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The nutritional status of children with cystic fibrosis

Alexia J. Murphy[1]*, Helen M. Buntain[2], Claire E. Wainwright[2] and Peter S. W. Davies[1]

[1]*Children's Nutrition Research Centre, Discipline of Paediatrics and Child Health, University of Queensland, Royal Children's Hospital, Brisbane, Queensland 4029, Australia*
[2]*Department of Respiratory Medicine, Royal Children's Hospital, Brisbane, Australia*

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The importance of nutritional intervention for children with cystic fibrosis (CF) is well recognised. It would be expected that the increase in knowledge over the past decade would be reflected in improvements in nutritional status for the CF paediatric population. The aim of the present paper was to evaluate the nutritional status of children with CF, cross-sectionally and longitudinally. Body cell mass adjusted for gender and size (BCM/Ht^p) was measured in sixty-four children with CF to represent nutritional status and expressed as a Z-score. The cross-sectional results showed a mean BCM/Ht^p Z-score of 0·54 (SD 1·21), with males having a slightly higher Z-score than females but with a larger variation. At the initial measurement, only one female and one male were considered sub-optimally nourished. The longitudinal analysis after 2 years showed that the mean population had a significantly decreased BCM/Ht^p Z-score; however, when each gender was analysed separately, this decrease was significant only in the males. At the final measurement, only two females and three males were considered sub-optimally nourished. It is evident from our results that children with CF are well nourished, with only a small percentage considered malnourished. It appears that nutritional status decreases with age, with this decline being more evident in males. These results signify that although children with CF are better nourished with current treatment support, intervention needs to continue throughout a CF patient's life to counteract the changes that occur with age.

Cystic fibrosis: Nutritional status: Body cell mass

Optimal nutritional status is vital in children with cystic fibrosis (CF) to enhance their quality of life and prognosis (Corey *et al.* 1988). However, maintaining optimal nutritional status in children with CF can be compromised by aspects of the disease. The malabsorption of fat and protein and increased energy demands have the potential to cause nutritional problems in the paediatric CF population (Sinaasappel *et al.* 2002). As poor nutritional status has been identified as a potential problem for the CF population, guidelines to prevent and manage malnutrition have been recommended, with nutritional support recognised as a vital component of the overall CF treatment plan (Borowitz *et al.* 2002; Sinaasappel *et al.* 2002; Sharma & Singh, 2003).

Studies have used a variety of assessment techniques and variables to determine whether the increased understanding of the nutritional needs of children with CF is being reflected in an improved nutritional status (Stettler *et al.* 2000; Ahmed *et al.* 2004; Marín *et al.* 2004). Many methods are available to measure the nutritional status of children with CF; however some methods, such as BMI, have been found to be inappropriate in this population (McNaughton *et al.* 2000; Stapleton *et al.* 2001). An assessment method that is considered suitable for use in this population is total-body K (TBK) counting, which provides a measure of body cell mass (BCM). BCM is the metabolically active component of fat-free mass (FFM), and is therefore the component of the FFM that is reduced most significantly in malnutrition (Moore, 1980). Unlike measurements of FFM, measurements of BCM are a better reflection of nutritional status in children with CF because they are independent of extracellular fluid shifts that may occur as a result of disease state.

Previous studies have measured BCM in children (Shepherd *et al.* 1995, 2001; McNaughton *et al.* 2000); however, these studies have not interpreted BCM results using Z-scores and have not adjusted BCM for body size. BCM data are ideally interpreted when adjusted for body size, because BCM is influenced by size and this is especially important in children who are growing. The present study uses BCM adjusted for gender-specific height constants (BCM/Ht^p) to represent nutritional status in our CF population, a principle examined previously in women (Wells *et al.* 2004) and used in bone marrow transplant patients (White *et al.* 2005). The primary aim of the present paper was to examine the nutritional status of children with CF at our centre, using the technique of BCM/Ht^p. The secondary aim was to investigate the longitudinal changes in nutritional status over a 2-year period.

Abbreviations: BCM, body cell mass; BCM/Ht^p, BCM adjusted for gender-specific height constants; CF, cystic fibrosis; FEV_1, forced expiratory volume in 1 s; FFM, fat-free mass; TBK, total-body K.

* **Corresponding author:** Alexia J. Murphy, fax + 61 7 36361981, email alexia.murphy@uq.edu.au

Materials and methods

Subjects

The study sample consisted of children diagnosed with CF over the age of 5 years, who were recruited from the Royal Children's Hospital, Brisbane, Australia. The children were a part of a longitudinal study concerned with bone mineral density and body composition (Buntain *et al.* 2004). Only those who completed longitudinal body composition measurements are reported here. Twelve children initially involved in the study did not complete longitudinal body composition measurements; 50 % withdrew consent, 25 % had travel limitations and 25 % were too sick to complete measurements. The study protocol was approved by the Royal Children's Hospital Ethics Committee. Written consent was obtained from all parents and children over 12 years, while verbal assent was obtained from children under 12 years.

Measurements

All measurements were taken in the Body Composition Laboratory at the Royal Children's Hospital. Body weight was measured to the nearest 0·05 kg using calibrated digital scales (Tanita BWB-600; Wedderburn Scales, Brisbane, Australia) and height was measured to the nearest 0·1 cm using a wall-mounted stadiometer (Holtain Instruments Ltd, Crymmych, UK). Height and weight Z-scores were calculated using the LMS values from the 2000 CDC Growth Charts (National Center for Health Statistics/Centers for Disease Control and Prevention, 2004). To describe the severity of lung disease, respiratory function tests were performed in accordance with the American Thoracic Society standards in the Respiratory Investigation Unit. Forced expiratory volume in 1 s (FEV_1) was recorded and expressed as a percentage of predicted (Hibbert *et al.* 1989).

Body cell mass measurements

K^+ is the primary intracellular cation and, as 98 % of the body's K is located within the BCM (Moore, 1980), it is possible to determine BCM from TBK analysis. TBK analysis was performed using a shadow shield whole-body counter (Accuscan; Canberra Industries, Boston, MA, USA), which contains three NaI crystal scintillation detectors arranged above a scanning bed. The crystals detect the 1·46 MeV γ-rays being emitted by the ^{40}K found in the body. As a fixed proportion of the body's K occurs as the natural isotope ^{40}K, TBK can be determined.

The measurement of TBK required the subject to lie supine on a bed that is moved under the detectors. Two 1100 s scans were performed for each subject with all personal metallic objects having been removed. Background and sensitivity checks were completed daily and considered in each measurement, with TBK in grams being reported. BCM was then calculated from TBK using the equation of Wang *et al.* (2004):

$$\mathrm{BCM(kg)} = [\mathrm{TBK(g)} \times 9{\cdot}18]/39{\cdot}1.$$

BCM was adjusted for height (BCM/Ht^p), with height being raised to the power of 2·5 for females and 3 for males (AJ Murphy, HM Buntain and PSW Davies, unpublished results). Gender-specific height corrections of BCM were formulated using log-log regression of normal paediatric data collected in our laboratory (313 healthy children; aged 5 to 18 years).

Statistical analyses

Mean and standard deviation were used to describe the study sample. BCM/Ht^p was expressed as a Z-score relative to laboratory reference data. In the present study we have chosen a cut-off of −1·65 SD to determine those individuals who have sub-optimal nutritional status when expressed as BCM/Ht^p. This cut-off is equivalent to the 5th centile. A paired *t* test was used to determine longitudinal changes in the group.

Results

A total of sixty-four children (thirty-one females) with CF were involved in the study, with the mean age of the group being 10·6 (SD 2·9) years at the initial measurement. The mean initial height of the population was 137·9 (SD 15·7) cm (Z-score: −0·59 (SD 0·92)) and the mean initial weight was 34·35 (SD 11·25) kg (Z-score: −0·32 (SD 0·99)). The mean lung function was within normal limits; however, there was a large range of FEV_1 (26–122 %). The subject characteristics are displayed in Table 1.

The cross-sectional results show that that the mean BCM/Ht^p Z-score for the total population at the initial measurement was 0·54 (SD 1·21). The mean BCM/Ht^p Z-score for males was 0·76 (SD 1·39) and for females was 0·30 (SD 0·94). One female and one male subject were considered sub-optimally nourished with Z-scores below −1·65.

When BCM/Ht^p was examined at the final measurement, the mean Z-score (0·03 (SD 1·34)) had decreased significantly ($P<0{\cdot}001$) over the 2-year period. When each gender was examined separately, the mean male BCM/Ht^p Z-score had decreased significantly ($P<0{\cdot}001$) over time; however, no significant changes ($P=0{\cdot}25$) were observed in female subjects. Seven per cent of female and 9 % of male subjects were considered sub-optimally nourished with Z-scores below −1·65 after 2 years.

The correlation between age and BCM/Ht^p Z-score was −0·35 ($P<0{\cdot}05$) for the total group using the final data set. However, when the relationship was analysed within each gender, the correlation remained significant for the males (r −0·49; $P<0{\cdot}01$) but was insignificant for the females (r −0·18; $P=0{\cdot}34$). The difference can be seen in the

Table 1. Characteristics of the population: cross-sectional (Test 1) and longitudinal (Test 2) measurement

(Mean values and standard deviations)

	Test 1		Test 2	
	Mean	SD	Mean	SD
Age (years)	10·6	2·9	12·6	2·8
Height (cm)	137·9	15·7	148·5	15·0
Weight (kg)	34·35	11·25	40·45	12·55
FEV_1 (%)	75·7	18·4	74·9	22·3

FEV_1, forced expiratory volume in 1 s (expressed as percentage of predicted).

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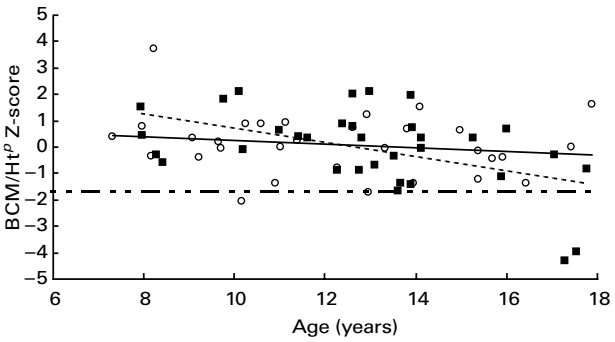

Fig. 1. The relationship between body cell mass adjusted for gender-specific height (BCM/Ht^p) Z-score and age at final measurement among female (○) and male (■) children with cystic fibrosis. A Z-score below −1·65 (-—-) was considered to indicate sub-optimal nutritional status. The regression line for males (---) is BCM/Ht^p = −0·269 × age + 3·425 and for females (—) is BCM/Ht^p = −0·062 × age + 0·95.

regression lines shown in Fig. 1. The change in Z-score with age in the females is virtually zero (−0·06). In the males, however, the mean Z-score decreases by 0·27 SD per year in the whole cohort.

Discussion

The primary aim of the present paper was to assess the nutritional status of children with CF at our centre, using size-adjusted BCM Z-scores. Our results showed that our CF population was on average well nourished, with BCM/Ht^p values similar to healthy reference values. When each gender was considered separately, both males and females had Z-scores above zero and there was no significant difference between the nutritional status in males and females at the initial measurement. At the initial assessment, only a small percentage of the population was considered sub-optimally nourished.

Our secondary aim was to examine the longitudinal change in nutritional status. The nutritional status for the total population decreased significantly over the study period; however, it must be recognised that although the BCM/Ht^p Z-score decreased with age, it still remained above zero. For the female subjects, there was no significant decrease in mean nutritional status. There was a slight increase to 9 % of males and 7 % of females who were considered sub-optimally nourished at the final measurement.

It was evident in our study that there was a significant negative relationship between nutritional status and age in males, but not in females. This finding was evident both in the cross-sectional trend and when the subjects were studied longitudinally. Our findings expand on those of Sood *et al.* (2003), who studied a CF population cross-sectionally and also reported a downward trend of nutritional status with age. The finding of sub-optimal nutritional status in boys compared with girls has also been supported by previous studies (Stettler *et al.* 2000; Ahmed *et al.* 2004). These findings contrast with the better prognosis in males than females with CF (Dodge *et al.* 1997; Rosenfeld *et al.* 1997).

The reasons why there was a decrease in nutritional status with age for children with CF, particularly in the males, cannot be determined from this study. This sexual dimorphism in changing BCM with age in children with CF is worthy of further study in other cohorts. It does not appear to be caused by a progression in lung disease in our cohort, because there was no significant decrease in FEV_1 over the 2-year period in either the males or females (results not shown). We recognise that there can be considerable lung structural damage with normal FEV_1, so FEV_1 may be a poor marker particularly in younger children and milder lung disease.

Size- and gender-adjusted BCM has not been used in a CF population previously and thus comparisons to other findings cannot be made; however, other methods have been used to define nutritional status in children with CF. A study by McNaughton *et al.* (2000), which used TBK as an indicator of nutritional status, found that 30 % of males and 22 % of females were nutritionally depleted, a higher percentage than found in the current study. Other studies using FFM from skinfolds as a measure of nutritional status have found that FFM is reduced in CF compared with controls (Groeneweg *et al.* 2002; Ahmed *et al.* 2004). However, a recent study by Marín *et al.* (2004) found that body composition was similar between CF children and controls, when using the measures of anthropometry and ^{2}H dilution.

All body composition methods have limitations; however, some methods, such as TBK, are more appropriate in clinical paediatric conditions. A limitation of our study is that there is no paediatric-specific equation available to convert TBK into BCM. The equation of Wang *et al.* (2004) used to convert TBK into BCM was formulated using data from healthy adults and thus is based on assumptions that may not apply to children with a clinical condition; therefore, this conversion may be a source of error in our study. It is recommended that future research formulates a child-specific BCM equation and that these equations are evaluated in clinical conditions.

Based on measurements of BCM, it appears from our results that children with CF at our centre are generally well nourished, with fewer children being considered sub-optimally nourished than previously reported. However, there appears to be a decrease in nutritional status with age, significantly in males, that needs to be acknowledged. It is recommended that nutritional intervention needs to play a major role throughout a CF patient's life to ensure that optimal nutritional status is maintained and that the decrease in nutritional status with age is counteracted with an increase in nutritional treatment.

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