COMPARTMENTAL NUTRITIONAL STATUS AND RESPIRATORY MUSCLE FUNCTION ASSESSMENT IN SUBJECTS WITH NEUROMUSCULAR DISEASES

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Abstract

There are few data devoted to the combined assessment of the nutritional and respiratory status of subjects with neuromuscular diseases. The objective was to establish correlations between compartmental nutritional variables and respiratory variables to identify respiratory muscle weakness determinants of patients with amyotrophic lateral sclerosis (ALS) and Duchenne muscular dystrophy (DMD). Cross-sectional study with ALS and DMD patients included in an Institutional Registry of Neuromuscular diseases. Nutritional status was assessed through body mass index (BMI), expected weight for zero muscle mass (ZMM%) and creatinine-height index (CHI%). Respiratory indices evaluated were spirometry, maximal static inspiratory and expiratory pressures at the mouth (MIP and MEP), and peak cough flow (PCF). A total of 36 ALS and 34 DMD patients were included. Both groups showed a decrease in the body muscle mass and an excess in body fat (p < 0.001). Only in the ALS group was there a weak uphill relationship between body mass index (BMI) and the respiratory variables. In both groups, the ZMM% index did not correlate with any respiratory variable. The CHI% showed the strongest (r > 0.700) positive linear relationship with FVC%, MIP%, MEP%, and PCF% in both ALS and DMD patients (p < 0.001). In this study our patients, BMI did not accurately reflect body composition and underestimated excess fat. This study puts into perspective the relevance of compartmental evaluation to assess respiratory muscle function and establishes that body muscle mass is the most relevant nutritional parameter in relation to respiratory muscle strength.

Key words: neuromuscular diseases, nutritional assessment, amyotrophic lateral sclerosis, Duchenne muscular dystrophy, pulmonary function testing

Resumen

Evaluación del estado nutricional compartimental y de la función muscular respiratoria en sujetos con enfermedades neuromusculares. Hay pocos datos relativos a la evaluación combinada del estado nutricional y respiratorio de sujetos con enfermedades neuromusculares. El objetivo fue establecer correlaciones entre las variables nutricionales compartimentales y las variables respiratorias para identificar los determinantes de la debilidad de los músculos respiratorios de los pacientes con esclerosis lateral amiotrófica (ELA) y distrofia muscular de Duchenne (DMD). Estudio transversal con pacientes con ELA y DMD incluidos en el Registro Institucional de Enfermedades Neuromusculares. El estado nutricional se evaluó mediante el índice de masa corporal (IMC), el peso esperado para masa muscular cero (ZMM%) y el índice de creatinina-talla (CHI%). Los índices respiratorios evaluados fueron espirometría, presiones inspiratorias y expiratorias estáticas máximas en la boca (MIP y MEP) y flujo espiratorio pico tosido (PCF). Se incluyeron un total de 36 pacientes con ELA y 34 con DMD. Ambos grupos mostraron una disminución de la masa muscular corporal y un exceso de grasa corporal (p <0.001). Solo en el grupo ELA hubo una débil correlación positiva entre el IMC y las variables respiratorias. En ambos grupos, el índice ZMM% no se correlacionó con ninguna variable respiratoria. El CHI% mostró la relación lineal positiva más fuerte (r > 0.700) con FVC%, MIP%, MEP% y PCF% tanto en pacientes con ELA como con DMD (p < 0.001). El IMC no reflejó con precisión la composición corporal y subestimó el exceso de grasa. Este estudio pone en perspectiva la relevancia de la evaluación compartimental para evaluar la función de la musculatura respiratoria y establece que la masa muscular corporal es el parámetro nutricional más relevante en relación a la fuerza de la musculatura respiratoria.

Palabras clave: enfermedades neuromusculares, valoración nutricional, esclerosis lateral amiotrófica, distrofia muscular de Duchenne, prueba de función pulmonar
Respiratory muscle weakness is the hallmark of most neuromuscular diseases (NMD), and together with malnutrition and weight loss, respiratory muscle weakness is a significant determinant of morbidity and mortality. Nutritional assessment and respiratory status are essential components of evaluating children and adults with NMD.

Clinical anthropometry is complicated for patients with NMD. The loss of muscle mass can be due to muscle atrophy from the primary pathology, muscle replacement by fat and fibrosis, and undernourishment. These factors can alter the compartmental distribution of muscle and fat mass and could not be reflected in the body mass index (BMI). It has been suggested that indices that incorporate the compartmental distribution of muscle (such as creatinine height index, CHI) and fat (zero muscle mass, ZMM) are more sensitive.

There are few data devoted to the combined assessment of the nutritional and respiratory status of subjects with NMD. This study aimed to assess the relationship between the compartmental nutritional status and respiratory muscle function measures in amyotrophic lateral sclerosis (ALS) and Duchenne muscular dystrophy (DMD) patients. Since only the CHI% considers muscle mass, we hypothesized that the respiratory muscle force could be more related to the muscle mass than with global nutritional status indicators such as BMI. We looked for correlations between compartmental nutritional variables and respiratory indices to identify respiratory muscle weakness determinants.

Material and methods

We conducted a cross-sectional study at a tertiary care teaching facility in Buenos Aires, Argentina. The information was extracted from an Institutional Registry of Neuromuscular Diseases with a validated quality data control process for extensive previous research. ALS and DMD patients were selected. All respiratory function tests, as well as anthropometric measurements correspond to routine measurements in these patients. The diagnosis of ALS was established according to the revised criteria for the diagnosis of amyotrophic lateral sclerosis, El Escorial. Regardless of gender and duration of disease, both subjects with bulbar and spinal predominance were included. Patients who used a wheelchair, had a gastrosomy, or received mechanical ventilation at home were also included. The diagnosis of DMD was established by clinical criteria and confirmed by dystrophin immunostaining. The Vignos Functional Scale was used to assess functional motor ability. At the time of evaluation, none of the selected patients presented unstable cardiac condition, active recent surgery, diabetes mellitus, and thyroid disorders, neither recent (6 weeks) episodes of acute respiratory exacerbation, infection, or hospitalization. Kidney function was normal. Patients were screened for eligibility during a regularly scheduled clinic visit. The candidates for the nutritional evaluation of the compartment were selected for their ability to perform urine collection indications and to live in the vicinity of the hospital. The Institutional Ethics Committee approved the study (CUDAP: TRI-UBA: 0051153/2018, #216).

We employed several measures to assess nutritional status and compartmental body mass distribution.

The body mass index (BMI) was calculated by dividing the patient’s weight by the height squared and was expressed as kg/m². Normal nutrition was defined by a BMI of 18.5 to 25 kg/m². Values greater than 25 or below 18.5 were considered overweight and underweight, respectively.

The percent of expected weight for zero muscle mass (ZMM%) was obtained after a creatine free diet for six days and total urinary creatinine excretion was averaged daily over the next three days. It provided a reliable estimation of muscle contribution to body weight according to the formula. The patient’s weight for zero muscle mass (pZMM) = body weight 24 h creatinine excretion in mmol * 2.2625. The theoretical bodyweight for zero muscle mass is ZMM, which is obtained by subtracting the normal theoretical muscle mass from the normal theoretical bodyweight. Thus, ZMM is obtained by the following equation: ZMM = theoretical body weight (normal values of 24 hr creatinine excretion * 2.2625). The pZMM divided by ZMM is the percent of expected weight for zero muscle mass (ZMM%). Normal nutrition was defined as having 90 to 110% ZMM%. Values higher than 110% and below 90% were considered overweight (fat mass excess) and underweight.

The creatinine height index (CHI%) in percent of predicted values was calculated as follows: measured 24 h urinary creatinine divided by expected 24 h urinary creatinine of normal individuals of same sex and height, expressed as a percentage. A CHI% higher than 80% of the standard was considered as normal protein status. Values of 60% to 80% represent a mild depletion in body muscle mass, values between 60% and 40% indicate moderate protein depletion, and less than 40% indicate a severe deficit of body muscle mass.

The respiratory muscle strength was assessed by measuring the maximum inspiratory pressure (MIP) and the maximum expiratory pressure (MEP) from residual volume and total lung capacity. The MIP reflects the strength of the diaphragm and other inspiratory muscles, whereas the MEP reflects the strength of the abdominal muscles and other expiratory muscles. At the mouth, these static maximum pressures were obtained with a snorkel-like (flanged) mouthpiece coupled with a unidirectional Hans Rudolph valve connected to a pressure transducer (Validyne MP 45, Validyne Engineering, Northridge, California). A 1mm leak was used to prevent glottic closure. Maximum effort was encouraged verbally, with simultaneous visual feedback from a monitor. Maneuvers were separated by at least 30-s rest periods and continued until no further increase in pressure could be obtained. Data were recorded in a digital format (MP100 Workstation, Biopac Systems, Goleta, California). The signals from the pressure transducers were filtered with low pass filters (30 Hz). They then were passed through an analog-to-digital conversion board.
TABLE 1. – Physical characteristics and pulmonary function testing in patients with amyotrophic lateral sclerosis (ALS) and Duchenne muscular dystrophy (DMD)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>ALS</th>
<th>DMD</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex M / F</td>
<td>21/15</td>
<td>34/0</td>
<td>--</td>
</tr>
<tr>
<td>Age (years)</td>
<td>57 ± 12</td>
<td>14 ± 5</td>
<td>0.001</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>64.2 ± 14.5</td>
<td>43.4 ± 16.4</td>
<td>0.001</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>169.0 ± 9.5</td>
<td>146.5 ± 19.2</td>
<td>0.001</td>
</tr>
<tr>
<td>FVC (liters)</td>
<td>2.01 ± 0.90</td>
<td>1.62 ± 0.63</td>
<td>0.059</td>
</tr>
<tr>
<td>FVC (% predicted values)</td>
<td>50.8 ± 21.7</td>
<td>45.9 ± 19.4</td>
<td>0.345</td>
</tr>
<tr>
<td>PF (liters/min)</td>
<td>228.5 ± 113.7</td>
<td>212.6 ± 62.8</td>
<td>0.981</td>
</tr>
<tr>
<td>PF (% of predicted values)</td>
<td>43.4 ± 19.9</td>
<td>55.1 ± 16.9</td>
<td>0.483</td>
</tr>
<tr>
<td>MIP (cmH2O)</td>
<td>45.1 ± 20.7</td>
<td>61.2 ± 16.9</td>
<td>0.001</td>
</tr>
<tr>
<td>MIP (% predicted values)</td>
<td>52.6 ± 24.4</td>
<td>46.7 ± 12.0</td>
<td>0.497</td>
</tr>
<tr>
<td>MEP (cmH2O)</td>
<td>54.3 ± 28.7</td>
<td>62.9 ± 21.5</td>
<td>0.175</td>
</tr>
<tr>
<td>MEP (% predicted values)</td>
<td>51.6 ± 27.3</td>
<td>36.6 ± 12.0</td>
<td>0.061</td>
</tr>
</tbody>
</table>

FVC: forced vital capacity; PF: peak expiratory flow rate; MIP: maximal inspiratory pressure; MEP: maximal expiratory pressure

Results

The DMD patients not receiving steroid treatment were excluded from the study. During the study period, a total of 74 patients were studied. Four were eliminated because of doubts about diet compliance or urine collection. All subjects in the DMD group started to be treated with steroid therapy (deflazacort 0.5-1.0 mg/kg) at 5 to 7 years old. A total of 36 ALS and 34 DMD patients were included in this study.

The physical characteristics and the pulmonary function test data of those enrolled in the study are shown in Table 1. There were no significant differences between our ALS and DMD groups regarding pulmonary function testing. Ten of the 36 patients with ALS were wheelchair users, four had gastrostomy tubes, and nine used long-term ventilatory assistance at home. Twenty-one of the 34 patients with DMD were wheelchair users, and the Vignos scale mean value was 6.6 ± 3.3.

The PCF in ALS subjects was 290.4 ± 157.0, while in DMD subjects was 296.0 ± 80.2 liters/min (p < 0.688). These values represent a mean increase of 21.3 for ALS (p < 0.154) and 39.2% for DMD patients (p< 0.001) of the PF, respectively. The FEV1/FVC ratio was within the predicted values.

Compared with the ALS group, the BMI was marginally lower in DMD (p < 0.048), while the nutritional compartmental variables of both groups were significantly different (Table 2). According to CHI%, and ZMM% both ALS and DMD groups showed a decrease in the body muscle mass and an excess in that body fat. The mean CHI% was higher in patients with ALS (p < 0.001), while the mean ZMM% was higher (p < 0.001) in patients with DMD (Table 2).

The relationship between nutritional compartmental parameters is shown in Table 3. In both groups, strong correlations uphill (positive) were found between ZMM% and BMI (r > 0.700, p < 0.001). Regarding DMD patients, no correlation was found between CHI% and BMI (r 0.091, p = 0.613), while in ALS patients, it was a sig-
The relationship between PCF and CHI% is shown in Figure 4. In both groups, the CHI% showed the strongest (r > 0.7) positive relationship with the PCF. In the ALS group, there was a moderate positive linear relationship between BMI and PCF (0.571, p < 0.001). In both groups of patients, the ZMM% index did not correlate with PCF.

**Discussion**

In this study, we correlated spirometry (mainly FVC), the maximal static pressures at the mouth (MIP and MEP), and a dynamic measure of cough effectiveness (PCF) with the global nutritional status according to BMI and with compartmental measurements such as body muscle mass according to CHI% and expected weight for zero muscle mass according to ZMM%. Our study’s most important finding is that the CHI% showed the strongest relationship with FVC%, MIP%, MEP%, and PCF%, both in ALS and DMD patients. The BMI correlated with all respiratory function parameters. The relationship between PCF and CHI% showed the strongest (r > 0.7) positive relationship with the PCF. In the ALS group, there was a moderate positive linear relationship between BMI and PCF (0.571, p < 0.001). In both groups of patients, the ZMM% index did not correlate with PCF.

Neuromuscular diseases represent a heterogeneous group of acquired or inherited conditions. The nutritional approach is complicated for these patients. Patterns of global nutritional parameters, anthropometric

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**TABLE 2.** Nutritional variables in patients with amyotrophic lateral sclerosis (ALS) and Duchenne muscular dystrophy (DMD)

<table>
<thead>
<tr>
<th>Variable</th>
<th>ALS</th>
<th>DMD</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/cm²)</td>
<td>22.4 ± 4.3</td>
<td>19.9 ± 5.1</td>
<td>0.048</td>
</tr>
<tr>
<td>CHI%</td>
<td>59.8 ± 22.2</td>
<td>31.4 ± 21.9</td>
<td>0.001</td>
</tr>
<tr>
<td>ZMM%</td>
<td>118.8 ± 27.0</td>
<td>152.9 ± 43.9</td>
<td>0.001</td>
</tr>
</tbody>
</table>

BMI: body mass index; CHI%: creatinine height index in % of predicted values; ZMM%: % zero muscle mass in % of predicted values

**TABLE 3.** Relationship between nutritional compartmental parameters in Duchenne muscular dystrophy (DMD) and amyotrophic lateral sclerosis (ALS) patients

<table>
<thead>
<tr>
<th>Relations</th>
<th>Equations</th>
<th>r</th>
<th>p value</th>
<th>Pw alpha</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMD</td>
<td>BMI vs. ZMM%</td>
<td>ZMM% = -6.362 + (8.064 * BMI)</td>
<td>0.972</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>BMI vs. CHI%</td>
<td>CHI% = 23.002 + (0.402 * BMI)</td>
<td>0.091</td>
<td>0.613</td>
<td>0.072</td>
</tr>
<tr>
<td>ALS</td>
<td>BMI vs. ZMM%</td>
<td>ZMM% = -2.988 + (5.444 * BMI)</td>
<td>0.858</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>BMI vs. CHI%</td>
<td>CHI% = 0.309 + (2.663 * BMI)</td>
<td>0.460</td>
<td>&lt; 0.007</td>
<td>0.778</td>
</tr>
</tbody>
</table>

BMI: body mass index; CHI%: creatinine height index in % of predicted values; ZMM%: % zero muscle mass in % of predicted values. Pw alpha: Power of performed test with alpha = 0.050
TABLE 4.– Correlation coefficients of nutritional and respiratory parameters in Duchenne muscular dystrophy (DMD) and amyotrophic lateral sclerosis (ALS) patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>ALS (n 36)</th>
<th>equation</th>
<th>r</th>
<th>p</th>
<th>Pw*</th>
<th>DMD (n 34)</th>
<th>equation</th>
<th>r</th>
<th>p</th>
<th>Pw*</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI FVC%</td>
<td>-3.439 + (2.424 * BMI)</td>
<td>0.480</td>
<td>0.003</td>
<td>0.852</td>
<td>41.796 + (0.204 * BMI)</td>
<td>0.045</td>
<td>0.759</td>
<td>0.049</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MIP%</td>
<td>-10.192 + (2.804 * BMI)</td>
<td>0.493</td>
<td>0.002</td>
<td>0.874</td>
<td>42.481 + (0.211 * BMI)</td>
<td>0.090</td>
<td>0.613</td>
<td>0.072</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MEP%</td>
<td>-16.688 + (3.052 * BMI)</td>
<td>0.480</td>
<td>0.003</td>
<td>0.852</td>
<td>32.812 + (0.191 * BMI)</td>
<td>0.081</td>
<td>0.648</td>
<td>0.066</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ZMM% FVC%</td>
<td>41.123 + (0.0818 * ZMM)</td>
<td>0.102</td>
<td>0.554</td>
<td>0.085</td>
<td>43.376 + (0.0162 * ZMM)</td>
<td>0.037</td>
<td>0.835</td>
<td>0.040</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MIP%</td>
<td>38.732 + (0.117 * ZMM)</td>
<td>0.129</td>
<td>0.453</td>
<td>0.112</td>
<td>44.948 + (0.0113 * ZMM)</td>
<td>0.041</td>
<td>0.816</td>
<td>0.042</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MEP%</td>
<td>43.391 + (0.0694 * ZMM)</td>
<td>0.069</td>
<td>0.690</td>
<td>0.059</td>
<td>34.804 + (0.0117 * ZMM)</td>
<td>0.043</td>
<td>0.810</td>
<td>0.043</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHI% FVC%</td>
<td>6.011 + (0.750 * CHI)</td>
<td>0.803</td>
<td>0.001</td>
<td>1.000</td>
<td>32.083 + (0.438 * CHI)</td>
<td>0.502</td>
<td>0.003</td>
<td>0.867</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MIP%</td>
<td>3.496 + (0.821 * CHI)</td>
<td>0.781</td>
<td>0.001</td>
<td>1.000</td>
<td>36.440 + (0.326 * CHI)</td>
<td>0.594</td>
<td>0.001</td>
<td>0.968</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MEP%</td>
<td>-7.932 + (0.996 * CHI)</td>
<td>0.847</td>
<td>0.001</td>
<td>1.000</td>
<td>25.740 + (0.345 * CHI)</td>
<td>0.630</td>
<td>0.001</td>
<td>0.908</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

FVC: forced vital capacity; MIP: maximal inspiratory pressure; MEP: maximal expiratory pressure; BMI: body mass index; ZMM%: % zero muscle mass in % of predicted values; CHI %: creatinine height index in % of predicted values. *Pw: Power of performed test (for alpha = 0.050, the desired power would be 0.800). Less than desired power indicates you are less likely to detect a difference when one actually exists. Negative results should be interpreted cautiously.

Even when BMI remains a useful clinical tool if these limitations are acknowledged\(^{22}\), classifying boys with DMD as overweight or underweight based solely on height and weight or BMI, without accurate concurrent estimates of nutritional status and respiratory parameters to assess the impact of NMD, years of evolution, steroid therapy\(^{22}\) and perhaps dietary interventions\(^{23}\).
body composition, can be problematic\textsuperscript{5, 24}. Our present results confirm significant differences between nutritional status diagnoses in DMD patients\textsuperscript{8}. The BMI does not accurately reflect body composition and underestimates excessive body fat. We found that in ALS patients, the diagnostic concordance was higher (Fig. 2B) than in DMD patients. It is an expected result because muscle atrophy in ALS patients does not follow muscle replacement by fat and fibrosis.

Our DMD group showed a more significant body fat (Table 2). Other authors have addressed body fat’s significant influence upon BMI\textsuperscript{12,23}. A child with pronounced muscle wasting can look cachectic, despite having excessive soft-tissue body fat\textsuperscript{22}. Our study suggests that DMD subjects, who look like normal BMI, from the compartmental approach, seem probably obese. Both in ALS and DMD patients, BMI correlated positively with ZMM\%. Interestingly, only a few DMD subjects lied into the concordance quadrants between ZMM \% and BMI (Fig. 1B).

In both groups, the body fat was definitively associated with BMI, whereas the muscle mass only was positively correlated with the BMI only in patients with ALS (Table 3). The replacement of muscle mass by fat tissue present in DMD patients does not occur in ALS patients. It is a fact that equal BMI may be present in a very different compartment distribution.

The restrictive pattern found in our ALS patients was explained by the inspiratory and expiratory muscles’ weakness (Table 1), while in DMD patients, the restrictive pattern results from a complex interaction between respiratory muscle weakness and progressive scoliosis\textsuperscript{25}.

The combined assessment of the nutritional and respiratory status in NMD, in theory, could depend on the nutritional approach performed. BMI correlated well with all respiratory variables only in the ALS group (Table 4). Perhaps the higher proportion of total body fat in DMD subjects precludes the BMI as an indirect indicator of muscle mass. Remarkably, the CHI\% was the nutritional compartmental parameter that showed the most robust positive relationship with all respiratory variables (Table 4, Figs 2, 3 and 4).

Fig. 2.– Nutritional and respiratory variables in the amyotrophic lateral sclerosis (ALS) group.
Vincken et al. studied patients with a stable chronic and clinically heterogeneous NMD not presenting with respiratory symptoms\textsuperscript{10}. BMI did not correlate with respiratory muscle strength in their patients.

In patients with ALS, Silva et al. found that BMI correlated significantly with both muscle area and fat area of the arm and respiratory parameters\textsuperscript{11}. Similarly to Vincken et al, the BMI did not correlate with muscle strength. It is an expected fact (at least in the DMD group) because it is a determination that does not discriminate fat from muscle. Furthermore, although it is known that severe malnutrition affects muscle strength, the low number of patients with severe malnutrition according to BMI in our DMD group makes it unlikely that a correlation with muscle strength can be established.

Canapari et al. designed his study to determine the relationship between central adiposity, BMI, and lung function in boys with DMD. FVC (% predicted) was not significantly correlated with BMI, and PCF was not associated with body fat parameters, including BMI\textsuperscript{12}. Truncal fat distribution was a significant predictor of lower FVC. Interestingly, they suggest that an increase in BMI at a given truncal fat percentage is protective of FVC. Since BMI includes muscle mass, it may suggest that higher BMI is consistent with greater muscle mass. The authors found a lack of association of total fat mass (directly measured) with pulmonary function.

Given the progressively degenerative nature of DMD, an increasing BMI or weight may not be a reflection of increasing muscle mass. Chew et al. found that body fat mass was adversely associated with FVC\textsuperscript{13}. Higher weight profile and lower adiposity have better respiratory outcomes. Our patients found that the respiratory muscle force was more related to the muscle mass than with global nutritional status indicators (Table 4).

The CHI% was the only parameter that correlated with respiratory functional abnormalities. This was valid for both ALS (Fig. 2) and DMD patients (Fig. 3). If we consider
that muscle mass is adequately evaluated with the CHI% and respiratory muscle strength depends not only on the muscle’s contractile characteristics and muscle mass, this association is expected.

PCF was significantly higher than PF in the DMD group. As a whole, patients with ALS showed a significantly higher dispersion of PCF relative to its mean than the DMD group, reflecting different degrees of bulbar involvement. PF is used to assess the effectiveness of the cough as well as bulbar involvement in NMD. There is currently a 1st-grade recommendation for the application of mechanically assisted cough in patients with NMD who present less than 270 L/min of PCF. Most of our patients were mechanically cough assisted devised users. Remarkably in both groups, the CHI% showed the most robust relationship with the PCF%. The moderate linear relationship between PCF and BMI found only in the ALS group means perhaps the relative better bound between BMI and muscle mass in this group (Table 3). Interestingly, a few DMD subjects showed a flattening shape regression curve at almost predicted CHI% values (Fig. 4), reflecting perhaps a myopathic component of weakness, a well-known fact in DMD subjects beyond muscle mass loss.

This study has several limitations that merit consideration. First, the findings represent the experience of
a single center. Second, day-to-day variation in protein intake and exercise cause significant variation in 24-hour creatinine excretion. Further, 24-hour urine creatinine excretion is problematic because it is often inaccurate.38,29 We trust in the subjects' high motivation to comply with the diet and collect urine. To obtain urine specimens, we used convenience sampling to create samples according to the ease of access, compliance with medical indications, and people's availability to be part of the study. Due to the sedentary characteristics of our patients, we dismiss that physical activity could be a confounding factor. Secondly, inaccuracies in anthropometric measures, especially height, may have influenced findings. Finally, since boys with DMD can move from over- to under-nutrition within their shortened life span, results should be restricted to our patients' age. However, the DMD group receiving long-term deflazacort therapy could serve to assess the impact of the compartmental nutritional status on respiratory muscle function.

In conclusion, although the relationship between nutritional status and respiratory muscle function has been established, data on this relationship in patients with NMD are scarce. BMI does not accurately reflect body composition and underestimates excess fat, it should be used cautiously to assess patients' nutritional status with NMD. In these patients, it seems more appropriate to use indices that incorporate the evaluation of the compartmental distribution of muscle and fat.

This study shows that the CHI% is most powerfully related to the three indices examined with respiratory and global muscle strength values. It also puts into perspective the relevance of compartmental evaluation to assess respiratory muscle function. It establishes that body muscle mass is the most relevant nutritional parameter concerning respiratory muscle strength. The clinical implications of our study should be explored. It must be outlined whether or not nutritional monitoring with a lot of elaborated indices than BMI and interventions targeted in body muscle mass modifies the development of respiratory muscle weakness.

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Conflict of Interest: None to declare

References


