EUROPEAN JOURNAL OF PHYSIOTHERAPY
https://doi.org/10.1080/21679169.2022.2053201

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ORIGINAL ARTICLE

The effects of reducing the frequency of long-term physiotherapy on patients with severe COPD: a Dutch multicenter study

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ABSTRACT

Purpose: To investigate if a reduction in the frequency of long term physiotherapy leads to an increase in exacerbations, prescriptions of medication and hospital admissions leads to an increase ofexacerbations, prescriptions of medication and hospital admissions in patients with chronic obstructivepulmonary disease (COPD).

Intervention: 296 adults with severe COPD (GOLD III & IV) followed a weekly physiotherapy program with a focus on endurance capacity, muscle function and education. In this study, participants were divided into two groups: a High-Frequency Group (HFG) and a Low Frequency Group (LFG).

Results: The HFG had consistent lower rates of exacerbations (LFG x̄ 4.14; HFG x̄ 2.71), prescriptions antibiotics LFG x̄ 28.63; HFG x̄ 12.64), number of hospital admissions (LFG x̄ 1.22; HFG x̄ 0.36) and days in hospital (LFG x̄ 8.85; HFG x̄ 1.36) compared to LFG. Differences between both groups (Independent samples *T*-test, $p < 0.05$) were significant for exacerbations ($p = 0.001$), antibiotic prescriptions ($p = 0.009$), hospital admissions ($p = 0.000$) and days in hospital ($p = 0.000$).

Conclusion: Reducing the frequency of long-term physiotherapy leads to significantly higher rates of exacerbations, medication use, hospital admissions and days in hospital in patients with severe COPD.

ARTICLE HISTORY
Received 4 November 2021
Accepted 4 March 2022
Published online 31 May 2022

KEYWORDS
COPD; physiotherapy; pulmonary rehabilitation; exacerbation; COPD management

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a lung disease that induces limitations in the lung airflow. COPD distinguishes two characteristics, namely bronchiolitis and emphysema. Most patients with COPD suffer from breathlessness (dyspnoea), excessive sputum production, chronic cough and limited exercise capacity [1–4]. Globally, COPD is the third leading cause of death [3]. An estimated 64 million people are diagnosed with COPD and 3 million people died as a consequence of COPD in 2004 [3,5].

In COPD management the influence of pulmonary rehabilitation (PR) is considered to be clinical of great importance [1,3]. PR can involve patient assessment, supervised exercise training, education, behaviour change, nutritional intervention and psychosocial support [3]. The cornerstone of pulmonary rehabilitation is physiotherapy (exercise training) [3]. PR reduces dyspnoea and physical fatigue [1,2]. Furthermore, improved health-related quality of life, increased patient empowerment, and reduction of anxiety and depression are reported due to PR [1]. An early initiation of PR after discharge from hospital is associated with lower mortality rates [5–20].

In The Netherlands, patients with COPD are referred to either a multidisciplinary rehabilitation centre or physiotherapy in an outpatient setting. However, there is no consensus on the optimal duration of PR and physiotherapy [1,3,16]. Ideally, the duration of PR is individually set by continued progress towards goals and benefits, however, often the duration is also influenced by the resources of the program and reimbursement [3,21,22]. Generally, longer programs, are recommended, because these are thought to produce greater gains and maintenance of benefits [3,16].

The number of sessions per week of physiotherapy included in PR varies widely. Outpatient programs commonly meet 2 or 3 sessions/week, inpatient programs are usually planned for 5 sessions/week [3,16]. In 2019, the Minister of Health, Welfare and Sports (VWS) of the Netherlands set a ceiling of 52 sessions per year of outpatient physiotherapy for patients with severe COPD [2,5,23]. This means that patients can only have one physiotherapy session each week, in contrast to more sessions allowed before this decision. To date, no studies are conducted to determine which frequency should be used to achieve the optimum effect in terms of the frequency per week of PR and physiotherapy over a 12-month period [1,3,16].

Therefore, the purpose of this study is to examine the difference in exacerbation rates between patients with severe COPD (GOLD III and IV) receiving low frequent physiotherapy versus patients receiving high frequent physiotherapy per

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week. Moreover, this study also aims to investigate the effect on medication prescriptions, hospitalisations and days of stay in a hospital for both groups. We hypothesise that reducing the frequency of long-term physiotherapy in patients with severe COPD will lead to an increase in exacerbations,medication prescriptions, hospital admissions and days of stay in hospital.

Methods

Study design and sample

This study was a prospective multicentre cohort study involving 22 physiotherapy practices in the Netherlands. The practices were recruited from May 2018 to December 2018 using the network of practices from the Dutch Physical Therapy & Science Association (PhyScience group) and social media [24]. Physiotherapists recruited patients with COPD in their practices. Recruited patients were provided with information about the study. The content of the information was about two different groups in this study. Allocation to a group by the physiotherapist (low frequency or high frequency) was dependent on the referral from a general practitioner or a lung physician and the capacity of patients to pay for extra treatment themselves. Researchers were blinded for the referrals received by physiotherapists and stated GOLD classifications and comorbidities. In the period 2018 higher frequency physiotherapy was reimbursed by the Dutch health insurance. From the first of January 2019, patients paid for the higher frequency sessions of physiotherapy themselves.

This allocation method had to be used because of the political decision for the change in reimbursement for physiotherapy in COPD from the first of January 2019 by the Ministry of Health, Welfare and Sport of the Netherlands [23]. After signing informed consent, patients were included in the study. Participation was voluntary and participants could withdraw from the study at any moment. The study was carried out in compliance with the Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects. Because the study did not fall within the remit of the Medical Research Involving Human Subjects Act (WMO) in the Netherlands, no formal medical ethical approval was required.

Procedures

In January 2019, 22 physiotherapy practices were inquired to retrospectively deliver data about the previous 12 months to the research group. The physiotherapists extracted the frequency of rehabilitation per week, the number of exacerbations, antibiotic/prednisone prescriptions, hospital admissions and days of stay in hospital from the files of their patients. From the 1st of January 2019, the prospective study started in two different groups with similar physiotherapy but with different frequencies per week. In this study, patients with average frequency physiotherapy equal or less than 1.5 times per week were included in the Low Frequency Group (LFG). Patients who received more than 1.5 times per week physiotherapy were included in the High Frequency Group (HFG). Both groups received both physiotherapy (exercise therapy) and education during each appointment. Cut off point of 1.5 times per week was chosen practically for when patients could not exactly meet the once or twice a week frequency.

Participants

To be eligible to participate, patients should have COPD stadium GOLD III or IV and should have followed physiotherapy or PR for at least 12 months prior to inclusion (to meet the long term criterion). All participants were diagnosed by a lung physician for GOLD III and IV according to the spirometry outcome and referred by a general practitioner, lung physician or lung nurse for physiotherapy. Participants were physically capable to participate in the outpatient rehabilitation. No other inclusion or exclusion criteria were used for an optimal generalisability of the study results.

Intervention

All participants received physiotherapy by their own physiotherapist in close proximity to their homes. Physiotherapy sessions were provided for an hour per session in small rehabilitation groups (2–5 patients per group). Physiotherapy was conducted according to the Dutch Guideline for Physiotherapy in COPD [25]. An outline of a rehabilitation session was discussed with each physiotherapist and contained the following goals: an increase of the exercise capacity; improved muscle function (strength/fat-free mass); education (encouragement of daily activities/stop smoking); and breathing-, sputum evacuation techniques. Dependent on the group allocation, patients received less than 1.5 times (LFG) or more than 1.5 times (HFG) physiotherapy per week.

Outcome measures and data collection

Physiotherapists were asked to accurately report the outcome measures of this study in patient files for maximum safety of the patient's data. Six months (July 2019) and twelve months (January 2020) after the start of the effect study all data were anonymised and sent in encoded files to the researchers. Data for all the outcome measures were collected three times in this study. In January 2019 (T0) retrospectively data was collected for the year 2018. Prospective data were administered in July 2019 (T1) and January 2020 (T2) for the effect study.

Primary outcome

The primary outcome measure was the frequency of exacerbations. Exacerbation rates in patients with COPD have a correlation with lung function [16,20,26]. This leads to respiratory symptoms. Moderate to severe exacerbations have a significant impact on health-related Quality of Life and deterioration of lung function. Therefore, this can predict medication prescriptions and hospitalisations [20,26]. In the

literature, the definition of an exacerbation is still a topic of debate [26]. In our study an exacerbation is a sustained worsening of the patient's condition, from the stable state and beyond normal day-to-day variations, necessitating a change in regular medication in a patient with underlying COPD [16,26]. Respiratory symptoms should include an increase in shortness of breath; an enlarged volume and purulence of sputum; coughing more than on a regular basis and shallow/rapid breathing. This definition was communicated to all physiotherapists.

Secondary outcomes

Secondary outcome measures were divided into medication prescriptions and hospitalisations. In case of an acute exacerbation, the number of prescriptions for antibiotics and prednisone was noted. Changing the medication back to a maintenance dose was noted. The number of hospitalisations and days of stay in the hospital was registered for the whole study period.

Statistical analysis

On the ratio level, the average frequency of therapy was chosen for T1 and T2. Data were retrospectively collected at T0 and used to analyse patients on the primary and secondary outcomes before the first of January 2019. On this date, the change in reimbursement was a fact.

An independent *t*-test was performed to check for significant differences in patient characteristics at baseline between both groups. Boxplots and histograms of the variables of the two groups (LFG and HFG) were compared. In addition, a Shapiro-Wilk's test was performed to check for the normality of the data. An independent-samples *t*-test was used to compare the mean groups differences in the primary and secondary outcomes at T2. All hypotheses were tested two-sided. In our analyses, $p < 0.05$ is set as statistically significant. The effect size Cohen's d was calculated for the primary outcome measure.

Based on a sample size calculation, a minimum sample size of 168 participants was needed to achieve a statistical power of 80% with an alpha level of 5%. To see if the equal variance assumption was met, we compared the GOLD level, gender and age of both groups. Mean rank and sum of ranks were calculated for variables of both groups.

When analysing data we found a low percentage of missing values (7%). Missing values were at random (MAR) so the mean imputation method was used for the specific variables. Adherence in both groups was calculated but generalisability and intention to treat reason were not taken into account for statistics. Continued variables were normally distributed therefore parametric measures were used.

Results

A number of 343 eligible patients were included from 22 physiotherapy practices. Baseline characteristics of the patients are presented in Table 1. 124 patients received LFG ($\leq$1.5 per week) and 219 patients received HFG (>1.5 per week). After six months, 25 patients dropped out because of not enough reimbursement from their health care insurance; co-morbidity; mortality; or moving to another place. For 6 patients the reason for dropout is unknown. After 12 months, another 22 patients dropped out of the study, in 7 patients the reason for dropping out is unknown. The total dropout was 47 patients (14%) for the total cohort. Figure 1 shows the flowchart for the recruitment of patients.

Treatment effect

We found a significant difference in the number of exacerbations between the groups after 12 months of PR. LFG had a significantly higher rate of exacerbations ($\bar{x}$ 4.14 at T2) in comparison to the HFG ($\bar{x}$ 2.71 at T2). Table 2 summarises the mean score on the primary outcome and secondary outcomes between the LFG and HFG group. On our primary outcome measure, we found a significant difference for exacerbations in LFG ($M = 4.14$, SD = 3.34) and HFG ($M = 2.71$, SD = 2.06); $t(174.92) = 3.32$, $p = 0.001$. According to the difference in the means (mean difference = 1.12, 95% CI: 0.46–1.79), there was a medium effect size (Cohen's $d = 0.52$).

For the secondary outcome measures antibiotics, hospitalisations and days of stay in a hospital we found significant differences. In LFG more antibiotics were prescribed ($M = 28.63$, SD = 62.84) in contrast to HFG ($M = 12.64$, SD = 38.93); $t(185.61) = 3.07$, $p = 0.002$. LFG was referred more to the hospital with an acute exacerbation ($M = 1.22$, SD = 1.65) than HFG ($M = 0.36$, SD = 0.76); $t(152.54) = 4.76$, $p = 0.000$. In addition, days of stay in the hospital showed significant differences. LFG stayed on average 8.9 days in the hospital ($M = 8.85$, SD = 11.89) versus 1.4 days on average for HFG ($M = 1.36$, SD = 3.05); $t(117.08) = 6.20$, $p = 0.000$. Prednisone use showed to be the only non significant secondary outcome measure after 12 months of PR. In order, LFG ($M = 22.33$, SD = 55.24) and HFG ($M = 8.65$, SD = 30.88); $t(249) = 1.83$, $p = 0.069$. All variables were tested for normal distribution with the Shapiro-Wilk's test ($p < 0.05$) and inspected for normality with box plots. All variables met the criteria for normality.

Adverse effects

No adverse effects related to the intervention were reported. The death of study subjects can be traced back to comorbidity and stopping physiotherapy because of physical incapacity.

Discussion

This is the first study that found that long term high frequency physiotherapy in patients with severe COPD (GOLD III and IV) is more effective in reducing rates of exacerbations than low-frequency physiotherapy. After 12 months, we also found significant between groups differences in medication prescriptions, hospital admissions and days of stay in the hospital in favour of high frequency physiotherapy. More

Table 1. Baseline characteristics of patients.

	LFG (*n*, %) (*n* = 124)	HFG (*n*, %) (*n* = 219)	*p*-value $p < .05$ (2-tailed)
Demography			
Male	64 (51.8%)	105 (47.9%)	0.77
Female	60 (48.2%)	114 (52.1%)	
Age (years)	69.12 (8.38%)	68.57 (7.75)	0.92
BMI	25.15 (4.43%)	25.30 (4.22)	0.37
GOLD III	85 (68.7%)	159 (72.8%)	0.35
GOLD IV	39 (31.3%)	60 (27.2%)	
Primary outcome at baseline (Mean (SD)			
Exacerbations	2.50 (2.03)	2.27 (1.79)	0.66
Secondary outcome at baseline			
Antibiotics	1.70 (1.61)	1.57	0.83
↘ numbers maintenance dose >98	11	20	
Prednisone	1.63 (1.64)	1.65 (1.76)	0.94
↘ numbers maintenance dose >98	6	10	
Hospitalisations	0.36 (0.69)	0.39 (0.82)	0.56
Hospital days	1.96 (4.19)	2.87 (7.22)	0.10

Data are presented as mean (SD) for continuous variables and as numbers or percentages for categorical variables. BMI: Body Mass Index; GOLD: Global Initiative for Chronic Obstructive Lung Disease; ↘: Patients with continued Antibiotics/prednisone.

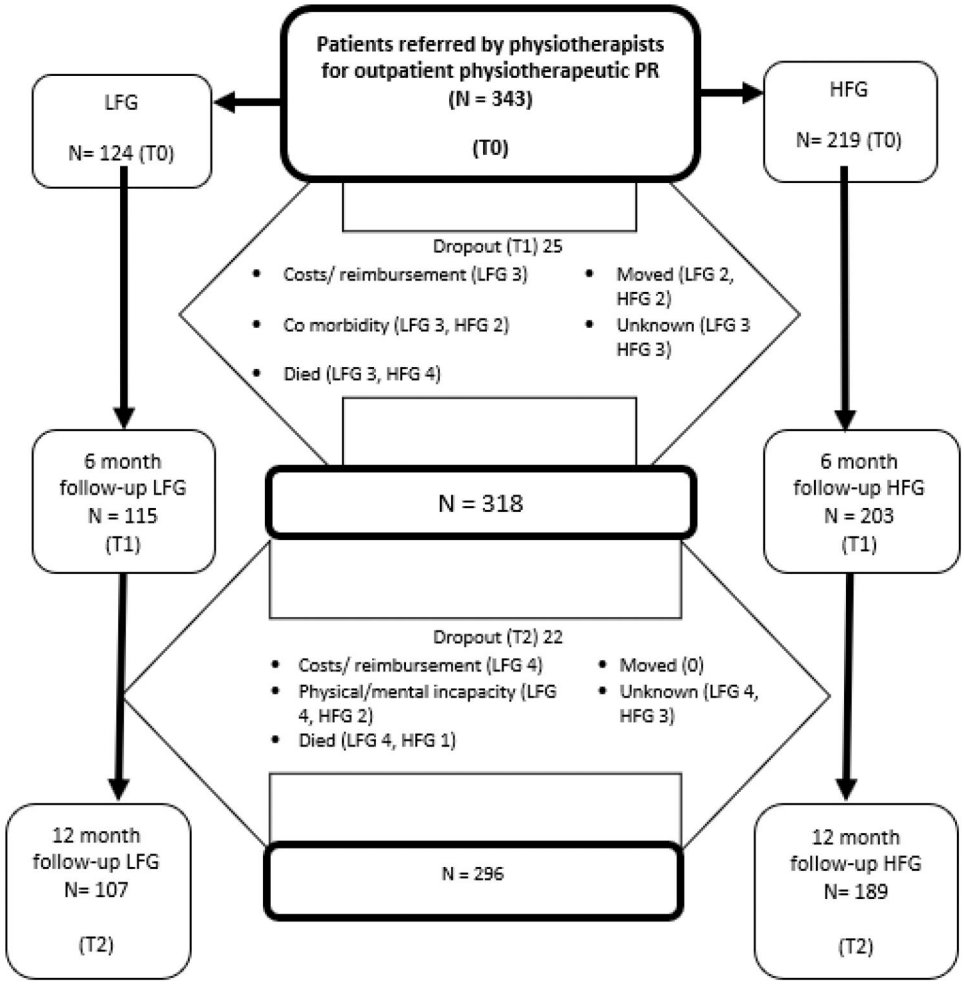

Figure 1. Patient flow-chart.

than 1.5 times per week long term physiotherapy leads to better health related outcomes over the full study length. Similarly, this effect was evident for medication prescriptions, hospital admissions and days of hospitalisation.

Prednisone prescriptions were not significantly different between LFG and HFG. This can possibly be explained by the difference in prescription behaviour of physicians. In theNetherlands, a physician and nurse practitioner conduct the prescription of meditational therapy.

Strengths of this study are the prospective component, the 12 months of follow-up, and the multi-centre design, including 22 physiotherapy practices, which increases generalisability of the study results. We used a large sample size in combination with a cohort. Moreover, the dropout rates

Table 2. Outcome measures mean scores (SD) of groups. mean between group differences.

	T0		T1		T2		Mean between group difference LFG-HFG		*p*-value	95% CI of the difference
	LFG ($N = 124$)	HFG ($N = 219$)	LFG ($N = 115$)	HFG ($N = 203$)	LFG ($N = 107$)	HFG ($N = 189$)	LFG	HFG	$p = 0.05$	Lower Upper
Primary outcome										
Exacerbations	2.40	2.30	1.48	1.60	4.14	2.71	1.12		0.001	0.46
Mean (SD)	(1.85)	(1.87)	(1.35)	(1.47)	(3.34)	(2.06)				1.79
Secondary outcomes										
Antibiotics	12.24	11.48	10.27	8.80	28.63	12.64	0.86		0.002	0.31
Mean (SD)	(30.42)	(29.59)	(28.55)	(26.31)	(62.84)	(38.93)				1.42
Prednisone	7.02	6.81	8.59	4.72	22.33	8.65	0.49		0.069	−0.04
Mean (SD)	(22.18)	(22.13)	(26.33)	(18.30)	(55.24)	(30.88)				1.02
Hospitalisations	0.35	0.40	0.22	0.41	1.22	0.36	0.67		0.000	0.39
Mean (SD)	(0.70)	(0.84)	(0.50)	(0.64)	(1.65)	(0.76)				0.95
Hospital days	1.95	3.13	1.26	2.24	8.85	1.36	6.12		0.000	4.16
Mean (SD)	(4.60)	(7.66)	(3.46)	(4.94)	(11.89)	(3.05)				8.07

Means scores (SD) presented for the outcome measures; LFG: Low frequency Group; HFG: High Frequency Group Mean between group differences with a *p*-value 0.05 and a 95% Confident Interval.

were relatively low (14%), which is surprising, as the burden of disease of COPD increases over the years [27]. Together with an overall low health status of the participants in addition to the higher average age, dropout rates were lower than we Fexpected.

A strong primary outcome measure (i.e. exacerbations) was used to evaluate the effects of the intervention. Exacerbations were chosen to be the primary outcome because of the relation to the deterioration of lung function. A stronger prognostic factor for deterioration of lung function and health status is not known in the literature [26].

This study also had some potential limitations. In The Netherlands, all physiotherapists perform physiotherapy according to the protocol of The Royal Dutch Society for Physiotherapy (KNGF) [25]. A potential source of bias is the possible difference in physiotherapy performed by the different included physiotherapy practices. The conformity of the physiotherapy among the practices was made on the evidence-based program of the KNGF. Our researchers did not instruct the physiotherapist about the content of the physiotherapy before the start of the effect study. Therefore, this could have led to a certain variation in the approach of the patients within the framework of the protocol.

Because of the start of COVID-19 at the beginning of 2020 in the Netherlands; practices were committed to stopping physiotherapy in order to guarantee the safety of the patient population. Therefore, this study only had 12 months of data collection rather than the planned two years of data collection for the effective study. The robustness of the results of this study would be of more importance when the effect study would have been running over two years. Despite this, we argue that the outcome of the present study is of clinical importance because significant benefits were observed for the HFG compared to the LFG.

We did not conduct an economic evaluation. It can be reasoned that hospitalisations are more expensive in comparison to the costs of physiotherapy. However, this hypothesis about differences in costs for the healthcare system was not evaluated in this study. Therefore, another analysis of the data and scientific research is needed to explore the differences in costs. Moreover, although we assume that the differences between the HFG and LFG can be attributed to the higher treatment frequency of the HFG, we cannot prove this because we did not investigate for confounders and did not perform a mediation analysis.

The change in reimbursement was a political decision of the Ministry of Health, Welfare and Sports (VWS) of the Dutch government [23,28]. The difference in frequency of rehabilitation was blind for researchers. The frequency of rehabilitation was dependent on two factors namely the referral of a general practitioner or lung physician, and the capacity of patients to pay partially/totally for the higher frequency of rehabilitation. In the first example patients are more likely to have more co-morbidities and therefore to have a lower overall health status. Patients who were capable of paying for the high frequency rehabilitation were to be expected from the higher socioeconomic backgrounds. Financial status may be associated with greater health literacy, which may influence adherence to other health behaviours like medication adherence. Therefore the comparison between the groups at baseline was critical to compare groups on effect in the study. Fortunately, the differences between groups at baseline were small for all characteristics.

To our best knowledge, no other multicenter study has examined what the optimum frequency is for conducting physiotherapy in patients with severe COPD in a cohort of a year with retrospective data of 12 months. In our study, we found significant mean differences between groups on our primary outcome measure. Therefore, we argue that there is a generalisability of our outcome for the whole population of patients with severe COPD, mainly because we used a multicenter design. However, we did not conduct an RCT, so we recommend confirming the results of this study in an RCT design. However, the results of this study provide a strong justification that a higher frequency of physiotherapy is beneficial. Based on this study, we recommend using a high frequency (>1.5 times per week) in physiotherapy in patients with severe COPD.

This study evaluated the consequences of reducing the frequency of long term physiotherapy in COPD and indirectly

the consequence of the political decision on this topic. The study showed lowering the frequency of long term physiotherapeutic pulmonary rehabilitation leads to higher rates of exacerbations, antibiotic and prednisone prescriptions, hospital admissions and days in the hospital for patients with severe COPD.

Ethical approval

The Research Ethics Committee of the Radboud University Medical Centre declared (file number 2022-13467) that this study was carried out in accordance with the applicable legislation concerning reviewal by an accredited research ethics committee such as Medical Research involving Human Subjects Act and Medical Treatment Contracts Act.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

The author(s) reported there is no funding associated with the work featured in this article.

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