

Original Article

The psychometric properties of the Leicester Cough Questionnaire and Respiratory Symptoms in CF tool in cystic fibrosis: A preliminary study ☆☆☆★



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Received 9 May 2016; revised 28 November 2016; accepted 29 November 2016

Available online 14 December 2016

Abstract

Background: There are few tools to quantify the impact of cough in cystic fibrosis (CF). The psychometric properties of the Leicester Cough Questionnaire (LCQ) and Respiratory Symptoms in CF (ReS-CF) tool were investigated in adults with CF.

Methods: Validity and reliability were assessed in clinically stable participants who completed the questionnaires twice, along with the Cystic Fibrosis Questionnaire – Revised (CFQ-R). Responsiveness was assessed by change in questionnaires following treatment for an acute respiratory exacerbation.

Results: Correlations between the LCQ and CFQ-R respiratory domain were moderate ($n = 59$, $r_s = 0.78$, $p < 0.001$). Correlations between ReS-CF and CFQ-R respiratory domain were fair ($r_s = -0.50$, $p < 0.001$). The LCQ total score was repeatable (ICC 0.92, 95%CI 0.87–0.96, $n = 50$). In those reporting improvement in symptoms following treatment ($n = 36$), LCQ total score had a mean change of 4.6 (SD 3.7) and effect size of 1.2.

Conclusions: The LCQ and ReS-CF appear to be valid, reliable and responsive in CF.

Trial Registration: www.anzctr.org.au: ACTRN12615000262505

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Keywords: Cystic fibrosis; Leicester Cough Questionnaire; Cough; Surveys and questionnaires; Signs and symptoms, respiratory

Abbreviations: CF, Cystic Fibrosis; LCQ, Leicester Cough Questionnaire; CFQ-R, Cystic Fibrosis Questionnaire (Revised); HRQOL, Health-related quality of life; VAS, Visual analogue scales; COPD, Chronic obstructive pulmonary disease; ReS-CF, Respiratory Symptoms in cystic fibrosis tool; GRCS, Global rating of change scale

☆ Results of this study have been presented as a poster at the Thoracic Society of Australia and New Zealand Annual Scientific Meeting, 2–6 April 2016, Perth, Australia.

☆☆ Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

★ The research underpinning this publication was undertaken by Nathan Ward whilst completing a PhD at La Trobe University, Melbourne, Victoria.

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1. Introduction

Cystic fibrosis (CF) is characterised by thickened respiratory secretions as a sequelae of the defective chloride transport in the respiratory epithelium. Inadequate clearance of respiratory secretions provides an environment conducive to a cycle of retained secretions, chronic infection and inflammation, resulting in progressive lung damage and eventual respiratory failure in the majority of sufferers.

Lung function testing, especially forced expiratory volume in 1 s (FEV₁), has historically been used as the primary outcome measure in studies investigating new therapies aimed at the respiratory system of people with CF. The occurrence and frequency of respiratory exacerbations are other frequently utilised

outcomes in CF trials, although a universally accepted definition of a respiratory exacerbation is still lacking. As the rate of decline in lung function has slowed as a result of improvements in available therapies, the suitability of FEV₁ or the rate/frequency of respiratory exacerbations as primary outcome measures in short and medium duration studies involving participants with CF has been questioned [1]. At the same time, there has been increasing interest in patient-reported outcomes as primary endpoints in CF clinical trials [2,3]. These encompass a broad range of assessments that measure how a patient feels or functions and includes generic and disease-specific health-related quality of life (HRQOL) assessments and more specific symptom evaluation tools [2]. The Cystic Fibrosis Questionnaire-Revised (CFQ-R), a 50-item, 12-domain tool assessing HRQOL, is currently the best validated HRQOL questionnaire for use in CF populations [4,5]. However, as recommended by the European Medicines Agency, there is a need to develop briefer, more targeted patient-reported outcomes for use in CF trials [4].

Cough is one of the most frequently reported respiratory symptoms in CF, with changes in cough behaviour a primary symptom identified by patients as an indicator of a respiratory exacerbation, even in the setting of mild lung disease [6–11]. Sawicki et al. [10] found that 94% of their sample of adults with CF reported cough, with the majority reporting it as being of high frequency and severity, with these frequency and severity ratings much higher than for other symptoms, including shortness of breath. A variety of tools have been developed to assess the frequency and impact of cough. Visual analogue scales (VAS) are a widely used evaluation tool and have been used to measure the impact of cough and other respiratory symptoms in people with non-CF bronchiectasis [12]. However, there is a paucity of data to support their use compared to other tools that evaluate the frequency and impact of cough [13]. Smith et al. [14] demonstrated, in a small sample of CF subjects treated for a respiratory exacerbation, that a change in VAS score assessing day and night cough correlated with a change in objective cough counts.

The Leicester Cough Questionnaire (LCQ) is a 19-item tool that assesses cough-related HRQOL. Originally developed in those with chronic cough, its validity and responsiveness has been demonstrated in patients with non-CF bronchiectasis and chronic obstructive pulmonary disease (COPD) [13,15–17]. The LCQ is moderately correlated with the number of explosive coughs and cough-seconds [18,19]. The LCQ has been used as an outcome measure in non-CF bronchiectasis airway clearance trials and in a case-series of cough changes related to laparoscopic fundoplication for reflux in CF [20–22]. However, the LCQ is yet to be formally validated for use in the CF population.

Given the prevalence and severity of cough across the disease severity spectrum in CF, there may be value in utilising a tool that specifically assesses the impact of cough on HRQOL in CF. The purpose of this study was therefore to investigate the psychometric properties of the LCQ in a cohort of adults with CF. As well as evaluating the psychometric properties of the LCQ in a sample of patients with CF, we also purpose-designed and evaluated a brief questionnaire comprising four simple

VASs that assessed respiratory symptoms (ReS-CF) to investigate if a briefer questionnaire may be useful as a screening tool.

2. Methods

2.1. Study design

All patients with a diagnosis of CF attending the Adult CF Service at the Royal Adelaide Hospital were eligible for inclusion. Patients unable to understand written English were excluded. The study was divided into two parts: one part investigating validity and reliability and the other investigating responsiveness. Recruitment for the two parts occurred concurrently between March and September 2015. Ethical approval was obtained from the Royal Adelaide Hospital Research Ethics Committee (HREC/15/RAH/2) and La Trobe University Human Ethics Committee. The study was registered with the Australian New Zealand Clinical Trials Registry (ACTRN12615000262505).

2.2. Questionnaires

The LCQ is a 19-item questionnaire that specifically assesses the impact of cough on HRQOL [16]. Each item requires a response using a 7-point Likert-like scale (e.g. 1 = all of the time, 7 = none of the time). These 19 items are divided into three domains that consider the physical impacts (e.g. effect of cough on chest and stomach pains, sputum production), psychological impacts (e.g. effect of cough on embarrassment/anxiety) and social impacts (e.g. cough interfering with job/daily life, enjoyment of life) of cough. Three domain scores and a total score are calculated, with domain scores ranging from 1 to 7 and total scores from 3 to 21, with higher scores indicating greater HRQOL [16].

The Respiratory Symptoms in CF (ReS-CF) tool was developed by the authors specifically for the purpose of this study as a means of briefly measuring patient's perceptions of their respiratory symptoms. It consists of four VASs assessing patient-perceived severity of their overall respiratory symptoms, cough, chest congestion and sputum production. Each VAS was scored separately, ranging from 0 (no symptoms) to 10 (extreme symptoms).

The CFQ-R is a 50-item, 12 domain, CF-specific HRQOL questionnaire and is currently the most widely used HRQOL questionnaire in the CF population [5]. The respiratory domain consists of seven questions, with the domain score being based on six of these questions. These questions assess cough, congestion, mucus expectoration, wheezing and trouble breathing and are scored on a 4-point Likert-like scale. The respiratory domain of the CFQ-R has been shown to have good internal consistency (Cronbach's alpha = 0.87), with a minimal clinically important difference of 4 points for clinically stable patients and 8.5 points in those receiving treatment for an acute exacerbation [23,24].

Participants were approached for inclusion in the study during outpatient appointments or on admission to hospital and given a package containing the full versions of all questionnaires to

self-complete. Whilst the questionnaires within the packages were in a set order, the order of completion was left to each participant. Participants in the reliability and responsiveness studies were given a second set of questionnaires to complete one week later (reliability) or four weeks later (responsiveness). Up to three reminders were provided to each participant to complete the repeat set of questionnaires that were given to the participant at the initial visit.

2.3. Validity and reliability study

Patients who were clinically stable were approached to participate in the validity and reliability component of the study. Validity was assessed by having participants complete the LCQ, ReS-CF and CFQ-R questionnaires on the same day, after undergoing any clinical assessments (e.g. spirometry). The following concepts of validity were assessed: concurrent validity and floor or ceiling effects. Internal consistency of the LCQ was also determined. Test–retest reliability was assessed by having the same participants complete the questionnaires again, one week after completing the initial set of questionnaires. Participants were excluded from the reliability analysis if they developed an acute respiratory exacerbation during the period separating the two assessment time points.

2.4. Responsiveness study

Patients diagnosed by their treating respiratory physician with an acute respiratory exacerbation, based on clinical assessment (e.g. drop in lung function [spirometry], increase in symptoms) and requiring treatment with new oral, inhaled or intravenous antibiotics were approached to participate. Participants completed the LCQ, ReS-CF and CFQ-R when commencing treatment and again four weeks later. A global rating of change scale (GRCS) was used at the four week point to determine participant-defined changes in respiratory symptoms, ranging from -7 (a very great deal worse) to $+7$ (a very great deal better). Participants were withdrawn if, during the assessment period, they developed a critical illness requiring intensive care unit admission, surgical intervention or had end of life care implemented.

2.5. Statistical analyses

Concurrent validity was assessed by calculating correlation coefficients using either Pearson's correlation coefficient or Spearman's rank correlation coefficient depending on the distribution of the data (determined by visual inspection and skewness and kurtosis statistics). Content validity was assessed by analysing for floor and ceiling effects, with $<15\%$ of subjects achieving either the minimum or maximum scores considered acceptable.

Reliability was assessed using several methods. Internal consistency of the LCQ (domain and total scores) was determined using Cronbach's alpha coefficient. Cronbach's alpha scores of 0.7 – 0.9 were selected as representing acceptable internal consistency. Test–retest reliability of the LCQ (domain and total

scores) and ReS-CF were determined using Intraclass Correlation Coefficients (ICC). An ICC of 0.7 was considered acceptable [25]. A Bland–Altman plot for the LCQ total score was constructed, with limits of agreement equalling $1.96 \times$ SD of the mean difference in scores.

Responsiveness was determined by calculating the effect size for those reporting an improvement in symptoms ($\text{GRCS} \geq 2$) four weeks after starting treatment for an acute respiratory exacerbation. Effect size was calculated as the difference in mean scores between the baseline and repeat assessments divided by the standard deviation (SD) of the baseline score. Anchor-based estimates of the minimum important difference (MID) were calculated using the change in LCQ total score for those reporting a small improvement in their symptom ($\text{GRCS} 2$ – 3). The sensitivity and specificity for the change in LCQ total score to discriminate between those who did and did not report an improvement in symptoms were calculated and a Receiver Operator Curve (ROC) obtained. The minimum important difference was determined as the data point closest to the upper left corner of the curve [26,27]. The distribution-based estimate of the MID was calculated as 0.5 SD of the mean change in LCQ total score.

Data analyses were conducted using SPSS version 23 (SSPS, Chicago, IL, US).

3. Results

3.1. Validity and reliability

3.1.1. Patients

Fifty-nine patients met the eligibility criteria and completed the initial questionnaires, with their descriptive characteristics and questionnaire scores summarised in Table 1. The LCQ, ReS-CF and CFQ-R respiratory domain results were not normally distributed.

3.1.2. Validity

3.1.2.1. Concurrent Validity. The physical, psychological and social domains of the LCQ were moderately correlated with the CFQ-R respiratory domain ($r_s = 0.71$ – 0.74 , $p < 0.001$). The three domains of the LCQ were moderately correlated with each other (0.74 – 0.78 , $p < 0.001$). The LCQ total score was moderately correlated with the CFQ-R respiratory domain ($r_s = 0.78$, $p < 0.001$). The ReS-CF overall domain had a fair negative correlation with the respiratory domain of the CFQ-R ($r_s = -0.50$, $p < 0.001$).

3.1.2.2. Floor and Ceiling Effects. Only two (3.4%) participants achieved the maximum score for the physical domain and total LCQ scores, with no participants achieving a minimum score for any of the domains or total score. However 14 (23.7%) and 18 (30.5%) participants achieved a maximum score on the LCQ psychological and social domains respectively, indicating a possible ceiling effect in these domains. For the ReS-CF, no participant achieved a maximum score and only five participants (8.5%) achieved the minimum value for any domain.

Table 1
Descriptive characteristics of the participants in the validity/reliability and responsiveness studies.

Characteristics	Validity and reliability study (n = 59)	Responsiveness study (n = 53)
Sex, male, n (%)	42 (71)	27 (51)
Age (yrs), mean ± SD (range)	29.0 ± 9.3 (17–59)	29.3 ± 7.4 (18–47)
FEV ₁ (L), mean ± SD (range)	3.05 ± 1.12 (0.82–5.85) ^a	2.40 ± 1.00 (0.55–4.20) ^b
FEV ₁ (% pred), mean ± SD (range)	75.3 ± 23.1 (20–118) ^a	63.0 ± 24.0 (16–102) ^b
FVC (L), mean ± SD (range)	4.21 ± 1.20 (1.71–6.82) ^a	3.68 ± 1.36 (1.06–7.29) ^b
FVC (% pred), mean ± SD (range)	86.2 ± 17.5 (41–126) ^a	80.1 ± 22.0 (27–117) ^b
BMI (kg/m ²), mean ± SD (range)	24.8 ± 4.8 (18.2–40.7)	22.3 ± 3.8 (15.7–38.8)
F508del homozygote	22 (37%)	28 (53%)
Pseudomonas aeruginosa colonisation (%)	36 (61%)	41 (77%)
Pancreatic insufficient (%)	44 (75%)	49 (92%)
CF-related diabetes (%)	7 (12%)	10 (19%)
LCQ, median (IQR)		
Physical	6.1 (5.4–6.5)	4.4 (3.4–5.0)
Psychological	6.7 (5.9–6.9)	4.1 (3.3–5.3)
Social	6.5 (5.8–7.0)	4.8 (3.3–5.5)
Total	19.2 (17.1–20.3)	13.3 (10.0–15.4)
ReS-CF, median (IQR)		
Overall	1.2 (0.4–2.3)	5.5 (4.4–6.8)
Cough	1.1 (0.3–2.3)	6.1 (4.4–7.9)
Congestion	1.0 (0.3–3.5)	6.2 (4.7–7.8) ^c
Sputum	1.7 (0.6–3.5)	6.4 (4.9–7.9)
CFQ-R, median (IQR)		
Respiratory	77.8 (66.7–88.9)	50.0 (38.9–61.1)

n = number of participants.

yrs = years.

SD = standard deviation.

%pred = percentage of predicted.

kg/m² = kilogrammes/m squared.

FEV₁ = forced expiratory volume in 1 s.

FVC = forced vital capacity.

L = litres.

BMI = body mass index.

LCQ = Leicester Cough Questionnaire.

IQR = interquartile range.

ReS-CF = Respiratory Symptoms in CF.

CRQ-R = Cystic Fibrosis Questionnaire – Revised.

^a n = 58.

^b n = 45.

^c n = 52.

Fig. 1 presents the scores from the three LCQ domains and the total LCQ score according to severity of disease as categorised by lung function results (based on forced expiratory volume in 1 s). Multivariate analyses revealed that the only significant difference was between the severe and both the mild and normal groups for the physical domain of the LCQ ($p < 0.05$).

3.1.3. Reliability

3.1.3.1. Internal consistency. The Cronbach's alpha for the physical, psychological and social domains of the LCQ were 0.84, 0.92 and 0.90 respectively and, for the LCQ total score 0.95.

3.1.3.2. Test–retest reliability. Of the 59 patients completing the initial questionnaires, 50 were eligible for the test–retest reliability analysis. Two patients were withdrawn as they developed an acute respiratory exacerbation in the time period between the two assessments and seven failed to return the repeat

questionnaires. The LCQ demonstrated good test–retest reliability, with all domains and the total score having an ICC > 0.7 (Table 2). The four ReS-CF VAS scores also achieved ICCs > 0.7 however the lower limit of the 95%CI for all except the sputum domain fell below 0.7 (Table 2). Repeatability of the LCQ total score over one week is shown in the Bland–Altman plot in Fig. 2. The mean (SD) difference in score was 0.2 (1.1) units, with the upper limit of agreement being 2.4 and the lower limit of agreement being –2.0.

3.2. Responsiveness

Fifty-three patients were recruited for the responsiveness part of the study. Table 1 summarises their baseline characteristics. Forty-eight (91%) participants completed and returned the repeat set of questionnaires. Thirty-six participants (75%) reported an improvement in respiratory symptoms post-treatment (GRCS ≥ 2).

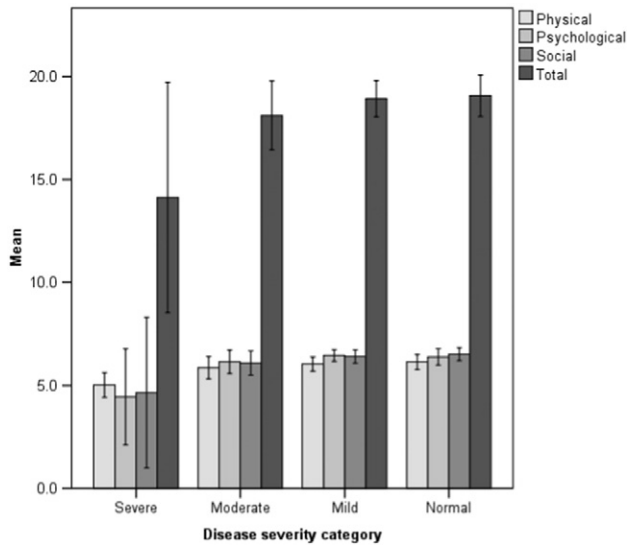


Fig. 1. LCQ domain and total scores by disease severity category. Data are mean and 95%CI. Disease severity category as measured by FEV₁ percentage of predicted: normal ≥ 90%, mild = 70–89%, moderate = 40–69%, severe < 40% predicted value.

The LCQ total scores increased by a mean (SD) of 3.6 (3.9) for the 48 participants. The ReS-CF scores changed by a mean (SD) of -2.2 (2.7), -2.9 (2.9), -2.6 (3.3) and -2.7 (2.8) for the overall, cough, congestion and sputum domains respectively. Data from the 36 participants reporting an improvement in symptoms (GRCS ≥ 2) were further analysed, with the pre- and post-treatment results for these participants summarised in Table 3. For these participants reporting an improvement in symptoms, the LCQ total score increased by 4.6 (3.7) units, with an effect size of 1.2. The ReS-CF scores in participants reporting an improvement in their symptoms changed by a mean (SD) of -2.9 (2.6), -3.5 (2.7), -3.5 (3.1) and -3.1 (2.7) for the overall, cough, congestion and sputum domains respectively, with effect sizes ranging from 1.3–1.6. Thirty two participants

Table 2
Test–retest reliability of the LCQ, ReS-CF and CFQ-R.

Questionnaire	ICC (95% CI)
LCQ	
Physical	0.85 (0.76–0.91)
Psychological	0.91 (0.85–0.95)
Social	0.86 (0.77–0.92)
Total	0.92 (0.87–0.96)
ReS-CF	
Overall	0.75 (0.60–0.85)
Cough	0.80 (0.67–0.88)
Congestion	0.78 (0.64–0.87) ^a
Sputum	0.82 (0.70–0.89)
CFQ-R	
Respiratory	0.84 (0.73–0.90) ^b

LCQ = Leicester Cough Questionnaire.

ReS-CF = Respiratory Symptoms in CF.

CRQ-R = Cystic Fibrosis Questionnaire – Revised.

^a n = 48.

^b n = 49.

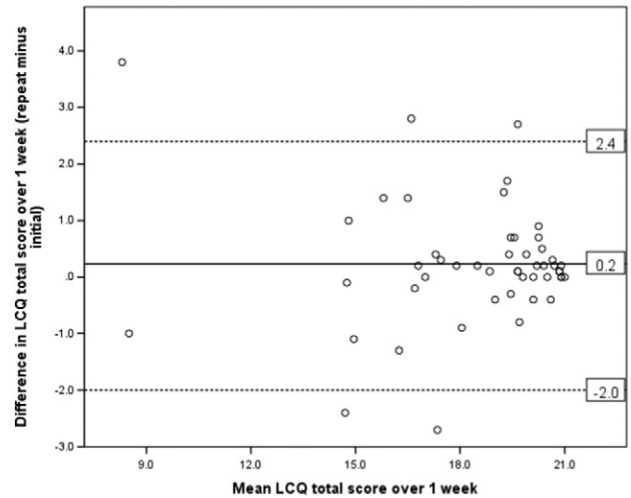


Fig. 2. Bland–Altman plot of the mean LCQ total score over one week. Difference in LCQ total score over 1 week equals repeat result minus initial result. The solid line represents the mean change in score and the dashed line represents the limits of agreement (1.96 × SD of the mean change in scores).

exceeded the previously identified minimum important difference (MID) for the CFQ-R respiratory domain (8.5 units), with these participants reporting a mean (SD) increase in LCQ total score of 5.3 (3.4) which was significantly higher than the mean (SD) change of 0.2 (1.9) in those not exceeding the CFQ-R MID (p < 0.001) [23].

Using the anchor-based method for determining the MID of the LCQ total score, participants reporting a small improvement in their symptoms on the GRCS [2–3] had a mean (SD) increase of 2.0 (3.2) units in their LCQ total score. Fig. 3 shows the ROC for the LCQ total score. Visual inspection of the ROC indicated a threshold change of 1.9 units for the MID (area under the curve 0.80, 95%CI 0.65–0.94, sensitivity 75% and specificity 75%). This is in agreement with the distribution-based method for estimating the MID (0.5 SD of the mean change in LCQ total scores), which estimated an MID of 1.9 units.

Table 3

Results for responsiveness data when commencing treatment for a respiratory exacerbation and four weeks later for the 36 participants who reported an improvement in symptoms.

	Baseline mean (SD)	Reassessment mean (SD)	Effect size
LCQ			
Physical	4.3 (1.1)	5.7 (1.1)	1.3
Psychological	4.3 (1.4)	5.9 (1.2)	1.1
Social	4.5 (1.4)	6.0 (1.1)	1.1
Total	13.0 (3.8)	17.6 (3.1)	1.2
ReS-CF			
Overall	5.5 (2.1)	2.6 (2.1) ^a	1.4
Cough	6.0 (2.3)	2.4 (2.0)	1.6
Congestion	6.2 (2.4) ^a	2.7 (2.2)	1.5
Sputum	6.1 (2.3)	3.0 (2.1)	1.3
CFQ-R			
Respiratory	47.4 (17.1)	71.0 (18.0)	1.4

LCQ = Leicester Cough Questionnaire.

ReS-CF = Respiratory Symptoms in CF.

CRQ-R = Cystic Fibrosis Questionnaire – Revised.

^a n = 35.

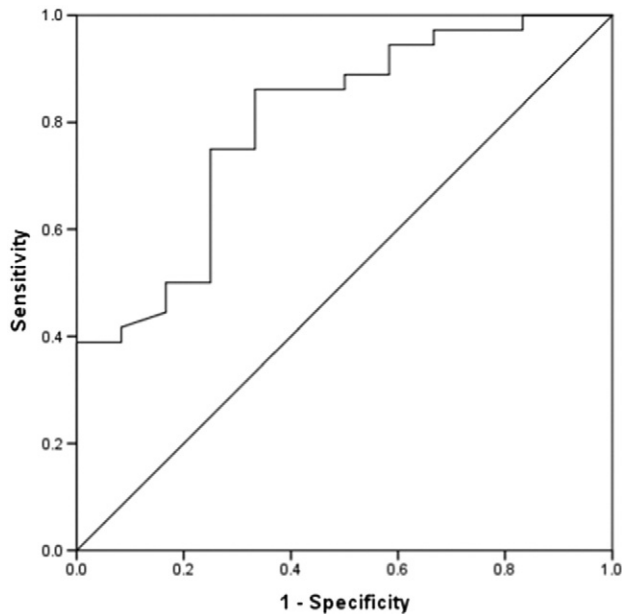


Fig. 3. Receiver Operator Curve for responsiveness of the LCQ total score. The area under the curve is 0.80 (95% CI 0.65–0.94).

4. Discussion

The current study found that the LCQ and ReS-CF were valid, reliable and responsive tools for the assessment of perceived respiratory symptoms in adults with CF. The LCQ total and domain scores were moderately correlated with the respiratory domain of the CFQ-R, currently the most widely used HRQOL in CF. The ReS-CF overall respiratory symptom domain had a fair correlation ($r_s = -0.5$) to the CFQ-R respiratory domain. The moderate correlation between the LCQ and CFQ-R respiratory domain suggests that the LCQ may have a complimentary role to the CFQ-R, with the cough-specific LCQ potentially having a place in the assessment of therapies where cough is a target.

Cough is a symptom that may have a significant social impact due to the stigma associated with coughing. It is therefore important to assess not only the physical symptom but also its psychological and social impact when determining HRQOL. Whilst the LCQ total score and physical domain, along with all domains of the ReS-CF, did not demonstrate a floor or ceiling effect, a ceiling effect was found for the psychological and social domains of the LCQ. The participants in this study generally had well preserved lung function which may have contributed to the ceiling effect demonstrated. Those achieving a maximum score for the two domains had a mean percent predicted FEV₁ of 82% for both domains respectively. For those not achieving the maximum score, it was 73% and 72% for the psychological and social domains respectively, suggesting, as expected, that those with milder respiratory disease may be more likely to achieve a maximum score. Given this potential ceiling effect, our recommendation would be that the LCQ total score be used as the primary outcome of interest when using the LCQ in people with CF, especially for those with mild respiratory disease pending larger, multi-centred investigations of the psychometric properties of the LCQ.

The LCQ demonstrated good internal consistency (Cronbach's alpha 0.84–0.95) with these results similar to those reported in the initial development study involving patients with chronic cough (Cronbach's alpha 0.79–0.92) and the Dutch-translation version (Cronbach's alpha 0.77–0.93) [16,28]. The internal consistency results in the current study are better than those seen in COPD (Cronbach's alpha 0.67–0.86) [15]. There is some debate about a suitable upper limit for Cronbach's alpha, with some suggesting 0.95 as opposed to 0.90 as the upper limit, therefore, the results of the current study with its values toward the upper limit of the commonly accepted range, indicate there may be some degree of redundancy in the LCQ when used to assess cough-related quality of life in CF [25,29,30].

Test–retest reliability was assessed by having participants complete the questionnaires one week apart which is within the repeat testing timeframes recommended by Deyo et al. [26]. We found that the LCQ and ReS-CF were both reliable, with ICCs greater than the recommended 0.7 cut-off [25]. Whilst the 95%CI for the LCQ domains and total score exceeded 0.7, it should be noted that only the sputum domain of the ReS-CF had the lower limit of the 95% CI above 0.7. The mean difference in the LCQ total score of 0.2 units between the initial and repeat testing is comparable with the -0.23 units reported by Murray et al. [17] in non-CF bronchiectasis and the 0.73 units reported by Berkhof et al. [15] in COPD.

The LCQ and ReS-CF were both responsive to change with effect sizes ranging from 1.1 to 1.3 for the LCQ and 1.3 to 1.6 for the ReS-CF. An effect size of >0.8 is generally considered to be large [31]. Our results are similar to those reported by Birring et al. [16] in the initial LCQ development study where they found effect sizes between 0.84 and 1.75. In the current study, the mean change in LCQ total score for those participants reporting an improvement in symptoms was 4.6, being consistent with the results reported by Murray et al. [17] in their cohort of patients with non-CF bronchiectasis undergoing treatment for an acute exacerbation. The anchor-based approach we used revealed 2.0 units as the mean change in LCQ score for those reporting a small improvement on the GRCS. Analysis of the ROC for the LCQ total score suggested a change of 1.9 units was able to detect those who reported an improvement in their symptoms, with an acceptable degree of sensitivity (75%) and specificity (75%). It must be noted however that the ROC had a wide confidence interval (0.65–0.94). The MID estimate of 2.0 is somewhat lower than the 3.0 suggested by Brokkaar et al. [32] in patients with chronic cough.

We developed the ReS-CF to see if a quick screening tool of respiratory symptoms consisting entirely of simple VASs might be useful in CF. The ReS-CF is very simple, taking less than 1 min to complete, whereas the LCQ takes around 5 min and the CFQ-R 10 min to complete. The ReS-CF seems well suited for use as a quick screening tool, particularly in the busy clinical setting where ease and speed of completion are important. The LCQ, with its higher test–retest repeatability and stronger correlation to the CFQ-R, may be a more robust and appropriate tool than the ReS-CF when considering outcome measures for clinical trials, particularly where cough is either a specific target or is likely to be affected by the intervention (e.g. airway

clearance trials) and where the time required to complete the questionnaire is less of an issue.

This study has several limitations. It only recruited a relatively small sample of patients attending a single adult CF service, so additional larger multi-centred trials would be of value. The participants in the validity and reliability analysis generally had well preserved lung function and therefore further evaluation of potential floor effects in those with more severe disease may be warranted. Our study recruited participants separately for the validity/reliability and responsiveness phases and we acknowledge that there may be value in evaluating the LCQ longitudinally and assessing LCQ in both stable and unstable disease states in the same participants. There were also some incomplete data due to several participants failing to answer all required questions, however there were less than 5% missing data for any individual analysis. Further research to evaluate the psychometric properties of the LCQ compared to more objective measures, such as genotype, *Pseudomonas aeruginosa* infection status and change in lung function, would also be of value. Another limitation is that we did not randomise the order of questionnaire completion, rather we left it to participant choice, so it is possible that there was an order effect. By chance, there were considerably more males than females (71% vs 29%) in the validity phase of our study. Further research with a more evenly mixed sample would be of value to determine if the gender bias in our cohort had any impact on the validity and reliability of the LCQ. It is important to note that, unlike the CFQ-R, the initial development of the LCQ did not include any participants with a diagnosis of CF. Nevertheless, our findings suggest that it may have psychometric properties that enable its use in the CF population, in keeping with those studies that found the LCQ useful for patients with COPD and non-CF bronchiectasis — populations that were also not included in the initial development of the LCQ [15,17]. Finally, it is acknowledged that, like previous research, the data from the questionnaires were treated as interval data, when it is possible that they are not truly interval (e.g. a 2 point change in score at the lower end of a scale may not mean the same as that seen at the upper end of a scale).

The results of this study indicate that further assessment into the role of the LCQ and ReS-CF in CF is warranted. The tools may have a role in the clinical assessment of patients when evaluating the impact of specific therapies added to a patient's regimen e.g. a change in airway clearance technique. Given that people with CF were not included in the initial development of the LCQ, further investigation into its structure and content in a CF-specific context is warranted prior to its potential use as a primary outcome measure in clinical trials.

5. Conclusion

The LCQ and ReS-CF appear to be valid, reliable and responsive tools for assessing the impact of cough in adult subjects with CF. The LCQ may be of use in evaluating clinical interventions that may impact upon cough, such as airway clearance techniques. Further assessment of these tools in multicentred studies and randomised controlled trials would be

of benefit to clarify their role in assessing HRQOL in CF in clinical practice and clinical trials.

Acknowledgements

We would like to thank the patients who participated in the study and staff of the Royal Adelaide Hospital CF Service for their assistance throughout this study.

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