ISSN 1669-9106

ORIGINAL ARTICLE MEDICINA (Buenos Aires) 2022; 82: 200-209

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

EDUARDO L. DE VITO, SERGIO G. MONTEIRO, SANTIAGO C. ARCE

Instituto de Investigaciones Médicas Alfredo Lanari, Facultad de Medicina, Universidad de Buenos Aires, Buenos Aires, Argentina

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 espiratorias 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

Received: 21-IX-2021 Accepted: 2-XI-2021

Postal address: Eduardo L. De Vito, Instituto de Investigaciones Médicas Alfredo Lanari, Combatientes de Malvinas 3150, 1427Buenos Aires, Argentina

e-mail: eldevito@gmail.com

KEY POINTS

- Current knowledge: There are few data devoted to the combined assessment of the compartmental nutritional and respiratory status of subjects with neuromuscular diseases.
- Contribution of the article to current knowledge: 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.

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[1,2]. Nutritional assessment and respiratory status are essential components of evaluating children and adults with NMD[3,4].

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 be not reflected in the body mass index (BMI)[5-7]. 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[8, 9].

There are few data devoted to the combined assessment of the nutritional and respiratory status of subjects with NMD[10-13]. 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*[14]. Regardless of gender and duration of disease, both subjects with bulbar and spinal predominance were included. Patients who used a wheelchair, had a gastrostomy, or received mechanical ventilation at home were also included. The diagnosis of DMD was established by clinical criteria and confirmed by dystrophin immunostaining[3]. The Vignos Functional Scale was used to assess functional motor ability[15]. 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[8].

The body mass index (BMI) was calculated by dividing the patient's weight by the height squared and was expressed as kg/m^2. Normal nutrition was defined by a BMI of 18.5 to 25 kg/m^2. Values greater than 25 or below 18.5 were considered overweight and underweight, respectively[16].

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[17]. 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 tZMM, which is obtained by subtracting the normal theoretical muscle mass from the normal theoretical bodyweight. Thus, tZMM is obtained by the following equation: tZMM = theoretical body weight (normal values of 24 hr creatinine excretion * 2.2625). The pZMM divided by tZMM is the percent of expected weight for zero muscle mass (ZMM%)[9, 17]. 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[16].

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

(Biopac Systems) at a 60-Hz sampling rate for acquisition. Reference values of maximal static pressures were obtained from Evans's equations[18].

The spirometry (flow-volume curves) were taken according to standard methodology. Subjects were seated and wearing nose clips. We reported the forced vital capacity (FVC) (Vitalograph Compact II Buckingham, U.K.); normal values were taken from NHANES III[19]. FVC, expressed either as an absolute value or a percentage of the predicted value for age and sex, was recorded for all patients. In a few poor collaborative patients, spirometry and maximal static mouth pressures were repeated in another day to obtain reliable data.

The peak expiratory flow rate (PF) was obtained with portable devices (Personal Best, normal or low range). PF with the cough (PCF) maneuver was obtained by adjusting a peak flow meter to a facial mask.

Descriptive statistics were used to summarize the groups' characteristics. Mean values of the data are followed by the standard deviation of the mean (SD). The comparison was tested for statistical significance using the Wilcoxon signed-rank or Mann- Whitney rank-sum test. Slopes were determined by linear regression analysis (SigmaPlot 12.0 Jandel Scientific Software, San Rafael, CA). The interpretation of the strength of the correlation (r-value) was made according to: > 0.7 strong, 0.5 moderate, 0.3 weak. Differences with $p< 0.05$ were considered significant. For alpha = 0.05, the desired power test would be 0.8.

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 łong-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-

TABLE 1.– *Physical characteristics and pulmonary function testing in patients with amyotrophic lateral sclerosis (ALS) and Duchenne muscular dystrophy (DMD)*

Characteristics	ALS	DMD	p value
Sex M / F	21/15	34/0	--
Age (years)	57 ± 12	14 ± 5	0.001
Weight (kg)	64.2 ± 14.5	43.4 ± 16.4	0.001
Height (cm)	169.0 ± 9.5	146.5 ± 19.2	0.001
FVC (liters)	2.01 ± 0.90	1.62 ± 0.63	0.059
FVC (% predicted values)	50.8 ± 21.7	45.9 ± 19.4	0.345
PF (liters/min)	228.5 ± 113.7	212.6 ± 62.8	0.981
PF (% of predicted values)	43.4 ± 19.9	55.1 ± 16.9	0.483
MIP (cmH_2O)	45.1 ± 20.7	61.2 ± 16.9	0.001
MIP (% predicted values)	52.6 ± 24.4	46.7 ± 12.0	0.497
MEP (cmH_2O)	54.3 ± 28.7	62.9 ± 21.5	0.175
MEP (% predicted values)	51.6 ± 27.3	36.6 ± 12.00	0.061

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

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

Variable	ALS	DMD	p value
BMI (kg/cm^2)	22.4 ± 4.3	19.9 ± 5.1	0.048
CHI%	59.8 ± 22.2	31.4 ± 21.9	0.001
ZMM%	118.8 ± 27.0	152.9 ± 43.9	0.001

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*

Relations		Equations	r	p value	Pw alpha
DMD	BMI vs. ZMM%	ZMM% = -6.362 + (8.064 * BMI)	0.972	< 0.001	1.000
	BMI vs. CHI%	CHI% = 23.002 + (0.402 * BMI)	0.091	0.613	0.072
ALS	BMI vs. ZMM%	ZMM% = -2.988 + (5.444 * BMI)	0.858	< 0.001	1.000
	BMI vs. CHI%	CHI% = 0.309 + (2.663 * BMI)	0.460	< 0.007	0.778

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

nificant and weak positive linear relationship ($r = 0.458$, $p < 0.007$).

No correlation between CHI% and BMI was observed in either of the two groups of patients (Fig. 1A). The 53% of ALS and 22% of DMD patients were located inside the three quadrants of diagnostic agreement between ZMM % and BMI method (Fig. 1B).

Correlation coefficients and equations of nutritional (BMI, ZMM%, and CHI%) and respiratory (FVC%, MIP%, and MEP%) parameters in ALS and DMD patients are displayed in Table 4. There was a weak positive linear relationship between BMI and the respiratory variables in ALS patients. Regarding DMD patients, we did not find a significant correlation between BMI and any respiratory variable. In both groups of patients, the ZMM% index did not correlate with any respiratory variable. The CHI% showed the strongest ($r > 0.7$) positive linear relationship with MIP%, MEP%, and FVC% in both ALS and DMD patients (Table 4).

The regression lines and their 95% confidence intervals for nutritional and respiratory variables are shown in Figures 2 (ALS group) and 3 (DMD group). Regarding the significant relationships (Table 4), the best reliability of the estimation procedure (95% confidence interval of the regression line) was for CHI%.

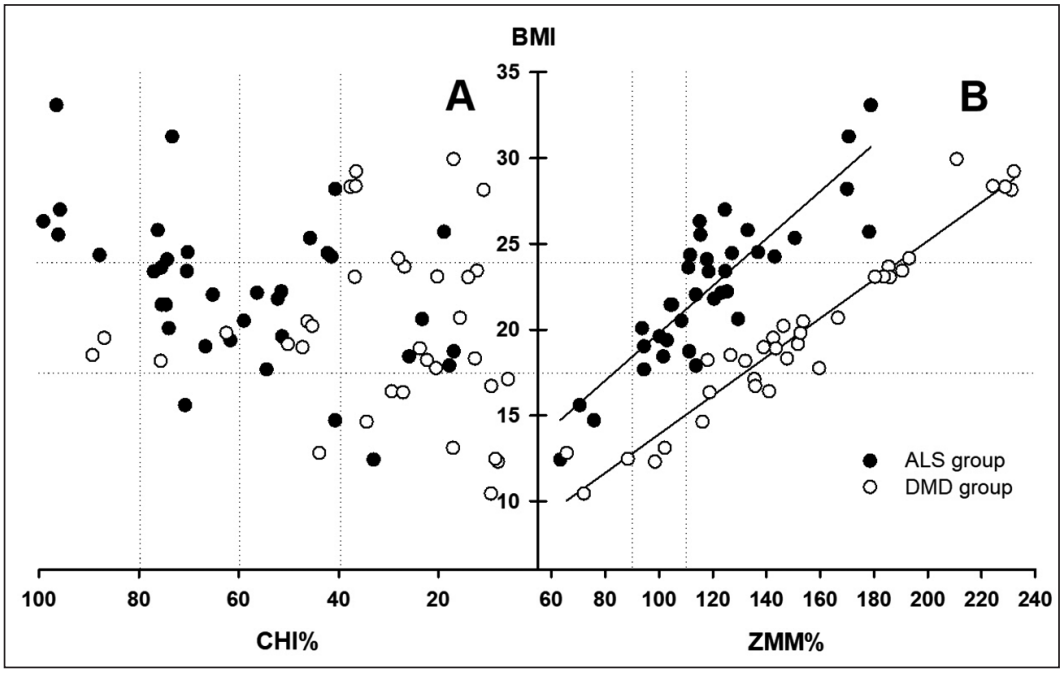
The relationship between PCF and CHI% is shown in Figure 4. In both groups, the CHI% showed the strongest ($r > 0.7$) positive relationship with the PCF. In the ALS group, there was a moderate positive linear relationship between BMI and PCF (0.571, $p < 0.001$). In both groups of patients, the ZMM% 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 variables in the ALS group but not in the DMD group, while the ZMM% did not correlate with any respiratory function parameters.

Neuromuscular diseases represent a heterogeneous group of acquired or inherited conditions. The nutritional approach is complicated for these patients[6,20]. Patterns of global nutritional parameters[21], anthropometric

Fig. 1.– Nutritional status concordance diagram for body mass index, expected weight for zero muscle mass and creatinine-height index



Left panel A: the relationship between creatinine-height index and body mass index. Right panel B: the relation between zero muscle mass and body mass index. Closed circles, amyotrophic lateral sclerosis (ALS) patients; open circles, Duchenne muscular dystrophy (DMD) patients. It can be observed in both ALS and DMD patients with a strong uphill (positive) linear relationship between body mass index and zero muscle mass. Most of the patients with DMD dystrophy were located outside the quadrants of concordance.

TABLE 4.– *Correlation coefficients of nutritional and respiratory parameters in Duchenne muscular dystrophy (DMD) and amyotrophic lateral sclerosis (ALS) patients*

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

*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*

measures[11], compartmental muscle mass[8], truncal fat distribution[12], and total body fat depend on such NMD, years of evolution, steroid therapy[22] and perhaps dietary interventions[23].

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

body composition, can be problematic[5, 24]. Our present results confirm significant differences between nutritional status diagnoses in DMD patients[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.

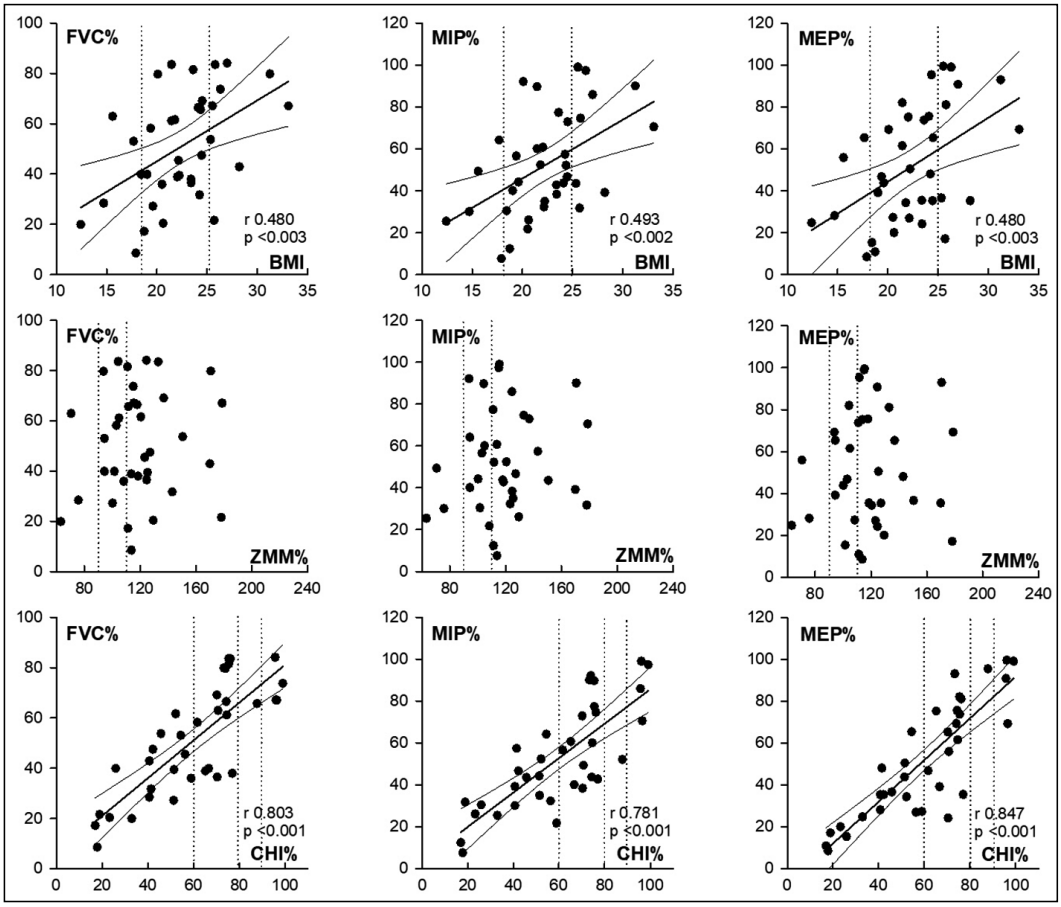
Our DMD group showed a more significant body fat (Table 2). Other authors have addressed body fat's significant influence upon BMI[12,23]. A child with pronounced muscle wasting can look cachectic, despite having excessive soft-tissue body fat[22]. Our study suggests that DMD subjects, who look like normal BMI, from the compartmental approach, seem probably obese. Both in ALS and DMD patients, BMI correlated positively with ZMM%. Interesting, 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[25].

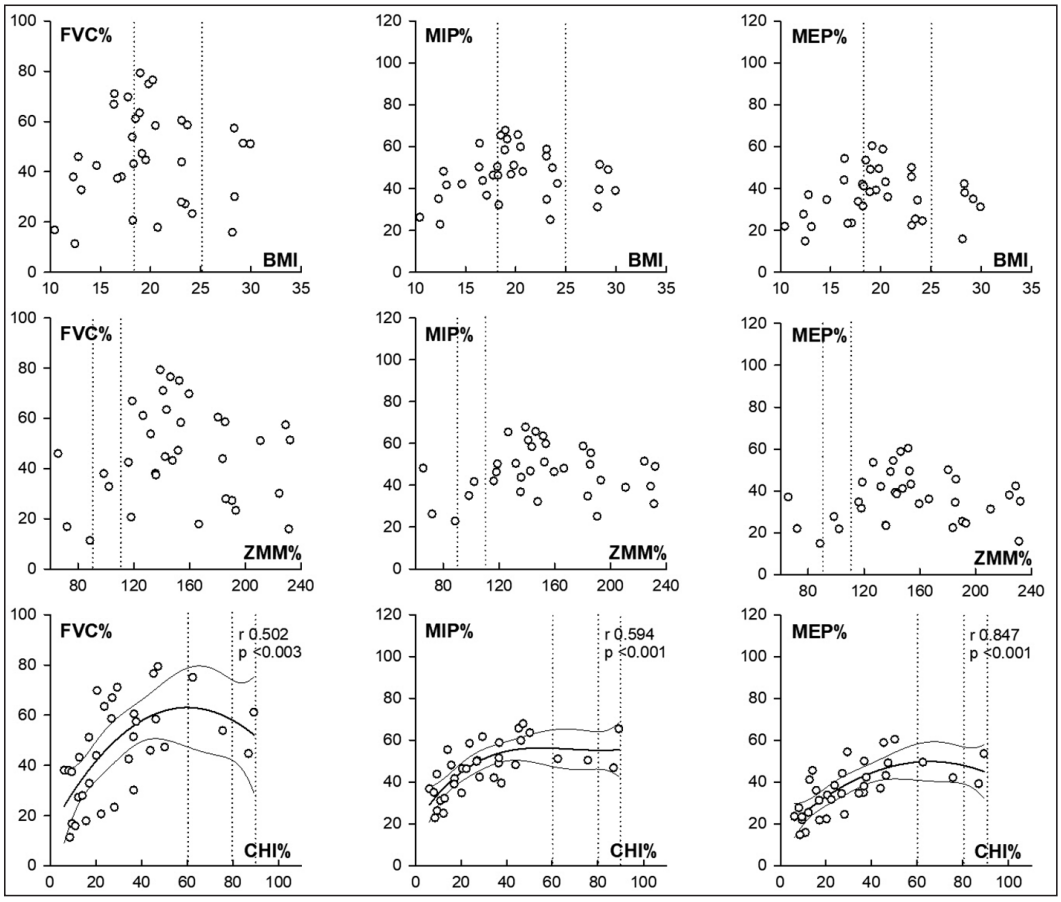
The combined assessment of the nutritional and respiratory status in NMD, in theory, could depend on the nutritional approach performed. BMI correlated well with all respiratory variables only in the ALS group (Table 4). Perhaps the higher proportion of total body fat in DMD subjects precludes the BMI 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



Regression lines for body mass index (BMI), expected weight for zero muscle mass (ZMM), creatinine-height index (CHI) and forced vital capacity (FVC), maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP). The regression line is the middle line, and the lower and higher lines are the upper and lower bounds of the 95% confidence interval of the slope

Fig. 3.– Nutritional and respiratory variables in the Duchenne muscular dystrophy (DMD) group



Regression lines for body mass index (BMI), expected weight for zero muscle mass (ZMM), creatinine-height index (CHI) and forced vital capacity (FVC), maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP). The regression line is the middle line, and the lower and higher lines are the upper and lower bounds of the 95% confidence interval of the slope.

Vincken et al. studied patients with a stable chronic and clinically heterogeneous NMD not presenting with respiratory symptoms[10]. BMI did not correlate with respiratory muscle strength in their patients.

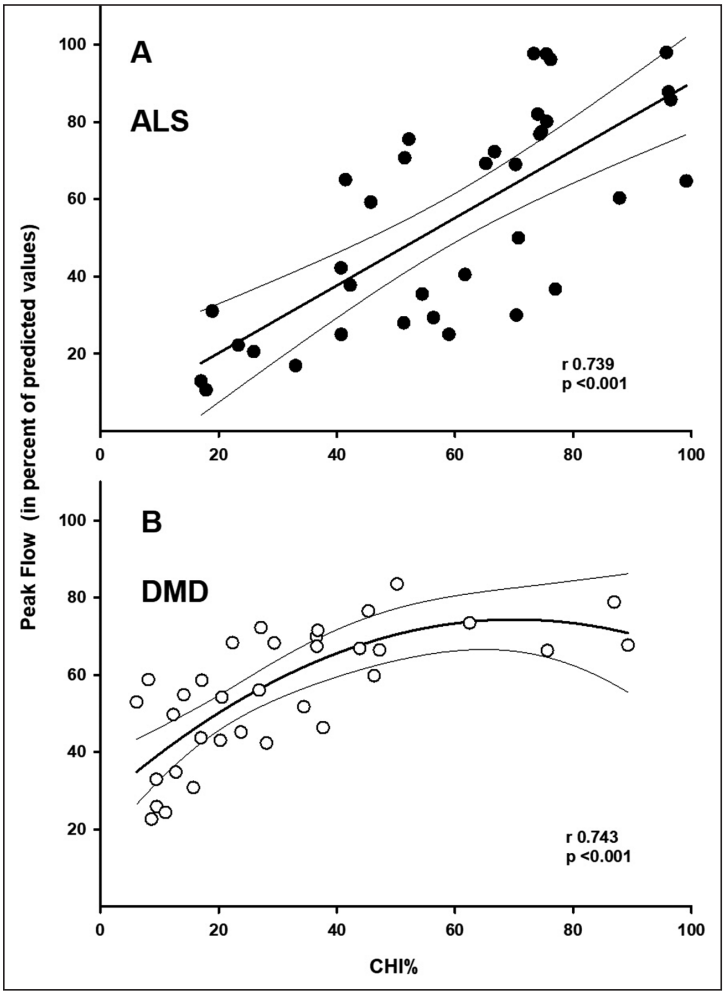
In patients with ALS, Silva et al. found that BMI correlated significantly with both muscle area and fat area of the arm and respiratory parameters[11]. Similarly to Vincken et al, the BMI did not correlate with muscle strength. It is an expected fact (at least in the DMD group) because it is a determination 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[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[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

Fig. 4.– Relationship between creatinine-height index and peak cough flow in amyotrophic lateral sclerosis, ALS, (A), and Duchenne muscular dystrophy, DMD, (B) group



The regression line is the middle line, and the lower and higher lines are the upper and lower bounds of the 95% confidence interval of the slope

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[26]. 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[27]. 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[3,5,7,8].

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[28,29]. 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.

Acknowledgements: The authors want to thank their co-worker and colleague Fernando Augusto Pessolano for his contributions. He passed away in total commitment to his tasks.

Conflict of Interest: None to declare

References

1. Park Y, Park J, Kim Y, Baek H, Kim SH. Association between nutritional status and disease severity using the amyotrophic lateral sclerosis (ALS) functional rating scale in ALS patients. *Nutrition* 2015; 31: 1362-7.
2. Jeronimo G, Nozoe KT, Polesel DN, Moreira GA, Tufik S, Andersen ML. Impact of corticotherapy, nutrition, and sleep disorder on quality of life of patients with Duchenne muscular dystrophy. *Nutrition* 2016; 32:391-3.
3. Birnkrant DJ, Bushby K, Bann CM, et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and neuromuscular, rehabilitation, endocrine, and gastrointestinal and nutritional management. *Lancet Neurol* 2018; 17: 251-67.
4. Greenwood DI. Nutrition management of amyotrophic lateral sclerosis. *Nutr Clin Pract* 2013; 28: 392-9.
5. McDonald CM, Carter GT, Abresch RT, et al. Body composition and water compartment measurements in boys with Duchenne muscular dystrophy. *Am J Phys Med Rehabil* 2005; 84: 483-91.
6. Liusuwan A, Widman L, Abresch RT, McDonald CM. Altered body composition affects resting energy expenditure and interpretation of body mass index in children with spinal cord injury. *J Spinal Cord Med* 2004; 27 Suppl 1: S24-8.
7. Willig TN, Carlier L, Legrand M, Rivière H, Navarro J. Nutritional Assessment in Duchenne muscular Dystrophy. *Dev Med Child Neurol* 2008; 35: 1074-82.
8. Pessolano FA, Súarez AA, Monteiro SG, et al. Nutritional assessment of patients with neuromuscular diseases. *Am J Phys Med Rehabil* 2003; 82: 182-5.
9. Griffiths RD, Edwards RH. A new chart for weight control in Duchenne muscular dystrophy. *Arch Dis Child* 1988; 63: 1256-8.
10. Vincken W, Elleker MG, Cosio MG. Determinants of respiratory muscle weakness in stable chronic neuromuscular disorders. *Am J Med* 1987; 82: 53-8.
11. Silva LB de C, Mourão LF, Silva AA, et al. Amyotrophic lateral sclerosis: combined nutritional, respiratory and functional assessment. *Arq Neuropsiquiatr* 2008; 66: 354-9.
12. Canapari CA, Barrowman N, Hoey L, et al. Truncal fat distribution correlates with decreased vital capacity in Duchenne muscular dystrophy. *Pediatr Pulmonol* 2015; 50: 63-70.
13. Chew K, Carey K, Ho G, Mallitt K-A, Widger J, Farrar M. The relationship of body habitus and respiratory function in Duchenne muscular dystrophy. *Respir Med* 2016; 119: 35-40.
14. Brooks BR, Miller RG, Swash M, Munsat TL. El Escorial revisited: revised criteria for the diagnosis of amyotrophic lateral sclerosis. *Amyotroph Lateral Scler Other Motor Neuron Disord* 2000; 1: 293-9.
15. Vignos PJ, Spencer Jr GE, Archibald KC. Management of progressive muscular dystrophy of childhood. *JAMA* 1963; 184: 89-96.
16. Gibson RS. Anthropometric assessment of growth. In: Principles of Nutritional Assessment. *New York, Oxford University Press* 1990, p 163-85.
17. Slowie LA, Paige MS, Antel JP. Nutritional considerations in the management of patients with amyotrophic lateral sclerosis (ALS). *J Am Diet Assoc* 1983; 83: 44-7.
18. Evans JA, Whitelaw WA. The assessment of maximal respiratory mouth pressures in adults. *Respir Care* 2009; 54:1348-59.
19. Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general U.S. population. *Am J Respir Crit Care Med* 1999; 159: 179-87.
20. Davis J, Samuels E, Mullins L. Nutrition considerations in Duchenne muscular dystrophy. *Nutr Clin Pract* 2015; 30: 511-21.
21. Skalsky AJ, Han JJ, Abresch RT, Shin CS, McDonald CM. Assessment of regional body composition with dual-energy X-ray absorptiometry in Duchenne muscular dystrophy: correlation of regional lean mass and quantitative strength. *Muscle Nerve* 2009; 39: 647-51.
22. Davidson ZE, Ryan MM, Kornberg AJ, et al. Observations

of body mass index in Duchenne muscular dystrophy: a longitudinal study. *Eur J Clin Nutr* 2014; 68: 892-7.
23. Davidson ZE, Billich NK. Are boys with Duchenne muscular dystrophy eating more than they need to? Maybe. *Muscle Nerve* 2019; 59: 277-9.
24. Gonzalez-Bermejo J, Lofaso F, Falaize L, et al. Resting energy expenditure in Duchenne patients using home mechanical ventilation. *Eur Respir J* 2005; 25: 682-7.
25. Choi Y-A, Shin H-I, Shin HI. Scoliosis in Duchenne muscular dystrophy children is fully reducible in the initial stage, and becomes structural over time. *BMC Musculoskelet Disord* 2019; 20: 277.
26. Suárez AA, Pessolano FA, Monteiro SG, et al Peak flow and peak cough flow in the evaluation of expiratory muscle weakness and bulbar impairment in patients with neuromuscular disease. *Am J Phys Med Rehabil* 2002; 81: 506-11.
27. Bach JR, Gonçalves MR, Hon A, et al. Changing trends in the management of end-stage neuromuscular respiratory muscle failure: recommendations of an international consensus. *Am J Phys Med Rehabil* 2013; 92: 267-77.
28. Gerber LM, Mann SJ. Development of a model to estimate 24-hour urinary creatinine excretion. *J Clin Hypertens (Greenwich)* 2014; 16: 367-71.
29. Mann SJ, Gerber LM. Addressing the problem of inaccuracy of measured 24-hour urine collections due to incomplete collection. *J Clin Hypertens (Greenwich)* 2019; 21: 1626-34.