Original Article

Development and electronic validation of the revised Cystic Fibrosis Questionnaire (CFQ-R Teen/Adult)  
New tool for monitoring psychosocial health in CF

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Abstract

Background: The Cystic Fibrosis Questionnaire-Revised (CFQ-R+14) is a disease-specific, health-related quality of life instrument for cystic fibrosis (CF) patients ≥14 years. We have developed a Spanish electronic version of the CFQ-R (e-CFQ-R+14 Spain). Our aim was to compare the paper and electronic versions and to validate the electronic version.

Methods: Fifty CF patients completed the study. All answered the paper and electronic versions on day 1 and repeated the e-CFQ-R version 15 days later.

Results: Concordance between the electronic and paper copy versions was high, with correlations above 0.9 in all domains. Test-retest reliability of the e-CFQ-R results was strong, with coefficients ranging from 0.8 to 0.9.

Conclusions: The e-CFQ-R version is reliable and valid and can replace the paper copy, thus simplifying the assessment of quality of life. It also provides immediate results with no errors in scoring. It is a useful new tool in CF care.

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Keywords: Cystic Fibrosis Questionnaire Revised; Patient reported outcomes; Cystic fibrosis; Diagnostic tool

1. Introduction

Patient-reported outcomes (PROs) are questionnaires completed by patients that detect changes in symptoms, perceptions of health, and daily functioning as perceived by the patient. They range from a single-item rating of pain to multi-dimensional, health-related quality of life instruments. PROs are important endpoints in clinical trials of new medications and can serve as outcome measures in clinical research and to improve clinical
care. Both the U.S. Food and Drug Administration and the European Medicines Agency have formally recognized their importance [1,2], and thus, PROs are increasingly used as primary or secondary outcomes in the drug approval process [3]. The most appropriate PRO depends on its purpose (natural course of disease, efficacy of treatment).

Health-related quality of life (HRQoL) measurements in PROs are very important in cystic fibrosis (CF) because they allow the inclusion of the patient’s perspective in research and clinical practice [4–8]. A validated CF questionnaire is the Cystic Fibrosis Questionnaire-Revised (CFQ-R). The CFQ-R was developed to evaluate the effects of the disease and its treatments on daily functioning in several domains (e.g., respiratory symptoms, physical functioning, and vitality) and has been used as an end-point for clinical trials of new medications [3,9–11]. Specific CFQ-R scales have been shown to predict pulmonary exacerbations and correlates with lung function, body mass index (BMI), and mortality [12–15]. Recently, the score of some scales of the CFQ-R has been used for the assessment of candidates for lung transplantation [16].

Despite the relevance of HRQoL measurements to monitor the impact of CF, the CFQ-R questionnaire is not routinely used in clinical practice in Europe. Among the reasons for this could be a lack of experience in the use of the questionnaire, the fact that it is time-consuming to analyze the data, there could be missing items in the paper copy, and the delay in receiving results in real time. These difficulties cause this valuable tool to be restricted to use in epidemiological studies and trials, and without a direct impact on daily clinical care [4,17]. Accordingly, an electronic version would help, and we have developed an electronic application of this questionnaire (e-CFQ-R+14). This version provides an automatic result in all domains, reduces data entry errors (which are common in the paper version) and the time required to enter and calculate the data [18]. The results are saved and stored in a secure database. The goal of our study was to evaluate the reliability and validity of the e-CFQ-R compared with the paper version.

2. Materials and methods

2.1. Description of the paper questionnaire

The Cystic Fibrosis Questionnaire-Revised Teen/Adult (CFQ-R+14) is a disease-specific, health-related quality of life instrument for adolescents and adults (≥14 years of age) with CF. The CFQ-R measures daily functioning from the patients’ perspective, and thus provides unique information to facilitate clinical interventions. More broadly, it provides systematic data on the frequency and severity of respiratory symptoms that are not measured using conventional clinical tests [17].

The CFQ-R+14 has 12 scales or domains that evaluate functioning over the previous 2 weeks in the following domains or scales: physical functioning, role, vitality, emotional functioning, social, body image, eating disturbances, treatment burden, health perceptions, weight, respiratory symptoms, and digestive symptoms [19–22]. The CFQ-R+14 includes 50 items across 12 domains. The first 6 domains measure general aspects of HRQoL: 8 items for physical functioning; 4 for role functioning; 4 for vitality; 3 for health perceptions, 5 for emotional functioning, and 6 for social functioning. The other 6 domains measure symptoms and effects of the disease: 3 items for body image, 3 for eating disturbances, 3 for treatment burden, 1 for weight, 7 for respiratory symptoms, and 3 for digestive symptoms. Each domain is standardized on a 0–100 scale; higher scores indicate better HRQoL [23]. In the paper copy, scores for each domain can be calculated if at least two-thirds of the questions are completed [9,23].

The CFQ-R has been translated and validated in various languages, such as Latin-American Spanish and for the Spanish population from Spain [9].

2.2. Construction of the electronic version

The e-CFQ-R+14 is the electronic version of the paper questionnaire. Patients can easily complete the questionnaire in its electronic format. The electronic application is linked to an online database that can be adapted for any electronic device, such as tablets, phones, or computers. Once the questionnaire has been completed, this application calculates the results, sends them by email to the caregiver, and saves the data in a centralized and protected database. As soon as the patient completes the survey, the result is available.

The e-CFQ-R+14 web version and cross-platform (Windows, Linux, Android, IOS) has been developed using PHP programming, and is linked to a MySQL database to record the calculated scores. It has been hosted at Strato, an ISO 27001-certified hosting provider, and is accessible through www.ecfqr.com, a domain specifically registered for this purpose. We have included two versions of the CFQ-R+14 in this program: English and Spanish. To access the English version, access this web address: http://www.ecfqr.com/en/ and for the Spanish version: http://www.ecfqr.com/sp. To grant privacy and security, access is restricted with an ID number and password, which is unique and personal for authorized staff.

We registered the www.ecfqr.com domain on 2015-11-26T00:00:00Z, where this application is hosted. By the end of 2015 and the beginning of 2016, we had performed the design and working tests on this electronic version to confirm its proper functioning.

2.3. Study procedure

Sixty patients with CF ≥14 years of age were consecutively enrolled in two CF adult units in Spain. At the end of the study, 50 patients had completed both questionnaires and repeated the electronic version 15 days later. The distribution was 24 patients in Málaga (Regional University Hospital) and 26 in Valencia (University Hospital La Fe). We used two centers to reduce single-center bias and to have a more heterogeneous sample. Recruitment took place during April and June of 2016. All the patients were in stable condition and completed the questionnaire before any other assessments to avoid bias (e.g., weight or pulmonary function test). On day 1, half the patients completed the paper version first and the other half started with the electronic version, but all the patients answered both formats on day 1. To
assess test-retest reliability, 15 days after the initial assessment, stable patients without signs or symptoms of a CF exacerbation completed the e-CFQ-R to assess the reproducibility of this new application. Test-retest reliability was completed by the 50 patients.

In all cases, to prevent cross-infection we followed current recommendations regarding infection control procedures while using tablets and other electronic devices [24,25]. Inclusion criteria: patients with CF older than 14 years who signed a consent form. Those who had significant intellectual disabilities, unstable disease, were transplanted or were listed for transplant were excluded, as were patients who did not complete the electronic version 15 days later (see Fig. 1).

2.4. Ethics

Validation of the electronic version was conducted in two Spanish teaching hospitals, in adult CF units, with patients >14 years of age. We received ethics approval from the Biomedical Research Committee of Research Institute la Fe. We followed the Spanish data protection law (Organic Law 15/1999 of 13/12/99 on the protection of personal data, BOE 298 of 12/14/99) and Law 41/2002 of the November 14 law on rights and obligations in the field of information and clinical documentation. All the participants signed an informed consent document. The local confidentiality law in Spain was followed.

Professor Alexandra Quittner, as developer of the CFQ-R for adolescents and adults, gave her permission to develop and validate this electronic version of her questionnaire in 2015. We registered this application and validated it in 2015 and 2016, respectively.

2.5. Statistical analysis

Validation of the e-CFQ-R was performed by assessing its concordance with results from the CFQ-R paper version, which was completed on the same day. In addition, test-retest reliability was evaluated by having a subset of patients complete the electronic version a second time, 15 days later. Concordance was estimated using Lin’s concordance correlation coefficient [26]. Additionally, Bland-Altman plots were performed to analyze concordances in the respiratory symptoms, physical functioning, and health perceptions domains. All the statistical analyses were performed using R (version 3.3.1) [27].

The paper copy CFQ-R administration was not repeated because this was not the aim of the study. We used the CFQ-R paper format as our gold standard; thus, we were not interested in the test-retest properties of the original questionnaire. The comparisons that made sense according to our aims were 1st day CFQ-R vs. 1st day e-CFQ-R and 1st day e-CFQ-R vs. 15th day e-CFQ-R.

3. Results

3.1. Demographics

The patients’ demographic and health data are presented in Table 1. On average, patients were in their late 20s, approximately half were male, BMI was in the normal range, and lung function indicated moderate disease severity. No significant variability was found across the two centers in age, sex, BMI, percentage of forced expiratory volume in the first second (FEV1%), and pancreatic insufficiency. The only significant differences were found in Pseudomonas aeruginosa colonization and dietary supplements.

All 50 patients completed the e-CFQ-R after 2 weeks; the results are shown in Table 2. The sample size was estimated using the formula provided by Bland JM and Altman [28]. For a precise standard deviation the estimated sample size was 50 patients.

Concordance between e-CFQ-R and CFQ-R (paper copy) completed on the same day was high, with coefficient correlations of 0.9 or higher across all scales. In fact, some domains such as physical functioning, role functioning, and health perceptions had a coefficient correlation of 0.99. Test-retest reliability over 15 days was also very strong, with all
values ranging from 0.8 to 0.9 (see Fig. 2). Limits of agreement estimated by the Bland-Altman plots were between −5.9 and 6.3 for the physical functioning score, between −5.7 and 5.7 for the health perception score, and between −7.4 and 8.5 for the respiratory symptoms score (Fig. 3).

4. Discussion

HRQoL instruments can provide a standardized, valid, and reliable way of gaining the patients’ perspective as to “how they are or feel” and the benefits and limitations of interventions.
In recent years, a number of instruments have been developed to measure patient health status and to assess how patients feel or function with regard to their health conditions [4,17,14,23]. The questionnaires that measure quality of life in patients with CF (the revised CF questionnaire [CFQ-R] and the Cystic Fibrosis Quality of Life [CFQoL] questionnaire) are considered valid instruments with demonstrated reliability, internal validity, and sensitivity.

PROs, such as the CFQ-R questionnaire, are important endpoints in clinical trials of new medications, can serve to improve clinical care, and can help caregivers make complicated decisions such as whether to send a patient with CF for lung transplant assessment [16]. Until now, the mode of administration for CFQ-R has been by paper format. It has been used mainly in CF clinical trials, and less frequently in clinical practice [1,3,5,10]. One of the main reasons is the time consumed by using the current paper format, and subsequently, the medical team does not have immediate results; therefore, it does not help the CF team to monitor the physical and psychosocial aspects of health.

This misbalance between the effort in analyzing the results of questionnaires and the lack of immediate results could be solved using electronic versions of the PROs, as we are presenting in this study.

Due to the underuse of PROs, we do not know the real impact of CF disease on HRQoL, nor if the current items measured in these questionnaires are adequate to evaluate the changes experienced by the patient as the CF is progressing.

Currently, the use of CFQ-R in clinical practice in most EU centers is scarce, and we are losing critical input from the patient.
that can orientate us to mood changes or poorer physical functioning better than a clinical interview or through lung tests [19,29]. One consequence of this loss is that there are limited data on HRQoL changes over time in adults with CF [19,30], and scarce physiological interventions are derived from this relevant information. In addition, patients may respond differently over time. Their health or HRQoL might or might not have changed, but their perceptions of them can evolve over time. These changes have important implications for HRQoL assessments, particularly in terms of the effects of interventions. A change in HRQoL could reflect an intervention effect, a change in response or both.

Two longitudinal HRQoL studies have recently been published in which they analyze the evolution of various questionnaires’ subscales, adjusting for demographic and clinical characteristics. In the first study, the physical domains of CFQ-R, such as respiratory symptoms, were stable. In contrast, population

Fig. 3. Bland-Altman plots for A: physical functioning; B: health perception; and C: respiratory symptoms scores.
changes in several psychosocial domains of CFQ-R suggest that differentiating between the physical and the psychosocial trajectories in health among adults with CF is critical when evaluating patient-reported outcomes [30].

Abbott et al. [19] published the largest study on longitudinal data that evaluates the association between changes in clinical variables and the CFQoL questionnaire. These longitudinal data highlight the inadequacy of cross-sectional data, which fail to recognize the full impact of the CF disease trajectory and its treatments on HRQoL. The authors demonstrated that the demands created by the CF disease trajectory and its treatments profoundly impact all aspects of a person’s quality of life.

Monitoring HRQoL adds additional information to routine assessments in chronic conditions such as CF. Understanding the natural history of HRQoL in a population with CF allows for a more accurate interpretation of such assessments over time. How CF is affecting HRQoL and whether there is any cutoff value in the subscales for alerting us, as a red flag, is unknown. Knowing the natural rate of change in HRQoL domains could provide a benchmark against which changes due to CF complications or interventions can be compared and should help reveal the clinical relevance of HRQoL changes.

Assessing changes in HRQoL over time would augment existing clinical assessments and population-based outcome tools and help direct management decisions for the care of adults with CF.

In our experience, the CFQ-R questionnaire can help not only in making management decisions, but could also be useful for complicated decisions such as whether to send the patient for lung transplant assessment or to be listed for transplantation [16].

Until now, the mode of administration for CFQ-R has been by paper format. To our knowledge, this is the first time that the electronic CFQ-R version has been validated. Our results revealed that the electronic version is equivalent to the paper version; in fact, the concordance between both versions was very high. In addition, it provides excellent test-retest reliability over 2 weeks. This electronic version presents many advantages: first, it calculates automatically and provides immediate results to the CF team. Second, it reduces data entry errors to zero and decreases the possibility of missing data (e.g., not being able to accidentally skip a question). Third, it makes this valuable instrument very easy to use for both clinical and research purposes. Finally, it provides in real time a view of how our patients are living with their disease, and allows us to incorporate the patients’ concerns. In addition, data are automatically entered into a secure database, which facilitates their use for other purposes, such as an annual registry.

In conclusion, the electronic version of the CFQ-R Teen/Adult version is reliable and valid, and can be used in place of the paper version. Future steps will include validation of the other versions of the CFQ-R (e.g., child and parent) in an electronic format, and also developing the electronic version of the other translations. The e-CFQ-R is a useful tool in the care of patients with CF, because it reduces the time associated with data entry and scoring, produces more accurate data, and is a great step forward in implementing the use of patient-reported outcomes in real-time care.

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Authors’ contributions

All the authors conceived of the study. AS, ALQ, VV and ANB drafted the manuscript. All the authors have critically revised and approved the final version.

Conflict of interests

The authors declare no conflicts of interest.

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References


