ORIGINAL ARTICLE

Relationship between nutritional status and lung function in cystic fibrosis: cross sectional and longitudinal analyses from the German CF quality assurance (CFQA) project

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A list of the 97 CF centres which reported patient data to the project is available on the *Thorax* website.

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Background: The German cystic fibrosis (CF) quality assurance (CFQA) project is a patient registry for CF which was founded in 1995. Relevant clinical and laboratory data, respiratory function test results, complications, and CF treatments are entered into the database once a year for each patient. Using the database, a study was undertaken to elucidate the relationship between nutrition and lung function in a large patient cohort by cross sectional and longitudinal analysis.
Methods: A cohort of 3298 patients above 2 years of age was analysed. Patients were grouped according to the presence or absence of malnutrition (wasting and/or stunting). Cross sectional and longitudinal analyses over 2 and 3 years including mixed model analyses were performed.
Results: The prevalence of abnormal weight for height (<90% predicted) increased with age from 19% in children aged <6 years to 38% in adults with CF. Patients with malnutrition had significantly lower mean values of vital capacity, arterial oxygen tension (P_{O_2}), and forced expiratory volume in 1 second (FEV_1) and higher serum IgG ($p<0.05$). *Pseudomonas aeruginosa* infection was also associated with decreased pulmonary function. Malnourished adolescents aged 12–18 years experienced a serious decline in FEV_1 of about 20% predicted, whereas mean FEV_1 values remained stable at above 80% predicted in adolescents of normal weight. Longitudinal follow up showed that malnourished patients of all ages and those with *P aeruginosa* infection had significantly worse lung function than their normally nourished counterparts and a greater yearly loss of FEV_1 % predicted. During 1 year of observation adolescents who experienced a >5% predicted decrease in weight for height had a concomitant mean loss of FEV_1 of 16.5% predicted during that year, whereas patients who gained relative weight had a parallel increase in FEV_1 of 2.1% predicted.
Conclusions: These data emphasise the close relationship between nutrition, lung function, and clinical course in CF. Normal body weight and absence of *P aeruginosa* infection was associated with better preservation of lung function.

Most patients with cystic fibrosis (CF) carry mutations at the CFTR gene which are associated with malfunction of the pancreas. Since malabsorption due to pancreatic insufficiency causes intolerance of nutritional fat, patients are at risk of low energy intake in addition to increased faecal nutrient loss. In the past malnutrition was considered one of the key clinical features of CF. A low fat diet was recommended by most CF centres until the mid 1980s when acid resistant pancreatic enzymes became available. At that time researchers from Toronto had reported that an energy rich diet not restricted in fat, together with additional (conventional) enzyme supplements, resulted in a better nutritional status and longevity of their patients compared with those treated in Boston, a comparably large and experienced centre.[1] Seventeen years later, with modified dietary recommendations in the US, substantially smaller differences in the growth indices of patients with CF between the US and Canada were observed.[2] Thus, there was evidence that improved nutrition was associated with better long term outcome, as had already been stated in an earlier paper by Kraemer *et al*.[3] A consensus report on nutrition in CF published in 1992 described nutritional management as an important part of the multidisciplinary approach to the disease.[4] Nowadays there is no reason to accept nutritional failure or growth retardation in any patient with CF.[5]

Patient registries for CF permit analysis of data from large cohorts of patients over many years. Results from Canada and the US, the UK, Australia, Europe, and Denmark have shown improved nutritional status, lung function, and survival of CF patients during the last decades.[2 6–12] Respiratory function tests, energy expenditure, growth status, and weight were more abnormal with increasing age. Later birth cohorts had improved outcome, and some authors described sex related differences in health. Most of these studies present cross sectional data, however, while the longitudinal course of certain patient groups over years has been addressed in only a few reports.[13 14]

The relationship between nutritional status and lung function has not been analysed in detail using data from patient registries. The German CF quality assurance project was founded in 1995 and data from more than 5000 patients with CF aged 1 month to 58 years have been documented up to the end of the year 2000. The aim of the present study was to describe the prevalence of malnutrition in these patients and to elucidate the relationship between nutrition and lung function by cross sectional and longitudinal analyses. We speculated that patients with normal weight would be in a better clinical condition than malnourished patients, and that the yearly decline in pulmonary function would be smaller if weight was normal.

METHODS

The German CF quality assurance (CFQA) project is a patient registry which contains relevant clinical and laboratory data,

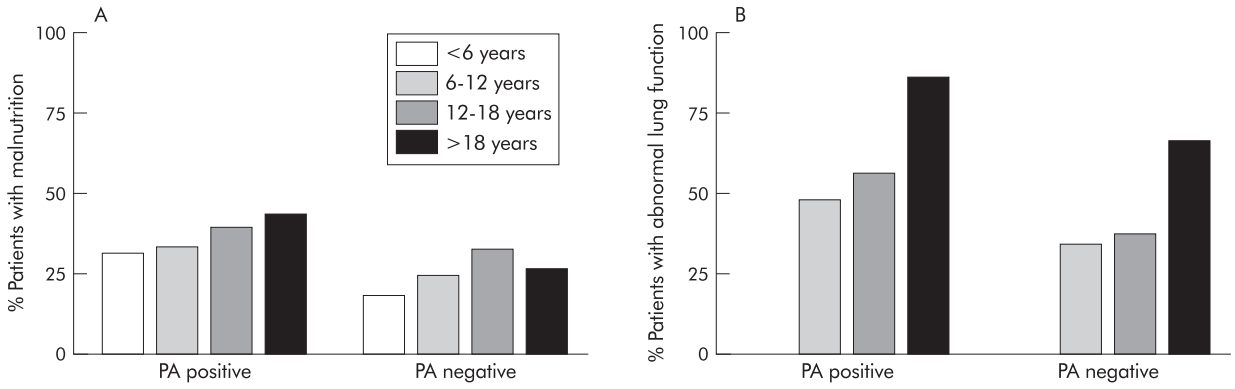

Figure 1 Frequency of (A) malnutrition and (B) impaired lung function in patients with and without *Pseudomonas aeruginosa* (PA) colonisation.

Table 1 Mean clinical data (95% confidence intervals) in 1997 by age group

Age group (years)	Weight for height (% pred)	Vital capacity (% pred)	FEV_1 (% pred)	IgG (g/l)	P_{O_2} (kPa)	MEF_{25} (% pred)
2–5.9 (n=459)	98.2 (97.3 to 99.1) [19.0]	–	–	8.1 (7.7 to 8.5) [14.2]	9.9 (8.1 to 11.7) [53.8]	–
6–11.9 (n=866)	96.6 (95.8 to 97.3) [25.3]	85.3 (84.2 to 86.4) [35.7]	86.7 (85.2 to 88.1) [25.4]	10.8 (10.5 to 11.1) [34.8]	10.8 (10.2 to 11.3) [47.7]	68.2 (65.5 to 70.9) [46.6]
12–17.9 (n=858)	97.6 (96.7 to 98.5) [31.5]	84.1 (82.7 to 85.5) [38.5]	78.8 (77.1 to 80.5) [42.0]	13.8 (13.5 to 14.2) [53.4]	10.7 (10.3 to 11.1) [50.0]	57 (54.3 to 59.7) [59.4]
> 18 (n=1115)	19.8 (19.7 to 20.0) [38.3]	71.4 (70.1 to 72.7) [62.8]	54.5 (53.1 to 56.0) [79.3]	15.9 (15.6 to 16.2) [65.4]	10.0 (9.7 to 10.3) [67.8]	29.2 (27.3 to 31.1) [88.9]

FEV_1=forced expiratory volume in 1 second; P_{O_2}=oxygen tension; MEF_{25}=mid expiratory flow at 25% of vital capacity.
Numbers in square brackets indicate percentage of patients with abnormal results.

Table 2 Mean differences (95% confidence intervals) between malnourished and normally nourished patients by age groups and by *Pseudomonas aeruginosa* colonisation

Age group (years)	Vital capacity (% predicted)	FEV_1 (% predicted)	MEF_{25} (% predicted)	IgG (g/l)	P_{O_2} (kPa)
P aeruginosa positive patients:					
6–11.9	–11.3 (–14.9 to –7.7)	–14.5 (–19.5 to –9.5)	–15.4 (–23.5 to –7.4)	2.9 (1.9 to 3.9)	–0.3 (–1.7 to 1.1)
12–17.9	–21.1 (–24.6 to –17.7)	–23.6 (–27.5 to –19.8)	–20.2 (–26.5 to –13.9)	3.6 (2.6 to 4.6)	–0.5 (–1.5 to 0.3)
⩾18	–18.9 (–21.6 to –16.3)	–20.4 (–23 to –17.7)	–11.4 (–14.5 to –8.4)	2 (1.2 to 2.7)	–1.1 (–1.6 to –0.5)
P aeruginosa negative patients:					
6–11.9	–9.9 (–13.2 to –6.5)	–11.8 (–16.5 to –7.2)	–13.8 (–22.4 to –5.2)	1.3 (0.4 to 2.2)	0.2 (–2.7 to 3.1)
12–17.9	–15.6 (–19.9 to –11.4)	–18.7 (–23.7 to –13.7)	–21.4 (–31 to –11.9)	1.3 (0.1 to 2.4)	–1.5 (–2.8 to –0.2)
⩾18	–18.0 (–23.6 to –12.3)	–20.9 (–27.2 to –14.6)	–22.8 (–32.5 to –13.1)	2.6 (1.3 to 3.9)	–1.1 (–2.4 to 0.1)

Example: In patients aged 6–11.9 years colonised with *P aeruginosa*, vital capacity was 11.3% of predicted lower in malnourished than in normally nourished children.
FEV_1=forced expiratory volume in 1 second; P_{O_2}=oxygen tension; MEF_{25}=mid expiratory flow at 25% of vital capacity.

respiratory function test results, and categorised CF treatment and complications.[15] Data are entered into the database once a year for each patient. In 1997, clinical data from 3448 patients aged 0–58 years were available from 97 different CF outpatient clinics in Germany. For the present study the cohort of 3298 patients aged above 2 years of age was analysed.

Cross sectional analysis

The 1997 data from all patients were divided into four different age groups: 2–5.9 years, 6–11.9 years, 12–17.9 years, and 18.0 years of age or older, since severity of disease increases with age. According to a publication by Lai and coworkers,[16] patients were defined as malnourished if data indicated wasting and/or stunting—that is, if (1) weight was below 90% of the predicted normal value for sex and height in children,[17] if body mass index (BMI) was <19 kg/m^2 in adults *or* if (2) weight was <80% of the median normal value for sex and age, *or* if (3) height was <90% of the median normal value for sex and age.[17] Pulmonary function was considered abnormal if (1) forced vital capacity (FVC) was <80% predicted *and* (2) if forced expiratory volume in 1 second (FEV_1) was below 75% of the predicted normal value.[18] Mid expiratory flow at 25% of vital capacity (MEF_{25}) was rated abnormal if values were less than 60% predicted. The lower limit of normal for oxygen tension (P_{O_2}) in oxygenised capillary blood was 10.7 kPa (80 mm Hg). Serum immunoglobulin G (IgG) values were considered increased if Z scores were ⩾2.[19] Reference values were used according to recommendations made by the Scientific Advisory Committee of the CFQA project who selected appropriate normal values for the population under consideration. The tabulated reference data for weight were related to a third degree polynomial equation of height. Comparisons between age groups were made for means of nutritional and lung function parameters, and the relative proportion of patients with abnormal results was determined for each age group. In addition, patients were grouped according to the presence or absence of risk factors such as *Pseudomonas aeruginosa* colonisation or malnutrition.

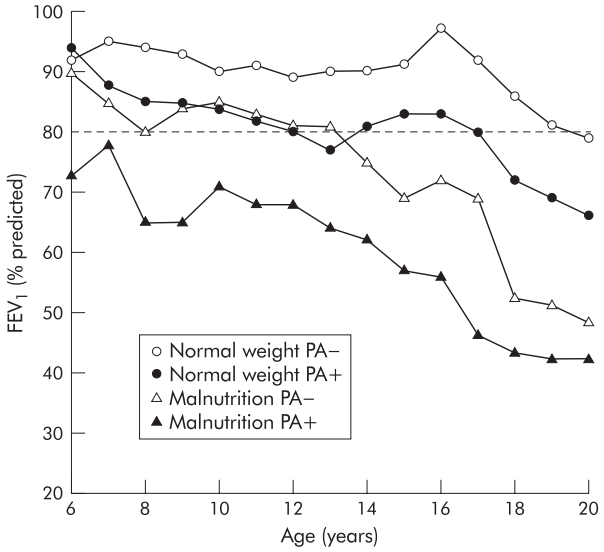

Figure 2 Cross sectional mean values of FEV_1 grouped by presence or absence of malnutrition and *Pseudomonas aeruginosa* (PA). The decline in % predicted FEV_1 at age 18 years is partly due to different reference values for adults.

Multifactorial variance analysis was performed to investigate the association between lung function and malnutrition and the confounders *P aeruginosa* infection and sex. The Student's *t* test for independent samples was performed to compare means between groups with normal or abnormal results. χ^2 and Fisher's exact tests were used to evaluate proportions of patients.

Longitudinal analysis

Patients who had complete data sets for 1995 and 1996 were eligible for the first part of the longitudinal analysis. 536 children aged 6–11.9 years and 477 adolescents aged 12–17.9 years were analysed in detail. For each patient the differences in weight for height and FEV_1 between 1996 and 1995 were calculated.

Three longitudinal groups were defined according to the resulting differences: "better" if the results in 1996 were at least 5% higher than those in 1995: "no change" if the differences were between –5% and +5%; and "worse" if the results were at least 5% lower than in 1995. For each of these groups mean changes in FEV_1 and weight for height between the two years were determined. When means from the three longitudinal groups were compared, one way analysis of variance with the Student-Newman-Keuls test was performed. All calculations were made using SPSS (SPSS Inc, Chicago, USA).

In a second longitudinal analysis the equality of FEV_1 slopes and intercepts in different risk groups was tested for 1995, 1996, and 1997. Mixed model analysis was performed using SAS Proc Mixed version 6.12 for Windows.[20] A multiple comparison adjustment for the p values and confidence limits for the differences of least squares means was performed with a Tukey test. An approximate F test was used to assess the effect of deleting a variable from the model. A level of $p=0.05$ was used to indicate statistical significance.

RESULTS

Cross sectional data

Clinical and lung function data were available for 3298 patients above 2.0 years of age (table 1). As expected, mean weight for height, vital capacity, FEV_1, and P_{O_2} decreased with age, and the proportion of patients with abnormal results was larger in older patients. Mean weight for height was below 90% predicted in 19.0% of children aged 2–6 years and in 31.5% of adolescents. In children below 12 years of age, P_{O_2} had the highest frequency of abnormal results. More than 50% of adolescents had abnormal MEF_{25}, IgG, and P_{O_2}, while FEV_1 was decreased in only 38.5%. A multifactorial analysis of variance revealed that FEV_1 was related to both malnutrition ($p<0.001$) and *P aeruginosa* colonisation ($p<0.001$) but was independent of sex ($p>0.05$) for all age groups.

Pulmonary function was decreased in 56.0% and 85.6% of *P aeruginosa* positive adolescents and adults, respectively, whereas only 37.4% and 66.3% of non-colonised patients had abnormal lung function ($p<0.001$, fig 1). An association between *P aeruginosa* colonisation and malnutrition was also observed. However, most patients had a weight for height above 90% predicted or a body mass index above 19 kg/m^2, irrespective of bacterial status.

Patients with malnutrition had significantly lower vital capacity and FEV_1 and higher serum IgG. As shown in table 2, this was independent of *P aeruginosa* infection. For example, in malnourished children aged 6–11.9 years who were *P aeruginosa* positive, mean vital capacity and FEV_1 were 11.3% and 14.5% predicted lower, respectively, than in normally nourished children (table 2). A similar difference between children of normal and decreased weight was observed in the absence of *P aeruginosa* colonisation—for example, FEV_1 was 11.8% predicted lower. In *P aeruginosa* positive and negative adolescents, malnutrition was associated with even larger differences in lung function, IgG, and P_{O_2}. The differences between normally nourished and malnourished adults with CF were comparable to those in adolescents, and the presence or absence of *P aeruginosa* had no additional effect.

Figure 2 shows cross sectional mean values of FEV_1 by age and bacterial status. FEV_1 values of at least 90% predicted were observed in children and adolescents with normal weight and no *P aeruginosa* infection. *P aeruginosa* positive patients with normal weight had mean FEV_1 values which were 10–20% predicted lower, but they remained at above 80% predicted except at age 13. In contrast, malnutrition was associated with a severe decline in FEV_1 of about 20% predicted between 12 and 18 years of age, irrespective of bacterial status. Malnourished patients colonised with *P aeruginosa* had the worst results at any age. For example, at ages 8 and 17 mean FEV_1 was only 65% and 46% predicted, respectively. These differences between the four groups were both clinically relevant and statistically significant ($p<0.001$).

Longitudinal analysis

Three patient subgroups were formed with respect to the patients' individual courses from 1995 to 1996. Malnourished adolescents who experienced a decrease of ≥5% predicted in weight for height during that year had a concomitant mean loss in FEV_1 of 16.5% predicted, whereas patients who gained relative weight had a parallel increase in FEV_1 of 2.1% predicted. These differences were statistically significant ($p<0.001$). In adolescents with normal weight in 1995, FEV_1 declined by 7.6% or 0.16% of predicted if weight decreased by at least 5% or remained stable, respectively, whereas patients who improved their weight by more than 5% had a concomitant increase in FEV_1 of 4.3% ($p<0.001$). Figure 3 shows the respective data for 6–11.9 year old children.

In a further step a mixed model analysis was performed to identify differences between sexes and between risk groups (patients with or without malnutrition or *P aeruginosa* infection, respectively) with respect to the decline in FEV_1 within a year. Malnourished patients of all age groups had significantly worse lung function than their normally nourished counterparts (table 3). At the initial visit in 1995, FEV_1 was 11.7–23.9% predicted lower if weight for height was decreased . During the 2 year follow up period, adolescents with malnutrition experienced a decline in FEV_1 whereas lung function remained stable in adolescents with normal body

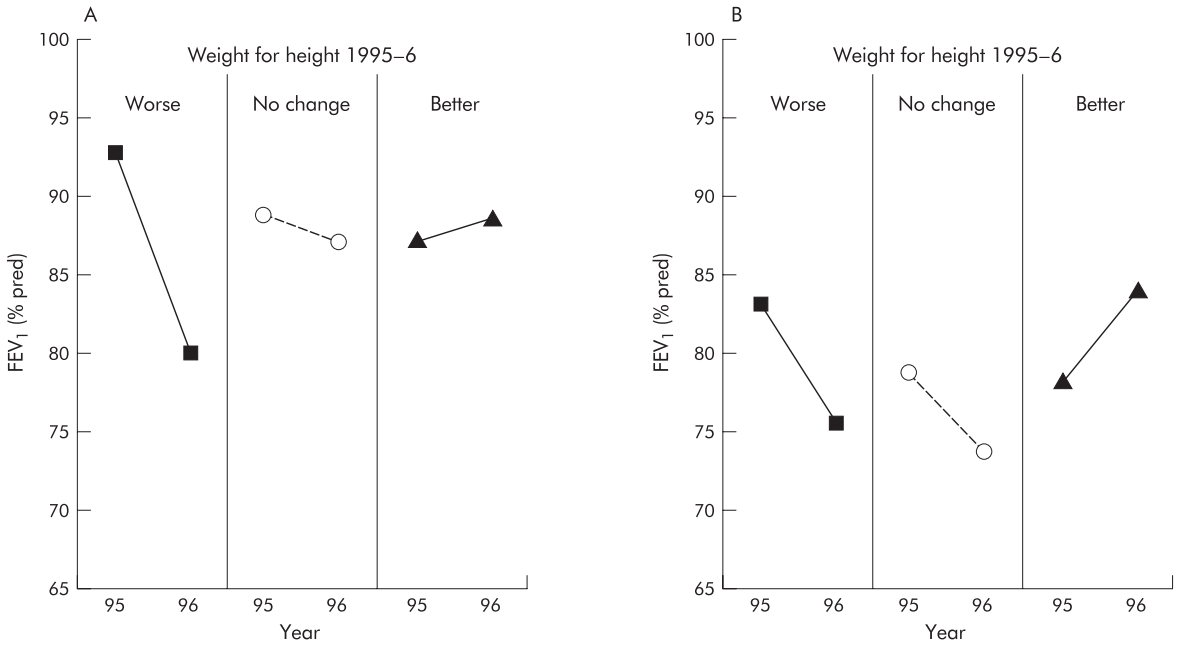

Figure 3 Mean values of individual differences in FEV_1 (% predicted) between 1995 and 1996 in 536 schoolchildren aged 6–11.9 years of age. (A) Normally nourished children. (B) Children who were malnourished in 1995 (weight for height (W/H) <90% predicted). If W/H decreased by 5% or more, a concomitant decline in FEV_1 of (A) 12.8% and (B) 7.5% predicted was observed.

Table 3 Longitudinal results: mixed model regression estimates for forced expiratory volume in 1 second (FEV_1) in 1995 (intercept) and for the mean decline in FEV_1 per year (slope)

	Estimated difference (95% CI) in FEV_1 (% pred) in 1995	p value	Estimated difference (95% CI) in change in FEV_1 per year	p value
6–11.9 years				
Malnutrition (yes *v* no)	–11.7 (–17.9 to –5.6)	0.0002	–1.57 (–3.8 to +0.6)	0.160
P aeruginosa (yes *v* no)	–5.8 (–10.2 to –1.6)	0.008	–2.77 (–3.9 to –1.7)	0.0004
12–17.9 years				
Malnutrition (yes *v* no)	–11.6 (–17.7 to –5.5)	0.0002	–1.63 (–3 to –0.3)	0.009
P aeruginosa (yes *v* no)	–5.8 (–10.1 to –1.5)	0.008	–2.79 (–4.3 to –1.3)	0.0004
Sex (female *v* male)	+3.6 (–0.7 to +7.8)	0.1	+1.58 (+0.1 to +3.1)	0.042
⩾18.0 years				
Malnutrition (yes *v* no)	–23.9 (–28.2 to –19.6)	0.0001	+1.21 (+0.1 to +2.4)	0.032
P aeruginosa (yes *v* no)	–10.1 (–15.1 to –5.1)	0.0001	–1.14 (–2.4 to +0.1)	0.08

Estimates are shown as mean differences between the subgroups malnutrition present *v* absent and *Pseudomonas aeruginosa* infection present *v* absent, respectively, and between male and female adolescents.

weight ($p<0.01$, fig 4). The FEV_1 slopes of patients colonised with *P aeruginosa* were significantly worse in children and adolescents with a 1.14–2.79% predicted faster decline in lung function ($p<0.001$). The only association with sex was found in adolescents, with females showing a slower progression of lung disease than males—that is, a 1.58% predicted difference in FEV_1 within a year (table 3).

DISCUSSION

The negative impact of underweight on the long term outcome of patients with CF has long been recognised.[3] The results of the present longitudinal analysis from a large cohort of patients confirm that nutrition and lung function are co-dependent variables in CF. Patients with normal weight had a significantly smaller decrease in lung function over a 2 year period than those with malnutrition, and this was shown in all age groups. A fall in weight for height of 5% predicted or more within 1 year was associated with a parallel decrease in FEV_1, whereas patients with improved nutrition showed constant or even improved FEV_1.

Cross sectional analysis revealed that the prevalence of malnutrition was 19% in children aged 2–6 years and increased considerably with age up to 38% in adults. Other disease related parameters, particularly P_{O_2} and MEF_{25}, were abnormal in even larger proportions of patients, and showed a similar deterioration with age. Of the 858 adolescents aged 12–18 years, more than one third had abnormal MEF_{25} (59%), serum IgG (53%), P_{O_2} (50%), FEV_1 (42%), and VC (39%). The figures for FEV_1 are comparable to data from other patient registries. For example, the US registry found that FEV_1 was less than 70% predicted in 68% of adult patients.[21] There are no data from other patient registries with respect to IgG, P_{O_2}, or MEF_{25} grouped by age.

In the present study, adolescent girls had better FEV_1 results and a smaller yearly decline in FEV_1 than boys. Younger children and adults showed no sex related differences by

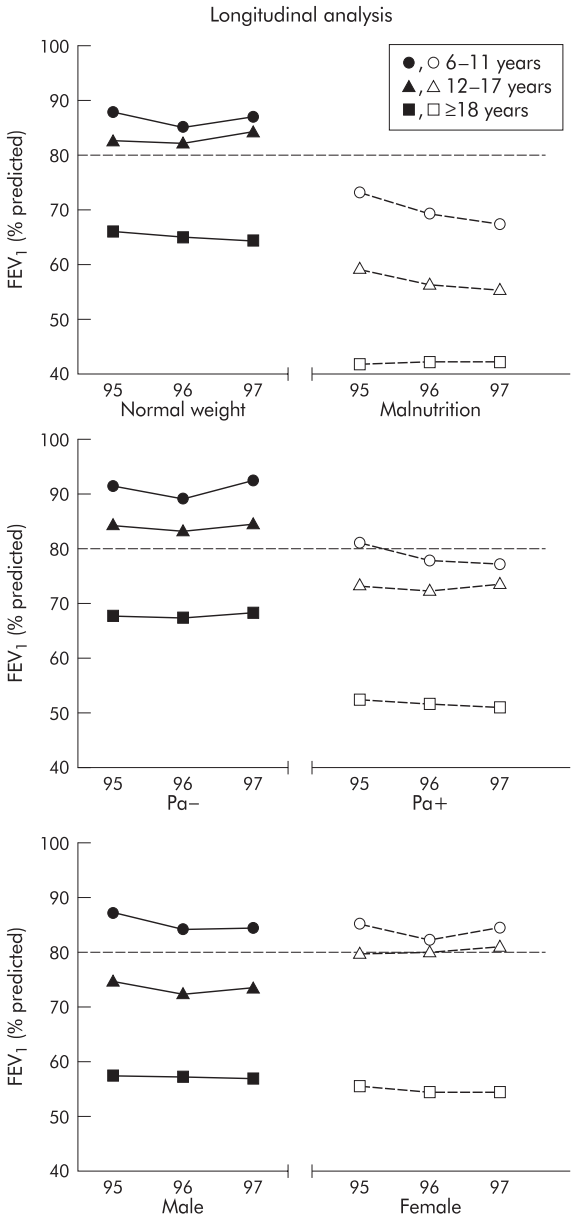

Figure 4 Mixed model analysis for the course of FEV_1 between 1995 and 1997 in the three age groups by risk factors (malnutrition and *P aeruginosa* (Pa) colonisation) and sex.

mixed model analysis. Data from the literature concerning the influence of sex on the course of CF are controversial. Zemel *et al* reported better weight (% predicted) in boys and higher Z scores for length and age in girls.[13] In contrast, the growth of boys with CF was impaired on the basis of height, fat free mass, and fat mass when observed longitudinally.[14] In the study by Corey *et al*, male patients had milder disease than females, as reflected by a smaller decline in FEV_1, decreased mortality, and higher survival.[22] No significant differences between males and females have been found in other studies.[11 23–25]

Chronic infection with *P aeruginosa* had a negative impact on pulmonary function, Po_2, and IgG. Significantly worse mean FEV_1 values were found in malnourished children, adolescents and adults, and the yearly decline in FEV_1 was larger in *P aeruginosa* positive patients. On the other hand, a large proportion of infected patients had normal weight and lung function. A recent report revealed a faster decline in FEV_1/FVC and an increased rate of worsening of chest radiographs after colonisation with *P aeruginosa*.[26] Previous studies found that infection with mucoid *P aeruginosa* was associated with an accelerated rate of decline in pulmonary function.[27 28] The CFQA project does not distinguish between mucoid or non-mucoid strains. From the data in the German registry, *P aeruginosa* infection must be regarded as a significant confounder for pulmonary function impairment in patients with CF.

When patients were stratified according to spirometric results, schoolchildren and adolescents with normal FEV_1 had a 4% and 10% predicted better mean weight for height, respectively, than children with impaired respiratory function. Zemel *et al* analysed patients with FEV_1 above or below 90% predicted and described significantly better data for weight and height in the group with normal lung function.[13] The North American Epidemiologic Study of Cystic Fibrosis (ESCF) reported that mean weight for age was at the 45th percentile in patients with an FEV_1 of ⩾100% predicted, whereas the mean weight for age percentile was only 20 if FEV_1 was significantly impaired (below 40% of normal).[25] Thus, a cross sectional perspective leaves no doubt that children with normal lung function have significantly better weight.

The detailed longitudinal follow up in the present study together with a mixed model analysis adds important information to previously published data. Corey *et al*[22] discussed the advantages of a mixed model analysis—for example, that repeated observations are properly accounted for in significance testing. They described a decline of only 0.7% FEV_1 per year in patients with normal pancreatic function compared with a decrease of 3.1% in patients with pancreatic insufficiency. Since patients with pancreatic insufficiency generally have a lower body weight, this is indirect evidence of the influence of nutrition on the longitudinal development of lung function. Wasting has also been shown to be an independent predictor of mortality in a recent paper published in *Thorax*.[29] In the study by Zemel *et al* which included a four year longitudinal analysis, Z scores for weight for age and height for age were positively associated with FEV_1 % predicted.[13] We have shown a 1.6% predicted smaller decline in FEV_1 in well nourished children and adolescents and a 12% difference in mean FEV_1 values between groups with or without malnutrition. When individual patients were categorised by change of weight and lung function within 1 year, those with a decrease in weight for height of ⩾5% had a parallel decrease in FEV_1 and vice versa, whereas patients with constant or even improved weight experienced no or only an insignificant decrease in FEV_1. We cannot tell what the reasons for the changes in weight were since the CFQA project reports treatment by categories only. Clinical trials confirm, however, a parallel improvement in nutritional status and lung disease: intravenous antibiotics for respiratory exacerbations have a positive effect on both lung function and weight,[30–32] and inhaled antibiotics not only improve pulmonary function but also the nutritional status of patients.[33 34] On the other hand, long term gastrostomy feedings induce favourable outcomes of nutrition as well as of pulmonary function.[35]

Possible reasons for the influence of malnutrition on chronic lung disease have been discussed in a comprehensive review.[36] In chronic obstructive pulmonary disease (COPD) emaciation has long been known to be accompanied by emphysema, and patients with COPD and severe airflow obstruction have lower body weight. Both oxygen consumption of respiratory muscles and resting energy expenditure were increased in patients with COPD. The flattened diaphragm present in emphysema diminishes the efficiency of respiratory muscles, and a myopathic process in malnutrition has also been suggested.[37] In animal studies biochemical abnormalities were associated with malnutrition—for example, increased collagen breakdown, impaired lung repair, and decreased surfactant activity. Relatively little information is

available on possible pathophysiological processes in CF. In particular, a cause/effect relationship remains to be proven.[5] In the malnourished mouse model of respiratory infections in CF, nutritional deficiency contributed to compromised innate lung defences, bacterial colonisation, and excessive inflammation in the CF respiratory tract.[38] A recent review summarised clinical studies on the relationship between lung function and nutritional status.[39] Correlations were found between FEV_1 and lean body mass, the body compartment which includes skeletal muscle, suggesting an influence of muscle wasting on pulmonary function. The detrimental effect of malnutrition on immune function in general[40] must also be considered as a relevant mechanism in CF. Treatment with intravenous antibiotics was associated with a concomitant decline in inflammatory parameters (C reactive protein, tumour necrosis factor-α), energy expenditure, and an increase in body weight.[32 41]

In summary, the results of this study suggest that normal body weight is associated with better lung function in CF. A significantly smaller decline in FEV_1 can be expected in all age groups if patients are well nourished, and this is independent of a concomitant colonisation with *P aeruginosa*.

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REFERENCES

1 **Corey M**, McLaughlin FJ, Williams M, *et al*. A comparison of survival, growth, and pulmonary function in patients with cystic fibrosis in Boston and Toronto. *J Clin Epidemiol* 1988;**41**:583–91.
2 **Lai HC**, Corey M, FitzSimmons S, *et al*. Comparison of growth status of patients with cystic fibrosis between the United States and Canada. *Am J Clin Nutr* 1999;**69**:531–8.
3 **Kraemer R**, Rudeberg A, Hadorn B, *et al*. Relative underweight in cystic fibrosis and its prognostic value. *Acta Paediatr Scand* 1978;**67**:33–7.
4 **Ramsey BW**, Farrell PM, Pencharz P. Nutritional assessment and management in cystic fibrosis: a consensus report. The Consensus Committee. *Am J Clin Nutr* 1992;**55**:108–16.
5 **Pencharz PB**, Durie PR. Pathogenesis of malnutrition in cystic fibrosis, and its treatment. *Clin Nutr* 2000;**19**:387–94.
6 **Laursen EM**, Koch C, Petersen JH, *et al*. Secular changes in anthropometric data in cystic fibrosis patients. *Acta Paediatr* 1999;**88**:169–74.
7 **Lewis PA**, Morison S, Dodge JA, *et al*. Survival estimates for adults with cystic fibrosis born in the United Kingdom between 1947 and 1967. *Thorax* 1999;**54**:420–2.
8 **Morgan WJ**, Butler SM, Johnson CA, *et al*. Epidemiologic study of cystic fibrosis: design and implementation of a prospective, multicenter, observational study of patients with cystic fibrosis in the US and Canada. *Pediatr Pulmonol* 1999;**28**:231–41.
9 **Fogarty A**, Hubbard R, Britton J. International comparison of median age at death from cystic fibrosis. *Chest* 2000;**117**:1656–60.
10 **Hill DJ**, Martin AJ, Davidson GP, *et al*. Survival of cystic fibrosis patients in South Australia. Evidence that cystic fibrosis centre care leads to better survival. *Med J Aust* 1985;**143**:230–2.
11 **Nir M**, Lanng S, Johansen HK, *et al*. Long-term survival and nutritional data in patients with cystic fibrosis treated in a Danish centre. *Thorax* 1996;**51**:1023–7.
12 **Morison S**, Dodge JA, Cole TJ, *et al*. Height and weight in cystic fibrosis: a cross sectional study. UK Cystic Fibrosis Survey Management Committee. *Arch Dis Child* 1997;**77**:497–500.
13 **Zemel BS**, Jawad AF, FitzSimmons S, *et al*. Longitudinal relationship among growth, nutritional status, and pulmonary function in children with cystic fibrosis: Analysis of the Cystic Fibrosis Foundation National CF Patient Registry. *J Pediatr* 2000;**137**:374–80.
14 **Stettler N**, Kawchak DA, Boyle LL, *et al*. Prospective evaluation of growth, nutritional status, and body composition in children with cystic fibrosis. *Am J Clin Nutr* 2000;**72**:407–13.
15 **Wiedemann B**, Steinkamp G, Sens B, *et al*. The German Cystic Fibrosis Quality Assurance project: clinical features in children and adults. *Eur Respir J* 2001;**17**:1187–94.
16 **Lai HC**, Kosorok MR, Sondel SA, *et al*. Growth status in children with cystic fibrosis based on the National Cystic Fibrosis Patient Registry data: evaluation of various criteria used to identify malnutrition. *J Pediatr* 1998;**132**:478–85.
17 **Reinken L**, van Oost G. Longitudinal physical development of healthy children 0 to 18 years of age. Body length/height, body weight and growth velocity. *Klin Padiatr* 1992;**204**:129–33.
18 **Quanjer PH**, Stocks J, Polgar G, *et al*. Compilation of reference values for lung function measuremetns in children. *Eur Respir J* 1989;**2**:184–261s.
19 **Pilgrim U**, Fontanellaz HP, Evers G, *et al*. Normal values of immunoglobulins in premature and in full-term infants, calculated as percentiles. *Helv Paediatr Acta* 1975;**30**:121–34.
20 **SAS Institute Inc**. *SAS/STAT user's guide*. Release 6.10. Cary, NC: SAS Institute, 1992.
21 **Cystic Fibrosis Foundation**. *Cystic Fibrosis Foundation Patient Registry. Annual Data Report 1996*. Bethesda, Maryland: Cystic Fibrosis Foundation, 1997.
22 **Corey M**, Edwards L, Levison H, *et al*. Longitudinal analysis of pulmonary function decline in patients with cystic fibrosis. *J Pediatr* 1997;**131**:809–14.
23 **Frederiksen B**, Lanng S, Koch C, *et al*. Improved survival in the Danish center-treated cystic fibrosis patients: results of aggressive treatment. *Pediatr Pulmonol* 1996;**21**:153–8.
24 **Konstan MW**, Butler SM, Schidlow DV, *et al*. Patterns of medical practice in cystic fibrosis: Part I. Evaluation and monitoring of health status of patients. *Pediatr Pulmonol* 1999;**28**:242–7.
25 **Konstan MW**, Butler SM, Schidlow DV, *et al*. Patterns of medical practice in cystic fibrosis: Part II. Use Of therapies. *Pediatr Pulmonol* 1999;**28**:248–54.
26 **Kosorok MR**, Zeng L, West SE, *et al*. Acceleration of lung disease in children with cystic fibrosis after Pseudomonas aeruginosa acquisition. *Pediatr Pulmonol* 2001;**32**:277–87.
27 **Demko CA**, Byard PJ, Davis PB. Gender differences in cystic fibrosis: Pseudomonas aeruginosa infection. *J Clin Epidemiol* 1995;**48**:1041–9.
28 **Parad RB**, Gerard CJ, Zurakowski D, *et al*. Pulmonary outcome in cystic fibrosis is influenced primarily by mucoid pseudomonas aeruginosa infection and immune status and only modestly by genotype. *Infect Immun* 1999;**67**:4744–50.
29 **Sharma R**, Florea VG, Bolger AP, *et al*. Wasting as an independent predictor of mortality in patients with cystic fibrosis. *Thorax* 2001;**56**:746–50.
30 **Wilmott RW**, Frenzke M, Kociela V, *et al*. Plasma interleukin-1 alpha and beta, tumor necrosis factor-alpha, and lipopolysaccharide concentrations during pulmonary exacerbations of cystic fibrosis. *Pediatr Pulmonol* 1994;**18**:21–7.
31 **Bradley JM**, Wallace ES, Elborn JS, *et al*. An audit of the effect of intravenous antibiotic treatment on spirometric measures of pulmonary function in cystic fibrosis. *Ir J Med Sci* 1999;**168**:25–8.
32 **Burdet L**, Hugli O, Aubert JD, *et al*. Effect of elective antibotic therapy on resting energy expenditure and inflammation in cystic fibrosis. *Eur J Pediatr* 1999;**158**:711–6.
33 **Steinkamp G**, Tummler B, Gappa M, *et al*. Long-term tobramycin aerosol therapy in cystic fibrosis. *Pediatr Pulmonol* 1989;**6**:91–8.
34 **Ramsey BW**, Schaeffler BL, Montgomery AB, *et al*. Survival and lung function during two years of treatment with intermittent tobramycin solution for inhalation in CF patients. *Neth J Med* 1999;**54**:S83–4.
35 **Steinkamp G**, von der Hardt H. Improvement of nutritional status and lung function after long-term nocturnal gastrostomy feedings in cystic fibrosis. *J Pediatr* 1994;**124**:244–9.
36 **Wilson DO**, Rogers RM, Hoffman RM. Nutrition and chronic lung disease. *Am Rev Respir Dis* 1985;**132**:1347–65.
37 **Rothkopf MM**, Stanislaus G, Haverstick L, *et al*. Nutritional support in respiratory failure. *Nutr Clin Pract* 1989;**4**:166–72.
38 **Yu H**, Nasr SZ, Deretic V. Innate lung defenses and compromised Pseudomonas aeruginosa clearance in the malnourished mouse model of respiratory infections in cystic fibrosis. *Infect Immun* 2000;**68**:2142–7.
39 **Schoni MH**, Casaulta-Aebischer C. Nutrition and lung function in cystic fibrosis patients: review. *Clin Nutr* 2000;**19**:79–85.
40 **Chandra RK**. Nutrition and the immune system: an introduction. *Am J Clin Nutr* 1997;**66**:460–3S.
41 **Elborn JS**, Cordon SM, Western PJ, *et al*. Tumour necrosis factor-alpha, resting energy expenditure and cachexia in cystic fibrosis. *Clin Sci (Colch)* 1993;**85**:563–8.