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Effects of In-Patient Pulmonary Rehabilitation in Patients with Interstitial Lung Disease

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ABSTRACT

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Introduction:

Pulmonary rehabilitation (PR) is recommended for patients with chronic lung diseases including idiopathic pulmonary fibrosis (IPF) according to international guidelines. However, data for patients with interstitial lung disease (ILD) are limited. We examined the effect of an in-patient PR on functional status and quality of life in ILD-patients.

Methods:

We evaluated 402 consecutive ILD-patients who were admitted to a specialized pulmonary rehabilitation centre (1999-2010). All patients performed a standardized PR program including pulmonary function tests, blood-gas analysis, 6-minute-walk test (6MWT), dyspnoea rating and health-related quality of life questionnaire (SF36) on admission and discharge.

Results:

Mean duration of PR was 30±1 days. 6MWT-distance improved by 46±3m (308±6m vs. 354±6m, $p<0.001$). Dyspnoea rating did not change. Lung function testing showed marginal improvement of vital capacity (+1±0%, $p=0.002$). SF-36-questionnaire demonstrated an increase in all eight sub-scores as well as in physical and mental health summary scores (physical: 6±1 points, $p<0.001$; mental-health: 10±1 points, $p<0.001$). Moreover, patients with signs of pulmonary hypertension also benefited from PR.

Conclusion:

In a large cohort of patients with ILD, PR had a positive impact on functional status and quality of life. Considering the limited treatment options in this patient-population PR appears to be a valuable adjunct therapy.

Key words: 6-minute walk test, idiopathic pulmonary fibrosis, interstitial lung disease pulmonary rehabilitation, quality of life, vital capacity.

INTRODUCTION

Interstitial lung diseases (ILD) comprise a diverse group of diagnoses including but not limited to idiopathic pulmonary fibrosis (IPF), acute and chronic interstitial pneumonias, ILD associated with connective tissues diseases (CTD) and sarcoidosis. Pathologically ILD are characterised by involvement of the lung parenchyma with varying amounts of inflammation and fibrosis leading to restrictive physiology and impaired gas exchange. Clinically ILD are characterized by dyspnoea on exertion, limited exercise tolerance and dry cough[1-2]. Increasing dyspnoea and decreasing exercise capabilities lead to disability of the patients and to impairments of their health-related quality of life (HRQL)[1]. Treatment options are often limited and without proven effect on survival and HRQL and associated with significant risks and side effects[3].

Pulmonary rehabilitation (PR) has been defined as an “evidence-based, multidisciplinary and comprehensive intervention for patients with chronic respiratory disease who are symptomatic and often have decreased daily life activities”[4]. Comprehensive PR-programmes involve not only exercise training with aerobic conditioning, strength and endurance training and respiratory therapy, but also educational lectures, nutritional interventions, behaviour modification techniques to improve self-managements and physiological support[3].

The ATS/ERS consensus report supports the use of PR in the management of chronic respiratory disease regardless of underlying disease[4]. The benefits of PR have been extensively reported in patients with chronic obstructive pulmonary disease (COPD) with the assumption that the recommendations are applicable to subjects with other lung diseases[4-5]. Benefits of PR in COPD-patients are reported in view of decreased dyspnoea, increased exercise endurance, improved HRQL and reduced health-care costs[5-9]. However, data supporting PR in patients with ILD are scant and the effects of PR in patients with ILD are largely unknown. While ventilatory limitation and skeletal muscle dysfunction are present in both, COPD and ILD, impaired pulmonary gas exchange and circulatory factors may be more important in ILD-patients[10-12].

So far, only a few studies have investigated the impact of in- and out-patient PR in ILD-patients. Unfortunately, none of these studies included a sufficient number of patients to conclusively demonstrate clinically meaningful benefits. Nevertheless, the authors of the recent official ATS/ERS/JRS/ALAT-evidence-based guideline for IPF recommend PR for the majority of IPF-patients (weak recommendation, low quality-evidence)[13]. Consequently the

authors suggested further investigations. Therefore, the aim of our study was to assess the impact of an in-patient PR in a specialised centre on a large cohort of ILD-patients.

METHODS

Patient population and study design

440 consecutive patients with ILD including IPF, collagen vascular disease, occupational lung disease, sarcoidosis, hypersensitivity pneumonitis and other forms of idiopathic interstitial pneumonias participating in an in-patient-PR at “Schoen Klinik Berchtesgadener Land” between 01/1999 and 05/2010 were analysed. 402 patients (91.4%) were included, 38 patients (8.6%) were excluded due to acute infectious disease, heart failure, non-compliance or inability to follow the program or missing data. Diagnoses were made in accordance with the ATS/ERS international consensus classification of idiopathic interstitial pneumonias[14]. Data were obtained from prospectively maintained medical records and computerised databases. The study was performed in accordance of the local board on medical ethics at Ludwig-Maximilians-University of Munich.

Patients participated in a standardized in-patient PR program (German health system does not offer an out-patient PR-program for ILD-patients yet). On admission all patients received a baseline examination including a full medical history and physical examination, resting ECG, laboratory screening, blood gas analysis, lung function test, six-minute walk test (6MWT), dyspnoea-rating with visual analogue scale (VAS) before and after 6MWT and health status measured by SF-36-questionnaire. The same investigations were performed one day before discharge. Admission data were compared to discharge data.

Pulmonary rehabilitation programme

Patients underwent a standardized in-patient PR program consisting of 5 hours of individually tailored and supervised exercise training and 30 minutes of breathing exercises four to five times per week, attendance of aerobic sessions with breathing exercises for 30 minutes five times per week and a group education three sessions per week. PR was individualized based on patient status and estimated exercise capabilities. Exercise training involved aerobic (treadmill, stationary bikes or similar apparatus) and resistance training (light weights, resistance bands etc.). Breathing training consisted of breathing techniques (pursued-lipped, controlled, and diaphragmatic breathing), pacing and energy conservation. Intensity and duration of RP were gradually increased to build tolerance and confidence with the goal of reaching maximum tolerated work load during each exercise period. Supplemental oxygen was given to maintain oxygen saturation above 90% if desaturation was observed.

Education sessions were aimed at promoting self-management and included self medication, management of infections and exacerbations, dyspnoea, use of oxygen, return to activities of daily living and maintaining and improving physical function. If needed, patients received psycho-social support.

Assessments

Spirometry and bodyplethysmography (Master Screen Jaeger, Wuerzburg, Germany) were measured according to ATS/ERS recommendations and results were compared with the predicted normal values from the ATS/ERS[15-16]. 6MWT was performed according to recommendations of the ATS[17]. Perceived dyspnoea was obtained using the VAS (0-10).

HRQL was evaluated using SF-36-questionnaire[18]. SF-36 is a 36-item health status questionnaire with 8 domains (physical functioning, bodily pain, physical role functioning, general health perceptions, vitality, social-/emotional role functioning, general mental health) and 2 component summary scores (physical and mental-health, each of which derives from 4 of the 8 domain scores). SF-36 Health Survey items were transformed to a 0-100 scale and scales were constructed using the Likert method of summated ratings[19].

Signs of right heart decompensation/failure were obtained from medical records (heart catheterization (50% of patients in PH-group) in referring hospitals and echocardiography in referring hospitals and/or rehabilitation clinic): Patients were considered to be affected by pulmonary hypertension (PH) according to ERS guidelines[20] in case of mean pulmonary artery pressure ≥25mmHg in right heart catheterization or at least two of the following echocardiographic parameters: systolic transtricuspid pressure gradient >35mmHg/ peak tricuspid regurgitation velocity > 2.8m/s, tricuspid annular plane systolic excursion (TAPSE) ≤17mm and/or right atrial surface area >27cm^2.

Statistical analyses

Descriptive statistics are reported as mean plus/minus standard error of the mean (SEM). Kolmogorov-Smirnov-test was used to examine the distribution of data showing that all data conform to a normal distribution. Demographic data between groups were compared using unpaired t-test. Within-group and between-group changes between/after PR were evaluated using paired t-test. A statistical software package (SPSS 18.0 for Windows, SPSS Inc., Chicago, IL) was used for all statistical analyses. Reported p-values were two-sided, $p < 0.05$ was considered statistically significant.

RESULTS

Patient cohorts

Study population included 402 patients with ILD performing PR. Mean duration for PR was 30±1 days. Baseline characteristics are summarized in table 1. Mean age of participants was 60±1 year (range 21-89). 202 patients (50%) had a confirmed pattern of IPF, 21 (5%) had idiopathic interstitial pneumonias other than IPF (non-specific interstitial pneumonia, cryptogenic organising pneumonia), 59 patients (15%) had hypersensitivity pneumonitis, 50 patients (12%) sarcoidosis, 24 (6%) ILD associated with CTD and 46 (12%) patients ILD of different etiology including drug induced-/radiogenic fibrosis, after bone-marrow transplantation or of unknown origin. 299 patients (74%) were listed for lung transplantation, 111 patients (28%) had documented signs of PH, 80% of patients were on LTOT, mean vital capacity (VC) was 54±1% predicted.

Blood gas analysis and lung function parameters

Complete lung function parameters and blood gas analysis from arterialized capillary blood from the ear lobe on admission and discharge were available in all patients (table 2). Statistically significant improvements were observed before and after PR in blood gas analyses and lung function parameters (table 2).

6-minute walk test parameters

369 pairs of 6MWT from admission and discharge were available, 33 (8 %) were missing due to exacerbation, cardiac failure and call for transplant. Mean baseline 6MWD distance on admission was 308±6m (range: 5-590m), the post PR-baseline on discharge was 354±6m (range 10-646m) (table 2, figure 1). The change was 46±3m (range -146 to 328m), approximately 15% of baseline value ($p<0.001$) (table 2). 50 (14%) patients showed a decreasing 6MWD before/after PR (n=10 decrease ≥50m; n=40 decrease <50m) due to various reasons including acute exacerbations and cardiac decompensations. 319 patients (86%) showed an increase of 6MWD during PR (n=153 increase 1-50m; n=103 increase 50-100m, n=47 increase 101-150m, n=16 increase >151m). VAS pre- and post-exertion did not differ significantly between admission and discharge (table 2).

Health related quality of life parameters

350 patients had completed SF-36 questionnaires on admission and discharge (52 (13 %) were missing). Mean physical health summary score was 31±1 points on admission and 37±1 points on discharge, mean mental health summary score was 47±1 on admission and 57±1 on discharge. All admission/discharge sub-scores are displayed in table 2. Analysis of

SF-36 questionnaire demonstrated a significant increase ($p<0.05$) in all eight sub-scores as well as in physical and mental health summary scores (physical: 6±1, $p<0.001$; mental 10±1, $p<0.001$) (table 2, figure 2).

Predictors of change

Of the variables tested (age, gender, body-weight-index, smoking history, use of LTOT, baseline FVC, baseline-6MWD and baseline-VAS), only baseline-6MWD was a significant predictor of change in 6MWD, but not for change in improvement of SF-36 scores. The improvement in 6-MWD was the smaller the higher the baseline-6MWD was ($p<0.01$) (figure 3).

Effect of pulmonary hypertension on outcome of PR

Baseline demographic characteristics from patients with and without signs of PH were statistically indistinguishable. Lung function parameters (blood gas analysis and lung volumes) improved during PR in the non-PH-group, whereas in ILD patients with signs of PH only VC improved (table 3). Patients not affected by PH had significant improvements in physical and mental-health sub-scores of SF-36, while in patients with signs of PH only significant improvements in mental-health sub-scores could be observed. 6MWD on admission were significantly lower in patients with signs of PH compared to those without signs of PH (277±12m vs. 322±8m, $p=0.001$). On discharge, both groups showed a significant improvement ($p<0.001$) (PH: 313±12m vs non-PH: 370±7m). However, patients with signs of PH had a smaller absolute increase in 6MWD compared to patients without signs of PH (36±6m vs. 48±3m, $p=0.045$) (table 3).

DISCUSSION

We evaluated the impact of an in-patient PR-program in a specialised centre on patients with ILD. Our data demonstrate that PR is beneficial in those patients and appears to be a valuable adjunct therapy. Our results show small but statistically significant improvements in lung function parameters before and after PR. More importantly, significant improvements in both functional status and health-related quality of life (HRQL) were observed. This benefit was seen regardless of age, gender, underlying disease or baseline pulmonary function. Additionally, our data suggest that patients with signs of PH also benefited from an in-patient PR, however, to a smaller extent. This finding is in line with Mereles et al., who showed that even patients with advanced PAH can improve with specialized PR[21].

PR is widely accepted for patients with COPD since many studies demonstrated benefits regarding exercise endurance, decreasing dyspnoea, improvement of HRQL and reducing health-care costs[5]. There is a good rationale for the use of PR also in patients with ILD. Exercise training improves aerobic capacity, muscle strength and flexibility, contributing to less dyspnoea on exertion and to improvement of functional status. Additionally PR has psychosocial benefits that help patients understand their disease and may mitigate anxiety and depression[22]. Due to these advantages it is widely supposed that patients with ILD might profit from PR. However, only a few studies have investigated the effect of PR in this population and most of published studies evaluated out-patient PR programmes.

We observed a small, statistically significant improvement of blood gas analysis and lung function parameters, which is in line with other published studies[10,23]. Although these improvements are statistically significant, their clinical relevance is probably negligible. With respect to the underlying pathophysiology this is also concordant to our expectations regarding the potential effects of a 30-day PR program.

We demonstrate a significant improvement in 6MWD of 46±3 metres, approximately 15% of the baseline value. Between different groups of underlying diseases of ILD (e.g. IPF, hypersensitivity pneumonitis etc.) we could not document significant different improvements in 6MWD before and after PR. Only few studies have investigated the effect of PR on the 6MWD in ILD-patients so far; in all of them PR was performed as an out-patient program. Nishiyama and colleagues observed a PR-effect of 46 metres in 6MWD, Holland et al. reported a mean increase in 6MWD of 35 metres in ILD patients and of 25 metres in a subgroup analysis of 34 patients with IPF[23-24]. Ferreira et al. measured an average increase of 56 metres in their study with 113 ILD-patients[22]. Swigris and colleagues documented an improvement of 61 metres in 6MWT in their study with 21 IPF-patients[25], in contrast, Kozu and coauthors found only an increase of 16 metres in 6MWT in 36 IPF-patients[10]. Based on lung function parameters, patients included in all of these studies showed less advanced ILD with a lower proportion of LTOT when compared to our study population (table 4).

The minimal clinically important difference (MCID) for the 6MWT in ILD is still under debate. In COPD-patients a distance of 54 metres has been identified for the MCID, although more recently this value has been questioned and the threshold for MCID may be lower in this group (35m. Puhan et al.) [26-27]. Based on a large cohort of 822 IPF-patients the MCID for the 6MWD was calculated to be 24-45 metres, depending on the statistical method employed[28]. This is in line with previous studies of Holland et al. who assumed an improvement of 6MWD in range 29-34 metres to be clinical relevant in people with

parenchymal lung disease, and Swigris et al. who calculated the MCID for 6MWD to be 28 metres[29-30]. Thus, the improvement in 6MWD of 46 metres is among the highest discussed MCID and reflects a meaningful increase in exercise capacity in our patients. In contrast to above cited study populations we have to highlight that 299 of our patients (74%) were listed for lung transplantation. This clearly demonstrates the efficacy of an in-patient PR even in a patient-group with end stage ILD.

In our study we could show that baseline-6MWD was a significant predictor of change of 6MWD after PR. Interestingly and in concordance with data from COPD-patients, the lower the baseline, the more likely the patient was to improve. Lower baseline-6WMD was associated with lower baseline-FVC and TLC and the use of LTOT. This observation emphasizes that especially patients with severe impairments may substantially benefit from PR. This observation is flawed slightly by the fact that patients with signs of PH had lower baseline 6MWD and less improvement. However, even in this subgroup the observed increase in 6MWD was still within the range of the assumed MCID.

Our observation, that lower baseline-6MWD predict higher benefits from PR is in line with data published by Ferreira et al.[22]. Nonetheless, PR is also effective in patients with high baseline 6MWD. This can be confirmed by our data showing an improvement in 6MWD which are in the range of the MCID even in patients with high baseline-6MWD (figure 3b).
Dyspnoea-rating using VAS before and after exertion did not change significantly in the current study. This is contrary to experiences from COPD-studies which show improved dyspnoea-ratings[5]. We speculate that ILD-patients walking at their highest possible capacities achieve their dyspnoea maximum more rapidly in contrast to COPD-patients independent from the distance walked. However due to conflicting data from different studies, dyspnoea-rating is still under debate in IPF patients[10,22-25].

In addition to increased exercise capacity another important aspect of PR is an improvement in HRQL. We observed a pattern of poor health-status measured by SF-36 questionnaire that is well established in patients with ILD[31]. In the current study we noticed a statistically significant improvement in both summary scores (physical and mental health) of SF-36 as well as in all eight sub-scores. Clinically meaningful changes in SF-36 questionnaire are not been firmly established in patients with ILD, but in general, a 5-point increase in SF-36 summary score is supposed to indicate a MCID[32]. Therefore our data show a significant and clinically important improvement in all sub- and summary-scores of SF-36. Our observation is in concordance with some published studies[8,23,31,33], while others did not detect any influence of PR in HRQL[10,24-25]. Naji and co-workers demonstrated in their

group of ILD patients a significant reduction of anxiety and depression after completing PR[31]. Some investigations including ours have noted that PR participants perceive greater improvements in mental health than in physical aspects. This is more interesting regarding the aspect that dyspnoea is the most important factor determining HRQL in ILD patients[34]. Although in our study dyspnoea-rating during 6MWT did not differ between admission and discharge, we speculate that improved physical ability resulted in a better feeling of health, since before PR, most patients claimed about decreasing physical ability.

There are some important limitations that warrant attention. First, the current study was an open clinical non-randomized study without involving a control group. Second, due to long study-duration an influence of changes regarding staff or training modalities as well as training effects of the team cannot be excluded. Third, although 6MWT was performed by specially trained medical staff and strictly according to current standards, it was obtained by several examiners. Finally, some patients were enrolled after an acute deterioration or after listing for lung transplantation, which may have introduced a selection-bias. The observation period in this study was restricted to the active PR phase. Long-term follow-up data are not available; consequently, the long-term effect of PR remains unknown. Further data concerning cost-effectiveness of such an inpatient PR are lacking.

Despite these limitations our study provides robust data demonstrating that in-patient PR is beneficial for ILD-patients. We were able to show statistically and clinically significant improvements in exercise capacity and HRQL in physical- as well in mental-health in a large cohort of ILD patients. These benefits are even more pronounced in patients with poorer functional status at baseline. Moreover, ILD patients with signs of PH also benefit significantly from RP.

Considering the limited treatment options in this patient population PR appears to be a valuable adjunct therapy which should be offered to ILD patients. Further research should focus on controlled trials and on the durability of the effects observed here.

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AUTHOR CONTRIBUTIONS:

HP wrote paper, analysed and collected data

SB, BM, WS, SU: collected data

NC, BJ: analysed data

KK: Designed study, collected and analysed data.

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ABBREVIATIONS:

ATS	American Thoracic Society
6MWD	Six-minute walk distance
6MWT	Six-minute walk test
COPD	chronic obstructive pulmonary disease
ERS	European Respiratory Society
HRQL	health-related quality of life
ILD	interstitial lung disease
IPF	idiopathic pulmonary fibrosis
LTX	lung transplantation
MCID	minimal clinical important difference
PAH	pulmonary arterial hypertension
PH	pulmonary hypertension
PR	pulmonary rehabilitation
RP	rehabilitation programme

TABLES

Table 1: Patient characteristics (n=402)

Age (years (y))	59.9 ± 0.6 <40y: 21 (5%), 40-49y: 56 (14%), 50-59y: 126 (31%), 60-69y: 122 (30%), >70y:77 (20%)
BMI (kg/m²)	26.7 ± 0.3 <18.5: 28 (7%), 18.6-25.0 131 (33%),m 25.1-30.0: 127 (32%), >30: 99 (25%); n.a: 17 (3%)
underlying disease	IPF: n=202 (50%), NSIP/COP: n=21 (5%), hypersensitivity pneumonitis: n=59 (15%), sarcoidosis: n=50 (12%), CTD: n=24 (6%), radiogenic/drug induced: n=11 (3%), asbestosis/silikosis/beryliosis: n=4 (1%), other: n=31 (8%)
gender	male: 203 (50%), female 199 (50%)
smoking status	never smoker: 200 (50%), ex-smoker: 165 (41%), continuing smoker: 12 (3%); n.a.: 25 (6%)
LTOT	yes: 321 (80%), no: 62 (15%), n.a.: 19 (5%)
vital lung capacity	54±1 %-predicted) >90%: 24 (6%), 70-89%: n=64 (16%), 50-69%: 124 (31%), <50%: 190 (47%)
signs of pulm.hyp.	no: 286 (71%), yes: 111 (28%); n.a.:5 (1%)
listed for LTX	yes: 299 (74%), no: 103 (26%)

Table 1: Patient characteristics on admission
Abbreviations: BMI: body-mass-index; dis.: disease; CTD: connective tissue disease; LTOT: long-term oxygen therapy; LTX: lung transplantation; n.a.: data not available; PH: pulmonary hypertension

Table 2: Lung function parameters, 6-minute walk test and health related quality of life parameters before and after rehabilitation programme

		Admission	Discharge	Delta	p
Lung function parameters	(n=402)				
pO2	mmHg	61 ± 1	63 ± 1	2 ± 1	0.012
pCO2	mmHg	39 ± 0	40 ± 0	1 ± 0	0.002
VC	% predicted	54 ± 1	55 ± 1	1 ± 0	0.002
TLC	% predicted	65 ± 1	65 ± 1	0 ± 0	0.322
FEV1	% predicted	55 ± 1	56 ± 1	1 ± 0	<0.001
6-MWT and dyspnoea-rating	(n=369)				
6MWD	m	308 ± 6	354 ± 6	46 ± 3	<0.001
dyspnoea-free walk distance	m	291 ± 7	343 ± 7	52 ± 4	<0.001
VAS (before exertion)	points	3.2 ± 0.1	3.3 ± 0.1	0.1 ± 0.1	0.572
VAS (after exertion)	points	6.5 ± 0.1	6.3 ± 0.1	-0.2 ± 0.1	0.176
Health status (SF-36)	(n=350)				
Physical functioning	points	24 ± 1	29 ± 1	5 ± 1	<0.001
Bodily pain	points	60 ± 2	66 ± 2	7 ± 2	<0.001
Physical role functioning	points	12 ± 2	17 ± 2	5 ± 2	0.009
General health perceptions	points	29 ± 1	33 ± 1	4 ± 1	<0.001
Vitality	points	32 ± 1	45 ± 1	13 ± 1	<0.001
Social role functioning	points	52 ± 2	63 ± 2	11 ± 2	<0.001
Emotional role functioning	points	49 ± 3	56 ± 3	7 ± 3	0.029
General mental health	points	58 ± 1	67 ± 1	9 ± 1	<0.001
Physical summary score	points	31 ± 1	37 ± 1	6 ± 1	<0.001
Mental summary score	points	47 ± 1	57 ± 1	10 ± 1	<0.001

Table 2: Lung function parameters, 6-minute walk test and health related quality of life parameters before and after rehabilitation programme
Abbreviations: 6MWD: Six-minute walk distance; 6MWT: Six-minute walk test; l: litre; FEV1: forced expiratory volume in the first second of exhalation; m: metre; pO2: partial oxygen pressure; pCO2: partial carbonic acid pressure; TLC: total lung capacity; VAS: visual analogue scale; VC: vital capacity;

Table 3: Lung function parameters, 6-minute walk test and health-related quality of life parameters for patients with and without signs of pulmonary hypertension

Parameters		no signs of pH				signs of PH			
		admission	discharge	delta	p	admission	discharge	delta	p
Lung function parameters	(n=402)								
pO2	mmHg	62 ± 1	64 ± 1	2 ± 1	0.013	57 ± 2	58 ± 2	1 ± 1	0.722
pCO2	mmHg	38 ± 0	39 ± 0	1 ± 0	0.003	41 ± 1	41 ± 1	0 ± 1	0.862
VC	% predicted	56 ± 2	57 ± 1	1 ± 1	0.041	50 ± 2	52 ± 2	2 ± 1	0.007
TLC	% predicted	66 ± 1	65 ± 1	1 ± 1	0.105	62 ± 2	63 ± 2	1 ± 1	0.506
FEV1	% predicted	57 ± 1	58 ± 1	1 ± 0	0.001	52 ± 2	53 ± 2	1 ± 1	0.267
6MWT and dyspnoea-rating	(n=369)								
6MWD	m	322 ± 8	370 ± 7	48 ± 3	<0.001	277 ± 12	313 ± 12	36 ± 6	<0.001
dyspnoe-free walk distance	m	305 ± 9	363 ± 8	58 ± 4	<0.001	256 ± 14	293 ± 14	37 ± 7	<0.001
VAS (before exercise)	points	2.9 ± 0.2	3.1 ± 0.2	0.2 ± 0.1	0.167	3.8 ± 0.3	3.6 ± 0.3	-0.2 ± 0.3	0.554
VAS (after exercise)	points	6.3 ± 0.1	6.1 ± 0.2	-0.2 ± 0.1	0.287	6.9 ± 0.2	6.9 ± 0.2	-0.1 ± 0.2	0.730
Health status	(n=350)								
Physical functioning	points	23 ± 1	26 ± 1	2 ± 1	<0.001	21 ± 2	23 ± 2	2 ± 1	0.058
Bodily pain	points	45 ± 1	48 ± 1	3 ± 1	<0.001	46 ± 1	48 ± 1	2 ± 1	0.060
Physical role functioning	points	30 ± 1	32 ± 1	2 ± 1	0.019	29 ± 1	30 ± 1	1 ± 1	0.162
General health perceptions	points	33 ± 1	36 ± 1	3 ± 1	<0.001	31 ± 1	33 ± 1	2 ± 1	0.067
Vitality	points	34 ± 1	41 ± 1	7 ± 1	<0.001	32 ± 1	40 ± 1	8 ± 1	<0.001
Social role functioning	points	32 ± 1	37 ± 1	5 ± 1	<0.001	29 ± 2	36 ± 2	7 ± 2	<0.001
Emotional role functioning	points	35 ± 1	37 ± 1	2 ± 1	0.117	35 ± 2	39 ± 2	3 ± 2	0.115
General mental health	points	40 ± 1	45 ± 1	5 ± 1	<0.001	40 ± 2	46 ± 1	6 ± 1	<0.001
Physical summary score	points	29 ± 1	32 ± 1	2 ± 1	<0.001	28 ± 1	29 ± 1	0 ± 1	0.600
Mental summary score	points	39 ± 1	45 ± 1	6 ± 1	<0.001	39 ± 2	46 ± 2	7 ± 2	<0.001

Table 3: Lung function parameters, 6-Minute walk test and health related quality of life parameters before and after rehabilitation programme
Abbreviations: 6MWD: Six-minute walk distance; 6MWT: Six-minute walk test; l: litre; FEV1: forced expiratory volume in the first second of exhalation; m: metre; pO2: partial oxygen pressure; pCO2: partial carbonic acid pressure; TLC: total lung capacity; VAS: visual analogue scale; VC: vital capacity;

Table 4: Comparison of results with recent published literature

	Holland (2008)	Nishiyama (2008)	Ferreira (2009)	Swigris (2011)	present study
N	57	28	99	21	402
in-/out-patients	out-patient	out-patient	out-patient	out-patient	in-patient
ILD group	ILD	IPF only	ILD	IPF only	ILD
Age (years)	67	68±9	66	71.5±7.4	60±1
Time of RP	8 weeks	8 weeks	8 weeks	8 weeks	30±1 days
VC (% predicted)	75	66±13	62	73±22	54±1
pO_2 (mmHg)	n.a.	80±12	n.a.	n.a.	61±1
LTOT (%)	n.a.	CI	65	n.a.	80
Δ 6MWD (m)	35	46	56	61±41	46±3

Table 4: Comparison of results with recent published literature
Abbreviations: 6MWD: Distance in 6-minute walk test; CI: contraindication; ILD: interstitial lung disease; IPF: idiopathic pulmonary fibrosis; m: metre; n: number of patients; n.a.: data not available;
Literature: Holland [20]; Nishyama [19]; Ferreira [18]; Swigris [21];

FIGURE LEGENDS

Figure 1: 6-Minute walk test on admission and discharge
Box- and whisker-plots show comparison of 6-minute-walk-test on admission and on discharge. The horizontal white line displays the median, the box-edges show the 25th and 75th percentiles and the whiskers show the smallest and highest value within 1.5 box lengths from the box.
Abbreviations: 6MWD: Six-minute walk distance; 6MWT: Six-minute walk test; m: metre

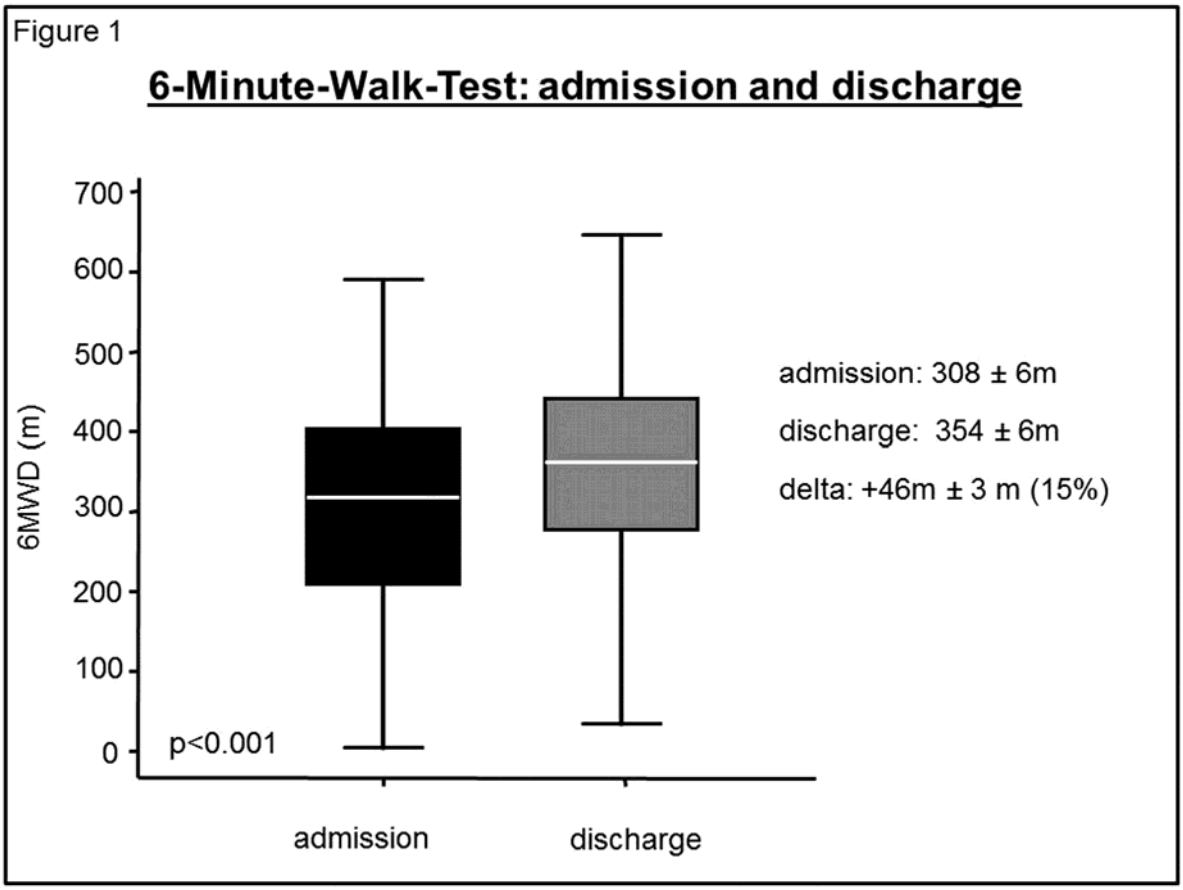

Figure 2: Health-related quality of life on admission and on discharge
Box- and whisker-plots show comparison of physical summary score and mental health summary score of SF-36 questionnaire on admission and on discharge. The horizontal white line displays the median, the box-edges show the 25th and 75th percentiles and the whiskers show the smallest and highest value within 1.5 box lengths from the box.
Abbreviations: HRQL: Health-related quality of life

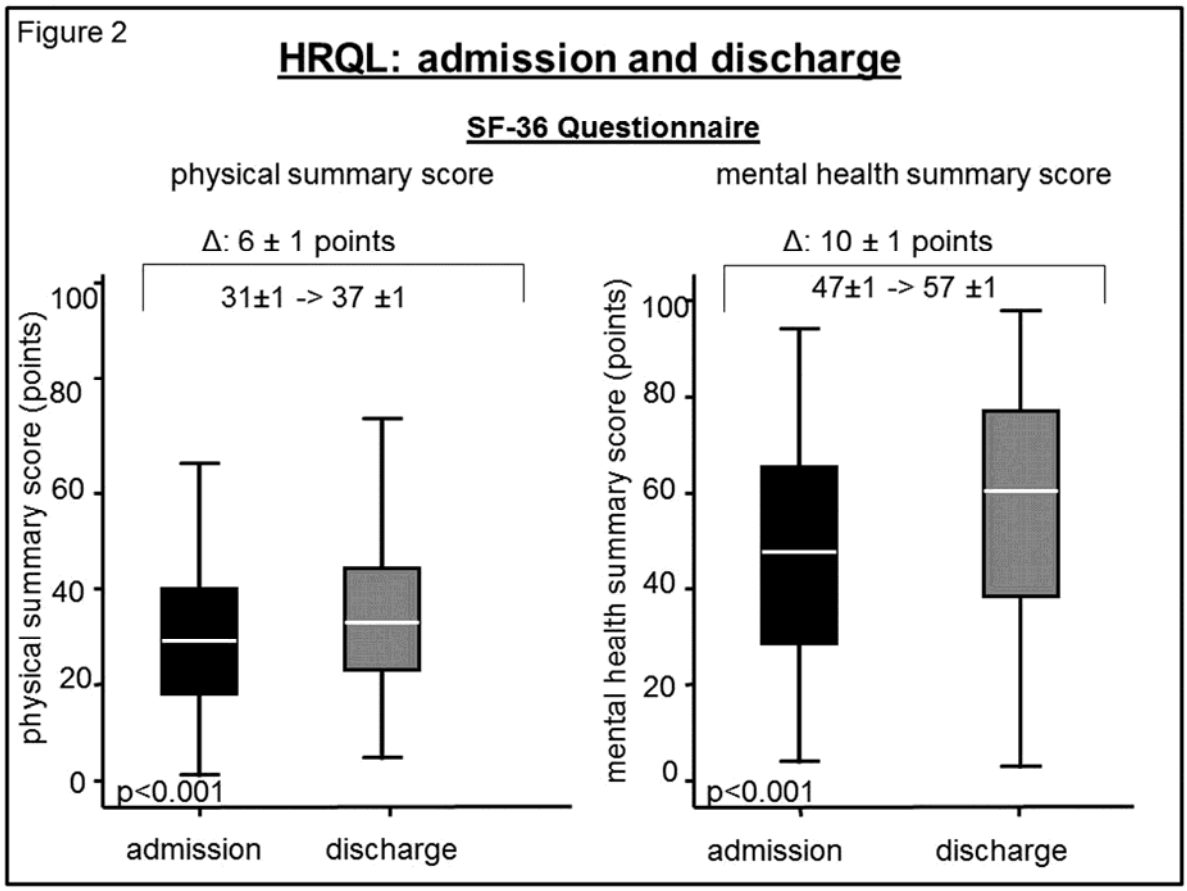

Figure 3: Baseline 6MWD (on admission) is predictor for improvement during pulmonary rehabilitation.
Figure 3a: Points display the difference of 6-minute walk test between admission and discharge (delta; y-axis) dependent on distance of 6-minute-walk-test on admission (x-axis)
Figure 3b: Bars show the mean change of 6-minute walk test between admission and discharge dependent on baseline 6-minute walk distance.
Abbreviations: 6MWD: Six-minute walk distance; 6MWT: Six-minute walk test; m: metre

Figure 3a

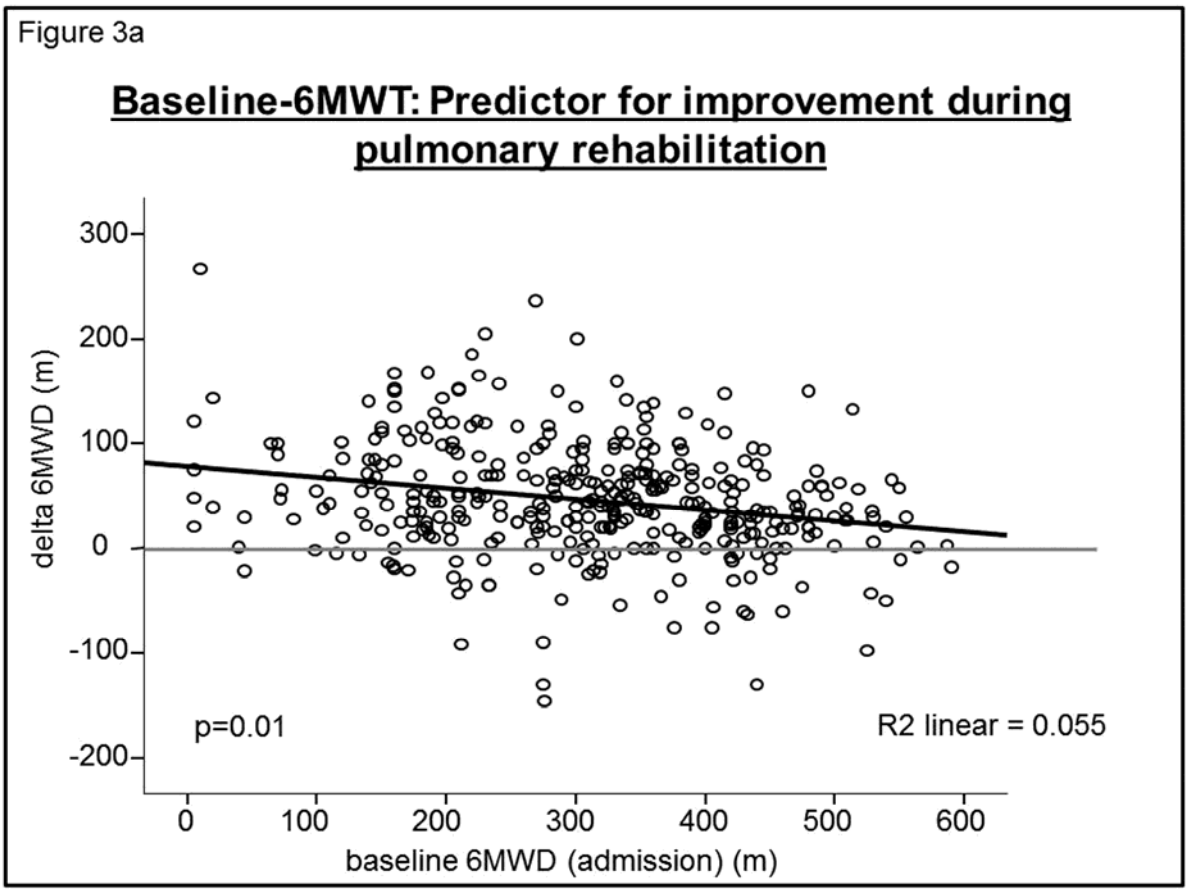

Figure 3b