Validity of a Spanish Version of the Leicester Cough Questionnaire in Children with Cystic Fibrosis

Resumen

Antecedentes: Los pacientes con Fibrosis Quística (FQ) presentan tos crónica como uno de los síntomas principales, afectando la calidad de vida y las relaciones sociales. Nuestro objetivo fue analizar la fiabilidad y validez de la versión española del Cuestionario de Tos Leicester (LCQ) en niños y adolescentes con FQ.

Métodos: Tras adaptarlo al español mediante el método de traducción y retro-traducción estandarizada, 58 pacientes con FQ estable de 7 a 18 años fueron reclutados de 3 centros especializados en FQ de España. El cuestionario fue administrado en dos ocasiones (LCQ_1 y LCQ_2) espaciadas con 2-4 semanas. Para correlacionar los resultados con la calidad de vida (HRQoL) se utilizó el Cystic Fibrosis Questionnaire-Revised (CFQ-R).

Resultados: La población estaba compuesta en un 62% por varones, con una media de edad 11,7±3,1 años, y con un índice de masa corporal de 19±3 kg/m^2. Las puntuaciones totales de LCQ fueron: LCQ_1 19 (17,75-21) vs LCQ_2 19 (16-21) *(p=0,199)*. El coeficiente Alfa de Cronbach fue de 0,83 para el LCQ_{total} y para cada dominio específico fue: 0,82 $LCQ_{physical}$; 0,74 $LCQ_{psychological}$ y 0,62 LCQ_{social}. El coeficiente de correlación intraclase fue: 0,69 $LCQ_{physical}$; 0,59 $LCQ_{psychological}$; 0,45 LCQ_{social} y 0,71 LCQ_{total}. Las correlaciones más significativas con el CFQ-R fueron: LCQ_{total} r = 0,51 *(p <0,001)* y para el dominio síntomas respiratorios r = 0,67 *(p <0,05)*.

Conclusión: La versión española del Cuestionario de Tos Leicester es fiable y válida para niños y adolescentes con FQ; además presenta buenas correlaciones con la calidad de vida en esta población.

Palabras clave: Fibrosis Quística, Tos, Cuestionario de Tos y Calidad de Vida relacionada con la salud.

Abstract

Background: Cystic Fibrosis (CF) patients present chronic cough as one of the main symptoms, which has an important effect on quality of life and social relations. Our goal was to validate the Spanish version of the Leicester Cough Questionnaire (LCQ) in a group of children and teenagers with CF.

Methods: After adapting to Spanish by standardized translation and retro-translation methodology a sample of 58 stable CF patients from 7 to 18 years were recruited from three CF specialized centers in Spain. The questionnaire was administered twice; the second administration (LCQ_2) was performed between 2-4 weeks later than the first one (LCQ_1), in order to analyse the reliability and validity of the Spanish version. To correlate results with health related quality of life (HRQoL) we used the Cystic Fibrosis Questionnaire-Revised (CFQ-R).

Results: Population was composed by 62% male, age 11.7±3.1 years and body mass index (BMI) 19±3Kg/m^2. Total scores from LCQ were: LCQ_1 19 (17.75-21) vs LCQ_2 19 (16–21) *(p=0.199)*. Cronbach's Alpha coefficient was 0.83 for the LCQ_{total} and for each specific domain was: 0.82 $LCQ_{physical}$; 0.74 $LCQ_{psychological}$ and 0.62 LCQ_{social}. Intraclass correlation coefficient was: 0.69 $LCQ_{physical}$; 0.59 $LCQ_{psychological}$; 0.45 LCQ_{social} and 0.71 LCQ_{total} (good reliability). Relations with CFQ-R, showed moderated and significant results: LCQ_{total} r=0.51 *(p<0.001)* and respiratory symptoms domain r=0.67 *(p<0.05).*

Conclusion: The Spanish version of the Leicester Cough Questionnaire is reliable and valid for children and adolescents with CF and it has good relations with health related quality of life in this population.

Keywords. Cystic Fibrosis, Cough, Cough Questionnaire and Health Related Quality of Life.

INTRODUCTION

Cystic Fibrosis (CF) is a genetic chronic and progressive disease that affects multiple organs such as exocrine cells placed in respiratory tract, pancreas, liver, sweat ducts and reproductive system.(1) The lungs pathophysiology is characterized by an absence or defective cystic fibrosis transmembrane regulator protein (CFTR) function, which causes an abnormal regulation of periciliary liquid volume, decreasing mucociliary clearance and producing plugging and lung obstruction.(2) Productive cough is a universal symptom in CF that becomes chronic with the evolution of the disease.(3) Pulmonary exacerbations are defined as an increase in cough and sputum production, appetite reduction and an exercise capacity impairment, which has a global impact in school absenteeism.(4) As CF progresses, exacerbations happened with more frequency and cough becomes a common daily symptom.(5)

Furthermore, cough shows a direct influence on survival, resulting in an important measure of evolution and treatment efficiency of the disease.(6–8) Clinical experience suggests that chronic cough interferes in the three patient's dimensions: physical, emotional and social. Consequently, diminishing considerably the patient's quality of life and affecting their social relations.(9,10) By monitoring health related quality of life and the cough impact it may be possible to improve the treatment efficiency, prolong longevity and decrease the economic costs of the disease.(11) Mainly, because cough might be an important symptom for predict and prevent possible exacerbations.(12)

Health related quality of life (HRQoL) assessment provides the base for evaluating the impact of the disease and treatments on daily life activities, which are not reflected by conventional clinical tests.(11,13) HRQoL questionnaires correlate

with chronic cough although its representation in these questionnaires is poor.(10) Therefore, the impact of cough in patient´s life is not fully characterized, especially in children. Cough is an exacerbation marker, which significantly alters HRQoL, becoming more significant in adolescent with CF.(14)

Leicester Cough Questionnaire (LCQ) was designed to evaluate objectively chronic cough and its impact on daily life. It is structured in three domains: physical, psychological and social.(15) Murray et al.(16) reported good results applying it in adults with non-cystic fibrosis bronchiectasis. LCQ has been translated in multiple languages like Dutch and Chinese among others;(17,18) and being a common tool for assessing the cough impact in different respiratory diseases showing solid results, even when cough is acute.(19) However, little is known about cough assessment in CF;(20) normally, it is only related to exacerbation periods and is poorly analyzed in children.(21)

After exploring the recent evidence, the LCQ seems to be an adequate tool for assessing cough in young CF population; in addition, it has not been investigated previously in this specific group.

The aim of the present study was to translate and validate the Spanish Version of the Leicester Cough Questionnaire in children and teenagers with Cystic Fibrosis, in order to provide a new tool to analyse the cough impact on this population. Therefore the Spanish Version of the Leicester Cough Questionnaire could constitute a simple and easy instrument to be incorporated for assessing cough in young CF patients.

METHODS

Participants

The population studied was selected in Spain from *Hospital de Sabadell, Corporació Sanitària Universitària Parc Taulí, Sabadell (Barcelona)*, *Hospital Ramón y Cajal* and *Asociación Madrileña de Fibrosis Quística* in Madrid. All participants were recruited during the period between May and September of 2013. Inclusion criteria were CF patients from 7 to 18 years old, with stable clinical conditions, without exacerbations since the previous four weeks to the study inclusion and were able to read and comprehend the questionnaires. First of all, sixty patients were included; two of them were excluded due to a respiratory exacerbation during the study process (Graph 1).

The study was approved by the Ethics Committee of the *Hospital de Sabadell, Corporació Sanitària Universitària Parc Taulí* and Pompeu Fabra University in Barcelona, Spain. Before the study, patients over 14 years old signed the informed consent form, and consent from children under 14 was signed by parents, accepting to participate in the study.

In order to better characterize patients, all of them performed a conventional forced Spirometry[24] using a portable spirometer Easyone™ Bluetooh Cradle model 2010BLT (Zurich, Switzerland) in the centers of Madrid, and by Datospir-600 Sibelmed (Barcelona Spain), in Sabadell.

Demographics

The final group was composed by 58 CF patients in stable clinical conditions, 38% of them were female with a mean age of 11.7±3.1 years; body mass index (BMI) 19±3Kg/m^2; and had a preserved lung function: Forced Vital Capacity (FVC) 2.68±0.93L; Forced Expiratory Volume in the first second (FEV_1) 2.25±0.79L; and the relation FEV_1/FVC 83.85±6.9%.

Cough questionnaire

The Leicester Cough Questionnaire (LCQ) measures cough impact on quality of life.(15) It is a self-administration questionnaire composed by 19 items divided in three domains: physical (8 items), psychological (7 items), and social (4 items). The answers were represented in a 7-point Likert scale. The total score, rang from 3 to 21, was obtained by adding the domains scores and dividing by three; in which higher scores represents lower cough impact on quality of life. Also, each domain could be analysed independently.

Quality of life

The *Cystic Fibrosis Questionnaire-Revised* (CFQ-R) consists of a quality of life questionnaire specifically designed for patients with Cystic Fibrosis older than 6 years old.(22) It was translated to a range of languages also into Spanish.(23) We used three versions of the questionnaire divided by groups of age: CFQ-R 6-11 (from 6 to 11 years), CFQ-R 12-13 (from 12 to 13 years) and CFQ-R 14+ (adolescents). The questionnaire is composed by self-reported items with different domains, including physical functioning, vitality, health perceptions, respiratory symptoms, treatment

burden, role functioning, emotional functioning, and social functioning. Answers were reported on 4-point Likert scale rating frequency, difficulty, or truth about selecting statements that described the patient´s situation. Final score is given by domains, each domain has a score from 0 to 100, higher scores indicate higher degrees of patient´s quality of life.

Validation process

For the validation process, we followed the standardized method of forward-backward translations. Firstly, we translated the original version into Spanish and then a native English official translator retranslated it to English. A panel of experts in respiratory diseases and cough discussed and compared the two versions in order to find the best expressions for better patients understanding. After this process, the preliminary version of the questionnaire was tested by a group of patients (n=8) to obtained their impressions and comments. During the final procedure, some simple modifications were introduced avoiding changes in the meaning of the questionnaire. Only two questions were adapted by including a simple common word, in parentheses, similar to the original to help children's comprehension (Graph 1).

To validate the Spanish version of the LCQ, the final version was applied twice in a period of 15-30 days to compare both results. During this period, patients were focussed not to change their routine management or initiate physical activities or change medication or any unusual activity that could interfere cough status during the validation. If that occurred, they were automatically excluded from the study.

Furthermore the floor or ceiling effects can be assessed if more than 15% of the patients achieve the lowest score, meaning higher impact of cough; or highest possible

score, meaning lower impact of cough in quality of life, respectively. Absence of floor or ceiling effects indicates a good content validity.(24)

Statistical Analysis

Statistic analysis was performed by using the PASW Statistics 18 (SPSS Inc., IBM. USA). Demographic characteristics are represented as median and Interquartil range. The Saphiro-Wilk test was used to analyse the distribution of the data. We used non-parametric statistics because most data were not normally distributed ($p<0.05$).

For reliability, internal consistency and reproducibility were examined. The questionnaire validity (internal consistency) was assessed by Cronbach alpha coefficient and item total correlation coefficients, while for the reliability was used the Intraclass correlation coefficient (ICC). We assume that the Cronbach's alpha coefficient should be >0.70. Reliability levels were defined based on the following classification: high reliability, ICC ≥ 0.90; good reliability, ICC ≥ 0.70 and <0.90; acceptable reliability, ICC ≥ 0.40 and <0.70; poor reliability, <0.40. Agreement over time was assessed by constructing a Bland-Altman plot for the LCQ total score by calculating the mean difference between 2 measurements and the standard deviation (SD) of the difference.(25) In this plot, 95% of the differences are expected to be less than 2 SDs.

The Minimal Important Difference (MID) is given by: $MID = \pm 1.96 \times v2 \times SEM$, where 1.96 derives from the 95% of confidence interval (CI).

Measurement error is expressed as a Standard Error of Measurement (SEM), which is calculated as: *SD x (V1-ICC),* where SD is the Standard Deviation of values from all participants and ICC is the reliability coefficient.(26)

The convergent validity was assessed by the Spearman correlation coefficient between the LCQ and the CFQ-R scores. A strong correlation was considered to be over 0.60; a moderate correlation between 0.30 and 0.60; and a low (very low) correlation below 0.30.(27)

RESULTS

Demographics

The demographics and clinical characteristics are showed in Table 1.

LCQ validation

The reproducibility of the Spanish version of the LCQ demonstrates no significative differences in median and interquartile range between both administrations, see table 2. The results obtained in the three domains and in the total score were similar between both administrations: $LCQ_{physical}$ 6.19 vs 6.50; $LCQ_{psychological}$ 6.43 vs 6.43; LCQ_{social} 6.75 vs 6.75; and LCQ_{total} 19 vs 19 [1^{st} vs 2^{nd} administration (p=ns)]. The Bland and Altman analysis, showed a higher concordance between total score results when comparing both administrations. A Bland-Altman plot of the LCQ total score is shown in Graph 2. The validity and reliability results obtained from the Cronbach Alpha coefficient and the intraclass correlation coefficient (ICC) are shown in table 3. Results showed acceptable reliability, ICC ≥ 0.40 and <0.70, except for de ICC of the LCQ_{total} domain that is was 0.71, showing good reliability. It is important to note that the questionnaire not presented floor effect (0%) in any of the domains.

The Minimal Important Difference (MID) for the LCQ was between 1.07 to 3 with a Standard Error Measurements (SEM) between 0.46 to 1.28 (table 3).

Relations between the Spanish version of the LCQ and health related of quality of life

In order to better understanding of the LCQ dimensionality, we compared the results of its dimensions with quality of life using the Cystic fibrosis Questionnaire-

Revised (CFQ-R). For this, we analysed all the domains of the questionnaire (physical capacity, role functioning, vitality, emotion functioning, social functioning, body image perceptions, eating, treatment burden, health perceptions, weight perceptions, and respiratory and digestion symptoms). The most significant and interesting correlations are shown in table 4. We can point-out the relations with CFQ-R revealing significant correlations in physical capacity, respiratory symptoms and body image domains ($p<0.001$).

DISCUSSION

The Spanish LCQ version is a valid and reliable questionnaire to evaluate the cough impact on quality of life in children and adolescents with Cystic Fibrosis. It is noticeable that this is the first study in which the LCQ was applied in children and on this population; there were no references found on this group of patients.

The Spanish LCQ version shows similar results to the original version done by Birring et al.(15) The original version showed a good reliability in all domains and in total score; on the other hand the Spanish version obtained lower values in both coefficients, ranging between: Cronbach Alpha coefficient 0.62 and 0.83; ICC 0.45 and 0.71. It should be highlighted that social domain coefficients obtained in the Spanish version were inferior in comparison with the original version and with other studies.(15,16) These results are probably explained by the low age of the sample. The majority of the studies based of LCQ feature adults, because children and adolescents perceive their surroundings in a different way than adults.(28) Consequently it affects the final score results, confirmed by the percentage of young patients (50%) who did not think having cough is equal to having a problem. Total score were repeatable with intraclass correlation coefficients above 0.7. So, repeatability of the LCQ in CF patients was adequate and in accordance with previous results.(29)

On the other hand, the excellent stability of the Spanish LCQ version reveals lower cough impact on quality of life in the population studied, likely due to age and low severity level of pulmonary disease; this also represented the plausible explanation for not to have found floor effect in the study. Gee et al.(30) confirms that gravelly affected patients tend to produce greater floor effect; however, those with moderated and mild levels, generate ceiling effects in most items. That is the case of

our patients where they presented more than 15% of celling effect in all domains. This could limited the internal validity of the Spanish version however, the obtained results could be explained because the mild respiratory severity and the age of the included patients. Secondly sex and age are stronger predictors of health related quality of life and children reported a lower treatment burden than their parents perceived them to have.(31) For all of this, the lower social domain coefficient obtained in the Spanish version it may be because by the young age of population (probably in this population, the social impact of cough is still unimportant and cough is not an obstacle for their normal life).

The LCQ represented a solid tool to measure cough impact on quality of life, as demonstrated by the strong and significant correlations observed between LCQ and CFQ-R, especially in the physical domain and respiratory symptoms. Therefore, it is safe to say that LCQ truly reflects quality of life related to cough impact in CF patients.

Subjective tools such as cough visual analogy scales, scores, and diaries are widely used to measure the cough impact. Although the optimal assessment of cough severity is not known, it is likely that a combination of subjective and objective assessments will be necessary. It is necessary to investigate about the well-validated cough severity assessment tools. Furthermore, it is important to emphasize the importance of the validation into Spanish, confirming its reliability even when complete by minors – not explored by previous studies.

Limitations

There were some limitations of the study that is worth mentioning.

First of all, researchers detected some difficulties on the items' comprehension during the experimental group in younger patients, which were solved in the final version by adding a synonym in parentheses next to the misunderstood word.

Another difficulty was the uneven age distribution that could lead to misinterpretation of some data since there is a distinct perception of sickness between teenagers and children. In addition, the low severity status of the disease could have overestimated the results increasing ceiling effect and revealing a better quality of life and lower cough impact.

It is noticeable that the sample was not selected specifically for the validation, they were collected from the ordinary respiratory hospital consultation. If the study group had been composed with severe and moderated CF patients, it would demonstrate that the Spanish version of LCQ really can distinguish the impact of cough in quality of life. The unequal medication regimen for each patient could also alter cough status, modifying LCQ results. To diminish this effect, during the validation process, the research team made sure there was no variation in drugs for each patient.

Despite those limitations, the aim of the study was to demonstrate the validity of the Spanish LCQ questionnaire version for young CF patients, and not to show if they have more or less cough.

In conclusion, the Spanish version of the Leicester Cough Questionnaire is valid to evaluate cough impact on quality of life in children and adolescents with Cystic Fibrosis. From these results we recommend their use regularly in order to detect any change in quality of life that could appear during the disease evolution.

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Tabla (Table)

Table 1. **Patients characteristics.**

Population Characteristics (n=58)	
Sex: M/F (%)	62/38
Age (years)	12 (9-14)
Height (m)	1.47 (1.33-1.58)
Weight (kg)	41.3 (30.2-52.1)
BMI (kg/m^2)	18.3 (16.6-21)
FVC (L)	2.45 (2.01-3.37)
FVC (%)	101 (83-114)
FEV_1 (L)	2.05 (1.72-2.92)
FEV_1 (%)	94 (83-114)
FEV_1/FVC (%)	84.4 (78.9-89.6)

Data are expressed as a median and interquartile range. BMI: body mass index; FVC: forced vital capacity; FEV_1: forced expiratory volume in the 1^{st} second; FEV_1/FVC: flow/volume ratio.

Table 2. Differences between both administrations of the Leicester Cough Questionnaire.

	1^{st} administration	2^{nd} administration	p-value
Physical Domain	6.19 (5.47-6.78)	6.50 (5.59-6.75)	0,504
Psychological Domain	6.43 (5.43-6.86)	6.43 (5.71-6.86)	0,838
Social Domain	6.75 (6.00-7.00)	6.75 (6.25-7.00)	0,975
Total	19 (17.75-21)	19 (16–21)	0,199

Data are expressed as a median and interquartile range. Wilcoxon's test *$p<0.05$

Table 3. Reliability and validity analysis of the LCQ.

Leicester Cough Questionnaire	Floor (%)	Ceiling (%)	Cronbach Alpha	ICC (95% CI)*	SEM	MID
Physical Domain	0	36.1	0.82	0.69 (0.52-0.81)	0.46	1.07
Psychological Domain	0	41.3	0.74	0.59 (0.38-0.74)	0.59	1.39
Social Domain	0	62.1	0.62	0.45 (0.20-0.65)	0.63	1.47
Total	0	29.3	0.83	0.71 (0.54-0.82)	1.28	2.99

ICC: Intraclass Correlation Coefficient; *95% Confidence Interval for ICC this study; SEM: Standard Error Measurements; MID: Minimal Important Difference

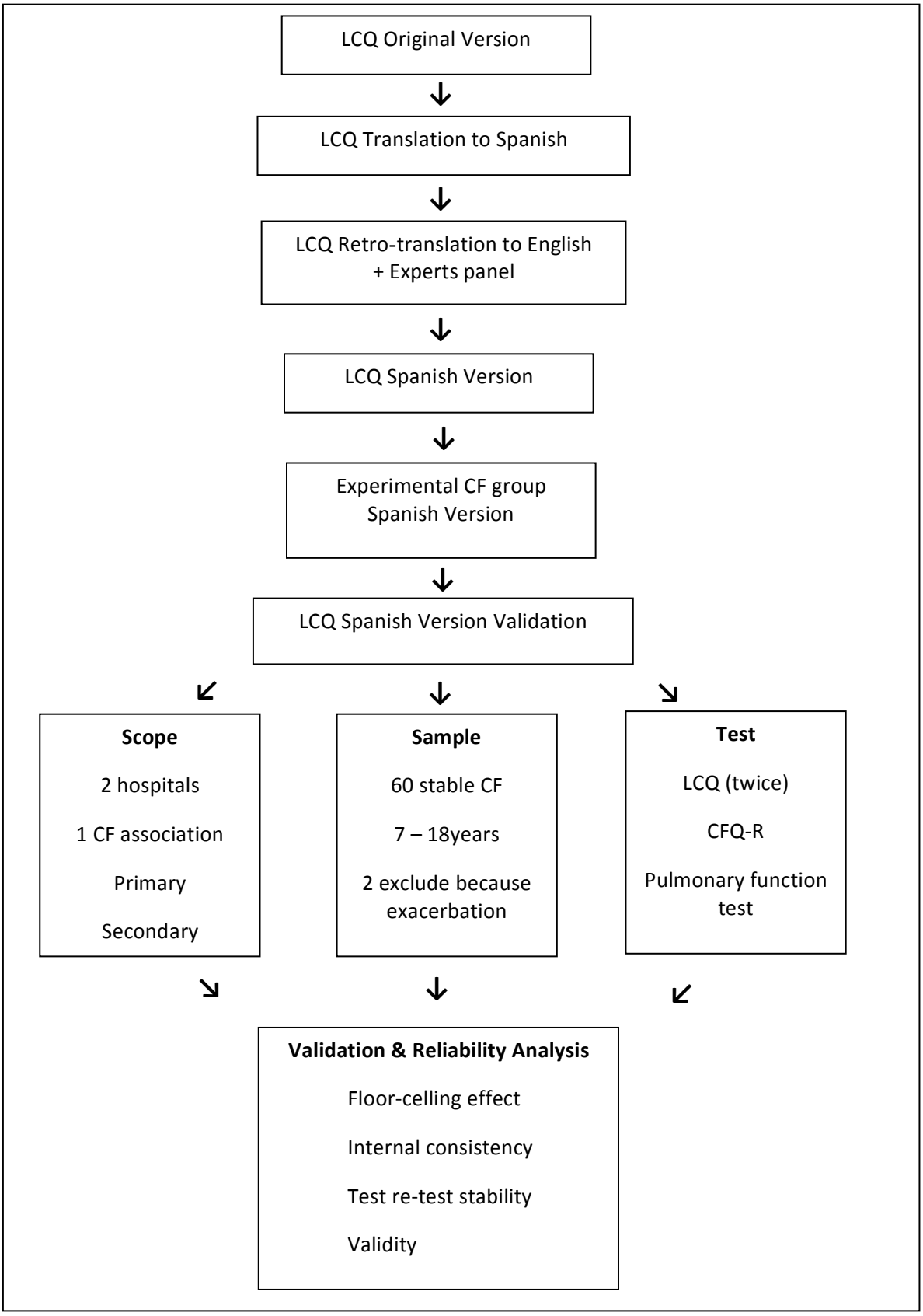
Table 4. **Correlations between the different domains of the LCQ, CFQ-R and pulmonary function.**

	Leicester Cough Questionnaire domains			
	Physical	Psychological	Social	Total
Respiratory Symptoms domain (CFQ-R Children)	0.624**	0.378*	0.236	0.513**
Physical Capacity domain (CFQ-R Adolescents)	0.653*	0.749**	0.739**	0.627*
Respiratory Symptoms domain (CFQ-R Adolescents)	0.700**	0.734**	0.684*	0.670*
Body image domain (CFQ-R Adolescents)	0.577*	0.575*	0.599*	0.637*
FVC (L)	0.427**	0.601**	0.462**	0.557**
FEV_1 (L)	0.487**	0.626**	0.456**	0.582**

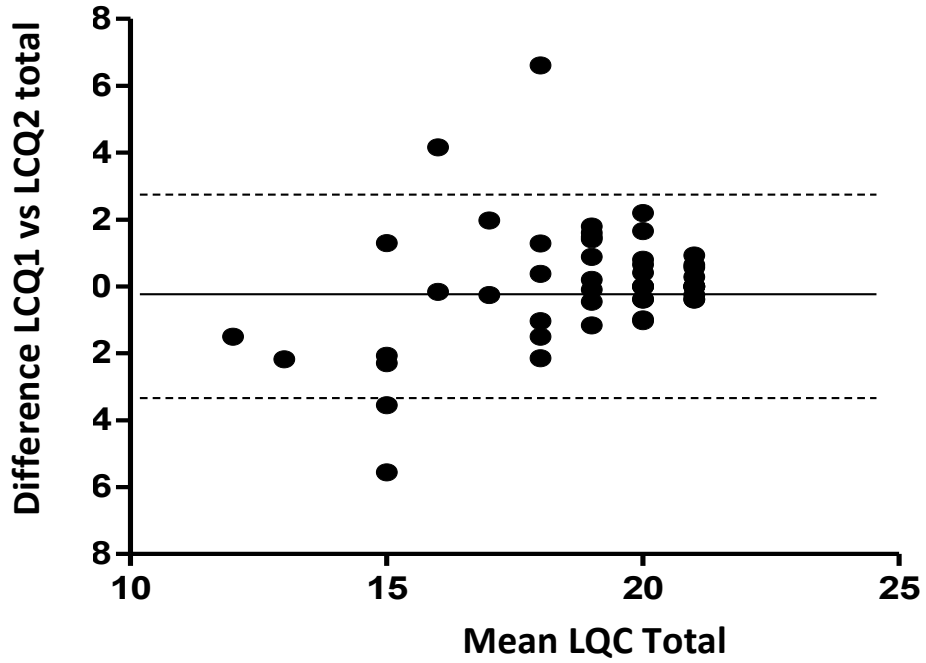
Spearman's correlations. CFQ-R Children: Cystic Fibrosis Questionnaire-Revised for children from 6 to 13 years; CFQ-R Adolescents: Cystic Fibrosis Questionnaire-Revised for adolescents over 14 years; FVC: forced vital capacity; FEV_1: forced expiratory volume in the 1^{st} second. *p<0.05. **p< 0.001.

Figura (Figure)

Graph 1: General scheme of the study process.



Graph 2. Bland-Altman plot of the LCQ total score and the changes between first and second administration.



Solid line represents the mean difference between over two administrations and the dashed lines are the limits of agreement, which represent 2 times the standard deviation of the mean difference.