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# Nutritional status, swallowing disorders, and respiratory prognosis in adult Duchenne muscular dystrophy patients

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## Abstract

Malnutrition and swallowing disorders are common in Duchenne muscular dystrophy (DMD) patients. We assessed, in adult DMD with home mechanical ventilation (HMV) and cough assist device, its prevalence and the relationships with respiratory muscle strength and long-term respiratory prognosis. We reviewed the patients ( $n = 117$ , age 18–39 years [median 24]), followed in a reference center, from 2006 to 2015, to obtain clinical baseline, nutritional status, vital capacity (VC), maximal inspiratory pressure (MIP), and maximal expiratory pressure (MEP). The median body mass index (BMI) was low ( $15.6 \text{ kg/m}^2$ ). Included patients had severe restrictive respiratory function with a median VC of 10.5% [7–17] of the predicted value. All patients were on HMV. Prevalence of malnutrition, swallowing disorders, and gastrostomy were respectively 62%, 34%, and 11%. BMI and serum albumin

level were significantly associated with MIP, MEP, and VC. The 1-year/5-years cumulative incidences of respiratory events (pulmonary sepsis and acute respiratory distress) were, respectively, 20.7%/44.5%. Using univariate analysis, predictive factors for respiratory events were swallowing disorders ( $p = .001$ ), transthyretinemia ( $p = .034$ ), MIP ( $p = .039$ ), and MEP ( $p = .03$ ) but not BMI or albuminemia. Using multivariate analysis, only swallowing disorders remained significantly associated with respiratory events (OR = 4.2, IC 95% 1.31–12.2,  $p = .01$ ). In conclusion, this study highlights the interrelationships between nutritional intake, swallowing function, airway clearance, and respiratory function in adult DMD. A multidisciplinary approach focusing on these previous factors is essential to optimize DMD patient health.

#### KEYWORDS

albumin, Duchenne muscular dystrophy, home mechanical ventilation, malnutrition, prognosis

## 1 | INTRODUCTION

Duchenne muscular dystrophy (DMD) is a rare inherited myogenic disorder due to mutations in the dystrophin gene on chromosome Xp21.1, affecting male patients. Respiratory muscle weakness, as well as dilated cardiomyopathy are frequent in this disease.<sup>1–3</sup> Respiratory impairment exposes patients to pneumonia, acute respiratory failure, and mortality.<sup>3–5</sup> Currently, with home mechanical ventilation (HMV) and cough assist devices, survival has improved in adult DMD.<sup>6–8</sup> However, nutritional status is a common clinical challenge in patients with chronic respiratory insufficiency, particularly in adult DMD patients, due to disability, macroglossia, dysphagia, and swallowing disorders.<sup>9–14</sup> Albumin level has been reported to be associated with respiratory function and is a reliable prognostic factor in hospitalized patients.<sup>15,16</sup>

Robust evidence-based nutrition research specific to DMD is lacking. Particularly, little is known about nutritional status, its relationship with respiratory function, and long-term respiratory morbidity in DMD in the area of HMV. We designed this study to determine the prevalence of malnutrition, the prevalence of swallowing disorders, the association between nutritional status and respiratory muscle strength, and the long-term respiratory morbidity in adult DMD patients on HMV.

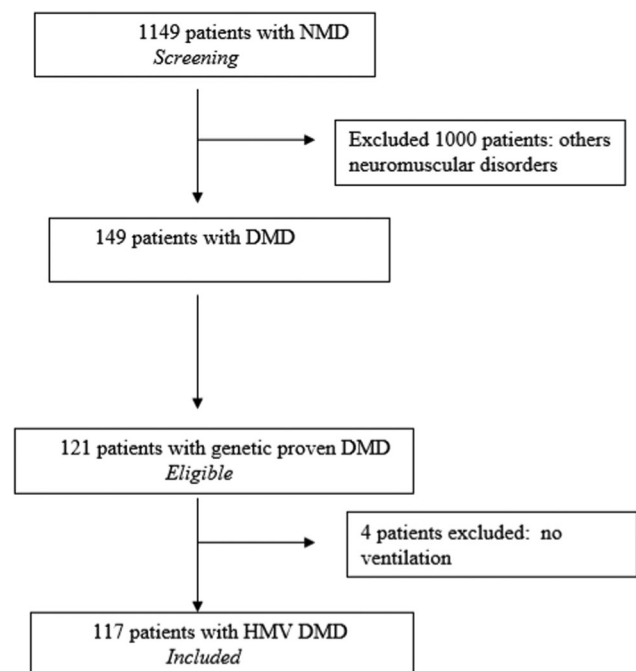
## 2 | METHODS

### 2.1 | Study design

We retrospectively reviewed the charts of all adult DMD patients followed at Raymond Poincaré University Hospital (University Paris Saclay, Garches, France), a tertiary neuromuscular center (CRMR: *centre de référence des maladies rares*, i.e., rare disease reference center), from 2006 to 2015. From the adult DMD population with

genetically proven DMD,<sup>17</sup> we included patients who have chronic respiratory insufficiency treated by noninvasive HMV. Figure 1 represents the flow chart of patients.

The initial visit in the unit, which includes a cardiac and respiratory functional assessment and a nutritional assessment (BMI, serum albumin, and transthyretin levels), was the baseline for the present study. From the medical records, for each patient, we collected clinical baseline, presence of swallowing disorders—by video endoscopic evaluation of deglutition function and Pharyngeal



**FIGURE 1** Flow chart diagram. DMD, Duchenne muscular dystrophy; HMV, home mechanical ventilation; NMD, neuromuscular disorders

Residue Severity Rating Scale score (Yale Pharyngeal Residue Severity Rating Scale),<sup>18</sup> presence of gastrostomy (percutaneous endoscopic gastrostomy or radiologically inserted gastrostomy), body mass index (BMI) calculation, serum prealbumin (transthyretin), serum albumin and C-reactive protein (CRP). In addition, pulmonary forced vital capacity (VC), maximal inspiratory pressure (MIP), maximal expiratory pressure (MEP), peak cough flow (PCF), and respiratory outcomes data were collected. As markers of efficiency of HMV, from the routinely performed morning daytime arterial or arterialized capillary blood gases, we recorded diurnal carbon dioxide tension (pCO<sub>2</sub>), base excess, and bicarbonates. In addition, we recorded the results of nocturnal oximetry, performed with a Covidien Nellcor oximeter (percentage of sleep time with oxygen saturation SaO<sub>2</sub> < 90%).

Patients remain in a wheelchair during periods of food intake or enteral nutrition. Patients who still received nutrition *per os* received adapted food, with a change in the texture (smooth or liquid, oral nutritional supplements), with caution. Management of patients with swallowing disorders includes a dietician involved in health practice for DMD patients and an orthophonist.<sup>19</sup> We noted the following parameters as acute respiratory events during the follow-up for this study: pulmonary sepsis, acute respiratory distress, pneumothorax, atelectasis, and the onset of tracheostomy procedure for invasive ventilation during follow-up. The study was performed in compliance with the ethical principles formulated in the declaration of Helsinki and was approved by the *Comité de Protection des Personnes* and the *Commission Nationale de l'Informatique et des Libertés*. The study was registered on [ClinicalTrials.gov](https://clinicaltrials.gov) (NCT02501083).

## 2.2 | Malnutrition and severe malnutrition definition

Patients were classified at the baseline in the group malnutrition in case of BMI < 20 kg/m<sup>2</sup> and/or serum albumin < 35 g/dl. Patients were classified in the group severe malnutrition in case of BMI < 18.5 kg/m<sup>2</sup> and/or albumin < 30 g/dl. For BMI as phenotypic criteria, we used the recent GLIM (Global Leadership Initiative on Malnutrition) criteria.<sup>20</sup> The criteria reduced muscle mass was not available due to the absence of measurement by a validated technic of body composition but all patients had severe reduction of muscle function, due to myopathy, and the criteria of sarcopenia were not considered for the diagnosis of malnutrition. All patients had CRP in the normal range at the baseline. All patients had the GLIM etiologic criteria, that is, DMD.

## 2.3 | Respiratory function and respiratory muscle strength

At baseline, pulmonary function tests were performed according to the ATS/ERS recommendations,<sup>21,22</sup> using a *Vmax 229 Sensormedics System* in the upright position. Forced pulmonary vital capacity (VC)

was also measured in the supine position. Measurements are expressed as a percent of predicted values.

Maximal sniff nasal inspiratory pressure (Psnip) and maximal inspiratory pressure (MIP) were measured from the functional residual capacity (FRC) in the upright position. Maximal expiratory pressure (MEP) was measured at total lung capacity (TLC). For each technique, the best value was recorded.<sup>22</sup> MIP and MEP were also expressed in the percentage of the estimated lower limit.<sup>22</sup> Peak-cough-flow (PCF) was measured with an appropriately fitted facemask (*Leadal Medical*) instead of a mouthpiece, placed around the mouth to allow mouth opening and reduce cheek compliance. Care was taken to avoid leaks around the mask. Patients were asked to cough as hard as possible, and the highest PCF obtained from three cough maneuvers, within 10% of the maximal value, was recorded. PCF cut-off values of 270 and 160 L/min were used to indicate cough disorders, as they are considered as indicative of, respectively, respiratory failure risk during respiratory tract infection and inability to clear airway successfully.<sup>23</sup>

MIP was measured using a flanged mouthpiece with the maneuvers repeated at least three times or until two identical readings were obtained. Once the operator was satisfied, the maximum value of three maneuvers that varied by less than 20% was recorded.<sup>24</sup>

## 2.4 | Statistical analysis

Continuous variables were described by median ± interquartile range (IQR) and compared by Wilcoxon Rank Sum test. Dichotomous or categorical variables were described by number of subjects and percentage and compared by Fisher's exact test. The associations between respiratory continuous parameters were explored by the nonparametric Spearman's correlation coefficient. Univariate and multivariate logistic models allowed to estimate the strength of association based on the odds ratio (OR). Statistical analysis was performed using R® (<http://www.R-project.org/>). A *p* < .05 was considered as statistically significant.

## 3 | RESULTS

### 3.1 | Patient characteristics and prevalence of malnutrition at baseline

A total of 117 male patients were included in the study. Age ranged from 18 years to 39 years with a median of 24. All patients were wheelchair bound. The median age of ambulation loss was 10 years. All patients have a history of the previous arthrodesis. All patients were on home mechanical ventilation. A volumetric setting was used for ventilation. Median BMI was 15.6 kg/m<sup>2</sup> [12.2–20.6] and swallowing disorders were present in 34% of patients. Five patients were overweighted (BMI between 25 and 30 kg/m<sup>2</sup>) and one patient was obese (BMI at 32 kg/m<sup>2</sup>). Gastrostomy was present in 11% (*n* = 13) of patients. Prevalence of malnutrition and severe malnutrition were,

**TABLE 1** Characteristics of the studied HMV DMD population ( $n = 117$ ) at baseline

Parameters	N (%) or median [IQR]
Age (years)	24 [21; 28]
Weight (kg)	41 [32; 56.5]
BMI (kg/m <sup>2</sup> )	15.6 [12.2; 20.6]
Age at arthrodesis (year)	14 [13–15]
Malnutrition	73 (62%)
Severe malnutrition	49 (42%)
Swallowing disorders	37 (34%)
Gastrostomy	13 (11%)
Tracheostomy	56 (48%)
Transthyretin concentration (mg/dl)	0.24 [0.2; 0.27]
Serum albumin concentration (g/dl)	41 [39; 43]
CRP (mg/L)	3.6 [1.9; 8]
VC (% predicted)	10.5 [7; 17]
MIP (cmH <sub>2</sub> O)	15 [10; 25]
MEP (cmH <sub>2</sub> O)	12 [8; 20]
PCF (L/min)	147 [105–171]
Bicarb (mmol/L)	26 [23.75–28.8]
Diurnal PCO <sub>2</sub> (kPa)	5.4 [4.67–6.12]
Nocturnal SatO <sub>2</sub> < 90% (%)	0 [0–1]
Ventilation duration (h)	24 [10–24]

Note: Nocturnal SatO<sub>2</sub> < 90%: percentage of sleep time with oxygen saturation SatO<sub>2</sub> < 90%.

Abbreviations: Bicarb, bicarbonates; BMI, body mass index; CRP, C-reactive protein; DMD, Duchenne muscular dystrophy; h, hours; HMV, home mechanical ventilation; MEP, maximal expiratory pressure; MIP, maximal inspiratory pressure; PCF, peak cough flow; PCO<sub>2</sub>, diurnal carbon dioxide tension; SatO<sub>2</sub>, oxygen saturation; VC, pulmonary vital capacity; y, years.

respectively, 62% and 42%. It is to note that only 16% had transthyretinemia below the normal range (<0.2 mg/dl) and 9% albuminemia below the normal range (<35 g/L). CRP values were in the normal range, so there were no patients with chronic inflammation. Left ventricular ejection fraction (LVEF) was reduced with a median at 47% [40–55]. Fifty-five 90% of patients were treated with angiotensin-converting enzyme (ACE) inhibitors and beta-blockers were prescribed in 52% of patients. Patients were not on steroids in this cohort. HMV was efficient with a median diurnal PCO<sub>2</sub> at 5.4 kPa, a median diurnal excess basis at 0.25 mmol/L, and a median % of sleep time with nocturnal oxygen saturation <90% at 0 [0–1]. Baseline characteristics of the population are detailed in Table 1.

Figure 2 displays all the correlations between variables, exhibiting large associations between maximal pressures, then with Peak-cough-flow and PCO<sub>2</sub>.

### 3.2 | Respiratory function and respiratory muscle strength

Included patients had severe restrictive respiratory function with a median VC of 10.5% [7–17] of the predicted value. Respiratory muscle strength was severely affected with median MIP at 15 cmH<sub>2</sub>O [10–25] and median MEP at 12 cmH<sub>2</sub>O [8–20] (Table 1). The PCF was severely reduced with a median at 145 L/min [105–171].

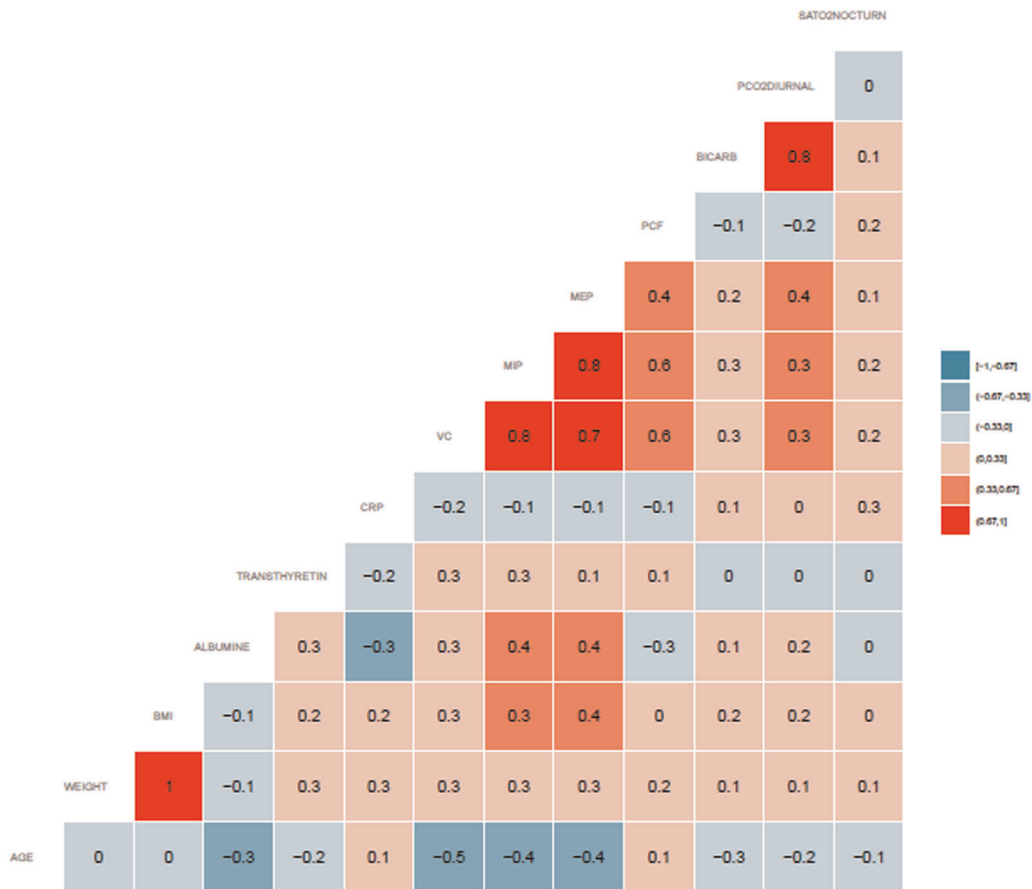
### 3.3 | Association between nutritional parameters and respiratory muscle strength

We found a significant association between serum albumin concentration and MIP ( $r = .43$ ,  $p < .0001$ ) and between serum albumin concentration and MEP ( $r = .36$ ,  $p = .00045$ ) (Figures 3 and 4). The PCF was not associated with serum albumin ( $p = .08$ ). The VC was significantly associated with serum albumin ( $r = .29$ ,  $p = .003$ ). VC, MIP, and MEP were also associated with BMI. Table 2 summarizes the association between nutritional parameters and respiratory function.

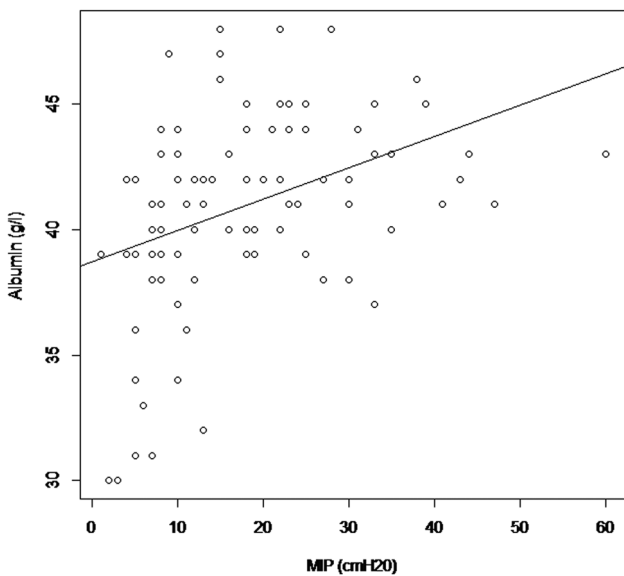
### 3.4 | Cumulative incidence of respiratory events and prognosis

One-year and 5-years cumulative incidence of respiratory events were, respectively, 20.7% [IC 95%: 13.3–28.2] and 44.5% [IC 95%: 34.6–54.3] (Figure 4; Kaplan–Meier method). Among events, pulmonary sepsis was the most frequent (56 patients, 48%) as well as acute respiratory distress (39 patients, 33%), and atelectasis (10.8%). Pneumothorax occurred in five patients. Invasive ventilation (ventilation using tracheostomy) was necessary in seven patients during the follow-up. Figure 5 (Kaplan–Meier method with log-rank test) represents the respiratory event-free survival in patients with swallowing disorders versus patients without swallowing disorders. During the follow-up, no patients were lost of view but 35 patients (29.9%) deceased. Among documented death, 40% were related to respiratory diseases and 60% were related to cardiac diseases (Figure 6).

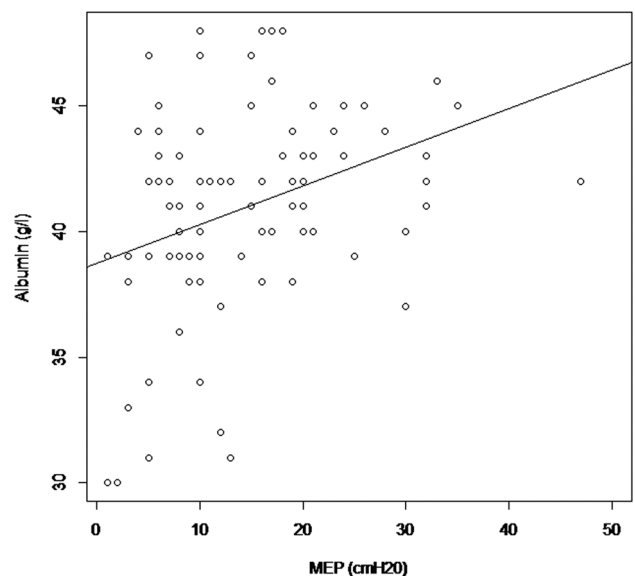
Additional gastrostomy was performed in eight patients during follow-up, because of severe malnutrition and/or swallowing disorders. All patients with additional gastrostomy experienced respiratory events during follow-up. Using univariate analysis, predictive factors for respiratory events were swallowing disorders ( $p = .001$ ), serum transthyretin concentration ( $p = .034$ ), serum albumin concentration ( $p = .057$ ), MIP ( $p = .039$ ), and MEP ( $p = .030$ ), but not presence of malnutrition even severe, BMI, or serum albumin concentration (Table 3). Using multivariate analysis, only swallowing disorders were associated with respiratory events (OR = 4.2, IC 95% 1.31–12.2;  $p = .01$ ).



**FIGURE 2** Matrix of correlations between variables. Bicarb, bicarbonates; BMI, body mass index; CRP, C-reactive protein; MEP, maximal expiratory pressure; MIP, maximal inspiratory pressure; PCF, peak cough flow; PCO<sub>2</sub>DIURNAL, diurnal carbon dioxide tension; SatO<sub>2</sub>NOCTURNAL, oxygen saturation nocturnal; VC, pulmonary vital capacity [Color figure can be viewed at wileyonlinelibrary.com]



**FIGURE 3** Relationship between serum albumin (g/L) and MIP (cmH<sub>2</sub>O) at baseline in the population of HMV DMD (*n* = 117). Spearman test *r* = 0.43 (*p* < .0001). DMD, Duchenne muscular dystrophy; HMV, home mechanical ventilation; MIP, maximal inspiratory pressure

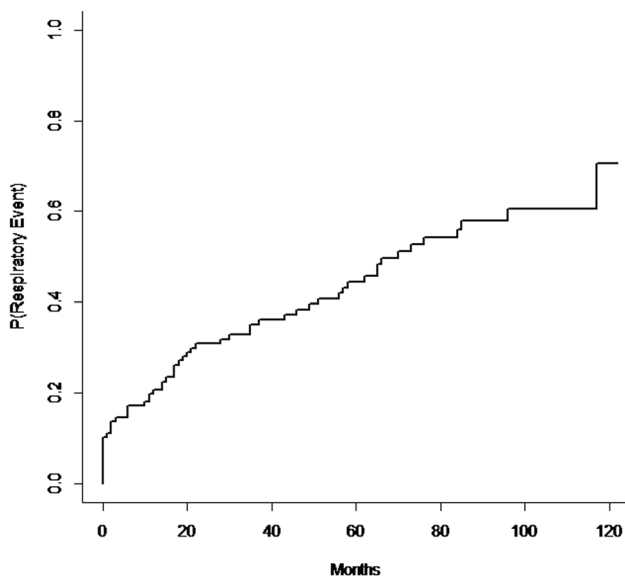


**FIGURE 4** Relationship between serum albumin (g/L) and MEP (cmH<sub>2</sub>O) at baseline in the population of HMV DMD (*n* = 117). Spearman test *r* = 0.36 (*p* = .00045). DMD, Duchenne muscular dystrophy; HMV, home mechanical ventilation; MEP, maximal expiratory pressure

**TABLE 2** Relationship between nutritional and respiratory function parameters at baseline in the 117 HMV DMD patients

	VC (%)	MIP (cmH <sub>2</sub> O)	MEP (cmH <sub>2</sub> O)
Serum albumin concentration (g/dl)	$p = .003$	$p < .0001$	$p = .00045$
	$r = .29$	$r = .43$	$r = .36$
Transthyretin concentration (mg/dl)	$p = .001$	$p = .003$	$p = .26$
	$r = .33$	$r = .33$	
BMI (kg/m <sup>2</sup> )	$p = .009$	$p = .001$	$p = .001$
	$r = .27$	$r = .35$	$r = .35$

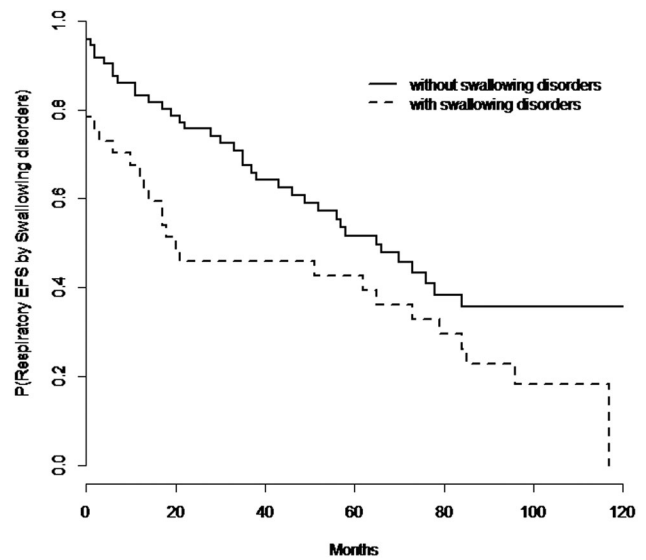
Abbreviations: BMI, body mass index; DMD, Duchenne muscular dystrophy; HMV, home mechanical ventilation; MEP, maximal expiratory pressure; MIP, maximal inspiratory pressure;  $r$ , Spearman coefficient correlation; VC, pulmonary vital capacity (predicted value).



**FIGURE 5** Cumulative incidence of respiratory events in the 117 DMD patients on HMV. DMD, Duchenne muscular dystrophy; HMV, home mechanical ventilation

## 4 | DISCUSSION

This study provides insights on nutritional status (BMI, serum albumin, and transthyretin concentrations) and long-term respiratory morbidity in adult DMD patients on HMV. The main findings of this study, with a large cohort of patients ( $n = 117$ ), not on steroids, is that (a) malnutrition (undernutrition) is frequent in adult DMD with a prevalence reaching 62% but is not per se a predictive factor of respiratory events, (b) respiratory muscle strength (evaluated by MIP and MEP) is associated with serum albumin concentration and BMI, (c) prevalence of swallowing disorders (evaluated by the presence of pharyngeal residues, defined as pre-swallow secretions and post-swallow food residue in the pharynx not entirely cleared by a swallow, as a clinical predictor of prandial aspiration) is high, reaching



**FIGURE 6** Event-free survival (EFS) in Duchenne muscular dystrophy (DMD) patients with swallowing disorders ( $n = 37$ ) versus DMD patients without swallowing disorders ( $n = 80$ );  $p = .001$

34%, and (d) respiratory morbidity is high, particularly in patients with swallowing disorders.

Upper airway muscle impairments have been reported in other neuromuscular disorders, particularly in amyotrophic lateral sclerosis (ALS) and affect prognosis.<sup>25</sup> Our data regarding the prevalence of malnutrition in adult DMD are similar to other studies reported in the pediatric literature, that is, 54% at about 18 years of age in the study by Willig et al.<sup>9</sup> Conversely, to young DMD patients who experienced high prevalence of obesity,<sup>23</sup> adult DMD disclosed weight loss and malnutrition<sup>9</sup> with its specific risks such as decubitus bedsores. In this cohort, only one adult DMD patient was obese and an overweight status was present in only five adult DMD patients. No patients were on steroids, which may influence the BMI distribution of the sample and impacts clinical applicability in places, such as the United States where steroids are standard practice.

In DMD, the presence of chronic respiratory failure in the late stage may increase energy expenditure, but is not the case in all situations.<sup>26</sup> Malnutrition may result from a reduction of food intake and/or an increase of energy expenditure. In DMD, weight loss is caused mainly by a negative energy and protein balance, in relation to a reduction in dietary intake. In DMD, reduced food intake is in relation with oral muscle weakness and dysphagia, swallowing disorders, reduced chewing, prolonged mealtime, and respiratory muscle weakness.<sup>27</sup> It is important to note that diagnosis of malnutrition is not easy in adult DMD. In this study, in the absence of body composition measurement and with a disease-related severe impairment of muscle function, we used the GLIM criteria<sup>20</sup> with additional data, like serum albumin as a prognostic indicator (as albumin is not sensitive for the diagnosis of undernutrition).

The prevalence of swallowing disorders, in adult DMD, is high, that is, 34% in this study. Usually, the swallowing process is characterized by a brief apnea followed by expiration, delaying the next

**TABLE 3** Parameters associated with respiratory events in the follow-up of the cohort of 117 HMV DMD patients

Parameters	No respiratory events (N = 59)	Respiratory events (N = 58)	p value	OR (95% IC)
Age (years)	24 [22; 27.5]	25 [21; 28.7]	.49	1.02 (0.96–1.10)
Weight (kg)	42.5 [35.5; 59]	39.5 [32; 53]	.13	0.98 (0.96–1.01)
BMI (kg/m <sup>2</sup> )	15.9 [13.2; 21.3]	15.2 [12; 20]	.30	0.96 (0.89–1.04)
Malnutrition	35 (59%)	38 (65.5%)	.49	1.3 (0.62–2.76)
Severe malnutrition	24 (41%)	25 (43%)	.79	1.1 (0.53–2.3)
Serum albumin (g/L)	42 [39; 44]	40 [38; 42]	.057	0.91 (0.82–1.00)
Transthyretin (mg/dl)	0.25 [0.22; 0.28]	0.23 [0.2; 0.26]	.034	0.00 (0.00–0.48)
CRP (mg/L)	3.2 [2; 5.4]	4.7 [1.7; 10.3]	.67	1.01 (0.96–1.06)
Swallowing disorders	10 (18.5%)	27 (49%)	.001	4.24 (1.78–10.1)
Gastrostomy	6 (10%)	7 (12%)	.80	1.17 (0.33–4.13)
Tracheostomy	24 (41%)	32 (55%)	.14	1.74 (0.84–3.64)
VC (%predicted)	13 [8; 21.5]	10 [6; 16]	.07	0.97 (0.93–1.00)
MIP (cmH <sub>2</sub> O)	18 [10; 27]	12 [7; 20]	.039	0.96 (0.93–1.00)
MEP (cmH <sub>2</sub> O)	13.5 [9; 21.5]	11 [8; 17]	.030	0.95 (0.90–0.99)
PCF (L/s)	2.49 [1.75; 2.96]	2.38 [1.84; 2.67]	.58	0.81 (0.39–1.69)
Bicarb (mmol/L)	26 [24.25; 28.6]	26 [23.6; 29.1]	.79	1.01 (0.92–1.12)
PCO <sub>2</sub> (kPa)	5.45 [4.7–6.18]	5.34 [4.33–6.06]	.27	0.82 (0.58–1.16)
Nocturnal SatO <sub>2</sub> < 90%	0.2 [0–1]	0 [0–1]	.31	1.04 (0.97–1.12)

Note: Values are expressed as median [interquartile range] or N, number (proportion). Nocturnal SatO<sub>2</sub> < 90%, percentage of sleep time with oxygen saturation SaO<sub>2</sub> < 90%.

Abbreviations: Bicarb, bicarbonates; BMI, body mass index; CRP, C-reactive protein; DMD, Duchenne muscular dystrophy; HMV, home mechanical ventilation; MEP, maximal expiratory pressure; MIP, maximal inspiratory pressure; PCF, peak cough flow; PCO<sub>2</sub>, diurnal carbon dioxide tension; SatO<sub>2</sub>, oxygen saturation; VC, pulmonary vital capacity.

respiratory cycle.<sup>27</sup> In DMD, this cycle is altered and Terzi et al.,<sup>28</sup> in a study that evaluated the swallowing-breathing interaction, reported frequent occurrences of inspiratory effort immediately after swallowing which may increase the risk of aspiration, particularly in the case of post-swallowing pharyngeal residue. HMV and cough assist devices have improved respiratory care and prognosis of patients with DMD.<sup>6–8</sup> However, the presence of swallowing disorders remains a major predictive factor for mortality<sup>29</sup> and morbidity, as underlined by our data (OR = 4.2 for acute respiratory events). This emphasizes the need for a multidisciplinary approach, including not only a respiratory care management but also a nutritional status and caloric intake evaluations with a dietician and a particular focus on swallowing disorders assessment with a swallowing therapist.

Since gastrostomy (endoscopic or radiologic) is indicated in DMD patients with swallowing disorders leading to infectious swallowing lung disease and malnutrition, according to the *DMD Care Considerations Working Group*,<sup>30</sup> an earlier gastrostomy may be discussed in selected DMD patients. The family and care team should consider gastrostomy tube placement to be a necessary and positive intervention when progressive weakness interferes with self-feeding and swallowing. Indications for gastrostomy tube placement include severe malnutrition that is unresponsive to interventions to improve

oral caloric intake, diagnosis of severe swallowing disorders, and inability to maintain adequate hydration. Assessment of the benefits of gastrostomy tube feeding should be discussed in the context of respiratory, cardiac, and anesthetic risks.<sup>30</sup> Enteral feeding by gastrostomy has been shown to improve nutritional status in adult DMD<sup>31</sup> and mechanical ventilation may improve swallowing function in patients with neuromuscular disorders.<sup>32</sup> Malnutrition may also alter immunologic responses. This feature increases the risk of pulmonary sepsis.<sup>33</sup> It is of note that in this study the prevalence of gastrostomy appears to be low (21 under 117 patients, i.e., 18%), due to the technical difficulties and delay of potential acceptance by patients and its family or care team. It is of note that in this study, all patients with a gastrostomy were maintained with an adapted (quantity and texture, liquid, or smooth) oral intake, in most situations for the quality of life.

This study highlights the significant relationship between malnutrition and respiratory function status. Indeed, a significant association was found between serum albumin and respiratory muscle strength. In addition, in DMD, the BMI has been reported to be associated with the respiratory function<sup>34</sup> and the regional lean mass is reduced and associated with decreased strength.<sup>35</sup> We found a significant association between nutritional parameters, namely



albumin, prealbumin (transthyretin) and BMI, and respiratory muscle strengths (MIP and MEP). In addition, malnutrition may affect diaphragm thickness and function.<sup>36</sup> Like a vicious circle, respiratory muscle failure may lead to a reduction of oral intake that inversely affects respiratory muscle strength. Recently, a group from Korea reported a relationship between the presence of eating disorders and the decrease of respiratory muscle strength in DMD.<sup>37</sup>

Swallowing function and respiratory function can track together or separately in DMD. In fact, a phenotypic discordance regarding cardiopulmonary function is common in DMD, reaching 34% in a recent study.<sup>38</sup> Swallowing function and respiratory function can be involved with a discordance phenotype. In our study, all patients were on home mechanical ventilation (bad respiratory function). We defined discordant respiratory–swallowing function as patients with bad lung function and good swallowing function. In this context, discordant respiratory–swallowing function was present in 66% of patients in our cohort. One explanation may be the presence of different isoforms in DMD.<sup>38</sup>

Nevertheless, our study has some limits. We do not have data for these patients on the possible reduction in weight and oral intake (of different causes like dysphagia, swallowing disorders, macroglossia) in the months before starting HMV and during the follow-up. This methodological aspect may misestimate nutritional status in DMD. We previously have shown that the food intake of these adult DMD patients on HMV was  $1.2 \pm 0.4$  greater than their resting energy expenditure.<sup>26</sup> Body composition may provide specific nutritional status evaluation of patients. Indeed, adult patients with DMD disclosed reduction in fat-free mass (bio-impedancemetry) and reduced resting energy expenditure (indirect calorimetry).<sup>26</sup> In DMD, body composition is characterized by a reduction of lean body mass and an increase of intramuscular fat mass.<sup>39</sup> In fact, patients with advanced forms of Duchenne muscular dystrophy have balanced energy intakes and resting energy expenditure.<sup>26</sup> In addition, serum albuminemia, as well as BMI, may underestimate nutritional status in DMD at the difference of body composition.<sup>40,41</sup> As albumin discloses a long half-time and reflects an index of chronic malnutrition; it can in fact be considered as a reliable global prognosis biomarker. It is important to note that in this study most, with the exception of 9%–16%, of patients had serum albumin—and transthyretin—in the normal usual range. This raises the question of the relevance of these protein biomarkers in DMD, a situation with a severe sarcopenia, as it is well known in anorexia nervosa for example. Finally, this study was mono-centric, but it is a rare disease followed in a tertiary reference center (CRMR: *centre de référence des maladies rares*, i.e., rare disease reference center), and retrospective and the results may be hampered by the recruitment specificities of a specialized unit.

## 5 | PERSPECTIVES

DMD is a neuromuscular disorder with a disability that affects not only the skeletal muscle system but also the respiratory muscles, and the swallowing function. These results highlight the need for a

multi-collaborative association in the management of these patients. Regular screening for swallowing disorders is necessary within addition a very regular nutritional status evaluation. It is possible that an analysis of body composition with a well-validated technique in this situation brings more prognosis information for these adult patients.

## 6 | CONCLUSION

This study highlights the interrelationships between nutritional intake, swallowing function, airway clearance, and respiratory function in adult DMD. A multidisciplinary approach focusing on these previous factors is essential to optimize DMD patient health.

### CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

### AUTHOR CONTRIBUTIONS

*Study design, practical performance, data collection, preparation of the manuscript:* Abdallah Fayssoil. *Data analysis:* Cendrine Chaffaut and Sylvie Chevret. *Practical performance, critical review of the manuscript:* Helene Prigent. *Practical performance, critical review of manuscript:* Pascal Laforet. *Practical performance:* Bernard Clair, Adam Ognà, and Paris Meng. *Practical performance, critical review of the manuscript:* David Orlikowski. *Study design, critical review of the manuscript:* Djillali Annane. *Study design, practical performance, critical review of the manuscript:* Frederic Lofaso. *Study design, preparation of the manuscript, critical review of the manuscript, the final form of the manuscript:* Pascal Crenn.

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