvements in 6MWD, PEmb QoL, actigraphy with peak 5-minute steps
Azzarito *et al.* 2024 [42] cohort study, N = 225 - preliminary data	acute PE	4-week in-patient ET: group 1 plus calisthenics, group 2 plus RT	Preliminary: improvements in dyspnea, physical performance. Echo: RV 93% back to normal
Haukeland-Parker *et al.* 2025 [43] two center-RCT, N = 159 (IG = 80, CG = 79)	persistent dyspnea following PE 6-72 months after diagnosis – 6-month follow-up of [38]	8-week out-patient ET, 2 60 min supervised exercise sessions (IT, RT), 1 educational session/week	IG: further non-significant improvement in ISWT

Abbreviations: BPA, balloon pulmonary angioplasty, CG, control group, CMR, Cardiac Magnetic Resonance, CO, cardiac output, CPET, cardiopulmonary exercise testing, CR, cardiac rehabilitation, CTEPH, chronic thromboembolic pulmonary hypertension, CWP, capillary wedge pressure, DVT, deep vein thrombosis, ESWT, Endurance Shuttle Walk Test, ET, exercise training, HIIT, High intensity interval training, IG, intervention group, IMT, inspiratory muscle training, ISWT, Incremental Shuttle Walk Test, IT, interval training, PAP, pulmonary artery pressure, MET, metabolic equivalent of task, MSTST, 1-min sit-to-stand test, n.a., not available, n.s., non-significant, NT-proBNP, non-terminal pro-brain natriuretic peptide, PAH, pulmonary arterial hypertension, peak VO_2, peak oxygen uptake, PE, pulmonary embolism, PEA, pulmonary endarterectomy, PEmb-QoL, Pulmonary Embolism Quality of Life questionnaire, PI_{max}, maximal inspiratory pressure, PPES, Post-Pulmonary Embolism Syndrome, PR, pulmonary rehabilitation, PVR, pulmonary vascular resistance, PVFS, Post-VTE Functional Status Scale, QoL, quality of life, RCT, randomized controlled trial, reps, repetitions, RHC, right heart catheterization, RV, right ventricular, SOBQ, Shortness of Breath Questionnaire, VTE, venous thromboembolism, W, watt.

3.1. Studies on Aftercare and Rehabilitation in PE-Patients (Incl. PPES)

In a first prospective randomized study, the safety and efficacy of early physical exercise in DVT and PE patients were evaluated over a period of 12 weeks. In the intervention group, maximum oxygen uptake (peak VO_2) and total weekly physical activity improved significantly. No clinical adverse events occurred under therapeutic anticoagulation [29].

Results of a retrospective cohort study (N = 422) showed no adverse events during a 3-week inpatient CR, especially in direct relation to physical activity and recent PE. In this feasibility-study, the PE-patients did not receive a specific program, but completed the multimodal CR together with other patients who were mainly attending CR due to coronary artery disease (CAD) [32].

In order to evaluate the prognosis of PE-patients during a 3-week CR, and in the first 12 months after completion of CR, a prospective cohort study was conducted by the same researcher. The rehospitalization rate was 3.9% during CR, and 28.6% in the follow-up phase. The mortality rate was 5.7% [33].

A retrospective study evaluated the effectiveness of participation in a 6-week outpatient exercise-based PR in 22 PE-patients with persistent exertional dyspnea (NYHA classification > 2), defined as PPES [28]. The median follow-up time was 39 months. Participation led to significant extension of the 6MWD. In addition, significant improvements were observed Pi_{max}, $Watt_{max}$, maximum strength of the upper and of the lower extremities. After an average follow-up period of 39 months after PR, 78% of patients reported an improved health status [28].

A small single-center RCT in 24 intermediate–high-risk acute PE-patients demonstrated that high-intensity-interval-training (HIIT) within a CR setting can be leveraged for acute PE patients as a safe and effective modality improving exercise capacity, pulmonary and RV function, as well as HRQoL significantly [31].

In the first multicenter randomized clinical trial, 140 PE-patients were randomly assigned to IG and CG [34]. The IG participated in an eight-week supervised home-based rehabilitation, starting 2 - 3 weeks following hospital discharge. Monitoring was carried out by telephone and through personal visits. The CG received one or more telephone consultations from specialized nursing staff. No relevant adverse events related to physical activity were observed. No significant benefits of the intervention were observed with regard to the primary endpoint or secondary endpoints. Reasons for this may include low comorbidity among PE-patients and the influence of the CG towards an active lifestyle due to the detailed examinations at the study entry. The latter may have reduced the CG's fear of physical activity after a severe acute illness [34].

In 27 PPES patients, participation in a 12-week outpatient rehabilitation led to a significant improvement in exercise intensity, PE-specific quality of life (PEQoL) and the extent of fatigue [37].

An analysis of cardiac magnetic resonance parameters in 26 PE-patients after an 8-week PR revealed, despite a significant improvement in dyspnea, only a non-significant reduction in the absolute longitudinal strain of the right ventricle and right ventricular mass, while the remaining parameters remained unchanged. The effects of PR were therefore not primarily attributable to cardiac adaptation. [41].

The results of a RCT involving 211 PE-patients suffering from persistent dyspnea 6 to 72 months after the event revealed that participation in an 8-week rehabilitation led to an improvement in physical performance and PEQoL. but it did not show superiority on its primary endpoint (with a non-significant difference in the Incremental Shuttle Walk Test (ISWT) of +53.0 m ($p = .035$)). No relevant adverse events occurred during the study [38]. These results were sustained and confirmed in a follow-up examination six months later. This confirms long-term health benefits of rehabilitation participation for PE-patients [43].

In a randomized pilot study, the IG participated in an 8-week home-based-exercise-program, while the CG received general recommendations on physical activity. Significant improvements in 6MWD, QoL and physical activity were observed in both groups, with no significant group differences. With regard to the primary endpoint of safety (defined as new or worsening pulmonary artery embolism during the eight-week program, syncope, hospital admission), the program was confirmed to be safe [39].

Recently published preliminary data on 225 PE-patients who began a 4-week inpatient exercise-based rehabilitation 8 days after the acute event are of interest. In all patients, treatment led to improvements in dyspnea and exercise capacity, regardless of the initial treatment for PE. However, the degree of improvement showed a clear correlation with existing comorbidities, particularly obesity and chronic obstructive pulmonary disease (COPD). There were no side effects from rehabilitation. All patients underwent a final echocardiography and pulmonary CT angiography after 4 weeks: the results showed normalization of right heart geometry and function in 93% and almost complete resolution of pulmonary artery thrombi in group 1. In group 2, significant residual thrombi remained in 61% of patients. After pharmacological or mechanical revascularization, the echocardiographic findings normalized after the first week of rehabilitation. The authors conclude that timely inpatient rehabilitation is suitable for high- and medium-risk patients. It is also suitable for low-risk patients, but they can participate on an outpatient basis [42].

3.2. Studies on Aftercare and Rehabilitation in CTEPH Patients

41 CTEPH patients who had previously undergone balloon angioplasty due to inoperability were randomly assigned to an IG with immediate 12-week CR and a CG with usual care. The remaining mean pulmonary artery pressure was 24.7 ± 5.5 mmHg, and physical performance remained impaired. After 12 weeks, maximum oxygen uptake (VO_2), percentage of maximum oxygen uptake, oxygen pulse, and maximum power in watts had improved significantly in the IG compared to the CG. No adverse clinical events or worsening hemodynamics were observed [30].

A sample of 45 patients who had previously undergone pulmonary endarterectomy (PEA) due to CTEPH participated in a three-week inpatient CR, followed by a 16-week home-based exercise. The exercise program was well tolerated and no serious side effects were documented. Within the first three weeks and over the following 19 weeks, there was a consistent improvement in physical performance, peakVO_2 and hemodynamic parameters, including right heart catheterization results [35].

In an RCT involving 12 patients with pulmonary arterial hypertension (PAH), including 2 patients with CTEPH, an 8-week inspiratory muscle training (IMT) significantly improved 6MWD but not peakVO_2 [36].

A three-week structured multidisciplinary CR in 84 patients after pulmonary endarterectomy (PAE), involving exercise, education, nutritional and psychosocial counseling, improved 6MWD, echocardiographic hemodynamic parameters and arterial oxygen saturation [40].

The results of a meta-analysis show that exercise is well tolerated by CTEPH patients and can improve physical performance, mean pulmonary artery pressure (mPAP) and quality of life. Larger multicenter studies are needed to confirm the efficacy and safety of exercise in these patients [44].

4. Discussion

The scientific evidence for benefit of a structured CR after PE is mixed, the largest acute PE trial did not show superiority on its primary endpoint (ISWT). Evidence quality remains low: most studies are small, heterogeneous, and frequently uncontrolled, limiting the strength of the recommendation for routine CR.

Nevertheless, there is a great need for structured follow-up care - including rehabilitation for PE-patients. The results of a study evaluating the frequency and predictors of physical limitations after PE, as well as their relationship to quality of life (QoL) and dyspnea in a group of 100 patients, support this assumption [45]. At 12-month follow-up, 40 out of 86 patients (46.5%) showed a reduced predicted peak $VO_2 < 80\%$. This was associated with a significantly reduced overall HRQoL, reduced PE-specific HRQoL, increased dyspnea and a significantly reduced 6MWD. The initial or residual thrombus burden on CTPA after 12 months or scintigraphy after 6 months was not associated with the predicted peak $VO_2 < 80\%$. Pulmonary function tests and echocardiographic parameters (pulmonary artery pressure, right and left ventricular systolic function) showed normal results, regardless of whether patients had limiting symptoms or not. The authors attribute the fact that almost half of PE-patients were restricted in their activities after one year primarily due to peripheral muscle deconditioning, particularly in connection with the acute event, and not to impaired respiratory or circulatory function [45].

These findings are supported by the results of study involving 20 patients with massive or submassive PE with 6 months follow-up [46]. The results show limitations in physical performance, measured by the predicted peak $VO_2 < 80\%$ (in %), regardless of echocardiographic or ventilatory/other cardiopulmonary stress test parameters. The restrictions were primarily related to general muscle weakness, particularly in connection with the acute even.

Other recent reviews of PR after PE have already confirmed safety and feasibility, a reduction in dyspnea and fatigue, and an improvement in functional capacity and QoL as outcomes of PR, particularly through exercise. However, study groups were small, and follow-up times short. There are still unanswered questions regarding the optimal timing and duration of rehabilitation after PE, the intensity of the exercises, and the use of new interventions that go beyond the six established methods (physical exercise, respiratory training, non-invasive ventilation, health education, psychological intervention, nutritional supplementation) [47] [48].

In a qualitative survey of 21 healthcare professionals, PE patients were viewed as a heterogeneous group with complex symptoms who require individualized care in terms of information needs and rehabilitation due to a lack of structured guidelines. Professional advice on physical activity in a safe and supervised environment was considered particularly important for patients with persistent respiratory problems [49].

Physical inactivity or reduced activity as a result of post-PE syndrome with dyspnea and reduced quality of life in almost half of all patients leads to a loss of one to two healthy years of life. The limitations are comparable to those associated with mild COPD, angina pectoris, heart failure or after a stroke. To date, there are no well-studied or effective therapeutic interventions for this syndrome. Patients' quality of life is significantly impaired for years due to dyspnea and reduced physical performance. In these patients, supervised individually adapted exercise intervention is currently the best option to improve quality of life. Endurance and strength training can furthermore have a positive impact on physical performance, weight stabilization, insulin sensitivity, macronutrient handling, myocardial compliance, mitochondrial density and function, and capillary density in skeletal muscle. In addition, NO production is increased and arterial remodeling is induced to improve vasodilation capacity [50]. In PH and CTEPH

patients, this leads to increased cardiac output, reduced vascular tone with a reduction in afterload, and improved metabolic efficiency. The precise mechanisms involved in this syndrome are still poorly understood. However, structured exercise-based rehabilitation clearly improves physical function and QoL, and reduces the occurrence of other subsequent cardiopulmonary diseases, such as heart failure, coronary artery disease, peripheral artery disease, COPD and CTEPH. Individually adapted exercise can and should be started as early as four weeks after an acute pulmonary artery embolism, even in cases of extensive embolism and right heart impairment at the time of pulmonary artery embolism. Available studies indicate a greater benefit from starting exercise intervention early [38].

Table 2 summarizes the most important practice statements with the actual level of supporting evidence.

Table 2. Practice statements with the actual level of recommendation and supporting evidence.

- PE as the 3rd leading cause of cardiovascular death worldwide with a high mortality rate can have far-reaching long-term health consequences (CTEPH, PPES) associated with persistent symptoms or limitations in physical performance and QoL
- Despite frequent occurrence and potential physical and psychosocial consequences no structured aftercare or rehabilitation programs (CR, PR) exist
- Current guidelines provide a class 1C recommendation for an "integrated patient care program" based on country-specific infrastructures or CR after PE
- Predominantly small studies show feasibility, safety and/or effectiveness of exercise-based rehabilitation or interventions, but considerable heterogeneity with regard to study design, characteristics of the included subjects, setting of the intervention, and the duration, volume and content of the exercise-based intervention or CR, as well as the outcome parameters evaluated.
- Exercise-based interventions lead to a prolonged 6MWD, an increase in peak VO_2 and physical performance, and an improvement in QoL, hemodynamic parameters, arterial oxygen saturation and respiratory parameters (evidence level B/C).

Abbreviations: CR, cardiac rehabilitation, CTEPH, chronic thromboembolic pulmonary hypertension, peak VO_2, peak oxygen uptake, PE, pulmonary embolism, PPES, Post-Pulmonary Embolism Syndrome, PR, pulmonary rehabilitation, QoL, quality of life, 6MWD, 6-minute walking distance.

5. Conclusions

To date, no evaluated standardized rehabilitation concept for PE patients has been introduced, the heterogeneity of rehabilitation needs in PE patients and available data support an individually tailored rehabilitation concept that is adapted to the national/local resources of the provider and the patient's personal living environment. Given the frequent occurrence of potential long-term limitations in PE patients, international guidelines [6] [21] [25] recommend structured follow-up care with exercise-based interdisciplinary rehabilitation in order to reduce/avoid possible persistent symptoms or limitations in physical performance with consequences for the personal/family/professional environment. There is a considerable need for improved scientific evidence, targeted and structured care pathways, and interdisciplinary cardiac/pulmonary rehabilitation in PE-patients.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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