

Effect of Hybrid Mode Rehabilitation on Aerobic Endurance and quality of Life: Evaluation Using 6MWT, VO2 Max, and PAH-SYMPACT Questionnaire in Stage 3 COPD Patients With Pulmonary Hypertension

Dr. Jai Kadam¹, Dr. Poovishnu Devi Thangavelu²

¹MPT, Department of Cardio Pulmonary Physiotherapy, Krishna Viswa Vidyapeeth Deemed to be University, Karad, Maharashtra.

Email ID: jaikadam17032000@gmail.com

²Dean Academics & Professor, Department of Cardio Pulmonary Physiotherapy, Krishna Viswa Vidyapeeth Deemed to be University, Karad, Maharashtra.

Email ID: deanacademicskcp@kvv.edu.in

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ABSTRACT

Introduction: Pulmonary hypertension (PH) is a frequent and serious complication in patients with chronic obstructive pulmonary disease (COPD), particularly in group 3 PH, where hypoxia and lung disease contribute to vascular remodelling and increased pulmonary arterial pressures. COPD-PH is associated with increased morbidity, reduced exercise capacity, and higher mortality rates. Despite the clinical burden, optimal management remains a challenge. Pulmonary rehabilitation has emerged as a promising intervention to improve exercise tolerance and quality of life in this population.

Methodology: A prospective, randomized controlled, single-blinded trial was conducted to compare the effects of a hybrid rehabilitation protocol (combination of aerobic, resistance, and breathing exercises) with conventional physiotherapy in patients with stage 3 COPD with PH. A total of 40 participants were randomized into two equal groups. Functional capacity was assessed using the 6-minute walk test (6MWT) and VO2 max. Quality of life was evaluated using the one day version of PAH-SYMPACT questionnaires. Statistical analysis included paired and unpaired t-tests and chi-square tests to assess within-group and between-group differences.

Results: Patients in the experimental group showed significant improvement in 6MWT distance (mean increase of 52.3 ± 10.6 meters, $p < 0.001$) and VO2 max ($p < 0.01$) compared to the control group. Quality of life scores, as measured by PAH-SYMPACT, also demonstrated statistically significant improvements in the experimental group ($p < 0.05$). The control group showed minimal changes in all outcome measures.

Conclusion: The hybrid rehabilitation protocol significantly improved functional capacity and quality of life in COPD patients with pulmonary hypertension compared to conventional physiotherapy. These findings highlight the role of comprehensive pulmonary rehabilitation in managing COPD-PH and suggest its potential to mitigate morbidity and enhance clinical outcomes in this high-risk population.

Keywords: COPD; Pulmonary hypertension; 6MWT; PAH-SYMPACT; Hybrid rehabilitation.

1. INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) represents a significant global health challenge and constitutes one of the leading causes of morbidity and mortality worldwide. According to data from the Global Burden of Disease (GBD) Study 2019, COPD ranks as the third leading cause of death globally, accounting for an estimated 3.23 million fatalities¹. The disease burden is disproportionately high in low- and middle-income countries, where delays in diagnosis and suboptimal management are prevalent¹.

Pulmonary hypertension (PH) is a frequent and severe complication associated with COPD, classified as Group 3 PH by the World Health Organization due to its etiological linkage with chronic lung diseases and hypoxemia². The coexistence of PH in COPD patients (COPD-PH) significantly exacerbates the clinical course, contributing to diminished exercise tolerance, impaired quality of life, and elevated mortality rates³. Notably, even mild elevations in pulmonary arterial pressure have been correlated with adverse prognosis and an accelerated progression to right ventricular failure⁴.

The pathophysiology of COPD-associated PH involves multiple mechanisms, including chronic hypoxic pulmonary vasoconstriction, inflammation-driven vascular remodeling, destruction of the pulmonary capillary bed secondary to emphysema, and endothelial dysfunction^{5,6}. Accurate diagnosis remains challenging due to overlapping clinical manifestations and limited availability of definitive diagnostic modalities such as right heart catheterization⁷. Although echocardiography is widely utilized as a non-invasive screening tool, its diagnostic precision is limited⁸.

Patients with COPD-PH often experience compounded physical impairments including severe dyspnea, skeletal muscle weakness, decreased peripheral oxygen utilization, and poor exercise capacity⁹. These physical limitations are frequently accompanied by emotional distress, depression, and social withdrawal, which further deteriorate the patient's overall quality of life¹⁰. Although pharmacologic treatments, such as bronchodilators, anti-inflammatory agents, and supplemental oxygen, remain central to disease management, they offer limited efficacy in reversing muscle dysfunction or restoring physical performance^{11,12}.

In recent decades, pulmonary rehabilitation (PR) has emerged as a cornerstone intervention in COPD care, demonstrating improvements in exercise tolerance, dyspnea perception, and health-related quality of life (HRQoL)¹³. Standard PR programs, typically delivered in clinical settings, consist of supervised aerobic and resistance training, breathing retraining, and patient education¹⁴. However, access to these programs is often hindered by logistical, financial, and geographical barriers, leading to poor adherence and underutilization, especially among individuals with advanced disease and mobility constraints¹⁵.

Hybrid rehabilitation models, which incorporate both supervised in-person sessions and home-based training components, have been developed to address these barriers and increase accessibility while maintaining clinical efficacy¹⁶. This blended approach allows for individualized exercise prescription, remote monitoring, and increased patient engagement, which can be particularly beneficial in populations at high risk for decompensation and functional decline¹⁷. Evidence suggests that hybrid rehabilitation can lead to sustained improvements in physical function, reduce hospitalization rates, and improve psychosocial outcomes by encouraging autonomy and self-efficacy^{18,19}.

Despite the growing body of evidence supporting hybrid rehabilitation in COPD management, data specific to its efficacy in patients with coexistent pulmonary hypertension remain scarce. Therefore, this study aims to investigate the effect of hybrid mode rehabilitation on functional outcomes and quality of life in Stage 3 COPD patients with pulmonary hypertension, with the goal of establishing a feasible and effective rehabilitation framework for this vulnerable subgroup.

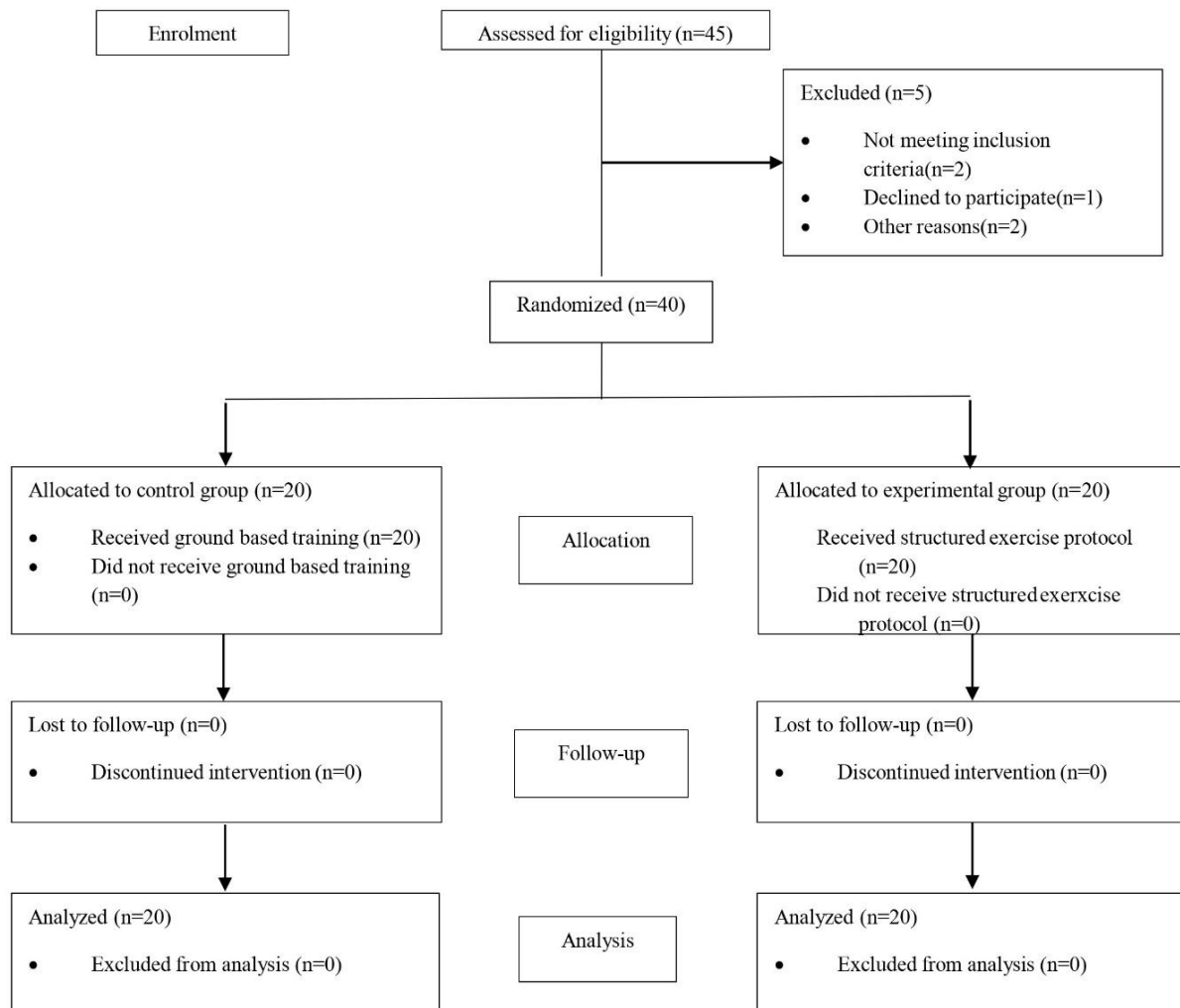
2. METHODOLOGY

This was a prospective, single-blind, randomized clinical trial, which recruited patients with COPD with PH diagnosis on the basis of ECHO finding attending a tertiary care university teaching hospital between March 2023 and March 2025. Patients who were diagnosed to have COPD along with PH (of either sex), age between 40-70 years, stable on medical therapy, and having a tricuspid regurgitant velocity 3.4 m/s with or without right ventricular dysfunction on transthoracic echocardiography were screened for inclusion. Patients with Chronic thromboembolism, left ventricular failure with ejection fraction < 40%, Obstructive sleep apnea, Patients with neuromuscular complications limiting rehabilitation, Coronary artery disease, Arrhythmias, Anemia, Renal and Liver disease patients were excluded from the study. Participants fulfilling criteria for inclusion and those consenting to participate were included into the study. The university ethics committee approved the study protocol, and all participants provided written informed consent.

A total of 45 patients were enrolled into the study. Among them only 40 patients completed the protocol. They were randomly allocated to receive ground-based walking (control group) or a hybrid rehabilitation program (experimental group), for 12 weeks. Details of these interventions are provided in the supplemental material. In addition to these interventions, both groups of patients also received a patient education, which has been shown to improve awareness of benefits of exercise in COPD-PH. The experimental group received a combined exercise protocol i.e. institutional along with home-based exercise program that was modified from a program used for patients with heart failure²⁰. The allocation was performed by a person from an external source who is not involved in the study and using block randomization of varying block sizes to minimize bias. At entry into the study, a baseline evaluation of demographic parameters and outcomes was performed. Functional capacity was assessed using the 6-min walk test (6MWT) as per the standard recommendations, in which the participant was asked to walk as far as possible in 6 min on a 30-m walk way before assessment, vitals were assessed, and the patient was made to perform the test, after providing detailed instruction and demonstration. Vitals were monitored continuously during the test, and no change to prescribed medications was made^{21,22}. Considering the possibility of adverse events during the 6MWT,²³ the test had a therapist walk behind the patient while continuously monitoring all vital signs. VO_2 Max was calculated using the formula depending on the value of 6MWT i.e. $VO_{2max} (mL/kg/min) = 12.701 + (0.06 \times 6\text{-minute walk distance}_m) - (0.732 \times \text{body mass index}_{kg/m^2})$ ²⁴. QoL and functional outcomes were assessed using the one day version of PAH-SYMPACT questionnaire. Patients in the intervention arm were provided an exercise log book to ensure they remained adherent to the program (i.e., performed exercises on at least 3 days of the week at home) for the 12-week duration. All outcomes were reassessed at the end of 12 weeks.

Sample size was calculated based on the study by Babu et al.²⁰ and a hybrid rehabilitation study in heart failure, aiming to detect a 35.55-meter difference in the 6MWT with a 30% attrition rate. The minimum sample size per group was 18, with 80% power and 95% confidence. Data analysis was conducted using SPSS version 22.0, with demographics summarized using descriptive statistics. Paired and unpaired t-tests were used to analyze dependent and independent variables, respectively, following normality testing with the Kolmogorov-Smirnov test.

FIGURE NO.1- Flow of participants using CONSORT Flow Diagram



3. RESULTS

A total of 45 participants were enrolled into the study, of which 40 completed the 12-week hybrid rehabilitation intervention. At entry into the study, there were no significant differences between demographic characteristics (Table 1). At the end of 12 weeks, the hybrid rehabilitation group demonstrated a statistically and clinically significant improvement in 6MWT performance compared to the control group (Mean Difference = -45.49 m; $p < 0.001$) (Table 2). An Independent t test was run to determine the effect of hybrid exercise training on postintervention outcomes (i.e., 6MWD and QOL) after controlling for various preintervention covariates (Table 3). For 6MWD, the experimental group demonstrated a significant improvement (mean difference = 45.50 meters, $t(38) = -4.675$, $p < 0.001$). The experimental group found an improvement of 53.76 m versus 2.5 m in the control group ($p < 0.001$). For VO_2 Max, although the experimental group showed a numerical increase in VO_2 Max from baseline, the post-intervention comparison between the experimental and control groups did not reach statistical significance. The mean difference between groups was 1.07 mL/kg/min ($t(38) = 0.649$, $p = 0.520$). For QOL, the experimental group demonstrated significantly greater improvements in certain domains of the PAH-SYMPACT compared to the control group. There was a statistically significant reduction in cardiopulmonary (CP) symptoms ($t(38) = 3.646$, $p < 0.001$; 95% CI = 1.179 to 4.121) and physical impact ($t(38) = 2.971$, $p = 0.005$; 95% CI = 1.020 to 5.380) in the experimental

group. The total mean PAH-SYMPACT score also showed significant improvement in the experimental group compared to controls ($t(38) = 2.870$, $p = 0.007$; 95% CI = 0.552 to 3.198). However, no statistically significant differences were found between groups in cardiovascular (CV) symptoms ($t(38) = 1.598$, $p = 0.118$) or cognitive impact ($t(38) = 1.137$, $p = 0.263$). No adverse events or fatalities were observed during the study. Adherence to the program was consistent.

Table 1 Comparison of baseline (pretest) descriptive statistics between control and experimental group using Chi-square test (χ^2) for categorical data and independent t test (t value) for continuous variables

Variables	Control (n =20)	Experimental (n = 20)	t/ χ^2	p value
Age, mean (SD)	61.15±5.89	63.35±7.16	-1.06	0.295
BMI, mean (SD)	23.55±1.34	23.92±1.74	-0.751	0.457
Sex, n%				
Female	08 (40)	11 (55)	0.902	0.342
Male	12 (60)	09 (45)		
Occupation, n%				
Farmer	14 (70)	07 (35)	6.93	0.074
Housewife	04 (20)	11 (55)		
Industry worker	02 (10)	01 (5)		
Retired	0 (0)	01 (5)		
2DEcho SPAP mmHg	28.05±1.82	28.15±1.79	0.010	1.0
TLC % predicted	107.80±11.64	111.45±14.61	-0.874	0.38
FVC % predicted	71.90±12.52	69.45±10.60	0.67	0.51
FEV1 % predicted	42.35±6.44	43.0±5.64	-0.339	0.736
DLCO	31.65±9.34	36.15±4.60	-1.93	0.061
6MWT	289.75±19.66	284.0±39.18	0.587	0.561
VO2Max	16.29±6.94	12.23±2.49	2.46	0.018
PAHSYMPACT CP symptoms	8.10±1.99	8.30±2.10	0.312	0.757
PAHSYMPACT CVS symptoms	3.75±1.80	3.65±1.84	0.173	0.863
PAHSYMPACT Phy Imp	13.75±3.57	14.15±3.57	0.354	0.725
PAHSYMPACT Cog Imp	4.25±2.35	5.40±2.26	-1.157	0.124
PAHSYMPACT Total average score	7.46±2.11	7.87±2.21	-0.603	0.550

Data are expressed as mean ± SD, BMI: Body Mass Index; SPAP: Systolic Pulmonary Artery Pressure; PFT: Pulmonary Function Test; TLC: Total Lung Capacity; FVC: Functional Vital Capacity; FEV1: Forced Expiratory capacity in 1 second; DLCO: diffusing capacity of the lungs for carbon monoxide; 6MWT: 6 Minute Walk Test; CP: Cardiopulmonary; CV: Cardiovascular; Phy Imp: Physical Impact; Cog Imp: Cognitive Impact.

Table 2 Within the group comparison of pre-test and post-test data of the outcome measures**Table 2a: Control group**

Paired Samples Statistics ^a									
a. Group = Control									
	Pre-Test		Post-Test			95%CI		t value	p value
Variables	Mean	SD	Mean	SD	Mean diff	Lower bound	Upper bound		
6MWT	289.8	19.7	292.3	18.0	-2.51	-6.9901	1.9701	-1.173	0.255
VO2Max	16.3	6.9	16.5	6.9	-0.23	-0.47787	0.01779	-1.943	0.037
PAHSYMPACT CP symptoms	8.1	2.0	8.1	2.2	0.00	-0.429	0.429	0.000	1
PAHSYMPACT Cv symptoms	3.8	1.8	3.5	1.6	0.25	-0.118	0.618	1.422	0.171
PAHSYMPACT Phy Impact	13.8	3.6	14.0	3.3	-0.20	-0.819	0.419	-0.677	0.507
PAHSYMPACT Cog Impact	4.3	2.4	4.3	2.3	0.00	-0.340	0.340	0.000	1
PAHSYMPACT Total mean Score	7.5	2.1	7.5	2.0	0.01	-0.27529	0.30029	0.091	0.929

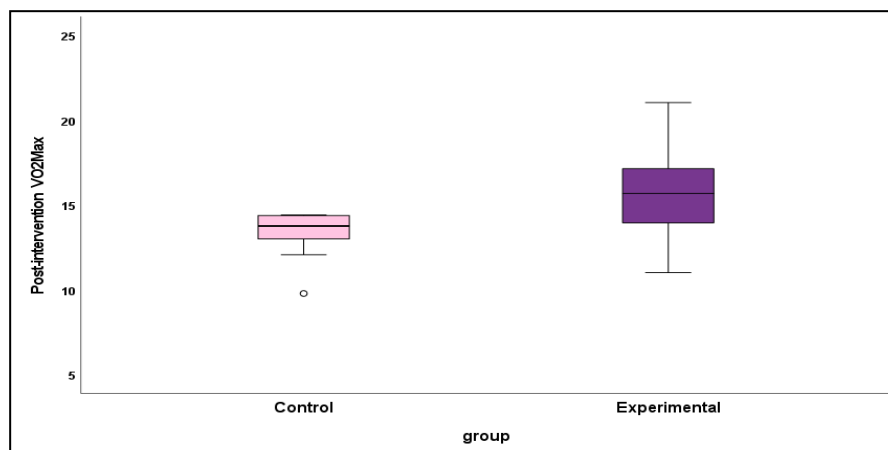
Table 2b: Experimental group

Paired Samples Statistics ^a									
a. Group = Experimental									
	Pre-Test		Post-Test			95%CI		t value	p value
Variables	Mean	SD	Mean	SD	Mean diff	Lower bound	Upper bound		
6MWT	284.00	39.18	337.76	39.62	-53.76	-73.53	-33.98	-5.69	0.000
VO2Max	12.2306	2.50	15.46	2.49	-3.23	-4.41	-2.04	-5.69	0.000
PAHSYMPACT CP symptoms	8.30	2.05	5.45	2.35	2.85	2.04	3.66	7.39	0.000
PAHSYMPACT CV symptoms	3.65	1.84	2.70	1.56	0.95	0.46	1.44	4.05	0.001
PAHSYMPACT Phy. Impact	14.15	3.57	10.75	3.51	3.40	1.65	5.15	4.06	0.001
PAHSYMPACT Cog. Impact	5.40	2.26	3.40	2.39	2.00	1.23	2.77	5.41	0.000

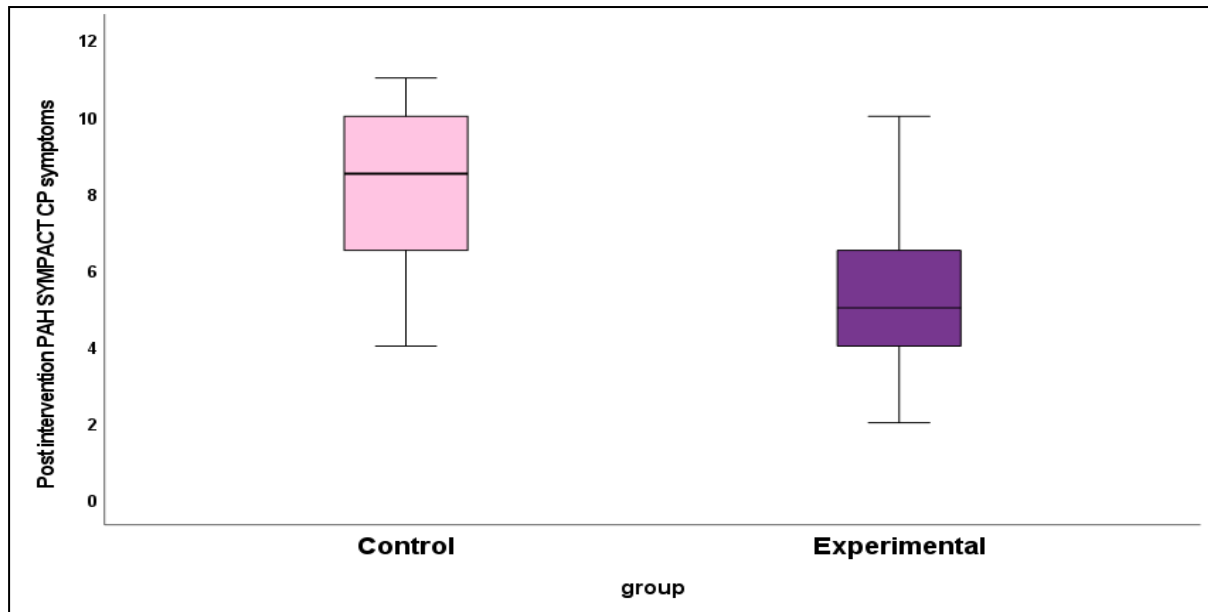
PAHSYMPACT			5.58	2.16	2.30	1.48	3.12	5.86	0.000
Total mean Score	7.8750	2.21							

Table 3 Comparison of post-intervention values of outcome measure between control group (n =20) and experimental group (n =20)

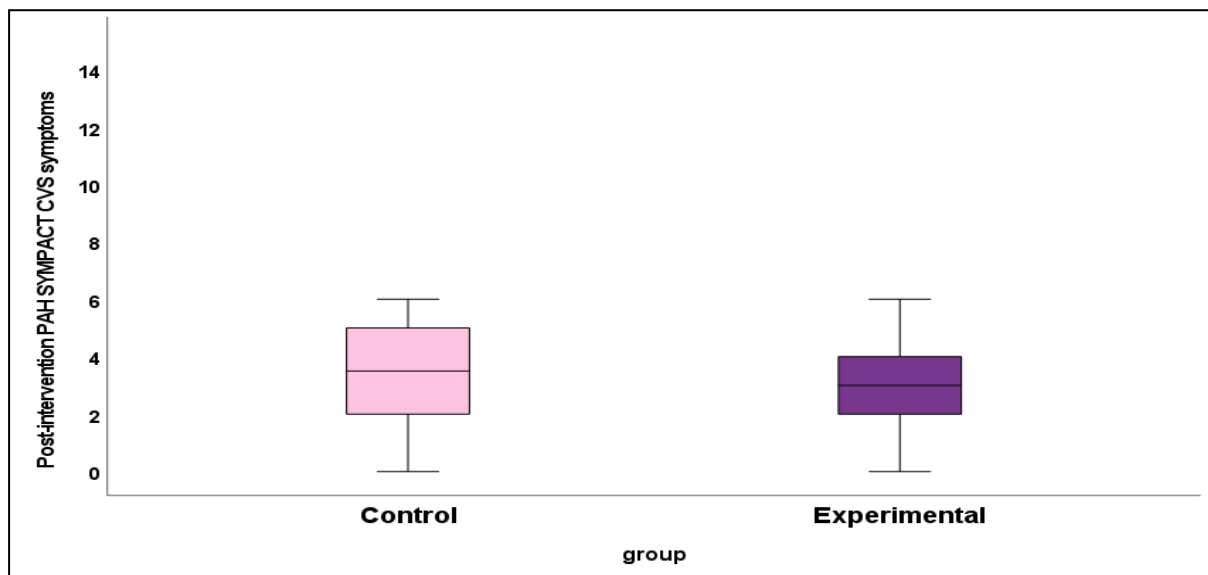
Independent Samples Test								
Variables	Levene's Test for Equality of Variances	t-test for Equality of Means					Sig. (2-tailed)	
		F	t	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference		
						Lower		Upper
6 MWT	5.362	-4.675	-45.4950	9.7310	-65.1943	-25.7957	< 0.001	
VO2Max	11.087	0.649	1.06938	1.64675	-2.26430	4.40306	0.520	
PAHSYMPACT CP symptoms	0.078	3.646	2.650	0.727	1.179	4.121	< 0.001	
PAHSYMPACT Cv symptoms	0.605	1.598	0.800	0.501	-0.213	1.813	0.118	
PAHSYMPACT Phy Impact	0.077	2.971	3.200	1.077	1.020	5.380	0.005	
PAHSYMPACT Cog Impact	0.011	1.137	0.850	0.748	-0.664	2.364	0.263	
PAHSYMPACT Total mean Score	0.009	2.870	1.87500	0.65336	0.55235	3.19765	0.007	



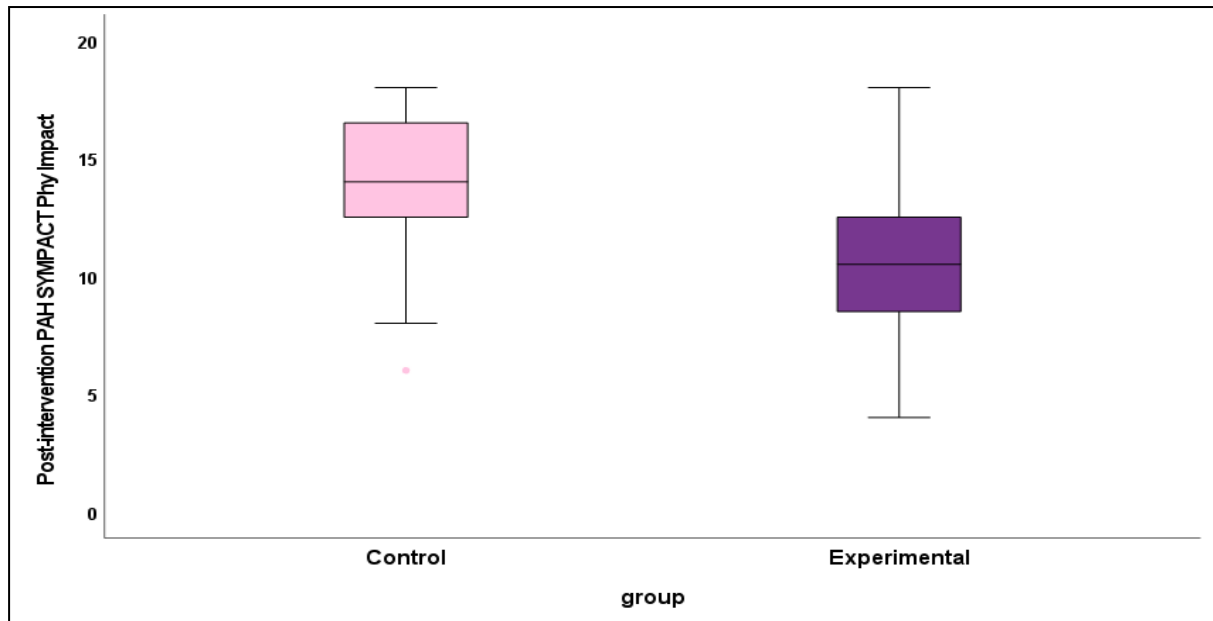
Graph 1: Comparison of Post-Intervention VO₂ Max between control and experimental groups.



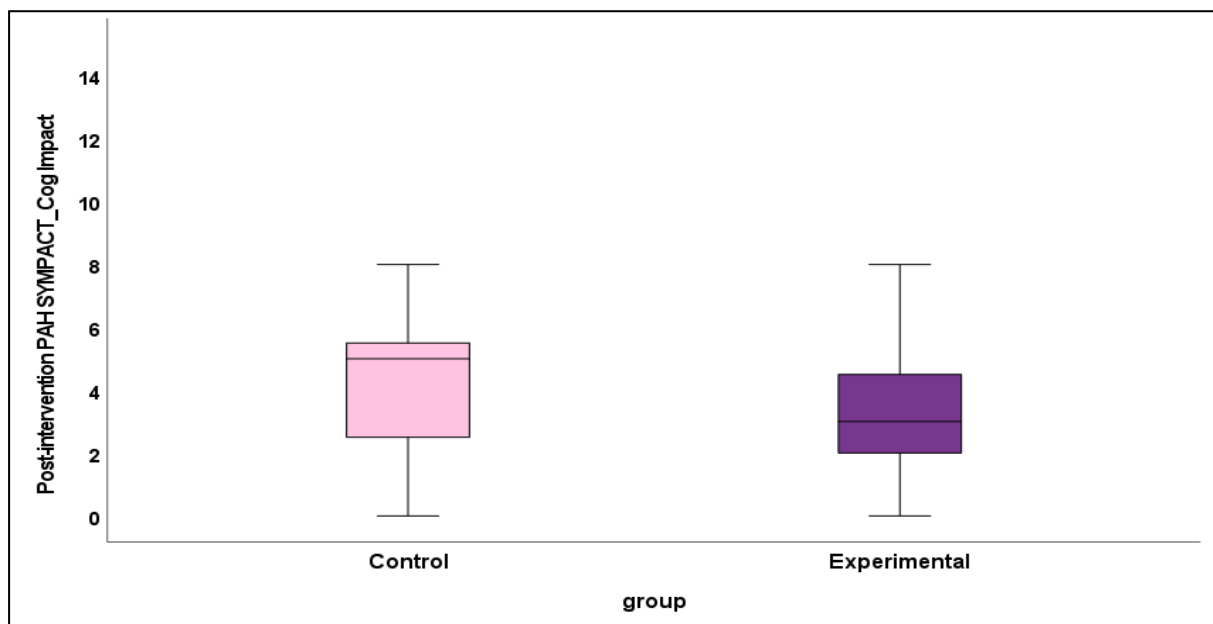
Graph 2: Comparison of Post-Intervention PAH-SYMPACT Cardiopulmonary symptoms between control and experimental groups.



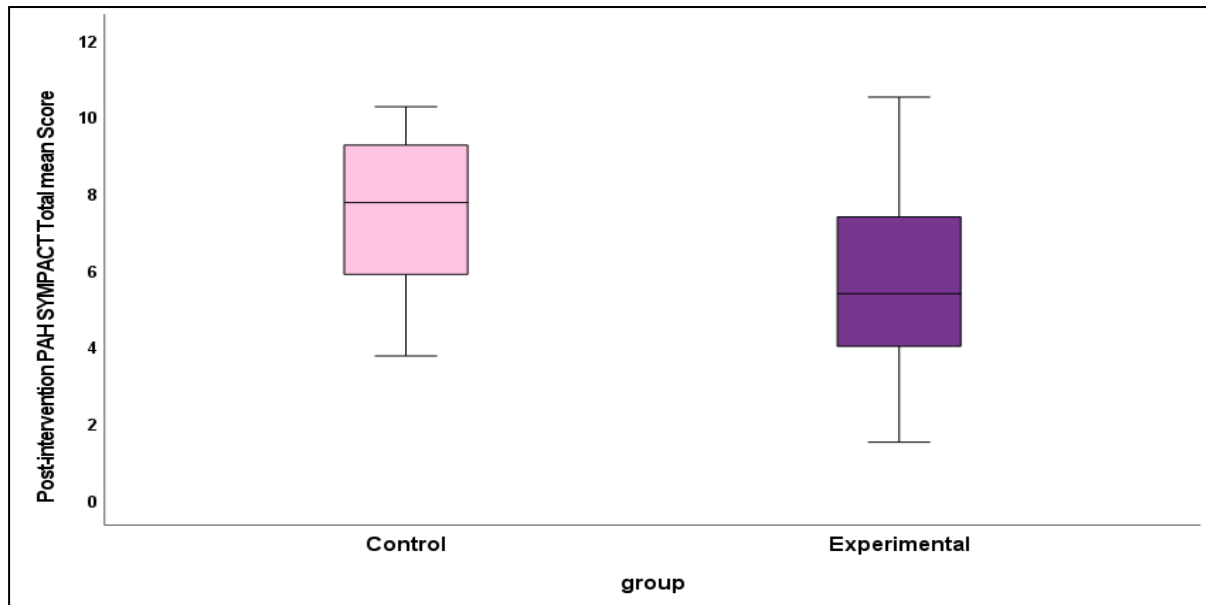
Graph 3: Comparison of Post-Intervention PAH-SYMPACT Cardiovascular symptoms between control and experimental groups.



Graph 4: Comparison of Post-Intervention PAH-SYMPACT Physical symptoms between control and experimental groups.



Graph 5: Comparison of Post-Intervention PAH-SYMPACT Cognitive symptoms between control and experimental groups.



Graph 6: Comparison of Post-Intervention PAH-SYMPACT Total Mean score between control and experimental groups.

4. DISCUSSION

The result of this prospective, randomized controlled, and single blinded study on the effect of hybrid rehabilitation in patients with stage 3 COPD along with pulmonary hypertension confirm that hybrid rehabilitation improves oxygen consumption and alleviates dyspnea in COPD patients with pulmonary hypertension, who are on stable medical target therapy. Additionally, the exercise capacity and peak VO₂ were increased along with improvement in quality of life.

In this study, we demonstrated that our hybrid rehabilitation is safe for COPD-PH patients, since no adverse events occurred during the 12-weeks training period. Moreover, there was a positive effect on primary outcome parameters, including exercise capacity measured by 6MWT and VO₂ Max, as well as QOL measured by the PAH-SYMPACT Questionnaire.

The hybrid rehabilitation group demonstrated a statistically and clinically significant improvement in 6MWT performance compared to the control group (Mean Difference = -53.76 m; $p < 0.001$). This indicates a notable enhancement in submaximal functional exercise capacity and physical endurance, which are often compromised in patients with COPD and pulmonary hypertension due to ventilatory limitations, gas exchange inefficiency, and peripheral muscle deconditioning. This finding is in line with a systematic review by Puhan et al. (2011), which found that structured pulmonary rehabilitation improved 6MWT by an average of 44–56 meters in moderate to severe COPD patients²⁵. Ferreira et al. (2015) reported similar improvements in PH patients undergoing exercise training, highlighting that such interventions can alleviate exercise intolerance by improving skeletal muscle oxidative capacity and cardiovascular response²⁶. In addition to surpassing the 44-meter minimal clinically important difference (MCID) reported by Babu et al. (2019)²⁰, this improvement also demonstrates the effectiveness of combining home-based and inpatient rehabilitation in this particular population, which has not been well-represented in interventional trials in the past. This increase is in line with findings from Yilmaz et al. (2019)²⁷, who reported that individuals with pulmonary hypertension improved by 53 meters following 12 weeks of intensive training. A similar improvement (96 m) was noted by Mereles et al. (2006)²⁸ with a comprehensive program that included interval cycling, resistance, and respiratory training over a period of 15 weeks. Although these studies included general PH populations, not exclusively COPD-PH, they support the conclusion that structured, multimodal training can substantially enhance exercise tolerance. In contrast, individuals undergoing outpatient pulmonary rehabilitation showed a smaller but still significant increase of 12.2 meters, according to Koudstaal et al. (2019)²⁹, suggesting that the setting and length of exercise may influence results. In their evaluation of pediatric PH patients, Zöller et al. (2017)³⁰ discovered that after 16 weeks of home-based training, treadmill performance improved by 30.6%, confirming the viability and efficacy of remote rehabilitation. By incorporating both inpatient and home-based components, our study expands on these findings by offering accessibility and flexibility without sacrificing effectiveness. Interestingly, Aslan et al. (2020)³¹ used threshold inspiratory muscle training with PH patients, and after 8 weeks, the 6MWT distance increased by 23.6 meters. This highlights the importance of respiratory training in increasing physical capacity, even though it is less than the gains shown in our mixed program. Significant improvements in 6MWT were also observed with the personalized remote physiotherapy intervention by Butane et al. (2022)³², indicating that customized home therapies can be just as effective as conventional in-person modalities.

Importantly, patients with COPD-PH are known to have significantly reduced baseline exercise capacity compared to COPD patients without PH. Blanco et al. (2009)³³ and Kalkan et al. (2020)³⁴ found that COPD-PH patients walked approximately 100 meters less on average than their non-PH counterparts. This reduction is attributed to increased pulmonary vascular resistance, impaired gas exchange, and right ventricular dysfunction^{35,36}. Therefore, the improvements observed in our study are particularly meaningful given the greater functional limitations of this population. Furthermore, systemic skeletal muscle dysfunction and impaired peripheral oxygen utilization—both exacerbated in COPD-PH—are well-recognized contributors to exercise intolerance^{35,37}. Our hybrid rehabilitation approach likely targeted these mechanisms through aerobic and resistance components, resulting in enhanced muscular efficiency and exercise performance. The significance of our findings is further supported by the systematic review conducted by Satyamurthy et al. (2023)³⁸. The 53-meter gain in our cohort closely matches the average 6MWT gain of 68.7 meters reported in 28 studies in PH patients following exercise training³⁸. Furthermore, the evaluation acknowledged that hybrid regimens, however less common, might provide benefits in terms of accessibility, flexibility, and adherence, particularly for people with significant respiratory impairments.

The observed improvements can be further explained through Wagner's oxygen transport cascade theory (1996), which postulates that enhancing peripheral muscle oxygen extraction and delivery—through repeated, moderate-intensity exercise—optimizes systemic oxygen utilization and contributes to increased exercise capacity³⁹. These physiological adaptations are likely potentiated in a hybrid model where regular professional supervision ensures safety and progression while at-home sessions promote frequency and patient autonomy⁴⁰.

Our study is one of the few to evaluate the effectiveness of a hybrid rehabilitation model in a COPD-PH cohort, demonstrating a clinically significant improvement in 6MWT distance. These results are in line with, and in some cases exceed, those reported in other PH and COPD rehabilitation studies. Our findings emphasize the need for continued development and implementation of tailored, multimodal rehabilitation strategies to improve the functional capacity and quality of life in this complex patient population.

Although the within-group improvement in VO_2 Max was significant in the experimental group, the between-group difference did not reach statistical significance ($p = 0.520$). This may be attributed to variability in baseline values, shorter intervention duration, or limited aerobic training intensity in the home-based sessions.

VO_2 Max, a marker of cardiorespiratory fitness, is typically responsive to structured, high-intensity interventions. Vogiatzis et al. (2002) showed that high-intensity interval training significantly increased VO_2 Max in COPD patients⁴¹. However, in hybrid settings, especially with less rigorous control over exercise intensity at home, gains in VO_2 Max may not be robust enough to yield inter-group significance⁴². According to the American College of Sports Medicine (2020), central adaptations affecting VO_2 Max—such as stroke volume and oxygen delivery—require sustained and progressively overloaded training, typically supervised in a clinical setting⁴³. Additionally, in PH patients, right ventricular dysfunction and vascular stiffness may limit aerobic adaptation, as highlighted by Grunig et al. (2011)⁴⁴.

A significant reduction in cardiopulmonary symptoms was recorded in the experimental group (Mean Difference = 2.65; $p < 0.001$), reflecting decreased dyspnea, wheezing, and chest tightness. These improvements likely stem from enhanced respiratory muscle efficiency and improved ventilatory mechanics achieved through aerobic and breathing exercises.

Spruit et al. (2013) emphasized that pulmonary rehabilitation desensitizes patients to dyspnea, increases ventilatory threshold, and reduces dynamic hyperinflation¹³. This effect is explained by O'Donnell's desensitization theory (2007), which states that graded physical exposure reduces cortical sensitivity to respiratory discomfort⁴⁵. The repetitive, structured nature of hybrid programs reinforces this process, leading to improved symptom perception.

Though there was a reduction in cardiovascular symptoms (e.g., palpitations, dizziness) in the intervention group, it did not reach statistical significance ($p = 0.118$). This may be due to the multifactorial etiology of cardiovascular symptoms in PH, which are less directly impacted by pulmonary rehabilitation alone⁴⁶. According to Galiè et al. (2015), the management of cardiovascular symptoms in PH requires pharmacological agents such as endothelin receptor antagonists (ERAs) and phosphodiesterase-5 inhibitors, along with supervised training⁴⁷. The lack of significance could also be attributed to variable baseline cardiac function, medication adherence, or the limited cardiovascular loading during home-based sessions.

The physical impact domain significantly improved in the experimental group (Mean Difference = 3.20; $p = 0.005$), indicating enhanced ability to perform activities of daily living (ADLs) such as walking, housework, or climbing stairs.

McCarthy et al. (2015) noted that pulmonary rehabilitation consistently improves physical performance, especially when the exercise regimen includes strength, balance, and mobility components⁴⁸. This outcome is further supported by Nagi's Disablement Model (1991), which explains that functional limitations can be reversed by targeted rehabilitation aimed at strengthening physical capacities and reducing environmental barriers⁴⁹.

The cognitive impact domain, while showing improvement in the hybrid group, did not reach statistical significance in inter-group comparison ($p = 0.263$). This outcome may reflect the relatively short intervention period, limited cognitive retraining components, or a ceiling effect in patients with already preserved cognition⁵⁰. Cognitive impairment in COPD is well-documented and is associated with hypoxemia, systemic inflammation, and medication side effects⁵¹. Yohannes et al. (2000)

highlighted that behavioral interventions, oxygen supplementation, and longer-duration therapy are more likely to impact cognition⁵².

The total PAH-SYMPACT score significantly favored the hybrid group (Mean Difference = 1.875; $p = 0.007$), indicating a comprehensive reduction in the overall burden of disease. This score aggregates the subscales and reflects global improvements in symptoms, physical limitations, and psychosocial well-being. The holistic improvements align with Wagner's Chronic Care Model (1996), which advocates for proactive, patient-centered, and community-linked care systems for chronic illnesses³⁹. Hybrid rehabilitation aligns with this model by combining clinic-based supervision with flexible, home-based support, promoting sustainability and empowerment⁵³.

Our results are in line with those of Bailey et al. (2024)⁵⁴, which was among the first to employ the PAH-SYMPACT method to evaluate HRQoL in PH-COPD. In their study, PH-COPD patients demonstrated significantly worse Physical Impact (PI) scores compared to PAH patients (1.79 vs. 1.13, $p < 0.001$) and overall higher (worse) PAH-SYMPACT scores (1.19 vs. 0.91, $p = 0.03$). The findings of Bailey et al.⁵⁴ highlight the increased physical and emotional restrictions experienced by PH-COPD patients, despite the fact that they mainly conducted a cross-sectional comparison without an intervention. In contrast, our interventional study demonstrates that despite these baseline challenges, HRQoL can improve with structured therapy, especially in domains related to participation, independence, and daily function.

Notably, the PAH-SYMPACT was not validated specifically for the PH-COPD population, according to Bailey et al.^{54,55} However, our research demonstrates its usefulness in this instance, especially for monitoring changes in perceived limitations induced by interventions. The non-significant change in the "Symptoms" category may reflect both the chronic and progressive nature of COPD and the limited sensitivity of the tool in detecting short-term changes in symptom severity—especially in smaller sample sizes like ours. This echoes findings from McKenna et al.⁵⁶, who also reported that the "functioning" category of the CAMPHOR questionnaire did not capture significant change in a similarly small pulmonary rehabilitation group. In terms of functional benefit, our results also resonate with studies by Mainguy et al. (2010)⁵⁷ and Gabbay et al. (2010)⁵⁸, which found that pulmonary rehabilitation improved exercise capacity, dyspnea, and QoL in PH patients, including those with overlapping chronic lung disease. Although those studies focused more broadly on PAH and mixed groups, the similarity in outcomes supports the generalizability of pulmonary rehabilitation strategies across different PH subtypes, including PH-COPD.

Our findings further support the hypothesis that targeted non-pharmacological interventions, such as structured rehabilitation, play a crucial role in the management of PH-COPD. As Howard et al. (2012)⁵⁹ and Spruit et al. (2013)¹³ suggest, pulmonary rehabilitation offers not only physiological benefits but also psychological and social gains, which are particularly meaningful for patients facing a dual burden of respiratory and cardiovascular disease.

The increase in 6MWT reflects enhanced skeletal muscle function and ventilatory efficiency⁶⁰. COPD-PH patients typically exhibit peripheral muscle atrophy, reduced oxidative enzyme capacity, and a shift from fatigue-resistant Type I fibers to glycolytic Type II fibers, which contribute to early fatigue during exertion⁶¹. Hybrid rehabilitation that combines aerobic and resistance training promotes muscle fiber type reversal and increases capillary density and mitochondrial content, improving endurance and delaying fatigue⁶¹. Additionally, exercise reduces dynamic hyperinflation, thereby improving thoraco-pulmonary mechanics and lowering the work of breathing during activity^{45,62}.

Reductions in dyspnea are attributed to improved inspiratory muscle strength, reduced respiratory drive, and better ventilatory efficiency⁴⁵. Regular aerobic training also improves ventilation-perfusion (V/Q) matching and gas exchange, thereby reducing hypoxemia and exertional desaturation⁶³. Furthermore, desensitization to dyspnea through graded exposure helps in modulating central perception of breathlessness¹³. Resistance training counteracts disuse atrophy and corticosteroid-induced muscle catabolism by increasing muscle cross-sectional area and neuromuscular efficiency¹³. These gains enable patients to perform activities of daily living with reduced effort, improving functional independence⁶¹. Improved aerobic capacity also increases oxygen delivery and utilization during physical tasks, reducing fatigue^{62,64}. Exercise-induced improvements in cerebral perfusion may mitigate cognitive impairment seen in COPD and PH populations⁶⁵. Exercise also reduces systemic inflammation (e.g., IL-6, TNF- α), which contributes to neuroinflammation and cognitive decline⁶⁶. Better sleep quality and mood stabilization through physical activity indirectly benefit cognitive function and psychological well-being¹³.

5. CONCLUSION

The randomized controlled trial demonstrates that a hybrid rehabilitation protocol—combining center-based and home-based physiotherapy—yields superior improvements in both functional capacity and quality of life in Stage 3 COPD patients with pulmonary hypertension compared to conventional rehabilitation. Statistically significant gains in 6-minute walk distance (6MWD), VO₂ max, and PAH-SYMPACT scores in the hybrid group underscore the potential of a structured, blended approach to enhance clinical outcomes in this high-risk population. These findings advocate for the integration of hybrid rehabilitation models into standard care frameworks for COPD-PH, with further multi-center studies recommended to validate long-term efficacy and scalability.

6. LIMITATIONS

Study sample was small; PH was not confirmed with right heart catheterization. Instead, we calculated mPAP, which yields results comparable to catheterization. In addition, certain information was not available to us such as current smoking status, laboratory values, imaging and medication use.

7. FUTURE RECOMMENDATION

Future studies should aim to include larger, more diverse populations across multiple centers to strengthen the generalizability of the findings. Stratification based on disease severity, age, and comorbidities may provide more nuanced insights into the effectiveness of hybrid rehabilitation.

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