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The relationship of body habitus and respiratory function in Duchenne muscular dystrophy

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ABSTRACT

Background: The multidisciplinary care of Duchenne muscular dystrophy (DMD) incorporates management of nutrition and the respiratory system, however the effect of body habitus on respiratory function in DMD is poorly understood. The present study examined the impact of nutritional status on respiratory function in DMD to guide further treatment strategies.
Methods: Anthropometric and respiratory parameters, such as body mass index (BMI) z-scores, forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1) were retrospectively analysed with a mixed linear model in 34 DMD patients. Cross-sectional analysis of cough peak flow (CPF) in upright and supine positions and body fat mass were examined in 12 DMD patients.
Results: Respiratory function in DMD patients was significantly related to BMI Z-score ($P < 0.001$), age ($P < 0.05$) and mobility ($P < 0.001$). DMD patients with greater BMI Z-score had increased respiratory function, even when adjusting for age and mobility status, with a 1 unit increase in BMI z-score associated with a 7.43% increase in FVC% predicted ($P < 0.001$). Body fat mass was adversely associated with FVC with a 1% body fat increase associated with a 1.5% reduction in FVC ($P < 0.05$). CPF values were significantly lower in supine compared to upright position ($P = 0.005$) and greater postural reductions in CPF were associated with higher body fat percent, with a 1% body fat increase associated with a 1.5% increase in postural CPF difference ($P < 0.05$).
Conclusion: The present study reinforces the importance of weight management in DMD, showing that a higher weight profile and lower adiposity have better respiratory outcomes. Furthermore, attention to body position with airway clearance techniques will maximize their effectiveness.

1. Background

Duchenne muscular dystrophy (DMD) is characterised by progressive muscle weakness and loss of respiratory function, caused by loss of function mutations in the dystrophin gene [1]. With an incidence of 1:3600–6000 live male births, DMD is the most common severe childhood muscular dystrophy. Recent advances in the multidisciplinary management of boys with DMD, widespread use of corticosteroids and the advent of international standards of care have resulted in increased life expectancy and respiratory function in DMD [2–7].

Despite these improvements, respiratory complications remain a leading cause of morbidity and mortality [8–10]. Respiratory function tests are used to monitor disease progression in DMD and determine initiation of respiratory interventions, with lung volume recruitment methods and assisted coughing preceding commencement of non-invasive ventilation. In addition, current guidelines promote adequate nutrition to support respiratory care and enhance quality of life, with avoidance of obesity or malnutrition [11]. Compared to an age and gender matched healthy population, patients with DMD have a tendency to the extremes of weight [11]. Obesity may be attributed to weight gain, reduced height velocity and increased body fat composition associated with chronic corticosteroid therapy and decreased energy expenditure related to reduced mobility [11,12], whilst weight loss and

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undernutrition are often features of the later stages of the disease [13,14]. The effects of being overweight or underweight on respiratory function in DMD are not fully defined and previous studies are inconsistent, in part related to variability in utilisation of chronic corticosteroid therapy affecting adiposity and respiratory strength and differences in measurement approaches [4,12–15]. Developing a further understanding of modifiable determinants of respiratory function such as body habitus is important in improving health outcomes in DMD.

The impact of nutrition on postural differences in respiratory function in DMD is also of therapeutic relevance, particularly as DMD patients may be managed lying down when unwell. Postural vital capacity is recognised to reduce with position change from standing to supine, yet this difference decreases with age in DMD and may not reflect functional respiratory status [16]. Cough effectiveness is critical in preventing atelectasis and recurrent respiratory tract infections, with cough peak flow (CPF) representing a simple alternative and highly relevant measure of postural changes in respiratory function to potentially guide therapy. This study aimed to examine the relationship of body habitus and postural differences on respiratory function in DMD.

2. Material and methods

2.1. Study design and population

The study incorporated DMD patients managed at the Sydney Children's Hospital multidisciplinary neuromuscular clinic from 2000 to 2015. Inclusion criteria comprised a clinical and genetic diagnosis of DMD, the ability to reproduce reliable respiratory function testing (age>5 years) and chronic corticosteroid therapy (>0.3 mg/kg/day). The South Eastern Sydney and Illawarra Area Health Service ethics committee approved the study.

A retrospective study was undertaken to describe the natural history of respiratory function and potential relationships with body mass index in DMD. Data were obtained from patient notes. Specific respiratory function parameters examined included forced vital capacity (FVC), forced expiratory volume in one second (FEV_1) and CPF. Additional characteristics recorded at the time of each respiratory function test included ambulatory status, dose and duration of corticosteroid therapy and BMI. Cross-sectional assessments of skin fold thickness, respiratory function testing and CPF were undertaken in DMD patients over 12 months from May 2014 to May 2015.

2.2. Study techniques

2.2.1. Respiratory function

Respiratory function testing was conducted according to the standards specified by the American Thoracic Society and European Respiratory Society [17] using the Vmax Encore 22D respiratory function testing system (SensorMedics, Yorba Linda). FVC and FEV1 were expressed as % of predicted for height and age. Respiratory function tests were performed in the sitting position. FEV1 and FVC manoeuvres were repeated until three acceptable results were attained with two or more sets of readings within 150 ml of each other.

CPF was measured both sitting and supine using a portable peak flow meter (HS755 Personal Best Peak Flow Meter, Philips Respironics) and postural differences calculated (ΔCPF). The highest of three sets of readings were obtained and the highest reading recorded. CPF % predicted values were then calculated from CPF reference values [18].

2.2.2. Anthropometric data

In ambulatory boys height and weight were measured using standing scales and stadiometers, while in non-ambulant DMD patients weight was obtained with a hoist and ulnar length was used to estimate height [19]. BMI was calculated from height (m) and weight (kg) where BMI = weight/height^2. Body mass index z-scores are measures of relative weight adjusted for child age and sex relative to an external reference. The z-score is the number of standard deviations away from the average value of the reference group. BMI z-scores were calculated using reference values from the 2000 Center for Disease Control and Prevention Growth Charts for boys between the ages 2–20 years. BMI z-scores were converted to BMI percentile units for interpretability and for each patient, were categorized as underweight (<5th percentile, $z < -1.65$), normal weight (>5th and <95th percentile, $z > -1.65$ and <1.65) and overweight (>95th percentile, $z > 1.65$) [20,21].

Skinfold thickness was measured from the mid-thigh and subscapular sites on patients using a Harpenden Skinfold Calliper (HSK-BI by British Indicators, Divisions of Quality Measurement Limited), according to previously described techniques [22]. Subscapular and supra-iliac skinfold thickness measurements have previously been demonstrated to be useful in accurately assessing nutritional status in DMD patients [14]. The callipers measure the 'pinched-off' skinfold thickness in millimetres (mm). The procedure was repeated until two measurements within 0.1 mm of each other were attained. Percent body fat (BFP) was determined from skinfold thickness measurements by first calculating body density using the formula established by Sloan and Weir [23].

$$\text{Males: density} = 1.1043 - (0.0133 \times \text{thigh skinfold}) - (0.00131 \times \text{subscapular skinfold})$$

Following that, percent body fat was determined using the Brozek formula [24].

$$\text{Percent body fat} = 100 \times ((4.57/\text{body density}) - 4.142)$$

2.3. Statistical analysis

Study data was collated with Microsoft Excel and statistically analysed using IBM SPSS 21. Demographic data were summarized as means, standard deviations, medians and ranges. A mixed linear model analysed possible associations between each respiratory parameter with age, BMI z-score and mobility status (ambulant vs. non-ambulant), including repeated data for each subject. Differences in positional CPF were tested with Student's paired *t*-test. Linear regression analysis also assessed the relationship between positional CPF changes and percent body fat. A probability (p) value of <0.05 was considered statistically significant.

3. Results

3.1. Respiratory function and clinical status in DMD: retrospective study

A clinical and genetic diagnosis of DMD was confirmed in 34 patients totalling 427 patient years receiving chronic corticosteroids and able to perform acceptable respiratory function tests attending the Sydney Children's Hospital multidisciplinary neuromuscular clinic. Scoliosis surgery was not performed in any patient. The characteristics of the DMD cohort at the time of their last follow-up are summarized in Table 1.

Latest respiratory function ranged from very severe restrictive