Monitoring quality of life in outpatients with cystic fibrosis: Feasibility and longitudinal results

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Abstract

Background: To investigate the feasibility of monitoring quality of life (QL) with cystic fibrosis (CF) in a clinical setting, to explore changes in subjective health and to describe the impact of multiple medical and psychosocial factors on the patients’ QL.

Methods: 108 adolescent and adult outpatients (age 15–47 years, FEV1 20–125% of the predicted) answered the Questions on Life Satisfaction repeatedly parallel to each pulmonary function test (2–16 assessments per patient within 18 months). Multiple regression analysis determined the contribution of medical and psychosocial factors to the patients’ QL.

Results: Good acceptance of the instrument was observed. The completion time was between 5 and 29 min per assessment (median 11 min). QL remained quite stable (r_{tt} = .69) with the previous QL score predicting most of the variance of the present score. Additionally, a longer interval between assessments, new colonization with Pseudomonas aeruginosa, infection exacerbations, partnership, vocation and living separately from parents significantly predicted QL at the second assessment. Pulmonary function varied independently of QL.

Conclusions: Medical factors such as pulmonary exacerbation and social living circumstances have an impact on the QL of patients with CF. Repeated QL assessments in clinical routine are feasible and useful to recognize the individual patient’s adaptation to the disease.

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Keywords: Adolescents and adults; Cystic fibrosis; Life satisfaction; Longitudinal assessment; Psychosocial aspects; Quality of life

1. Introduction

Although quality of life (QL) is considered increasingly important in chronic conditions, there is a lack of prospective longitudinal studies and clinical trials involving QL with cystic fibrosis (CF) [2–4]. Therefore, the knowledge of changes in patients’ subjective health and its determinants is limited. So far, monitoring QL in clinical practice is mostly done routinely by the “How are you?” question. The use of standardized psychometric instruments is still limited, although several disease-specific instruments have been developed over the past ten years [5–9]. Lack of staff trained in applied psychometrics and limited practicability of these instruments may be responsible for the abstinence from structured routine assessment of QL in clinical practice.

With regard to its definition as a multi-dimensional measure integrating self-reported physical, emotional and social functioning and well-being [10], QL is a dynamic psychological construct, which describes the subjective health perception of the patients independently of objective health parameters [11]. QL scores reflect the impact of disease-related stressors and other life stressors in relation to the psychological adaptation of the individual [12]. Patients may maintain good QL in spite of being seriously ill, and other patients may report a bad QL although they have a mild manifestation of the disease [13,14].

There is an ongoing discussion on the best way of measuring QL in CF [9,15,28]. Some questionnaires such as the
disease-specific Cystic Fibrosis Questionnaire CFQ [8] or the generic SF-36 [6] assess primarily the patients' perceptions of their functional health. The Questions on Life Satisfaction (FLZ) have been proposed as a reliable and valid instrument to reflect the subjective perspective of the patient by considering the importance and satisfaction ratings by the individual for different life domains [7]. So far, the FLZ has been used in a study with CF patients evaluating the effectiveness of inpatient rehabilitation programmes [16], but the feasibility of the FLZ in an outpatient setting has not yet been demonstrated. Therefore a purpose of the present study is to demonstrate the feasibility of repeated QL assessments in clinical routine. Feasibility in clinical routine is dependent on the practicability of the instrument, for example by its shortness, its costs, and its easiness of data collection and analysis. We assessed feasibility by observing the acceptance of repeated assessments by patients and professionals, by the proportion of missing data, and by measuring the time needed to fill in the instrument.

Another area of interest is the identification of factors impacting on patients' QL with CF. Multiple factors have been analysed, but the findings are only partially consistent. The following aspects have been reported to correlate with QL in CF patients: socio-demographic factors such as age [17,18] and gender [9,18–21]; cultural background [22]; disease factors such as pulmonary function [5,7,14,17,20,21,23–25], infection [19,26,27], body mass index [5,20,28], or concurrent medical conditions [26]; treatment factors such as intra-venous [29] or inhalative therapy with antibiotic drugs [25,30], recombinant human DNase [17], hospital admission [17,27], heart and lung transplantation [21,31], daily time for therapy [32], and the number of different medications [26]; and psychosocial factors such as work status [33], coping with the disease [12], psychopathology, hope for the future and family functioning [34]. However, most of the findings are based on cross-sectional studies and cannot estimate determinants of changes in QL. Only few prospective longitudinal studies with QL as the primary variable have been done so far. Based on multiple regression analysis, Bradley et al. [29] reported that changes in exercise capacity and sputum output contributed significantly to changes in QL. With the same method, Johnson et al. [17] found that only previous scores of QL and the number of hospital admissions showed a substantial quantitative association with QL. In another longitudinal QL study, Kotwicki et al. [26] found that changes in QL were associated with changes in the number of respiratory infections, changes in the number of concurrent medical conditions, and changes in different medications. Vermeulen et al. [31] showed improvements in QL after heart lung transplantation, and in a study of the course of QL during pulmonary exacerbations Yi et al. [27] reported that hospitalization was associated with an improvement in psychosocial QL by the post-exacerbation assessment.

Most of the QL research with CF patients is based on cross-sectional clinical studies with selected samples of participants. It is not clear whether these results can be generalized to the average CF population. The only community-based longitudinal survey study by Sawyer et al. [35,36] followed up 123 children and adolescents with CF for two years and found a stagnation of QL as measured by the Child Health Questionnaire. However, to our knowledge a clinic-based naturalistic approach to measuring QL in CF has never been done. Therefore the purpose of the present study was to include a non-selective sample of typical patients attending outpatient CF clinics in Germany and follow them up by repeated QL assessments. In accordance with the previous findings in the literature, this study explores multiple determinants of QL with CF and investigates intra-individual changes of QL in a naturalistic design of outpatient treatment. The following explorative research questions are addressed:

1. How stable is quality of life with CF under naturalistic conditions of outpatient treatment? In which domains of QL is there a higher or lower extent of intra-individual change?
2. Which factors out of a broad range of psychosocial, socio-demographic, medical and treatment factors have a significant impact on QL with CF? Are changes in health condition as a decrease in pulmonary function or pulmonary exacerbations correlated with changes in QL, and to what extent is QL determined by different factors?

2. Methods

2.1. Study design

The study took place in four German outpatient CF centres. All patients with a minimum age of 15 years were asked to participate. Informed consent of adult patients and of legal guardians of adolescent patients, and informed assent of adolescents themselves were acquired according to the guidelines of the local medical committee. In a prospective longitudinal approach, QL was assessed repeatedly parallel to each pulmonary function test during the observational period of 18 months. Forced expiratory volume in one second as a percentage of the predicted value (FEV, %), body mass index (BMI), infection parameters, antibiotic i.v. therapy within the four weeks prior to assessment, socio-demographic data and psychosocial living circumstances such as partnership status, vocation and housing were recorded at each QL assessment. The interval between the assessments depended on the standards of routine monitoring of pulmonary function (1–4 times per year), on the patients’ compliance with these standards, or on specific clinical indications, for example in the case of pulmonary exacerbation. Therefore the interval between the assessments varied from 1 to 405 days with a median of 86 and a standard deviation of 66 days.

2.2. Participants

148 patients were enrolled in the study with a total of 460 assessments. All patients were Caucasians. 108 patients were
able to be assessed repeatedly (2 to 16 times). 40 patients provided only baseline data because they appeared only once in their CF centre during the course of the study. For details of the study sample see Table 1.

### 2.3. Instruments

The Questions on Life Satisfaction FLZ\textsuperscript{M} are a multi-dimensional instrument measuring general life satisfaction, satisfaction with health, and satisfaction with CF-specific aspects of life. The FLZ\textsuperscript{M} was originally developed as a multi-dimensional generic questionnaire [37], which allows the respondent to weight her/his satisfaction with each of the 16 domains of daily life in relation to her/his subjective importance of each domain. Eight general dimensions of life satisfaction are measured: Friends/acquaintances, leisure time/hobbies, general health, income/financial security, occupation/work, housing/living conditions, family life/children and partner relationship/sexuality. Eight dimensions are health-related without reference to disease-specific problems: Physical condition/fitness, ability to relax, energy/zest for life, mobility, vision and hearing, freedom from anxiety, freedom from aches and pain, and independence from help/care. An additional disease-specific module [7] comprises nine CF-specific life dimensions: breathing difficulties/cough, abdominal pain/digestive trouble, eating, sleep, integration of therapy into daily routine, adherence to therapy, understanding by others, being needed by others, and disadvantage because of CF. First, the respondent rates her/his subjective importance of each dimension on scales between 1 (not important) to 5 (extremely important). Second, the present satisfaction with each of these dimensions is rated, again on 1−5 scales (1 = dissatisfied, 5 = very satisfied). The weighted scores are calculated by the formula weighted satisfaction = (importance rating − 1) × [(2 × satisfaction rating) − 5]. Three sum-scores can be computed adding the eight health-related, the eight general satisfaction, and the nine CF-specific scores. A total life-satisfaction score is derived by adding all 26 weighted satisfaction scores. For further details of the measurement concept and the psychometric properties of the FLZ\textsuperscript{M} see Goldbeck et al. [7]. The questionnaire is available from the authors.

The patients answered the FLZ\textsuperscript{M} during their visit to the outpatient clinic. In two thirds of the assessments the questions were administered by a laptop computer, in one third the paper-and-pencil version was used. The use of the paper–pencil questionnaire was due to the inconsistent training of staff members in using the computer system, and due to the inconsistent availability of hardware. We included paper–pencil questionnaires as a substitute to reduce missing data that would have occurred if we had used computer-administered assessments only. Comparisons of the scores by modality of assessment revealed a statistical tendency to report lower scores in the paper–pencil version in some domains, but these differences were not significant and could therefore be neglected in the further analyses. The advantage of the computer-version would be to provide an immediate analysis of the results for the patient and the therapists, but this feature was not used in our study for technical reasons in several CF centres. Good reliability and validity of the FLZ\textsuperscript{M} have been previously reported [7,37,38]. The reliability scores (Cronbach’s \( \alpha \)) in the current study ranged from .73 for the general life satisfaction module and .83 for the health-related life satisfaction module, indicating sufficient internal consistency of the scales. The QL sum-score (across all life domains) had a good reliability with \( \alpha = .92 \).

The following medical parameters were taken from the charts: present pulmonary function (per cent of the predicted FEV\textsubscript{1}), body mass index (BMI), colonization status with Pseudomonas aeruginosa and Burkholderia cepacia, recent i.v. antibiosis (in the past 4 weeks), current oxygen therapy, and exacerbation of pulmonary infection at the time of assessment according to the clinical judgement of the physician. Socio-demographic data and time for daily therapy were recorded by the patients in an additional questionnaire.

### 2.4. Statistical analyses

Weighted satisfaction scores were calculated for each life domain, and their intra-individual variance was determined by paired comparisons between the QL scores at the first and second assessments of each patient. All weighted satisfaction scores were normally distributed. Feasibility was tested by acceptance rates for the repeated assessments by the patients (vs. dropout of patients refusing repeated assessments), by the proportion of missing data, and by the time needed to answer the questions. The relation of changes of pulmonary function and changes of QL was analysed using Pearson correlations between intra-individual difference scores. This procedure allows inclusion of all pairs of assessments into the analyses regardless of how many assessments each patient performed. QL difference scores of patients in a
3. Results

3.1. Feasibility

The completion time for the individual QL assessments ranged from 5 to 29 min with a median of 11 min (SD = 4.4). According to the feedback from patients and staff, the acceptance of the method was good, and both the computer-assisted version and the paper-pencil version were considered practicable. This was also indicated by the absence of any missing data. After initial instructions provided by the CF nurses who were responsible for the assessment at the outpatient clinics, the patients were able to fill in the questionnaires without further assistance. Once enrolled in the study, only one patient did not want to repeat the QL assessments during the ongoing observation period.

3.2. Changes in quality of life

Each individual course of QL was analysed in episodes of two subsequent assessments. The intra-individual difference between both time points was determined for each weighted QL assessment. A ranking list according to the variability of weighted satisfaction in different life domains is provided in Table 2. It can be seen that weighted satisfaction scores were relatively stable in social domains such as friends/acquaintances, perceived understanding by others, being needed by others or family, whereas most intra-individual variability occurred in the health-related domains breathing, digestion, general complaints, and in partnership/sexuality.

Longitudinal single case analyses of courses with more than four assessments (see Fig. 1 for a case example) demonstrated an oscillation of QL scores around an individual mean, with several peaks in both directions, but without a general trend of increasing or decreasing QL. As can be seen in Fig. 1, the intra-individual variance of QL is larger than the patient’s variance in FEV1, and the course of QL is apparently independent from the course of FEV1.

Paired retest correlations (Pearson coefficients) for the different QL dimensions were on a medium to high level with rtt between .41 and .74 (see Table 2). The length of the interval between assessments correlated neither with absolute nor with relative intra-individual difference scores of QL.

3.3. Determinants of quality of life

A repeated measures analysis of variance (ANOVAR) with two time points (T1, T2) demonstrated no main effect of time on QL. Paired difference scores of FEV1 % and QL were not significantly correlated.

The comparison between those patients who showed a clinical significant decrease of their pulmonary function between two subsequent assessments (defined as a loss of 10% of the predicted FEV1 or more) and those patients in a stable health status demonstrated a more negative course of...
the life satisfaction of the patients with decreasing \( \text{FEV}_1 \) in the following domains: breathing \((F=7.1, \ p=.008)\), sum-score of health-related life satisfaction \((F=4.8, \ p=.029)\), independence from help/care \((F=5.4, \ p=.020)\), income/financial security \((F=6.7, \ p=.010)\), and leisure time/hobbies \((F=5.6, \ p=.019)\).

A multiple regression analysis was performed to determine the relative contribution of the different medical, treatment, socio-demographic and psychosocial factors on QL as measured with the FLZ\(^M\). We chose the weighted life satisfaction sum-score at T2 as the response variable and included all factors with a significance of \( p < .15 \) in the final regression model (see Table 3). This cutoff significance level for inclusion of a factor was chosen with regard to the explorative character of this study and to minimize type II errors considering the relative small sample size and the fact that some events such as new colonization with \( \text{P. aeruginosa} \) were rare in our study sample and could therefore not reach high significance levels in its prediction of QL.

QL at T1 was included as a factor to control for the individual QL baseline level. Neither age, gender, level of education, \( \text{FEV}_1 \)% at T2, changes in \( \text{FEV}_1 \)% between T1 and T2, BMI, time for daily therapy, oxygen therapy, status of colonization with \( \text{P. aeruginosa} \), nor recent i.v. antibiotic therapy met the criterion of \( p < .15 \) for the significance of the partial correlation with QL within the multiple regression model. Compared with all other explanatory variables, previous QL had the strongest effect in predicting present QL. Additionally the following six factors contributed significantly to the prediction of QL at T2: the length of the interval between the assessments, vocation, partnership status, living separately from parents, acquisition of \( \text{P. aeruginosa} \) between T1 and T2, and acute exacerbation of infection. The multiple coefficient of determination \( (R^2) \) reflects the amount of variation in the response variable that can be explained by the explanatory variables. Within the final regression model, 45\% of the variance of life satisfaction was determined by previous QL, and the above mentioned six factors explained another 29\% of the variance of QL. The direction of the effects in determining QL was as follows: the longer the interval between assessments, the better the QL at second assessment. Full-time occupation was associated with poorer QL compared with part-time or no occupation. Patients with a partner reported better QL than patients without partner. Living in a household separate from the parents was associated with lower QL than living together with the parents. Recent colonization of \( \text{P. aeruginosa} \) or acute exacerbation of infection had an independent negative effect on QL within the model.

### Table 3

Results of multiple regression analysis predicting the quality of life sum-score\(^1\)

<table>
<thead>
<tr>
<th>Independent variables</th>
<th>Standard coefficient</th>
<th>( t )</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous QL</td>
<td>.69</td>
<td>11.7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Interval between assessments</td>
<td>.13</td>
<td>2.3</td>
<td>.025</td>
</tr>
<tr>
<td>New colonization with ( \text{P. aeruginosa} )</td>
<td>.09</td>
<td>1.6</td>
<td>.117</td>
</tr>
<tr>
<td>Exacerbation of infection</td>
<td>.14</td>
<td>2.5</td>
<td>.013</td>
</tr>
<tr>
<td>Partnership status</td>
<td>.13</td>
<td>2.2</td>
<td>.032</td>
</tr>
<tr>
<td>Household independent from parents</td>
<td>-.20</td>
<td>-3.5</td>
<td>.001</td>
</tr>
<tr>
<td>Vocation (none/part-time/full-time)</td>
<td>-.16</td>
<td>-2.9</td>
<td>.005</td>
</tr>
<tr>
<td>Multiple ( R^2 )</td>
<td>.74</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^1n=98\); \( df=7/94 \); after stepwise exclusion of non-significant independent variables from the model (criterion \( p < .15 \)).

### 4. Discussion

This longitudinal study of a heterogeneous sample of adolescent and adult CF patients was done within a naturalistic design. The results are based on data from typical patients with CF being treated according to international clinical guidelines [39].

The feasibility of the FLZ\(^M\) for measuring QL in an outpatient population is demonstrated by its broad acceptance by patients and staff, by the completeness of the collected data, and by the shortness and convenience of the assessment procedure, which can be done either by computer administration or by paper and pencil.

The most prominent findings with regard to the longitudinal analyses are the stability of QL, indicated by the medium to high level retest correlations, the lack of significant general time effects on QL in a positive or negative direction, and the independence of QL and pulmonary function (with respect to level as well as change of function). The previous personal level of QL predicted most of the variance of re-assessed QL. Single case analyses with many repeated assessments demonstrate that individual QL curves oscillate around a personal average level. These findings are consistent with the Australian study on children and adolescents with CF by Sawyer et al. [35,36] who also demonstrated stability of QL over a 2 year-period. Many different explanations for this tendency are possible. Most patients may

![Fig. 1. Case example of a 22-year old female with CF based on 15 reassessments of quality of life and \( \text{FEV}_1 \)%.

The diagram illustrates the re-assessment of quality of life and \( \text{FEV}_1 \)% over a 2 year-period for a 22-year old female with CF.
effectively cope with their progressive disease without experiencing a decrease in their subjectively perceived QL. This phenomenon of adjusting the subjective estimation of one’s QL has also been referred to as response shift [40,41]. Moreover, QL may be considered rather a trait than a state and therefore the personality of the patients may have a greater impact on their QL than changes in their health status or in their personal living circumstances. More longitudinal studies are needed to investigate the possible mediating or moderating effects of coping and personality on QL.

Besides the personal level of QL which is represented by moderate retest correlations, six additional factors were demonstrated to contribute to the prediction of QL with CF by our exploratory multiple regression analyses: From a set of socio-demographic variables, partnership and closeness to the parents even in adulthood could be identified as protective factors. These factors indicate the availability of social support for the patients, and the protective effect of social support in buffering a potential negative impact of chronic diseases is known from previous studies [42,43]. On the other hand, a full-time vocation seems to conflict with QL, indicating that CF patients with limited time resources due to their daily therapy regime and limited physical resources due to their impaired objective health status may pay a certain price for their job engagement.

In accordance with the previous findings [19,26,27], the differential effects of the medical and disease-related variables in this study demonstrate that infection exacerbations and being newly colonized with *P. aeruginosa* have an impact on QL whereas the level of pulmonary function (FEV1%) and body mass index do not. Only patients with a clinical significant decrease of their pulmonary function, defined as a minimum loss of 10% of the predicted FEV1, show worse QL trajectories in some domains compared to patients with stable FEV1. These findings may be explained by the different impacts of acute symptoms compared with slowly progressing symptoms. Stress and coping theory postulates that it is more difficult to adapt to acute stressors than to changes which proceed slowly, as acute stressors strain the coping capacity of the individual [44].

The positive correlation of interval between assessments and level of QL can be explained by a less severe disease. The interval between QL assessments in this study was determined by the frequency of pulmonary function tests within the observation period. Frequent pulmonary function tests probably indicate a more severe disease. Especially in the case of decreasing pulmonary function therapists would try to prescribe a more aggressive therapy (for example, additional courses of antibiotic i.v. treatment) and they would consequently evaluate the effects of treatment by repeated pulmonary function tests.

Additionally, the knowledge of being free from potential dangerous germs may help the patients to maintain an optimistic view of their lives. Most of the patients in our study were well educated with regard to their CF, and they were aware of their prognosis worsening with the acquisition of specifically pathogenic germs. Only 16% of the patients were free from *P. aeruginosa* at the beginning of the study. Once colonized, these patients would probably expect a progression of their disease, and therefore they may perceive a worse QL by anticipating a negative course of their disease.

The following limitations of this study have to be acknowledged, entailing a cautious interpretation of the results. First, the sample size of this pilot study did not allow for the analysis of a more comprehensive set of risk and protection factors. The statistical power of the analyses was limited, and only strong or moderate effects could be detected. Other variables that were not included in this study may also have a significant impact on the patients’ QL.

Secondly, only outpatients were included in this study. Therefore our results cannot be generalized to patients in a very critical medical condition who are often hospitalized.

Third, the non-standardized time schedule for reassessments of QL may have affected the results of our study. Although it would be hard to realize in clinical routine, standardized intervals of QL may lead to different results. For example, assessments every 6 or 12 months independent of the measurement of pulmonary function would allow us to take a glimpse of the patient’s subjective health estimation more regularly.

Another limitation of this study is that the FLZM was not consistently completed prior to the other clinical examinations. In most cases the patients answered the questions during the waiting time before their clinical appointment, but sometimes the assessment was done after information on present clinical data such as the results of the pulmonary function test. This information may have systematically influenced the QL ratings, and future studies should strictly use a certain order of assessment.

5. Conclusions

The results of our longitudinal analyses provide further evidence that QL is predominantly independent of slow changes in pulmonary function. Clinicians should take into account the fact that the patients’ perceptions of their personal situation may depend more on their personal style of living with the disease, individual coping strategies, and available social support than on pulmonary function. On the other hand, infection exacerbations and the colonization status with problematic germs such as *P. aeruginosa* should be considered relevant medical parameters for the patients’ QL.

With little additional effort it would be possible to monitor QL in outpatient clinical routine as demonstrated in this study. Especially the computer-assisted assessment with its options of immediate analyses and automatic documentation of individual results can facilitate the implementation into clinical routine. Multiple benefits of such a procedure for the patients can be expected. In times of downsizing health care budgets it becomes increasingly important for the therapists to recognize the patients’ situation adequately within the
restricted time limits for medical consultations. Regular and standardized QL assessments would easily provide additional information on the effects of changes in individual treatment schedules, on unexpected changes in the patients’ subjective health perception or on potential special needs arising from a difficult social situation that may reduce adherence to treatment. Those patients who are not used to communicating their subjective health-related perceptions to their therapists spontaneously may be enabled to report their personal situation in a more comprehensive way than when responding to global “how are you?” questions. Taking QL into account may allow therapists to understand more deeply their patients’ subjective health-related cognitions. This would enhance the integration of the patients’ subjective perspective into the process of shared decision making. Future studies should evaluate different methods and designs for monitoring QL and the effect of the immediate feedback of assessment results on patient–therapist communication.

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