Nutritional Issues in Cystic Fibrosis

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KEYWORDS

• Cystic fibrosis • Nutritional status • Nutritional assessment • Malnutrition • Pancreatic insufficiency • Malabsorption • Cystic fibrosis–related diabetes • Enteral nutrition

KEY POINTS

- Patients with cystic fibrosis (CF) are at risk for malnutrition secondary to increased losses from malabsorption and increased energy demands from infections, chronic disease, and decreased oral intake.
- Complications, including pancreatic insufficiency, CF-related diabetes, and CF-related liver disease, place patients with CF at further risk for poor nutritional status.
- Optimizing growth and nutrition has a clear positive influence on lung health and overall survival.
- Comprehensive nutritional assessments at regular intervals are necessary to identify those at risk of nutritional failure even before malnutrition occurs.
- Aggressive nutritional support should be implemented early, and patients should be monitored closely to ensure optimal growth and nutritional status.

INTRODUCTION

The importance of nutritional status in individuals with cystic fibrosis (CF) and the impact on pulmonary function and survival has been well established.[1–3] Clinically characterized by progressive lung disease, nearly 90% of patients with CF have exocrine pancreatic insufficiency and subsequent malabsorption.[4] This malabsorption, along with increased energy requirements and chronic infections, place patients with CF at significant risk for malnutrition. Pancreatic-sufficient (PS) patients with CF are also at risk for poor nutrition and micronutrient deficiencies. Chronic undernutrition and poor growth are well-known causes of mortality and morbidity among patients with CF. This article focuses on nutritional issues in children, adolescents, and adults with CF.

EFFECT OF NUTRITIONAL STATUS ON CYSTIC FIBROSIS LUNG DISEASE AND SURVIVAL

The earliest study to elegantly highlight the relationship between nutritional status and survival in CF was published in 1988 by Corey and colleagues.[5] This retrospective comparative study identified a marked difference in the median survival between patients at 2 centers in Boston and Toronto. Although there was no significant difference in the pulmonary therapy between the centers, the approach to nutritional care was quite different. Adoption of a high-calorie, high-fat diet with aggressive pancreatic enzyme replacement therapy (PERT) by the Toronto team resulted in improved nutritional status, which in turn was associated with significantly better survival. This study did not identify any significant difference in

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the pulmonary function between the patients in the 2 centers, which suggested a direct detrimental impact of poor nutritional status on survival.

In a 2003 study of nearly 1000 subjects between 3 and 6 years of age, children with a weight for age less than the fifth percentile at 3 years of age had significantly lower pulmonary function at 6 years of age compared with those with a weight for age greater than the 75th percentile at 3 years.[6] A more recent study of more than 3000 pediatric patients with CF prospectively followed outcomes from birth to 18 years of age and found that the weight-for-age percentile at 4 years was associated with improved height and improved pulmonary function, fewer complications, and increased survival at 18 years.[7]

The relationship between nutritional status and pulmonary function seems to be linear to a certain extent. The CF Foundation Patient Registry data consistently show that children and adults with a higher body mass index (BMI) percentile and BMI, respectively, have better lung function. Based on analysis of registry data from 1994 to 2003, the CF Foundation recommends a goal BMI of greater than 50th percentile in children and a BMI greater than or equal to 22 in women and 23 in men.[8] Children with BMIs between the 10th and 25th percentiles are considered at nutritional risk, and those with BMIs less than the 10th percentile are considered to have nutritional failure.[9] A 2-year longitudinal analysis of more than 3000 patients in the German CF patient registry revealed that a greater than 5% decrease in weight for height had a concomitant mean loss of forced expiratory volume in the first second (FEV_1) of 16.5% predicted, whereas patients with improved nutrition showed consistent or even improved FEV_1.[10] The transition from adolescence into adulthood is a critical stage in CF with a mortality peak seen in young adults. This peak follows acceleration in lung function decline even in adolescents with mild lung disease. One of the most important predictors of this decline is a faster rate of decline in BMI during adolescence.[11] Therefore, a more rigorous monitoring of nutritional status and early and aggressive nutritional intervention is crucial during adolescence, even in those with mild lung disease.

LUNG TRANSPLANTATION AND NUTRITIONAL STATUS

Lung transplantation is an established and very effective means of therapy for end-stage lung disease; however, because of the limited organ supply, 20% to 30% of patients die while on the waiting list.[12] Lung transplant candidates are often malnourished; even those with normal weight tend to have depleted lean body mass, which is associated with a higher mortality, while awaiting a lung transplant, and even after transplant.[13] A recent retrospective study investigated the nutritional status in patients with CF before and after transplant and identified that a BMI of 18.5 kg/m^2 or less and a fat-free mass index (FFMI) of 16.7 kg/m^2 or less (men) or 14.6 kg/m^2 or less (women) was associated with impaired survival in lung transplant candidates with CF whereby FFMI is calculated by substituting the fat-free mass (FFM) (which only includes muscle mass and bone mass) for the body mass.[14] Another study identified female sex as a risk factor for increased waiting-list mortality, such that the combination of BMI less than 18 kg/m^2 and female sex was associated with only 21% 1-year waiting-list survival without transplantation.[15] Many centers recommend aggressive nutritional support for undernourished patients during the pretransplant period to improve weight and lean body mass; however, studies reveal conflicting success with this approach. Earlier studies showed that it was possible to increase energy intake and/or weight by intensified nutritional support, including with gastrostomy tube feedings.[16,17] Conversely, other studies failed to show an increase in energy intake or weight gain by intensified nutritional support or with dietetic intervention with oral nutritional supplements, tube feeding, or both.[14,18] After transplantation, studies uniformly show that weight and nutritional status improves. However, unique transplant-related complications, such as osteoporosis and diabetes related to steroids, should be closely monitored.[14,19,20]

PATHOGENESIS OF DISORDERED NUTRITION IN CYSTIC FIBROSIS

Significant progress has been made in the nutritional status of both the pediatric and adult CF population since the 1980s. However, according to the latest CF Patient Registry Report, 45.3% of children and 52.6% of adults with CF have nutritional measures that decrease to less than the nutritional goals.

Undernutrition

Undernutrition in CF results from an imbalance between energy demand and energy intake. Unique complications of CF further aggravate the situation by increasing energy loss (**Fig. 1**).

Increased demand

There seems to be increased resting energy expenditure (REE) in children and adults with