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ORIGINAL RESEARCH

Effects of community-based pulmonary rehabilitation in 33 municipalities in Denmark – results from the KOALA project

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Background: The positive impact of pulmonary rehabilitation (PR) in patients with COPD is well documented. However, little is known regarding the effect of this treatment in community-based settings. Since 2007, all Danish municipalities have been offering PR to patients with moderate to severe COPD, whereas patients with very severe disease or those suffering from many comorbidities were referred to outpatient hospital-based PR.

Objective: To analyze the effect of a standardized PR program conducted in a community-based setting on exercise capacity and health-related quality of life (HRQoL).

Methods: This is a real-life study including data from patients attending PR at one of the 33 healthcare centers in Denmark during the period 2011–2012. For the purpose of registration and for quality assurance, the KOALA database was established and this web-based registration instrument was offered free of charge to every municipality. Measures included sociodemographic and health-related variables and outcomes were exercise capacity and HRQoL assessed by 6-minute walking distance (6MWD) and the 15D questionnaire, respectively, at the beginning (baseline) and after completion of PR. Relative improvements in 6MWD and 15D were analyzed with multivariable linear models in patients who attended >50% of the sessions.

Results: A total of 581 patients completed the PR (72% of those included). We found statistically significant and clinically meaningful differences between baseline and end of rehabilitation values for both main outcomes with a mean change in 6MWD of 45 m, and the magnitude of improvement corresponds to other findings. Furthermore, relative improvements in 6MWD and 15D were correlated, as was the relative change in 15D and baseline Medical Research Council scores.

Conclusion: Standardized, multidisciplinary PR conducted in a community-based setting showed good adherence to the program and produced effects on exercise capacity and HRQoL that were clinically meaningful and comparable in size to hospital-based PR.

Keywords: COPD, community-based, exercise capacity, pulmonary rehabilitation, quality of life

Introduction

The beneficial effects of hospital-based pulmonary rehabilitation (PR) on exercise capacity, perception of dyspnea, and quality of life in patients with moderate to very severe COPD have been extensively documented.[1,2] According to the Cochrane authors, studies comparing PR with usual care are no longer warranted; instead, future studies should focus on settings, intensity, and duration of the PR program as well as of the achieved effect.[1] With respect to the impact of rehabilitation on these outcomes in patients with less advanced disease, the evidence is limited, even more so when

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evaluating the effect of this intervention in a home-based or community-based setting.[3,4] Most of the studies included small sample size, and there was no consensus as to recommended type of training or the duration and maintenance of PR in these settings compared with the in- or outpatient hospital-based programs. However, one reasonably large randomized controlled trial of 199 patients with moderate COPD showed that community-based rehabilitation was effective in improving exercise performance and quality of life and was also cost-effective compared with usual care.[5,6] In this 2-year study, the exacerbation rate did not differ between the intervention group and the usual care group. A recently published meta-analysis also resulted in a weak recommendation for routine PR in patients with perceived dyspnea corresponding to modified Medical Research Council (mMRC) ≥ 1.[7]

In Denmark, the National Board of Health recommended in 2006 that all COPD patients with a dyspnea grade of 3 or above according to the MRC scale should be offered PR. Furthermore, the intention was that patients with mild to moderate disease were referred to this service in primary care, while patients with severe to very severe COPD (GOLD D with frequent exacerbations) were referred to hospital-based outpatient clinics.[8] Hence, since 2007, all 98 municipalities in Denmark have gradually implemented rehabilitation programs for patients with COPD. To comply with this task, many municipalities have established one or several healthcare centers with a multidisciplinary staff, though usually not including medical doctors. To our knowledge, only two studies have compared the effects of standardized PR programs conducted either in a healthcare center/community site or in a hospital outpatient setting.[9,10] Both studies concluded that the two settings were equally effective in terms of improving endurance shuttle walking time (ESWT) and quality of life; however, in the Danish study, improvement in the ESWT was significantly greater in the hospital setting.[9] Due to the lack of data registration and quality assurance instruments for PR in primary healthcare, the KOALA project was launched in 2007 by Boehringer Ingelheim Denmark A/S as an opportunity for the newly established healthcare centers to enter the data and clinical parameters of participating patients into a Web-based database.

The aim of this non-randomized, real-life study was to analyze the efficacy of community-based rehabilitation programs in a large COPD patient population on exercise capacity, measured using the 6-minute walking distance (6MWD) test, and health-related quality of life (HRQoL), measured using 15D questionnaire, as primary end points.

Methods

The overall purpose and design of the KOALA project has previously been described in detail.[11]

Brief description of the KOALA database

The main objective of the KOALA database was to construct a digital platform for recording relevant indicators of PR, which could be used in healthcare across all municipalities in Denmark. Other objectives included implementation of the database as a quality assurance instrument and a forum for sharing of knowledge and evaluation. The project was organized with a steering committee consisting of key healthcare professionals and a daily manager employed by Boehringer-Ingelheim. The variables were assessed and measured pre- and post-PR and included, among many, demographic and behavioral characteristics of the participants, such as medication for COPD, smoking habits, frequency of exacerbations, previous PR, comorbidities, and dyspnea measured as MRC and Borg dyspnea scale (BORG). HRQoL was measured using a generic 15-item questionnaire 15D, which has proven to be valid and reliable in assessing and detecting changes in HRQoL in chronic conditions including COPD.[12,13] Exercise capacity was tested using 6MWD[14] and in some centers also included the incremental and endurance shuttle walk test (SWT), and was recorded at baseline, at completion of the PR, and at eventual subsequent follow-up visits. Upon completion of the rehabilitation program, relevant clinical information was sent electronically via EDIFACT to the patients' general practitioners.

Inclusion of healthcare centers and referral of patients

The daily manager of the KOALA project invited healthcare centers to participate by face to face meetings preceded by e-mail or phone correspondence. The healthcare professionals employed by the municipalities are mainly represented by specially trained nurses, physiotherapists, and dieticians – preferably as a multidisciplinary team – depending on the size and facilities in the municipality. However, all patients attending COPD rehabilitation must be referred by a doctor (general practitioner or pulmonary specialist) based on a diagnosis of COPD, a spirometry conducted in less than 1 year, and assessment of the subject's degree of dyspnea on exertion. Whenever possible, the patient also had his/her lung function measured at the healthcare center before rehabilitation was started. Although minor deviations exist, most healthcare centers have implemented the standard PR program with respect to content and duration, ie, focusing on aerobic exercise endurance and lasting for 6–12 weeks and

in some centers with 1–2 subsequent follow-up visits within the following year. All the community-based PR programs in Denmark provide supervised aerobic and strength training at least twice a week, breathing exercises, and group educational sessions comprising, at a minimum, management of dyspnea and exacerbations and inhalation technique. If available, nutritional support, psychosocial interventions, and home-training programs were provided. In general, the healthcare centers have adopted the Danish outpatient hospital-based PR recommendations.[15]

By February 2011, all 78 municipalities, who at that time offered standardized PR in Denmark, were contacted, and of these 33 agreed to participate in the KOALA project. We report data that were extracted from the database at Danish Technical University (DTU) in August 2012.

Ethical considerations

All patients provided written consent as it is mandatory for participation in PR, and the study was approved by the Danish Data Protection Agency. However, ethical approval was not indicated due to the non-interventional setting of this study.

Statistical analyses

In this paper, we present results from the changes recorded during rehabilitation, ie, the difference between the first (baseline) visit and at the end of the rehabilitation program. Categorical variables were summarized by frequency and percentage. Continuous variables were summarized by median and interquartile range (IQR) as the data were not normally distributed. The improvement in the two primary outcomes of interest, 6MWD and 15D, was tested univariately by Wilcoxon signed-rank test for paired observations.

Factors associated with the relative improvement in 6MWD/15D were analyzed in a multivariable linear regression model. For continuous factors, the association with the relative improvement was estimated by restricted cubic splines (non-parametric smooth functions) and the effect reported as the effect corresponding to interquartile range increases. The association between the relative improvement in 15D and the initial score and the association between absolute changes in 6MWD and 15D were tested by Spearman correlation coefficients and corresponding *P*-values.

The statistical analyses were performed using the statistical software R version 2.11.1 (R Development Core Team [2009]). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. ISBN 3-900051-07-0, URL http://www.R-project.org.), and a 5% significance level was used in all tests.

Results

The results from this study are based on data from 33 participating centers and included patients that were referred and participated in PR between October 2011 and August 2012. A total of 803 COPD patients were included in the study, and at the time of analysis 581 patients completed the full rehabilitation program (>50% attendance) with pre- and post-rehabilitation data. The rehabilitation period was 64 days (median).

Demographic data including assessment of comorbidities for patients completing rehabilitation program are shown in Table 1. The majority of patients had moderate disease severity according to GOLD criteria, however, with median FEV_1 only just above 50% of expected and

Table 1 Baseline characteristics of the patients

Baseline data for patients completing PR (n=581)	Median (IQR)/N (%)
Gender	
Female	58.4%
Male	41.7%
Age (years)	68.1 (11.1)
FEV_1 (% pred)	53.5% (25.2)
COPD stage (GOLD 2007)	
Mild	4.7%
Moderate	45.8%
Severe	25.7%
Very severe	6.7%
Missing information	17.2%
MRC	
1	6.9%
2	33.6%
3	43.7%
4	11.4%
5	3.6%
Missing information	2.4%
Pack-years	37.5 (24.0)
BMI (kg/m^2)	25.7 (7.2)
Smoking status	
Never	4.1%
Ex	67.5%
Current	27.9%
Missing information	0.5%
Osteoporosis	9.3%
Heart disease	20.1%
Depression	11.9%
Diabetes	9.1%

Abbreviations: BMI, body mass index; MRC, Medical Research Council; PR, pulmonary rehabilitation.

moderate degree of dyspnea. Overall, the prevalence of comorbidities was low with cardiovascular disease being the most frequent.

Key parameters for effect of rehabilitation showed significant and clinically meaningful changes as displayed in Tables 2 and 3 for 6MWD and 15D, respectively. 6MWD improved by an average of 45m ($P<0.001$) and the change was significant across COPD stage groups. Furthermore, looking at quartiles of 6MWD based on initial distance achieved, changes were consistent in all groups, although patients with the best walking distance at baseline improved the least. The multivariable analyses also revealed that women, older patients (>75 years), those with MRC =5, and current smokers had significantly less improvement in 6MWD compared to reference groups. Relative changes in 6MWD are positively correlated to changes in 15D ($P=0.016$), as shown in Figure 1.

The HRQoL and 15D improved by a score of 0.03 ($P<0.001$), which is considered to be clinically relevant. The analyses showed that the individuals with the lowest 15D at baseline on average improved the most on the relative scale

Table 2 Multivariate linear regression models of the effect of PR on 6MWD at the end of the program adjusted for baseline 6MWD, gender, age, FEV_1, BMI, pack-years, COPD stage, MRC, and smoking status

Improvement in the 6MWD after pulmonary rehabilitation			
Variables		**95% CI**	***P*-value**
6MWD mean change m (SD)	445.0 (151.0)–400.0 (132.5) (N=579)	[38.0–46.0]	<0.001
6MWD at baseline, m	[22–320] (N=88)		
	[321–395] (N=85)		
	[396–463] (N=106)		
	[463–663] (N=94)	[–0.18, –0.08]	<0.001
Gender	Female (N=210)		
	Male (N=163)	[0.00, 0.10]	0.04
Age (years)	[30–62] (N=111)		
	[63–69] (N=112)		
	[70–74] (N=70)		
	[75–90] (N=80)	[–0.13, –0.04]	0.02
FEV_1		[–0.01, 0.20]	0.55
BMI (kg/m^2)	[9.16–22.42] (N=76)		
	[22.43–25.70] (N=93)		
	[25.70–29.63] (N=97)		
	[29.64–48.69] (N=107)	[–0.04, 0.06]	0.55
Pack-years	[0–22.5] (N=103)		
	[22.6–37.5] (N=100)		
	[37.6–50.0] (N=87)		
	[50.1–200.0] (N=83)	[–0.01, 0.08]	0.13
COPD GOLD stage	Mild (N=27)		
	Moderate (N=199)	[–0.11, 0.15]	
	Severe (N=117)	[–0.05, 0.25]	
	Very severe (N=30)	[–0.09, 0.29]	0.30
MRC	1 (N=26)		
	2 (N=127)	[–0.14, 0.00]	
	3 (N=164)	[–0.15, –0.01]	
	4 (N=39)	[–0.21, –0.03]	
	5 (N=7)	[–0.34, –0.06]	0.03
Smoking status	Never (N=19)	[–0.43, –0.04]	
	Ex-smoker (N=253)		
	Smoker (N=101)	[–0.06, 0.02]	0.05

Abbreviations: BMI, body mass index; MRC, Medical Research Council; 6MWD, 6-minute walking distance; PR, pulmonary rehabilitation.

Table 3 Multivariate linear regression models of the effect of PR on quality of life (15D) at the end of the program adjusted for baseline 15D, gender, age, FEV_1, BMI, pack-years, COPD stage, MRC, and smoking status

Improvement in quality of life after pulmonary rehabilitation			
Variables		**95% CI**	***P*-value**
15D mean change (IQR)	0.854 (0.121)–0.826 (0.122) (N=558)	[0.023, 0.035]	<0.001
15D at baseline	[0.43–0.75] (N=72)		
	[0.76–0.82] (N=86)		
	[0.83–0.88] (N=100)		
	[0.88–1.00] (N=99)	[–0.10, –0.05]	<0.001
Gender	Female (N=207)		
	Male (N=150)	[–0.04, 0.00]	0.08
Age (years)	[30–62] (N=96)		
	[63–69] (N=110)		
	[70–74] (N=77)		
	[75–90] (N=74)	[–0.03, 0.02]	0.23
FEV_1		[–0.05, 0.06]	0.22
BMI (kg/m^2)	[9.16–22.42] (N=69)		
	[22.43–25.70] (N=84)		
	[25.70–29.63] (N=96)		
	[29.64–48.69] (N=107)	[–0.03, 0.02]	0.65
Pack-years	[0–22.5] (N=89)		
	[22.6–37.5] (N=96)		
	[37.6–50.0] (N=88)		
	[50.1–200.0] (N=84)	[–0.03, 0.01]	0.90
COPD GOLD stage	Mild (N=29)		
	Moderate (N=182)	[–0.01, 0.12]	
	Severe (N=120)	[–0.01, 0.15]	
	Very severe (N=26)	[–0.02, 0.17]	0.36
MRC	1 (N=18)		
	2 (N=114)	[–0.04, 0.04]	
	3 (N=172)	[–0.04, 0.04]	
	4 (N=45)	[–0.04, 0.06]	
	5 (N=8)	[–0.07, 0.08]	0.88
Smoking status	Never (N=19)	[–0.12, 0.11]	
	Ex-smoker (N=245)		
	Smoker (N=93)	[–0.02, 0.03]	0.92

Abbreviations: BMI, body mass index; MRC, Medical Research Council; PR, pulmonary rehabilitation.

($P<0.05$). No other factors were associated with changes in 15D. The positive changes in 15D correlated with the initial MRC score such that patients with higher MRC improved more in 15D ($P=0.042$) (Figure 2).

Discussion

Results from this database of community-based PR showed statistically significant and clinically meaningful effects of the chosen outcomes: exercise capacity measured as 6MWD and quality of life measured using the 15D questionnaire. The overall magnitude of the effect on 6MWD corresponds to "moderate response" to PR as suggested by a Dutch group but clearly exceeds the revised minimal clinical important difference (MCID) of 30 m for this test.[16,17] Furthermore, our results are almost identical to other recently published studies of community-based multicenter PR from Australia and the UK.[18,19] The latter study also found that the patients with the lowest 6MWD at baseline improved the most and that there was no independent association between baseline variables and change in HRQoL.[19]

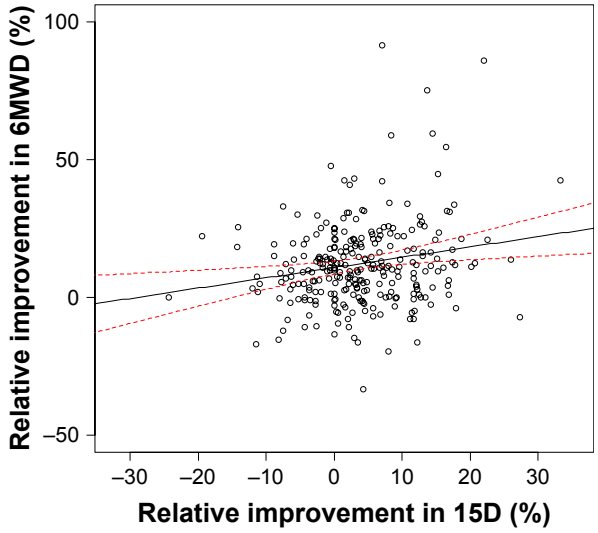

Figure 1 Relative improvement in 6MWD vs relative improvement in 15D.
Note: The solid black line is the fitted regression line and the red dashed lines are 95% confidence bands (*P*=0.016).
Abbreviations: 15D, 15-item questionnaire; 6MWD, 6-minute walking distance.

Successful PR in this setting was defined as participation in >50% of the sessions and this was achieved by 72% of the patients, which we consider is in alignment with and even better than current evidence.[1,18,19] However, in the London study comprising nearly as many patients as in our study, the criterion for completion of the PR was at least 75% of the visits. The adherence in our study was slightly higher than in another study of similar size that included two hospitals and five community PR sites.[20] It could be hypothesized that adherence to a PR program would be better in a community setting which, in many countries including Denmark, receives patients with less severe disease and is thus at lower risk of dropout due to exacerbation.

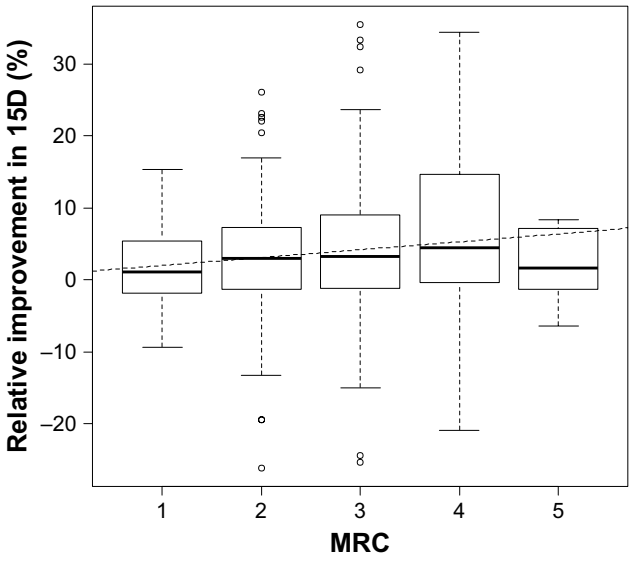

Figure 2 Spearman rank correlation for relative improvement of 15D and correlated to MRC at visit 1 (baseline).
Note: *R*=0.088, *P*=0.042, N=530.
Abbreviations: 15D, 15-item questionnaire; MRC, Medical Research Council.

Baseline characteristics of the patients referred for PR in this real-life setting are also comparable to other studies,[1] and overall the KOALA project also captures those intended for community-based PR. Unfortunately, data on GOLD stage (and thereby registration of FEV_1 and FVC) were missing for 17% of the participants. Nevertheless, the majority were in GOLD stage II and III (moderate and severe COPD). It is noteworthy that ~40% of the patients were registered as having less dyspnea (MRC 1–2), which at that time was considered a "contra-indication" for referral to PR. Due to the increasing evidence for the benefit of PR in patients with milder disease based on FEV_1 and/or less symptom burden,[7,21,22] it is considered appropriate in the new Danish guidelines for PR to refer patients with MRC 2, who also show signs of muscle depletion.[23] While it is generally recognized that most patients with COPD have one or more comorbidities,[24] only one in five reported heart disease as the most common comorbidity and ~10% reported other comorbidities such as depression, diabetes, or osteoporosis. Most likely this also reflects the milder disease status in this setting.

We have previously shown that most municipalities in Denmark quickly complied with the task of performing PR in non-healthcare facilities and that the KOALA database was a feasible instrument for data recording.[11] Now the efficacy results of the standardized training have proven to be in accordance with the above-mentioned evidence, which has emerged during the recent years, and the outcomes are favorable and comparable to hospital-based PR in terms of exercise capacity and quality of life.

Strengths and limitations

A strength of the present study is that it reflects current clinical practice and thus has greater relevance than the selected populations normally recruited to clinical trials. This is, however, also a weakness, since the results cannot be confirmed by comparison with a control group. However, it is now generally recognized that it would be unethical to allocate patients in need of PR to a control group without such intervention. The large number of participants, inclusion of many centers, and application of the KOALA database also contribute to the external validity of the study. Limitations are we have no data on further follow-up visits after completion of rehabilitation program, no registration of

healthcare utilization, some missing data on lung function measurements, and no recording of reasons for dropout during the PR. Furthermore, more than half of the approached healthcare centers/PR facilities declined to use the KOALA database, the most common reasons being that they already had a registration tool or that they did not want to cooperate with the pharmaceutical industry as previously described.[9] Another potential source of bias comes from the fact that some small municipalities deliver generic PR, meaning that the physical training sessions are performed together with patients suffering from other chronic conditions such as heart failure or musculoskeletal disorders. This would, however, tend to dilute the efficacy parameters and thus underestimate the results.

Conclusion

We conclude that pulmonary rehabilitation is effective when conducted in community-based facilities and that a significant improvement in walking distance of 45 m is similar to current knowledge regarding PR in a less intensive setting. There is also a positive effect on HRQoL, which is most pronounced in patients with the largest baseline symptom burden.

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Disclosure

The authors report no conflicts of interest in this work.

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