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Pulmonary function and nutritional morbidity in children and adolescents with congenital diaphragmatic hernia

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ABSTRACT

Background: Malnutrition is common among congenital diaphragmatic hernia (CDH) survivors and may result from elevated respiratory effort. We evaluated body mass index (BMI), measured resting energy expenditure (mREE) and pulmonary function test (PFT) results in children and adolescents with CDH to determine if there is a correlation.
Methods: With ethics approval (REB# 1000035323), anthropometrics, indirect calorimetry (IC) results and PFTs were collected from patients 5–17 years of age during CDH clinic visits between 2000 and 2016. Malnutrition was defined as BMI z-scores <−2.0; mREE (as percent predicted REE) was measured using IC; z-scores for forced expiratory volume in 1 s (FEV1) and forced vital capacity (FVC) were normal if <−1.64. Statistics: GraphPad Prism 6, San Diego, CA.
Results & discussion: Of 118 patients who attended clinic, 33 had reproducible PFTs, anthropometrics and IC results. Mean BMI z-score was −0.89 ± 1.47 and 24% of patients were malnourished; mean FVC z-score (−1.32 ± 1.39) was within normal range, whereas mean z-scores for FEV_1 (−2.21 ± 1.68) and FEV_1/FVC ratio (−1.78 ± 0.73) were below normal. A correlation was noted between BMI and PFTs (FEV_1 $r = 0.70$, $P < 0.0001$; FVC $r = 0.74$ $P < 0.0001$). Mean mREE was 112% ± 12% of expected and 67% of patients were hypermetabolic (mREE < 110% predicted). IC results did not correlate with z-scores for either FEV_1 ($r = 0.10$, $P = 0.57$); or FVC ($r = 0.28$, $P = 0.12$).
Conclusions: These preliminary results suggest that a correlation is present between BMI and lung function in CDH children and adolescents, whereas lung function does not seem to correlate with mREE.
Level of evidence: II.

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Malnutrition is frequently documented in young children with CDH [1–9] but information on nutritional morbidity in CDH survivors beyond early childhood is just starting to emerge. At our institution, the prevalence of low weight and body mass index (BMI) z-scores (scores ≤2.0) in children and adolescents with CDH between 5 and 17 years of age was 19% and 14% respectively [10]. A Japanese group recently reported a prevalence of growth retardation (using the Waterlow criteria [11]) at age 6 years of 13.5% [12]. Similarly, height z-scores have been shown to be lower in young adults with CDH when compared to age-matched controls treated for other forms of respiratory failure of infancy [13]. Many factors are associated with malnutrition in infancy including the type of surgical repair, degree of respiratory compromise at hospital discharge [7], increased resting energy expenditure (REE) [14] and inadequate energy intake owing to comorbidities such as oral aversion, and gastrointestinal reflux disease (GERD) [4]. Far less is known about the etiology of nutritional morbidity as CDH survivors reach late childhood and adolescence. We recently reported that 58% of children and adolescences with CDH evaluated by indirect calorimetry (IC) demonstrated elevated measured REE (mREE) [10]. Although we did not find any correlation between BMI and mREE, it was postulated that BMI did not account for altered body composition and associated changes in metabolically active tissue (i.e. reduced muscle mass) [10].

Increased respiratory effort leading to increased energy expenditure is a long-standing hypothesis within the respiratory [15] and CDH communities [7,8,16,17], but minimal evidence is available. In a group of CDH infants, mREE did not correlate with surrogate markers of pulmonary hypoplasia (oxygen requirement and respiratory rate), but the sensitivity of these surrogates was likely insufficient [14].

The objective of this study was to examine the relationship between BMI, mREE and pulmonary function in children and adolescents who had CDH corrected in infancy and followed in the multidisciplinary

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Table 1
Anthropometrics, lung function and measured energy expenditure of children and adolescents with CDH.

N = 33	
Weight (mean ± sd)	−0.80 ± 1.48
Height (mean ± sd)	−0.38 ± 1.11
BMI (mean ± sd)	−0.89 ± 1.47
Malnutrition Prevalence, n (%)	8 (24)
FEV_1 z-score (mean ± sd)	−2.21 ± 1.68
Prevalence of low FEV1, n (%)	21 (63)
FVC z-score (mean ± sd)	−1.32 ± 1.39
Prevalence of low of FVC, n (%)	12 (36)
FEV_1/FVC z-score (mean ± sd)	−1.78 ± 0.73
Prevalence of low FEV_1/FVC, n (%)	17 (52)
Percent pREE (mean ± sd)	112 ± 12
Prevalence of elevated mREE, n (%)	22 (67)

BMI: body mass index; FEV1: forced expiratory volume in 1 s; FVC: forced vital capacity; mREE; measured resting energy expenditure; pREE: predicted resting energy expenditure.

CDH clinic at our institution. We hypothesized that reduced lung function as measured through routine pulmonary function tests (PFTs) correlates with elevated mREE and low BMI.

1. Methods

With ethics approval (REB# 1000035323), a retrospective review of patients followed in the multidisciplinary CDH clinic in our institution was performed. Inclusion criteria were Bochdalek CDH patients aged 5–17 years, CDH clinic attendance between January 2010 and January 2016 and surgical repair performed at our institution between 1996 and 2010.

Anthropometrics, age, sex, side of defect, type of surgical repair, and PFT results were collected. Anthropometrics (height, weight and BMI) were plotted on Canadian Pediatric Endocrine Group (CPEG) charts (adapted from WHO growth standards) [18]; z-scores were obtained using the same (z-score of 0 is equivalent to 50th percentile, −1 to the 16th percentile, and −2.0 is equivalent to 2nd percentile). A BMI z-score ≤ −2.0 was indicative of malnutrition [19]. Clinic surveillance protocol, including the addition of indirect calorimetry, has been previously reported [10,20]. In short, calorimetry is offered to all patients between 5 and 17 years of age by voluntary participation. The VMax™. Encore 29 Viasys Health Care (Palm Springs, CA) calorimeter was used; as per convention, mREE results were expressed as percentage predicted REE (pREE) using the FAO/WHO/UNU equations; a variance of 10% in REE is accepted in healthy controls (90%–110% of predicted values) [21]. Results were considered valid only if steady state was achieved during the test.

Spirometry was performed on VMax™ Encore systems (Carefusion, Yorba Linda, CA, USA) according to the American Thoracic Society (ATS)/European Respiratory Society (ERS) Task Force Standardization of Spirometry guidelines [22], with only those tests deemed to meet acceptability and reproducibility criteria included. The highest obtained forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC) were recorded and the FEV_1/FVC ratio calculated. Results were compared to patient-specific predicted normal values obtained from the Global Lung Initiative (GLI) spirometry reference equations [23], with those having a z-score < −1.64 being deemed abnormal.

Pearson's correlation coefficient was used to explore associations between variables and statistical significance level was set at P = 0.05. Statistics were completed using GraphPad Prism 6, San Diego, CA.

2. Results

In total, 178 unique patients attended the multidisciplinary CDH clinic during the study period and 118 met the inclusion criteria for age. IC testing occurred in 50/118 (42%); of these, 43/50 (86%) also underwent PFT testing. PFT results were excluded for an additional 10 patients: 6 were unable to produce satisfactory results based on established standards and 4 were excluded owing to BMI > +2.0 with the known effect of obesity on pulmonary function [28]. Based on these exclusions, 33/118 patients (28%) with both reproducible PFT and IC results were included in analysis. Their mean age was 11.3 ± 3.4 years; 18/33 (55%) patients were male; 26/33 (80%) had left sided defects; 18/33 (55%) required patch repair; 1/33 (3%) had been treated with ECMO; and 2/33 (6%) had gastrostomy tubes in use at the time of the clinic visit. The mean BMI z-score was less than zero (−0.89 ± 1.47 l) and median (range) was −0.57 (−3.00 to 3.00) and 8/33 (24%) were considered malnourished (Table 1). Means for FEV_1 and

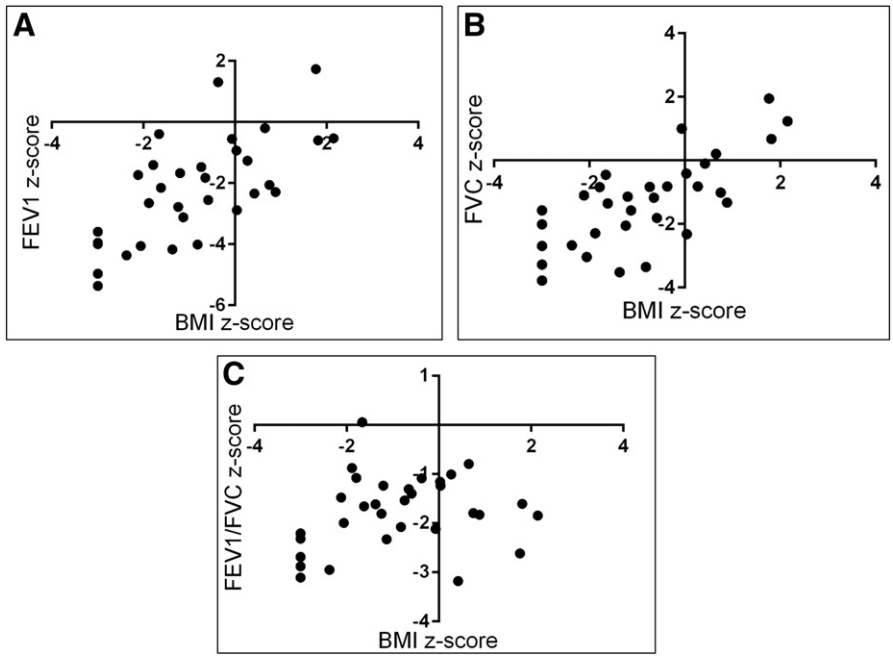

Fig. 1. Correlation analysis of pulmonary function and BMI in children and adolescents with CDH. A: FEV_1 z-scores correlate with BMI z-scores (r = 0.64, P < 0.0001). B: FVC z-scores correlate with BMI z-scores (r = 0.73 P < 0.0001). C: FEV_1/FVC z-scores do not correlate with BMI z-scores (r = 0.27, P = 0.13).

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