THE EFFECT OF THE WALK-BIKE ON QUALITY OF LIFE AND EXERCISE CAPACITY IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS: A FEASIBILITY STUDY

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Abstract. Idiopathic pulmonary fibrosis (IPF) is characterized by progressive loss of pulmonary function and exercise capacity, leading to loss of quality of life and often social isolation. A new walking aid, the walk-bike, showed an improvement in exercise performance in COPD patients. Aims of this pilot study were to evaluate feasibility of a home-based walk-bike intervention study in IPF patients and to explore the effect of the walk-bike on quality of life (QoL) and exercise capacity. Twenty-three patients with IPF were included in a randomized multicenter crossover study with 8 weeks of standard care and 8 weeks of walk-bike use at home. Ten patients completed both study phases. Study barriers included reluctance to participate and external factors (e.g. weather and road conditions) that hampered adherence. Patients' satisfaction and experience with the walk-bike varied greatly. After training with the walk-bike, health-related QoL (St. George’s Respiratory and King’s Brief Interstitial Lung Disease questionnaires) demonstrated a tendency towards improvement, exercise capacity did not. A clinically important difference was found between 6-minute walk test with the walk-bike and the standard test; median (range) respectively 602 m (358-684) and 486 m (382-510). Conclusions: Due to practical barriers a larger study with the walk-bike in patients with IPF seems not feasible. Individual patients may benefit from the use of a walk-bike as it improved action radius and showed a tendency towards improvement in QoL. No effect on exercise capacity was observed. (Sarcoidosis Vasc Diffuse Lung Dis 2020; 37 (2): 192-202)

Key words: Idiopathic Pulmonary Fibrosis, Home-based training, Quality of Life, Exercise training, Exercise capacity

Introduction

Idiopathic Pulmonary Fibrosis (IPF) is a chronic, progressive and life-threatening disease of unknown cause (1). Symptoms such as dyspnea, cough, and fatigue lead to a reduction of daily physical activities, exercise tolerance, muscle strength and quality of life (QOL). Problems reported by IPF patients are social isolation, increased level of dependency and immobility (1-5).

Pharmacologic treatment options are limited (5). There are two drugs that reduce pulmonary function decline in patients with IPF, however their effect on QoL is not convincingly established (6-8). In a selected, limited group of patients with IPF, lung transplantation can be an option. Non-pharmacolog-
logic treatments that could improve QoL are increasingly investigated (4, 9-11). Pulmonary rehabilitation (PR) programs are recommended by expert opinion for the majority of IPF patients to improve QoL and exercise tolerance (1, 5, 12). Cochrane reviews on physical training in patients with different interstitial lung diseases (ILD), including IPF, indicate PR has a beneficial effect on QoL and functional exercise capacity in IPF patients (3, 13, 14). Another problem is that the long-term effects of PR are debated (15-20). Furthermore, PR programs are offered in outpatient clinics and specialized rehabilitation centers with a duration of usually 6-12 weeks (14). Due to the limited life expectancy of IPF patients and practical problems with decreased mobility and transport, patients are often hesitant to participate in these external programs. Therefore, in recent years home-based (supervised) training has become increasingly investigated (20-22). An earlier study has demonstrated that a new-walking aid, the walk-bike, improved exercise performance in Chronic Obstructive Pulmonary Disease (COPD) patients due to the more efficient way of moving without excessive metabolic demand (23). To assess whether a study using this new method for home-based training is feasible and of benefit for IPF patients, we designed a crossover pilot study. We hypothesized that use of this walk-bike in daily life extends the range and everyday mobility of IPF patients, thereby decreasing the level of dependency and social isolation and improving QoL. If daily activities of IPF patients increase, exercise capacity might improve too. The objectives of this pilot study were (1) to evaluate the feasibility of a home-based walk-bike intervention study in IPF patients, and (2) to explore the effect of the walk-bike on QoL and exercise capacity.

Methods

Subjects

Patients were eligible to participate in this study if they were diagnosed with IPF according to the international guidelines criteria (1), had a diffusing capacity of the lung for carbon monoxide (TLCO) ≥ 25% predicted, a Forced Vital Capacity (FVC) ≥ 50% predicted, a 6-minute walk distance (6MWD) ≥ 150 meters and were clinically stable without a decline in TLCO and FVC of 10% or more in the past six months.

Exclusion criteria were participation in an official rehabilitation program 4 months preceding enrolment, musculoskeletal disorders, severe cardiac diseases (an ejection fraction < 30%, daily angina, or otherwise specified by treating cardiologist), unable to understand informed consent or other conditions that could hamper the use of a walk-bike. Patients were recruited at the outpatient clinics of three respiratory medicine departments in the Netherlands, Denmark and Spain (NTR5334, www.trialregister.nl). The study was approved by ethic committees of all participating sites and all patients gave written informed consent to participate (MEC-2014-047, Erasmus University Medical Center).

Study design

This prospective multicenter pilot study followed a 2-period crossover design with an intervention period and a control period of each 8 weeks. The intervention was a home-based training program using a walk-bike in daily life during 8 weeks, with the aim of a minimum of 1 hour per day. Patients were asked to record the time of real use of the walk-bike in a diary. At baseline, instructions and training were given. During the control period patients received standard treatment only. The walk-bike is an ambulation aid, a form of a bicycle but without pedals (Figure 1). By sitting on the seat the load on the muscles of ambulation is reduced which results in a lower cost of transport (oxygen uptake in mL/min per meter distance) (23).

Study procedure

Prior to randomization clinical stability was assessed by the physician. Pulmonary function and exercise performance were tested by spirometry, TLCO and 6MWT. Patients were randomly allocated to start with the intervention- or control period by an independent research nurse not involved in the study and using sealed nontransparent envelopes. Block randomization was used to ensure that the numbers of participants assigned to each group were equally distributed during the different seasons. After 8 weeks of intervention- or control period, patients were asked to cross over. Outcome variables were
measured at baseline, after 9 weeks and at the end of the study at 18 weeks. Pulmonary function tests including FVC and TLCO were done as part of the routine medical follow up of treatment.

**Feasibility outcomes**

Outcomes of feasibility comprised the number of patients assessed for eligibility, the proportion of patients that were randomized, the number of patients that finished both periods of the crossover study and adherence with the intervention (1 hour use of the walk-bike per day). Throughout the study, comments and suggestions for improvement from patients and the medical team were collected to explore potential barriers of this study for future research. After the study, patients were asked about their experience and satisfaction with the use of the walk-bike. Feasibility outcomes of all patients that signed informed consent were used.

**Patient-reported outcomes**

The primary outcome was change in total score in health-related QoL measured with the St. George's Respiratory Questionnaire (SGRQ) after 8 weeks of standard of care and after 8 weeks of walk-bike use at home. Although designed for patients with obstructive disease, the SGRQ has been found to be a valid measure of health-related QoL in patients with restrictive disease including IPF (24, 25). A change of 7 points in SGRQ total score (0-100) is known to be the minimal clinically important difference (MID) for IPF patients (26). Secondary outcome was change in total score of the disease-specific King's Brief Interstitial Lung disease health status questionnaire (K-BILD) (27). The MID range in ILD for the total score is 6-10 units (28).

Other secondary outcomes are change in SGRQ and K-BILD domain scores, and in scores measured with the General Anxiety Disorder Screener (GAD-7) (29).

**Exercise capacity**

Additional secondary outcomes were change in functional exercise capacity, determined by the 6MWT (30) after 8 weeks of standard of care or 8 weeks of walk-bike use at home, and change in the number of steps per day as a proxy for daily physical activities, measured with a pedometer (Yamax Digi-walker SW-200)(31). To compare exercise performance with or without the walk-bike, patients were asked to perform an additional 6MWT using the walk-bike, after the regular 6MWT. This was done at the visit after the intervention period (in week 9 or week 18 depending on allocation). The assessor that measured the regular 6MWT at 9 and 18 weeks was blinded for the allocation and patients were instructed not to inform the care provider. Patients were asked to wear the pedometer for a week at baseline, at the crossover moment and after the study.

**Pulmonary function tests**

PFT’s were performed according to ATS/ERS 2005 criteria(32, 33). FVC and TLCO were recorded and expressed as percentage of the predicted value (%pred).

**Analysis**

Due to the explorative nature of this pilot study, no sample size calculations were done and results are given in a descriptive way. As it concerns a small group of patients, results are described without statistical analysis.
Results

Feasibility outcomes

One hundred and twenty five outpatients with IPF were assessed for eligibility for the study, 23 (18%) were interested in participating, signed informed consent, and were randomized. Twelve patients were allocated to start in the intervention group and 11 patients to the control group. Sixteen patients finished the first phase of 8 weeks of the study and after crossover, 10 patients also completed the second phase. Two patients who started in the intervention group did not crossover because they wanted to continue using the walk-bike. Other reasons for not completing the full protocol are shown in Figure 2.

Ten of the 14 patients that completed the walk-bike period, recorded the actual use of the walk-bike in a diary; the median (min-max) use of the walk-bike was 5.3 (2.0- 6.9) days a week and 43.9 (11.3-60.6) minutes per actual usage day. An overview of potential barriers and solutions as reported by patients and medical staff during this study is provided in Table 1.

Patient satisfaction and experience with the walk-bike are shown in Table 2. Comments differed from very satisfied with continuation of using the walk-bike after the study, to not satisfied because using the walk-bike was too heavy or because of feelings of embarrassment.

One patient reported two fall-incidents due to wet and slippery roads, without any physical complaints, and decided to stop with the study.

Explorative outcomes

Baseline characteristics (Table 3) demonstrate

![Study flow chart of patients screened and enrolled](image-url)
that patients were predominantly male with a decreased FVC, TLCO, exercise tolerance and health-related QoL. The patients who dropped out during the study showed on average worse scores in diffusing capacity, exercise measures and health status. The results of the 10 patients that followed the complete protocol are given in Table 4.

SGRQ- and K-BILD total score, as well as the domain scores, tended to improve after training with the bike (Figure 3), with the most striking improvement in SGRQ symptoms- and K-BILD chest scores.

No change after training was observed in the 6MWD, the anxiety score or perceived health status (Table 4).

A meaningful difference in distance covered was found between the 6MWT performed with the walk-bike and the unaided 6MWT with a median (min-max) 6MWD of 602 meters (358-684) vs. 486 meters (382-510); (Figure 4). The lowest oxygen saturation during the 6MWT with the walk-bike and unaided did not differ with a nadir SpO2 of 86% (80-91) vs. 87% (78-90).

During the study, the lung volume remained stable with a median (min-max) FVC at baseline of 69%pred (53-87) vs. 70%pred (57-86) in week 18.
Table 2. Comments on the walk-bike

| Positive comments                                                                 |
|----------------------------------------------------------------------------------|
| Bike is really good for training; feel fit after 8 weeks of training             |
| Although not comfortable with the bike because of shoulder pain, would like to continue using it |
| Able to walk further with less dyspnea                                           |
| Enables me to leave the house and e.g. go to the bakery without being dependent of my spouse |
| Easier and nicer to walk                                                         |
| Able to walk further; it is more comfortable and gives possibility to rest       |
| The walk bike has been a good means of contact with other people, it has the interest of news. |

| Negative comments                                                                 |
|----------------------------------------------------------------------------------|
| Too heavy in combination with oxygen; difficult to use with oxygen bottle        |
| Difficult way of making steps                                                    |
| Able to walk further because of better stability but feel embarrassed when using walk bike |
| Uncomfortable with bike, roads are too slippery                                  |
| For small hills walking with the help of the walk-bike is more difficult than without |

Table 3. Baseline characteristics of the study patients

|                                      | Randomized (N=23) | Completed study (N=10) | Drop outs (N=13) |
|--------------------------------------|-------------------|------------------------|------------------|
| Male                                 | 18 (78%)          | 8 (80%)                | 10 (77%)         |
| Age (years)                          | 71 (54-88)        | 71 (60-88)             | 72 (54-88)       |
| **Pulmonary function**               |                   |                        |                  |
| FVC (%pred)                          | 69 (48-97)        | 69 (53-87)             | 72 (48-97)       |
| TLCO (%pred)                         | 43 (26-67)        | 51 (26-62)             | 40 (26-67)       |
| **Exercise measures**                |                   |                        |                  |
| 6MWD (m)                             | 443 (278-593)     | 481 (360-540)          | 433 (278-593)    |
| Nadir SpO2 (%)                       | 87 (78-96)        | 89 (81-95)             | 85 (78-96)       |
| Average steps/day                    | 3521 (478-9869)   | 4016 (707-9636)        | 3185 (478-9869)  |
| **Health status scores**             |                   |                        |                  |
| SGRQ total [0-100] §§                | 50 (16-62)        | 44 (32-52)             | 55 (16-62)       |
| K-BILD total [0-100] ¶¶             | 63 (30-83)        | 66 (56-78)             | 58 (30-83)       |
| Perceived health status [1-5] ¶¶     | 3 (2-4)           | 3 (3-4)                | 3 (2-3)          |
| GAD-7 [0-21]                          | 2 (0-11)          | 2 (0-8)                | 5 (0-11)         |

Data are presented as absolute number (%) or median (min-max). FVC: forced vital capacity (% predicted), TLCO: diffusing capacity of the lung for carbon monoxide (%predicted), 6MWD: distance walked in a 6-minute walk test (meters), SpO2, oxygen saturation from pulse oximetry measured during 6MWT, SGRQ: St George’s Respiratory Questionnaire, K-BILD: King’s Brief quality of life questionnaire for Interstitial Lung Diseases, GAD-7: Generalized Anxiety Disorder 7-item scale. *: n=22, †: n=17, ‡: n=19, §: n=21, ¶: n=7, ¶¶: n=8, §§: n=12, ††: n=10, ‡‡: n=11, §§: SGRQ lower scores indicate better health-related QoL, II: K-BILD lower scores indicate worse health-related QoL, ¶¶: Assessed with the SGRQ, ***: GAD-7 higher scores indicate more anxiety.
Gas exchange parameters showed a tendency toward decline with a TLCO at baseline of 50%pred (26-62) vs. 45%pred (25-59) in week 18.

We also analyzed the data including the four patients that did not cross over; no changes in results were found.

**Discussion**

In this crossover pilot study, we explored the feasibility of a home-based walk-bike intervention study in IPF patients, and evaluated its effects on QoL and exercise capacity.

The feasibility outcomes demonstrate that a home-based walk-bike intervention study in its current design is difficult to accomplish. Potential barriers for feasibility of the study include reluctance to participate in the study, but also external factors such as weather and road conditions that may hampered adherence to the protocol. Patients satisfaction with the bike greatly varied. Despite the moderate usage intensity of the walk-bike, we found a tendency towards improvement in QoL after the 8-week homebased training program with the walk-bike. Functional exercise capacity did not change. Mobility increased with an average of 116 meters in distance covered when using the walk-bike during the 6MWT, compared to an unaided regular 6MWT. Use of the walk-bike proved to be safe.

A larger future RCT to detect clear walk-bike training-effects on QoL and exercise capacity does

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**Table 4. Change in health status and exercise measures of patients that completed both phases (N=10)**

|                          | ΔControl period          | ΔWalk-bike period         |
|--------------------------|--------------------------|---------------------------|
| **SGRQ* **               |                          |                           |
| Total (n=8)              | 1.2 (-12.3 - 8.3)        | -7.1 (-17.8 - 5.9)        |
| Symptoms (n=9)           | 6.7 (-22.7 - 38.9)       | -7.9 (-42.6 - 16.0)       |
| Activity (n=9)           | 0.0 (-18.1 - 6.3)        | -5.2 (-14.2 - 1)          |
| Impact (n=8)             | 0.3 (-12.3 - 8.9)        | -7.4 (-22.3 - 9.9)        |
| **K-BILD † **            |                          |                           |
| Total (n=8)              | 1.8 (-14.7 - 15.3)       | 6.5 (-10.0 - 29.4)        |
| Chest (n=8)              | 0.0 (-25.0 - 25.0)       | 12.5 (0.0 - 37.5)         |
| Breathlessness & activity (n=9) | 0.0 (-29.8 - 14.9) | 0.0 (-21.8 - 46.8) |
| Psychological (n=8)      | 0.0 (-11.1 - 23.5)       | 6.2 (-16.1 - 18.5)        |
| **Other**                |                          |                           |
| GAD-7 (n=9)              | 0 (-2 - 6)               | 0 (-2 - 0)                |
| Perceived health status (n=9) ‡ | 0 (-2 - 0) | 0 (-2 - 2) |
| **Exercise measures**    |                          |                           |
| 6MWD (m) (n=7)           | -4 (-25 - 28)            | -3 (-34 - 23)             |
| Nadir SpO2 (%) (n=7)     | -1 (-3 - 6)              | -3 (-7 - 2)               |
| Average steps/day (n=6)  | 132 (-903 - 3056)        | -461 (-4335 - 1063)       |

Data are presented as median (min-max) [n]; FVC: Forc vital capacity (%predicted), TLCO: transfer capacity of the lung for carbon monoxide (%predicted), 6MWD: distance walked during 6-minute walk test, SpO2: oxygen saturation from pulse oximetry, SGRQ: St George’s Respiratory Questionnaire (MID for total score is 7 points), K-BILD: King’s Brief quality of life questionnaire for Interstitial Lung Diseases (MID range for total score is 6-10 points), GAD-7: Generalized Anxiety Disorder 7-item scale. *: A negative change in SGRQ score indicates an improvement in health-related QoL, †: A positive change in K-BILD score indicates an improvement in health-related QoL, ‡: Assessed with the SGRQ.
not seem feasible unless potential barriers detected in our study are being solved. We chose a crossover design as it holds the advantage over a parallel study that the patient is its own control, thereby reducing the influence of confounding variables. However, this crossover design warrants a longer duration of study for the individual patient (16–18 weeks). Despite the block randomization to account for seasonal changes, weather changes during the study period turned out to affect the use of the walk-bike. A study incorporating both walk-bike use as well as a home-based indoor training alternative, maybe a better design for a home-based training program. As table 1 shows, another potential barrier is the collection of correct information of the intensity of training. In our pilot study patients recorded the time of walk-bike use in a diary. However, this patient-recorded time may have included time spent waiting and resting on the bike without movement. Accelerometers are devices that if worn by the patient, can record intensity duration and frequency of activities and makes assessments of the potential effects of the walk-bike more accurate.

Patient satisfaction with the walk-bike varied greatly from positive to negative. Patients positively evaluated the walk-bike because it enabled them to walk further with less dyspnea, or made it possible to leave the house again. The feeling of an increased level of independence and social participation are both important aspects of IPF patients’ QoL (9, 34). Negative comments related to being afraid to be stigmatized when using the walk-bike. Swigris et al. investigated how IPF affects QoL from patients’ perspective and noted many patients feel the need to try to hide the fact that they have a chronic illness when they are in public (34). This aspect, together with unfamiliarity with this new walking-aid, may also have

Fig. 3. Individual changes in SGRQ- and K-BILD total scores during control and intervention period. A negative change in SGRQ score indicates an improvement in health-related quality of life, a positive change in K-BILD score indicates an improvement in health-related quality of life.
played a role in the difficult inclusion of patients in our study. Other patients noted that the walk-bike was too heavy when used outdoors e.g. on hilly roads. It might well be that when the road includes obstacles or hills, use of the walk-bike is more complicated, which was also observed in another study (35).

In this pilot study, the use of the walk-bike led to improvement of the SGRQ total equal to the minimal important difference (MID) of 7 points, with a median difference in change of 8.3 points between the intervention period and control period. This improvement in SGRQ scores is comparable with the effects reported in a recently published systematic review on PR in IPF. (36) Meta-analysis on the results of three studies demonstrated a weighted mean difference SGRQ total score of -8.34 (95% CI, -11.30 - -5.39; n = 82) between intervention and control groups, favoring PR. In our study, we also assessed QoL with the ILD specific K-BILD questionnaire and found similar results in magnitude and direction of changes compared to the SGRQ. The K-BILD holds advantages for clinical use, being much shorter and disease specific.

We found no effect in exercise capacity (6MWD). In studies that assessed the effect of exercise training or PR programs in patients with IPF, 6MWD usually improved (14). The previous mentioned review of Gomes-Neto et al. (36) showed a weighted mean difference in 6MWD of 44 meters (95% CI, 5.3-82.8; n = 113) favoring PR. Most PR- or physical training programs contain supervised exercise protocols with a combination of endurance and resistance training (37). In our walk-bike intervention, the primary aim was to increase QoL. Participants were encouraged to use the walk-bike for at least one hour daily, and it was up to the discretion of the patients whether to use it continuously or in intervals. Practical factors such as weather conditions and day to day changes in wellbeing turned out to limit participants from using the walk-bike stringently and may have minimized the effect on exercise capacity. In patients with severe COPD it was shown that interval training at low burden could still have a positive effect on exercise capacity (38). We hypothesized that by increasing daily activities, patients would also exercise more at low burden which may eventually result in improving or maintaining exercise capacity and improving QoL.

The advantage of a home-based physical exercise program is increasingly recognized (14, 20). It remains to be evaluated if a more structured and supervised use of the walk-bike could play a role in such programs.

We found a meaningful improvement of 116 meters in distance covered during a 6MWT with use of the walk-bike, compared to an unaided test. This is in line with the improvement found by Vaes et al. who assessed the effects of the walk-bike on exercise performance in COPD patients (23). Improvement of mobility by using the walk-bike could potentially...
lead to a higher level of independence and social participation. These factors may have been the main contributing factors to the tendency toward improvement in QoL in our study, even though exercise capacity did not improve.

One of the limitations of our study is the small sample size. We aimed to include 22 patients, enrolled 23 patients but after randomization, a part of the patients did not start or discontinued. Only 10 patients completed both phases which underlines the difficulties encountered when trying to set up an interventional study for such a vulnerable patient group. If patients still had a reasonably well-preserved exercise tolerance, they did not wish to use a walk-bike. On the other side, when patients were more impaired and wished to use the walk-bike, risk of dropout increased, leaving a small subgroup that potentially benefits from this intervention. A potential limitation of the study design could be a carry-over effect. However, we believe this can be neglected as 8 patients were allocated to the control period in the first phase and trained with the walk-bike in the second phase, only 2 patient participated in the reverse order. Moreover, with gas exchange parameters that tended to decline across the study, a potential order effect might have led to underestimation of the effect of the walk-bike. Furthermore, 2 patients that started with the walk-bike decided to continue with the walk-bike instead of crossing over to the control arm.

In conclusion, this pilot study showed that a larger RCT may not be feasible unless most of the potential barriers are being solved. Despite the small group studied we found that the use of a walk-bike led to a meaningful improvement in QoL for patients with IPF after an 8-weeks homebased training program. Use of the walk-bike also increased mobility for patients but did not result in an improvement in exercise capacity. Patient satisfaction varied greatly and the use of the walk-bike seems only beneficial for a small selected group of patients with IPF.

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References

1. Raghu G, Collard HR, Egan JJ, Martinez FJ, Behr J, Brown KK, et al. An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. Am J Respir Crit Care Med. 2011;183(6):788-824. Epub 2011/04/08. doi: 10.1164/rcrm.2009-040GL. PubMed PMID: 21471066; PubMed Central PMCID: PMC3459933.
2. Raghu G, Rochwerger B, Zhang Y, Garcia CA, Azuma A, Behr J, et al. An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline: Treatment of Idiopathic Pulmonary Fibrosis. An Update of the 2011 Clinical Practice Guideline. Am J Respir Crit Care Med. 2015;192(2):e3-19. PubMed PMID: 26177183.
3. Holland A, Hill C. Physical training for interstitial lung disease. Cochrane Database Syst Rev. 2008;(4):CD006322. PubMed PMID: 18843713.
4. Swigris JJ, Gould MK, Wilson SR. Health-related quality of life among patients with idiopathic pulmonary fibrosis. Chest. 2005;127(1):284-94. PubMed PMID: 15653996.
5. American Thoracic Society. Idiopathic pulmonary fibrosis: diagnosis and treatment. International consensus statement. American Thoracic Society (ATS), and the European Respiratory Society (ERS). Am J Respir Crit Care Med. 2000;161(2 Pt 1):646-64. PubMed PMID: 10673212.
6. Noble PW, Albera C, Bradford WZ, Costabel U, Glassberg MK, Kardatzke D, et al. Pirfenidone in patients with idiopathic pulmonary fibrosis (CAPACITY II): randomised controlled trial. Lancet. 2014;377(9779):1760-9. doi: 10.1016/S0140-6736(14)00405-0. PubMed PMID: 24836310.
7. Behr J, Gunther A, Bonella F, Geissler K, Koschel D, Kreuter M, et al. German Guideline for Idiopathic Pulmonary Fibrosis - Update on Pharmaceutical Therapies 2017 S2k-Leitlinie Idiopathische Lungenfibrose - Update zur medikamentosen Therapie 2017. Pneumologie. 2018;72(2):155-68. PubMed PMID: 29341047.
8. Vries JD, Kessels BLJ, Drent M. Quality of life of idiopathic pulmonary fibrosis patients. European Respiratory Journal. 2001;17(5):954-61.
9. Verma G, Marras T, Chowdhury N, Singer L. Health-related quality of life and 6 min walk distance in patients with idiopathic pulmonary fibrosis. Canadian Respiratory Journal. 2011;18(5):283-7.
10. Richeldi L, du Bois RM, Raghu G, Azuma A, Brown KK, Costabel U, et al. Efficacy and safety of nintedanib in idiopathic pulmonary fibrosis. N Engl J Med. 2014;370(22):2071-82. PubMed PMID: 25064589.
11. Behr J, Gunther A, Bonella F, Geissler K, Koschel D, Kreuter M, et al. An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. Am J Respir Crit Care Med. 2011;183(6):788-824. Epub 2011/04/08. doi: 10.1164/rcrm.2009-040GL. PubMed PMID: 21471066; PubMed Central PMCID: PMC3459933.
12. Spruit MA, Singh SJ, Garvey C, ZuWallack R, Nici L, Rochester C, et al. An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation. Am J Respir Crit Care Med. 2013;188(8):e13-64. Epub 2013/10/17. doi: 10.1164/rcrm.201309-1634ST. PubMed PMID: 24127811.
13. Kenn K, Gloeckl R, Behr J. Pulmonary rehabilitation in patients with idiopathic pulmonary fibrosis—a review. Respiration. 2013;86(2):89-99. Epub 2013/08/15. doi: 000354112 [pii] 10.1159/000354112.
