EuroQoL in assessment of the effect of pulmonary rehabilitation COPD patients

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Summary

Background: The effect of pulmonary rehabilitation on EuroQol in COPD patients has not been investigated previously.

Methods/materials: Two hundred and twenty nine consecutive COPD patients who had completed a 7-week pulmonary rehabilitation programme were assessed with EuroQol five-dimension questionnaire (EQ-5D), endurance shuttle walk test (ESWT), and the St George's Respiratory Questionnaire (SGRQ) before and after the programme, and at the 3-month follow-up visit.

Results: Two hundred and two (88.4%) patients had $FEV_1 < 50\%$ predicted and all but four (1.7%) had dyspnoea score at least 3 on MRC scale. At completion of the programme, statistical significant improvements were seen for ESWT 157.3 s; $p < 0.001$, EQ-5D utility score -0.019; $p = 0.03$, EQ-5D VAS -2.1; $p = 0.056$, SGRQ total score -2.8 units; $p < 0.001$. The effects of rehabilitation on ESWT and SGRQ were maintained at 3-month follow-up (158.9 s and -2.9 units), while the effect on EQ-5 utility decreased (0.013; $p = 0.18$). At baseline, there was a maximum score (''ceiling effect'') for EQ-5D utility and EQ VAS in 29 (12.7%) and five (2.2%) of the patients, respectively. After rehabilitation these number increased to 41 (17.9%) and seven (3.1%).

Conclusions: In COPD patients receiving rehabilitation, responsiveness of EQ-5D utility was poor. One explanation might be a ''ceiling effect'' of this instrument.

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Introduction

Pulmonary rehabilitation is an established treatment for COPD patients, which improves both physical performance and health-related quality of life (HRQoL)[1] However, not all studies have shown improvements in HRQoL after rehabilitation.[2] This may be related to the responsiveness of the chosen HRQoL instrument. Typically, HRQoL is measured by disease specific instruments, such as St. George Respiratory Questionnaire (SGRQ) and Chronic Respiratory Questionnaire (CRQ).[1] With a generic HRQoL measure more global issues related to HRQoL can be assessed, such as

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social role, mental health, and general well being. In addition, generic instruments make it possible to compare HRQoL across different diseases. The EuroQoL five-dimension questionnaire (EQ-5D), a generic preference-based instrument, is increasingly used as global measures of HRQoL in cost-effectiveness studies.[3] It generates utility scores, which can be used in calculation of quality-adjusted life years (QALY). Few studies in COPD patients have used EQ-5D as an outcome,[4,5] and only three studies have examined the responsiveness of EQ-5D to intervention (lung transplantation, self-management, and Tiotropium).[6–8] and in particular, the effect of PR on EQ-5D in COPD patients has not been evaluated previously.

In a comparison of different outcome measures, Harper et al. found, that many COPD patients were unable to complete the SGRQ, and that many patients at baseline scored either minimum ("floor effect") or maximum ("ceiling effect") in SF-36, a generic HRQoL instrument.[9]

The primary aim of the present study was to evaluate the responsiveness of EQ-5D to pulmonary rehabilitation in COPD patients. The secondary aims were to compare the complete rates, "floor effect", and "ceiling effect" of EQ-5D and SGRQ.

Methods

Rehabilitation programme

The programme used in this study is adopted from Glenfield Hospital, University Hospital of Leicester.[10] Patients attended twice weekly for 7 weeks with each session lasting 2 h. The session was divided into 1 h of supervised training and 1 h of education. Relaxation techniques, disease education, dietary advise, benefits advise, energy conservation, medication advise, chest clearance, and breathing control techniques comprised the main components of the education. The supervised aerobe training sessions consisted of walking and cycling. Patients were instructed to exercise at a level equal to 85% of predicted peak oxygen uptake as calculated from the Incremental Shuttle Walk Test (ISWT). During the 7-week programme total continuous walking times (with 85% of maximal intensity) were measured with a stopwatch and recorded in a diary both at the supervised training sessions and during unsupervised daily training at home. Their diary was looked over at the supervised training sessions. After the 7-week programme patients were asked to continue the self-monitored daily exercise at home as the only maintenance training. In addition, they received an illustrated folder with some of the exercises included in the supervised sessions. When the weather prevented them from walking outside, they were encouraged to use the stairs in their apartments or to do the exercises from the folder. Patients were advised to increase the duration of the walk rather than the intensity.

Selection of patients

Two hundred and twenty nine consecutive patients constituted our study group (Fig. 1). Eligibility criteria included: stable COPD (forced expiratory volume in 1 s (FEV$_1$) <80% and FEV$_1$/forced vital capacity <70%; motivated for

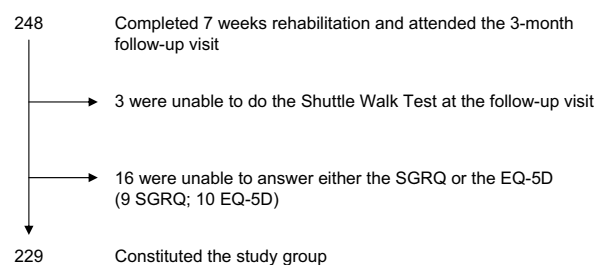| 248 | Completed 7 weeks rehabilitation and attended the 3-month follow-up visit |
	3 were unable to do the Shuttle Walk Test at the follow-up visit
	16 were unable to answer either the SGRQ or the EQ-5D (9 SGRQ; 10 EQ-5D)
229	Constituted the study group

Figure 1 Flow chart of patients completing 7-week pulmonary rehabilitation and attended 3 month follow-up visit.

pulmonary rehabilitation; completion of a 7-week rehabilitation programme and followed-up 3 months later. Exclusion criteria were: significant musculo-skeletal, cardiac, or cognitive problems.

Outcome measures

Measurements were made before and after the programme, and at 3 month follow-up. Endurance Shuttle Walk Test (ESWT), EQ-5D, and SGRQ were the outcomes. An Incremental Shuttle Walk Test (ISWT) was used to measure the maximal exercise performance. The ESWT measured the sub-maximal exercise performance, when the patient walked at a constant speed equating to 85% of predicted peak oxygen uptake as calculated from the ISWT.

The SGRQ is a disease specific questionnaire, which comprises of three domains (dyspnoea, impact, and activity) and has been valid, reproducible, and responsive in patients with COPD.[11]

The EQ-5D is a self-administered generic instrument in two sections, a descriptive and a valuation section.[3] The first section measures the following five-dimensions of health: mobility; self-care; usual activities; pain/discomfort; and anxiety/depression (EQ-5D utility). Each dimension is divided into the following three levels of functioning: no problems; some problems; and extreme problems. From these five answers a single index is derived on a scale anchored at 1, which represents perfect health and 0, which represents death. The second section is a visual analogue scale measuring global health (EQ-5D VAS). It is presented in the form of a thermometer with 100 intervals, in which 100 represent the best imaginable state and 0 the worst imaginable state. We asked patients to reflect the health status in their score as it was the day of examination.

Statistics

Data were analysed in the statistical package (SPSS) version 12.0 SPSS Inc. (Chicago, USA). Analysis of variance (ANOVA) was used to test the difference over time. Non-parametric statistics (Wilcoxon) were applied in comparing EQ-5D utility scores and ESWT because of non-normal distribution. The theory of Wilcoxon signed-rank test is that the absolute values of the differences between observations are ranked from smallest to largest (rank 1 to the smallest, rank 2 to the next smallest, and so on). If the null hypothesis is true, the sum of the ranks of the positive differences should be

about the same as the sum of the ranks of the negative differences. Note that this is different from the null hypothesis of the paired *t*-test, which is that the mean difference between pairs is zero. A two-sided *p*-value of <0.05 was considered significant.

Results

Patients had severe airflow limitation (88.4% had FEV_1 less than 50% of predicted value) and dyspnoea while walking (98.3% had at least MRC score 3) (Table 1, Fig. 2). Completion rates for SGRQ and EQ-5D were 96.3% and 95.1%, respectively. After supervised rehabilitation, statistical significant improvements were seen for ESWT 157.3 s ($p < 0.001$), EQ-5D utility score −0.019 ($p = 0.034$), SGRQ total score −2.8 ($p < 0.001$), but not for EQ-5D VAS −2.1 ($p = 0.56$) (Table 2). At 3-month follow-up the effects on ESWT and SGRQ were maintained, while the effects on EQ-5D were no longer present (Table 2).

At baseline, there was a ''ceiling effect'' for EQ-5D utility and EQ VAS in 29 (12.7%) and 5 (2.2%) of the patients, respectively. After rehabilitation, these numbers increased to 41 (17.9%) and 7 (3.1%), and at follow-up, the numbers were 45 (19.7%) and 2 (0.9%). There was no ''ceiling effect'' for SGRQ-total score. Patients who scored maximum for EQ-5D utility at baseline had a mean FEV_1 37.8%, MRC score 3.2, ESWT 201 s, and SGRQ-total score 42.7 units.

Discussion

The 7-week supervised pulmonary rehabilitation programme improved EQ-5D slightly. However, this effect was not maintained at 3-month follow-up. In contrast, the positive effects on exercise tolerance and disease specific health status remained unchanged.

The effect of rehabilitation on EQ-5D has not previously been studied. The gain in EQ-5D utility score of our rehabilitation programme was comparable to the fall seen after 6 months in COPD patients, who acted as controls in a study of self-management.[7] In that study, self-
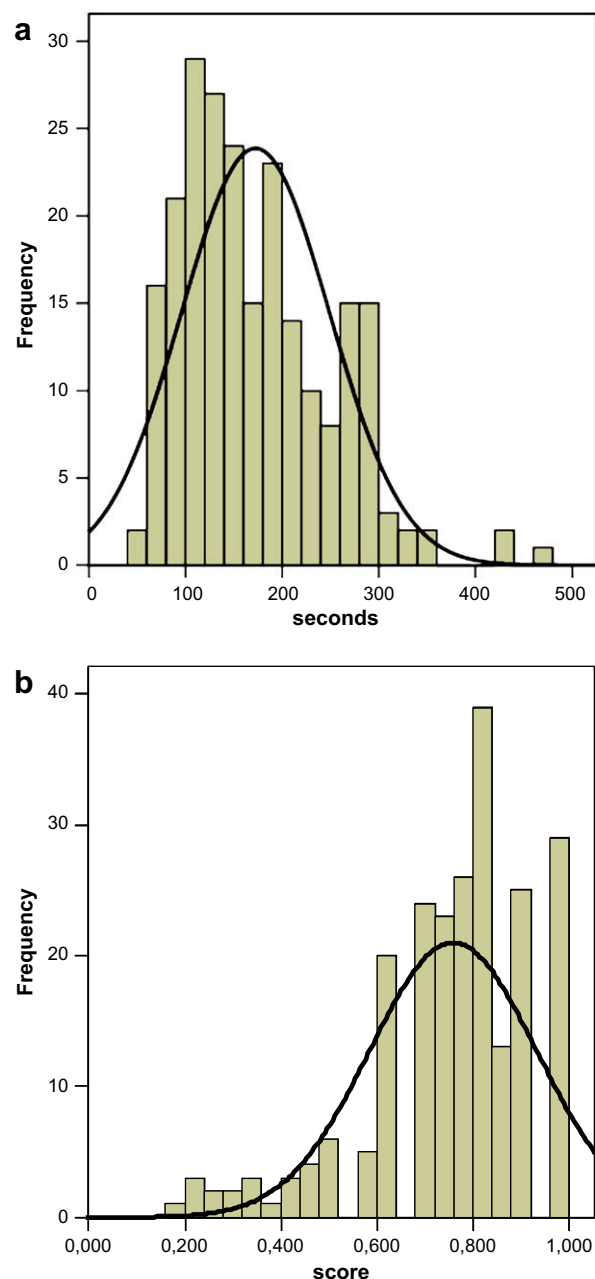

Figure 2 Distribution of endurance shuttle walk time (ESWT) (a) and EQ-5D (b) at baseline.

management didn't changed the EQ-5D utility score.[7] Not surprisingly, lung transplantation improved EQ-5D utility score considerably more (approximately 0.35).[6] Tiotropium was associated with statistically significant improvements in the visual analogue component of the EQ-5D and with non-statistically significant trends in the utility scores.[8] Only one study has provided information on minimum clinically important difference (MCID) for the EQ-5D. Walters & Brazier analysed eight longitudinal studies in 11 patient groups that used both EQ-5D and SF-6D.[12] They suggested that the MCID for the EQ-5D was 0.074 (range −0.011−0.140). Looking specifically at COPD patients (in total 55 patients) the MCID was negative! More studies are needed to determine the MCID for EQ-5D.

Table 1 Patients' characteristics at baseline for patients who completed the 3-month follow-up period

Age, years	69.1 (8.1)
Gender, % males	31.9
FEV_1 %-predicted value ($n = 225$)	34.1 (12.2)
Body mass index, kg/m^2 ($n = 226$)	24.8 (5.3)
Current smokers, % ($n = 228$)	19.7
Package years (minimum−maximum) ($n = 226$)	38.0 (0−100)
Musculo-skeletal diseases, %	21.8
Cardiac co-morbidity, %	29.7
Systemic corticosteroid, %	10.9
Long-term oxygen therapy, %	9.2
Oxygen saturation at rest and with air, %	94.0 (2.1)
Medical Research Council (MRC) dyspnoea score (minimum−maximum)	3.7 (2−5)

Continuous variables are presented as mean (SD) unless otherwise indicated.

Table 2 The effect of 7-week rehabilitation on endurance shuttle walk time (ESWT), SGRQ, and EuroQol 5-dimension questionnaire (EQ-5D)

	Pre-rehab.	Post-rehab.	3-month follow-up	p-value	
				Pre-rehab. vs post-rehab.	Pre-rehab. vs 3-month follow-up
EQ-5D utility score	0.759 (0.174)	0.778 (0.180)	0.771 (0.192)	0.034	0.18
EQ-5D VAS	58.6 (16.6)	60.7 (19.0)	59.2 (17.8)	0.056	0.30
SGRQ-total score	55.7 (12.9)	52.9 (13.3)	52.8 (14.4)	<0.001	0.001
ESWT, s	172.3 (76.6)	329.6 (289.8)	331.2 (345.2)	<0.001	<0.001

Variables are presented as mean (SD).

The UPLIFT trial had measured EQ-5D at baseline.[13] Although, their patients had the same mean EQ-5D utility score, they had higher EQ-5D VAS score (64.8) and FEV_1 (48% of predicted). Compared to the study of Maninkhof et al. where the effect of self-management was investigated, our patients had worse SGRQ-total score 55.7 vs 37.2 and EQ-5D utility score 0.76 vs 0.81.[7]

In accordance with other studies, we found that a disease specific instrument is more responsive than a generic measure, when used for evaluation of PR.[2,14–16] Yet, there are several reasons for also using generic instruments: (1) a disease specific instrument may fail to capture all aspects of HRQoL, e.g. co-morbidities such as cardiac and musculo-skeletal problems, and side effects of intervention; (2) generic instruments allow comparisons of HRQoL across different diseases; and (3) utility instruments can be used in economic evaluation.

The ideal health status instrument should be valid, reliable, and responsive, and besides it should not be expensive to use or too difficult or time consuming to answer/fill in for the patient. In our study, completion rates for SGRQ and EQ-5D were very high. This is in line with findings from other studies.[17,18] Ståhl et al. showed that only 10–20% of the patients reported difficulty with completing SGRQ and EQ-5D,[17] and in a study of 573 patients with various chronic diseases, 60–75% of the respondents found EQ-5D easy to respond to and easy to understand.[18] In contrast, Harper et al. found a completion rate of only 30% for SGRQ-total score, but 92% for EQ-5D.[9]

Despite decreased FEV_1 %-predicted, physical performance, and SGRQ-total score, 12.7% of our patients scored maximum at baseline for EQ-5D utility, and many more were in the top category of each of the five-dimensions. Similar results were found in a data set of 2436 cases, covering patients with various diseases, where 10% of the observations showed a maximum score (full health).[19] The consequence of this "ceiling effect" is less room for improvement. It is possible that the responsiveness of EQ-5D is better in patients with more severe COPD, where the "ceiling effect" is expected to be less frequent. In an attempt to minimise the "floor effect" and the "ceiling effect" and to improve responsiveness of EQ-5D, a 15-dimension (15D) questionnaire each with five levels instead of three levels has been developed.[20] So far, it has only been used in one study of COPD patients.[21] Change in EQ-5D, 15D, and SF-36 over a 1-year period was assessed in 59 COPD patients from an outpatient. Compared to EQ-5D, the "ceiling effect" was much less pronounced for 15D, and it seemed more responsive.[21] The 15D needs to be tested in larger studies and different groups of COPD patients.

In conclusion, SGRQ is more responsive than the EQ-5D to measure the effect of outpatient rehabilitation in COPD patients. Completion rates were high for both instruments. There was no "floor effect" but a significant "ceiling effect" for EQ-5D, which might explain the poor responsiveness of this instrument.

Conflicts of interest statement

There are no conflicts of interest.

References

1. Lacasse Y, Maltais F, Goldstein RS. Pulmonary rehabilitation: an integral part of the long-term management of COPD. *Swiss Med Wkly* 2004;**134**:601–5.
2. Ries AL, Kaplan RM, Limberg TM, Prewitt LM. Effects of pulmonary rehabilitation on physiologic and psychosocial outcomes in patients with chronic obstructive pulmonary disease. *Ann Intern Med* 1995;**122**:823–32.
3. The EuroQol Group. EuroQol—a new facility for the measurement of health-related quality of life. The EuroQol Group. *Health Policy* 1990;**16**:99–208.
4. Simon Pickard A, Wilke C, Jung E, Patel S, Stavem K, Lee TA. Use of a preference-based measure of health (EQ-5D) in COPD and asthma. *Respir Med* 2008;**102**:519–36.
5. Roche N, Dalmay F, Perez T, et al. Impact of chronic airflow obstruction in a working population. *Eur Respir J* 2008 Jan 23 (online).
6. Al MJ, Koopmanschap MA, van Enckevort PJ, et al. Cost-effectiveness of lung transplantation in the Netherlands: a scenario analysis. *Chest* 1998;**113**:124–30.
7. Monninkhof E, van der Valk P, Schermer T, van der Palen J, van Herwaarden C, Zielhuis G. Economic evaluation of a comprehensive self-management programme in patients with moderate to severe chronic obstructive pulmonary disease. *Chron Respir Dis* 2004;**1**:7–16.
8. Covelli H, Bhattacharya S, Cassino C, Conoscenti C, Kesten S. Absence of electrocardiographic findings and improved function with once-daily tiotropium in patients with chronic obstructive pulmonary disease. *Pharmacotherapy* 2005;**25**:1708–18.
9. Harper R, Brazier JE, Waterhouse JC, Walters SJ, Jones NM, Howard P. Comparison of outcome measures for patients with chronic obstructive pulmonary disease (COPD) in an outpatient setting. *Thorax* 1997;**52**:879–87.
10. Singh SJ, Smith DL, Hyland ME, Morgan MD. A short outpatient pulmonary rehabilitation programme: immediate and longer-term effects on exercise performance and quality of life. *Respir Med* 1998;**92**:1146–54.

11. Jones PW, Quirk FH, Baveystock CM, Littlejohns P. A self complete measure for chronic airflow limitation — the St. George's Respiratory Questionnaire. *Am Rev Respir Dis* 1992;**145**:1321—7.

12. Walters SJ, Brazier JE. Comparison of the minimally important difference for two health state utility measures: EQ-5D and SF-6D. *Qual Life Res* 2005;**14**:1523—32.

13. Rutten-van Mölken MP, Oostenbrink JB, Tashkin DP, Burkhart D, Monz BU. Does quality of life of COPD patients as measured by the generic EuroQol five-dimension questionnaire differentiate between COPD severity stages? *Chest* 2006;**130**:1117—28.

14. Guyatt GH, King DR, Feeny DH, Stubbing D, Goldstein RS. Generic and specific measurement of health-related quality of life in a clinical trial of respiratory rehabilitation. *J Clin Epidemiol* 1999;**52**:187—92.

15. Singh SJ, Sodergren SC, Hyland ME, Williams J, Morgan MD. A comparison of three disease-specific and two generic health-status measures to evaluate the outcome of pulmonary rehabilitation in COPD. *Respir Med* 2001;**95**:71—7.

16. Puhan MA, Guyatt GH, Goldstein R, et al. Relative responsiveness of the Chronic Respiratory Questionnaire, St. Georges Respiratory Questionnaire and four other health-related quality of life instruments for patients with chronic lung disease. *Respir Med* 2007;**101**:308—16.

17. Ståhl E, Jansson SA, Jonsson AC, Svensson K, Lundbäck B, Andersson F. Health-related quality of life, utility, and productivity outcomes instruments: ease of completion by subjects with COPD. *Health Qual Life Outcomes* 2003;**1**:18—24.

18. Nilsson E, Wenemark M, Bendtsen P, Kristenson M. Respondent satisfaction regarding SF-36 and EQ-5D, and patients' perspectives concerning health outcome assessment within routine health care. *Qual Life Res* 2007;**16**:1647—54.

19. Brazier J, Roberts J, Tsuchiya A, Busschbach J. A comparison of the EQ-5D and SF-6D across seven patient groups. *Health Econ* 2004;**13**:873—84.

20. Sintonen H, Pekurinen M. A fifteen-dimensional measure of health-related quality of life (15D) and its applications. In: Walker SR, Rosser R, editors. *Quality of life assessmentKey issues in the 1990s*. Dordrecht: Kluwer Academic Publishers; 1993.

21. Stavem K. Reliability, validity and responsiveness of two multi-attribute utility measures in patients with chronic obstructive pulmonary disease. *Qual Life Res* 1999;**8**:45—54.