



Pulmonary rehabilitation for interstitial lung disease: A26 Systematic Review and Meta-analysis – An Update

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Introduction

Interstitial Lung Diseases (ILD) include more than 200 parenchymal pulmonary disorders, from which the majority are considered rare diseases [1]. These disorders can result from some known etiological factors, such as environmental and occupational exposure or auto-immune conditions. Nevertheless, the most common variant of ILDs is the idiopathic type [2]. The overall pathophysiological manifestations in ILD patients are persistent inflammation and/or fibrosis within the lung's parenchyma[3-4], which may compromise its normal mechanical and structural properties [3]. Consequently, dyspnea and intolerance to exercise [4] are the main symptoms, and generally there is a decrease in the patient's quality of life [5].

Pulmonary Rehabilitation (PR) is a non-pharmacological therapy, which consists of a group of physical exercises that aim to alleviate some ILDs symptoms [6]. It has been largely recommended for patients with chronic pulmonary diseases [6] and there are evidences of beneficial effects of PR in individuals with ILDs [7]. However, the literature lacks studies that try to assess the safety and efficacy of PR in ILD patients. This work aims to update previous systematic reviews and meta-analyses about PR effects in the health condition in cases of ILD.

Methods

The research was carried out in the following electronic databases: MEDLINE, Science Direct, Google Scholar and ISI Web of Science. Five articles resulting from the previous systematic review and meta-analysis were included [8-12]. To perform this update, five more articles were found, from 2015 to 2021. However, only three of them were considered [13-15]. The inclusion and exclusion criteria are in agreement with the previous meta-analysis.

Two groups of participants were considered: participants with ILD treated with PR (intervention group) and participants with ILD not submitted to PR (control group). The control group could also be submitted to other therapies. The clinical parameters explored in this update were: six-minute walk test (6MWT, 216 participants in the PR group and 189 in the control group), dyspnea (188 participants in the PR group and 162 in the control group) and quality of life (QoL, 150 participants in the PR group and 142 in the control group). All the outcomes were measured before and immediately after the intervention, in order to compare the changes between groups. Mean differences (MD) and standardized mean differences (SMD) were used to quantify the effect of PR in each outcome. Heterogeneity was assessed using Cochran's Q test and I2. Furthermore, sensitivity analysis were made to complement the original meta-analysis.

All statistical analyses were performed using R (version 4.1.0).

Results

Heterogeneity was assessed for each outcome. Dyspnea was the only outcome that showed significant heterogeneity ($X^2 = 9.71$, p = 0.05, $I^2 = 59\%$). ILD patients from the PR group improved in all the clinical parameters compared with the control group. The MD between both groups regarding 6MWT improvement was 42.13 meters (95% CI 29.42 to 54.83, p<0.01), in favor of the PR group. The SMD concerning the amelioration of dyspnea and QoL scores were -0.50 (95% CI -0.69 to -0.30, p<0.01) and 0.48 (95% CI 0.11 a 0.85, p=0.03), respectively.

Sensitivity analysis demonstrated consistency in the overall effect in favor of the PR group, regarding the 6MWT and Dyspnea (Figure 1 and 2, respectively). The results concerning QoL were significant, mainly because of the presence of Holland 2008 study (Figure 3), since its omission leads to the loss of significance in the overall effect (SMD = 0.29, 95% CI - 0.22 to 0.80).

Keywords:

Dyspnea, Interstitial lung disease, Pulmonary rehabilitation, Quality of life, Six-minute walk test

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EXTENDED ABSTRACT

Study	Mean Diffe	erence	MD	95%-CI
Omitting Holland, 2008			43.93	[29.73; 58.14]
Omitting Nishiama, 2008			41.70	[28.31; 55.09]
Omitting Perez-Bogerd, 2011			41.72	[28.69; 54.75]
Omitting Vainshelboim, 2013			38.68	[25.42; 51.93]
Omitting Jackson, 2014			43.80	[30.78; 56.83]
Omitting Jarosch, 2020			40.22	[26.89; 53.55]
Omitting Dowman, 2017			50.15	[34.75; 65.54]
Omitting Wang, 2021		-	38.95	[25.48; 52.42]
Fixed effect model			42.13	[29.42; 54.83]
	-60 -40 -20 0	20 40 60		

Figure 1 - Sensitivity analysis for the omission of an individual study regarding the 6MWT outcome.

Study	Standardised Mean Difference	SMD	95%-Cl
Omitting Holland, 2008 Omitting Nishiama, 2008 Omitting Vainshelboim, 2013 Omitting Jarosch, 2020 Omitting Dowman, 2017 – Omitting Wang, 2021	*	-0.48 [-0 -0.51 [-0 -0.44 [-0 -0.47 [-0 -0.67 [-0 -0.48 [-0	.70; -0.27] .72; -0.30] .65; -0.24] .68; -0.26] .96; -0.38] .69; -0.26]
Fixed effect model		-0.50 [-0	69; –0.30]
	-0.5 0 0.5		

Figure 2 - Sensitivity analysis for the omission of an individual study regarding the dyspnea outcome.



Figure 3 - Sensitivity analysis for the omission of an individual study regarding the QoL outcome.

Discussion

This meta-analysis demonstrated a significant effect of PR in the improvement of ILD patients in all clinical parameters (6MWT, dyspnea and QoL) compared with the control group. These results are in agreement with the conclusions from the previous meta-analysis. However, the overall effect on QoL lost its statistical significance with the omission of Holland 2008 study. Further studies are needed to improve the robustness of these findings.

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EXTENDED ABSTRACT

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