ELSEVIER
SAUNDERS

Clin Chest Med 28 (2007) 319–330

CLINICS
IN CHEST
MEDICINE

Nutrition and Lung Disease in Cystic Fibrosis

Carlos E. Milla, MD

Department of Pediatrics, Center for Excellence in Pulmonary Biology, Stanford University, 770 Welch Road, Suite 350, Palo Alto, CA 94304, USA

It is well recognized that among patients who have cystic fibrosis (CF), lung disease is a significant reason for morbidity and pulmonary function is the primary predictor of death [1]. Consequently, the rate at which pulmonary function is lost is the most important variable predicting mortality [2]. To this day, despite the importance given to pulmonary cares and the multiple advances in this aspect of the disease, the long-term preservation of lung function remains difficult to accomplish. Long-term preservation of lung function is likely a multifactorial process whereby the factors with the strongest influence remain unclear or difficult to control. Nutritional status is clearly recognized as a factor that is tightly intertwined in this process, and the temporality of this association has long been debated. Still, from the time when the first effective therapeutic strategies for the management of CF were described [3,4], aggressive nutritional support has been a fundamental component of the recommended treatment regimens.

Magnitude of the problem

The most recent consensus statements on nutritional management for patients who have CF [5,6] introduced important changes in the assessment parameters and categorization schemes recommended for the classification of nutritional status (Table 1) [7,8]. With the availability of the Centers for Disease Control and Prevention body mass index (BMI) percentiles and the increased familiarity of adult care providers with this parameter, BMI is now favored over percentage ideal body weight (%IBW) as the preferred assessment parameter for children and adults. Added to the fact that the calculation of %IBW remains cumbersome, comparative studies have demonstrated a better discriminatory ability of BMI percentile over %IBW for the detection of underweight malnutrition [9,10]. Further, recent reviews of the US Cystic Fibrosis Foundation Patient Registry (CFFPR) have revealed that BMI percentile in children and BMI values in adults are directly and strongly correlated with pulmonary function parameters such as forced expiratory volume in 1 second (FEV_1) (Fig. 1). In view of this finding, the current recommendation is to aim for a BMI at the 50th percentile for children and a BMI of 22 kg/m^2 for adult women or 23 kg/m^2 for adult men [11]. In addition, added emphasis is given to the assessment of linear growth in children not only in terms of height-for-age percentile but also by interpreting this percentile in relation to the child's growth potential as determined by the target adult height percentile.

Epidemiologic studies

Given that many early studies showed good correlation between the degree of malnutrition and the severity of pulmonary disease, this finding has been taken as indirect evidence for the influence that nutrition has on the course of the lung disease and subsequent mortality [12]. Despite these observations, malnutrition continues to be one of the main clinical manifestations of CF across the age span, regardless of the time from diagnosis. The most recent estimates in the United States continue to indicate that inadequate weight gain and linear growth retardation are highly prevalent among children who have CF. Data reported by the CFFPR show that 22% of children who have CF

E-mail address: cmilla@stanford.edu

doi:10.1016/j.ccm.2007.02.006

Table 1
Consensus criteria for the assessment of nutritional status in patients who have cystic fibrosis

Status	Height %ile[a] 2–20 y	%IBW[b] All ages	W/H %ile 0–2 y	BMI %ile 2–20 y	BMI (kg/m^2) >20 y
Adequate	At or above genetic potential	≥90%	>25th %ile	>25th %ile	22 (women) 23 (men)
At risk	Not at genetic potential	≥90% but weight loss or plateau	10th–25th %ile	10th–25th %ile	19–22 (women) 19–23 (men)
Malnutrition	<5th %ile	<90%	<10th %ile	<10th %ile	<19

Values are taken from the Centers for Disease Control and Prevention 2000 normative data.

Abbreviations: BMI, body mass index; %IBW, percentage ideal body weight; %ile, percentile; W/H, weight-for-height.

[a] For height %ile, genetic potential is estimated by first calculating the target adult height (TAH) from the parents' heights and then obtaining the percentile that will correspond to that height at age 20 years. TAH can be obtained by calculating the midparental height (MPH) and then applying the formulas proposed by Luo and colleagues [7]:

Females: $\text{TAH (cm)} = 37.85 + 0.75 \times \text{MPH}$

Males: $\text{TAH (cm)} = 45.99 + 0.78 \times \text{MPH}$

[b] %IBW is calculated by dividing the actual weight by the IBW and multiplying by 100. The IBW in children can be estimated by obtaining first the height %ile and then estimating the weight that will correspond to the same percentile in the growth curve. Alternatively, the IBW formulas proposed by Budd and colleagues [8] can be employed, which apply across the age span:

Females: $\text{IBW (kg)} = \mathbf{e}^{(-0.3198 \times \text{Ln}(\text{Ht}^4) + 7.5767 \times \text{Ln}(\text{Ht}^3) - 63.306 \times \text{Ln}(\text{Ht}^2) + 222.74 \times \text{Ln}(\text{Ht}) - 299.6)}$

Males: $\text{IBW (kg)} = \mathbf{e}^{(-1.0504 \times \text{Ln}(\text{Ht}^4) + 20.689 \times \text{Ln}(\text{Ht}^3) - 151.4 \times \text{Ln}(\text{Ht}^2) + 490.3 \times \text{Ln}(\text{Ht}) - 592.49)}$,

where Ht is height in centimeters and Ln is natural logarithm.

fall below the 10th percentile for weight and that 14% fall below the fifth percentile for height [11]. In addition, and not surprising given its high prevalence in childhood, as age increases, so does the prevalence of malnutrition among adult patients. According to the most recent estimates available, on average, 60.8% of adults who have CF have a BMI below the recommended levels [11], and the rate of nutritional failure (BMI<19 kg/m^2) is estimated to be 38.5% [13].

In contrast, over 2 decades ago, the Toronto Cystic Fibrosis Center reported that their patient population had growth parameters that did not differ from the available normative data [14]. Their data showed, on average, fairly normal height percentiles in male and female patients. In addition, although weight percentiles were lower in female patients, underweight rates were lower than those reported from other centers. This report was followed by the classic Boston–Toronto comparison study. The study demonstrated clear-cut differences in the median survival of the two cohorts of patients: 21 years in Boston versus 30 years in Toronto. There was also a sharp contrast in the average growth parameters observed at each clinic, with the children in Toronto being ahead in their percentiles, particularly for height. Most interesting was the fact that pulmonary function parameters were comparable between the two groups. Given the differences noted in growth parameters, the survival advantage of the Toronto cohort was ascribed to their better nutritional status [15].

A second important finding of this study was that the main difference between the treatment programs was the approach to dietary intervention, with the Toronto site being unrestrictive in terms of fat intake [16]. A second look 10 years later at the United States and Canadian data revealed that although there were still differences in the nutritional parameters, the gap noted on the previous study had already narrowed [17], probably as a reflection of the adoption of the Canadian nutritional support approach by United States centers [18].

Multiple previous longitudinal and cross-sectional studies that have looked at the relationship between morbidity and nutritional status concur that in CF patients, growth abnormalities and development of lung disease are linked [19–21]. Further, there is also evidence that interventions to establish weight gain are associated with improvements in pulmonary function [22–24]. In