

Research Report

Age Related Burden of Swallowing in Adult Patients Affected by Duchenne Muscular Dystrophy

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Abstract.

Background: In Duchenne muscular dystrophy (DMD), dysphagia is a common but often overlooked symptom, which may affect quality of life (QoL). Its possible causes are progressive deterioration of muscle groups involved in swallowing function (oropharyngeal, inspiratory muscles) or impairment of autonomic function.

Objectives: In adult patients with DMD, we aimed to identify predictors of swallowing-related QoL and to compare swallowing-related QoL at different ages.

Methods: Forty-eight patients aged 30.0 ± 6.6 years were enrolled. Questionnaires were administered: the Swallowing Quality of Life questionnaire (SWAL-QOL) for swallowing-related QoL assessment, and the Compass 31 for autonomic symptoms assessment. The Brooke Upper Extremity Scale was used for upper limbs muscular function assessment. Respiratory and muscle function tests were performed, including spirometry, arterial blood gases, polysomnography, maximal inspiratory pressure (MIP), maximal expiratory pressure and sniff nasal inspiratory pressure.

Results: An abnormal composite SWAL-QOL score (≤ 86) was found in 33 patients. Autonomic symptoms were mild, while a severity impairment was shown by the Brooke Upper Extremity Scale. Spirometry and muscle strength tests demonstrated severe alterations, while diurnal and nocturnal blood gases were normal, due to effective use of noninvasive ventilation. Independent predictors of the composite SWAL-QOL score were age, MIP and Compass 31. A MIP < 22 had an accuracy of 92% in predicting altered swallowing-related QoL. The composite SWAL-QOL score was worse in subjects > 30 years old than in younger patients (64.5 ± 19.2 vs 76.6 ± 16.3 , $p < 0.02$), due to worse scores in items pertinent to mental and social functioning; scores in domains pertinent to the physical function were similar in both groups.

Conclusions: In adult DMD, swallowing-related QoL, which is altered in most patients, can be predicted by age, inspiratory muscles strength and autonomic dysfunction symptoms. While swallowing function is already altered in young patients, swallowing-related QoL can progressively worsen with advancing age due to psychological and social factors.

Keywords: Swallowing dysfunction, respiratory function, autonomic symptoms, quality of life, Duchenne muscular dystrophy

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INTRODUCTION

Duchenne muscular dystrophy (DMD) is a progressive disease due to absence of dystrophin, which involves striated and smooth muscles. Muscle dysfunction leads to several problems, including motor impairment, respiratory failure and loss of independence. In patients with DMD, quality of life (QoL) scales have shown variable degrees of satisfaction. Indeed, while motor impairment negatively affects well-being, the psycho-social sphere is often preserved [1–4]. However, other poorly considered factors may contribute to reduce QoL in this disease.

Dysphagia can be an important component of the symptomatology of patients with DMD, although it is often overlooked [5, 6]. In addition to swallowing disturbances, patients with DMD often complain symptoms of gastrointestinal dysfunction, such as gastric dilatation and intestinal pseudo-obstruction, [7–9].

In DMD, dysphagia is considered mainly a consequence of the impairment of oropharyngeal striated muscles function, which leads to slower and effortful bolus transportation [5]. Absence of dystrophin in gastro-intestinal smooth muscles and a dysfunction of the enteric autonomic nervous system may also contribute, as suggested by studies in mice models of DMD [10, 11]. Furthermore, altered autonomic control in the gastroenteric duct, which was demonstrated by the Compass 21 questionnaire [4], could also play a role. Some studies observed a relationship between swallowing performance and respiratory function, as assessed by common respiratory tests [12, 13], or by the severity of ventilator-dependence [14]. Since the alterations responsible for dysphagia in DMD worsen over time, it is conceivable that older DMD patients complain worse dysphagia symptoms, which may be associated to a deterioration of QoL.

To our knowledge, only one study evaluated how dysphagia impairs QoL in adult DMD patients [15]. In that study, the Sydney Swallow Questionnaire (SSQ) was used, which demonstrated to satisfactorily detect dysphagia in subjects with DMD. However, the study did not include patients older than 26. Today, thanks to current management methods, most patients affected by DMD can survive long beyond that age, so that there is a gap in our knowledge about QoL in older DMD patients. Besides, data from a recent review suggest that for the assessment of the impact of dysphagia on QoL the Swallowing Quality of Life questionnaire (SWAL-QOL) should be preferred over other tools. This indication was based on psychomet-

ric evaluation and clinical utility, including adherence to the WHO ICF framework [16]. The SWAL-QOL probes for the body function and structure across multiple stages of swallowing, such as oral, pharyngeal and esophageal [17, 18].

In this study, we administered the SWAL-QOL to adult patients with DMD. The aims were: 1) to describe swallowing-related QoL in this category of patients; 2) to identify potential independent predictors of its impairment; 3) to evaluate the functional impact of swallowing disorders on QoL at different ages.

PATIENTS AND METHODS

This was a prospective, cross-sectional study. We recruited consecutive adult patients with diagnosis of DMD, defined by clinical and genetic criteria, who came to the regional center for respiratory complications of neuromuscular diseases of Villa Sofia-Cervello hospital between 2017 and 2020 for a periodic follow-up evaluation. Criteria of inclusion were age ≥ 18 years and ability to perform a complete battery of tests of respiratory muscle strength. In all patients, dysphagia related QoL, as well as autonomic function impairment, were assessed by questionnaires. Questionnaires were self-administered or were answered with the help of a trained interviewer. Upper limb muscle function was assessed according to standard criteria. Finally, both diurnal and nocturnal respiratory function were evaluated. A clinician especially skilled in neuromuscular disorders was in charge of the functional assessment of the patients (GC). The study was approved by the local ethical committee (Palermo 2 verb 14, prot. amm.vo 325 AOR 05.10.2016) and all patients gave informed consent.

Dysphagia related quality of life assessment

The impact of dysphagia on QoL was evaluated by the SWAL-QOL questionnaire [19]. The first thirty items of the questionnaire are used to assess ten quality of life concepts, seven of which are dysphagia-related (food selection, burden, mental health, social functioning, fear, eating duration, eating desire) and three pertain to general QoL (communication, sleep and fatigue). The questions are intended to reflect experience within the preceding month and are scored on a 5-point Likert scale, which can be transformed to achieve scores ranging from 0 (least favorable state) to 100 (most favorable state). A

134 composite SWAL-QOL score can be derived by aver-
135 aging the ten scale scores. As a clinical cut-off score
136 to identify individuals with significantly altered QoL,
137 previous research suggested a decrease ≥ 14 points
138 from the maximum SWAL-QOL composite score
139 (100 points) [20]. The SWAL-QOL also includes a
140 symptom frequency battery of 14 questions (DSB,
141 dysphagia symptoms battery), which has been used
142 as an of index dysphagia status. Possible responses
143 range from 0 to 100, where 100 is the best score.
144 Responses to all items are averaged to obtain a mean
145 score.

146 The SWAL-QOL has been used in patients affected
147 by neuromuscular disease but no one of these
148 patients was affected by DMD [21]. Therefore, in
149 the patients of this study we tested its reliability with
150 the evaluation of internal consistency and test-retest
151 reproducibility when administered two weeks apart.
152 This period is considered adequately long to prevent
153 recall, but short enough to expect no clinical change
154 to occur [19]. No participant underwent a therapeutic
155 intervention for dysphagia either before or between
156 the questionnaire administrations.

157 *Autonomic symptoms assessment*

158 Autonomic symptoms were evaluated by the Com-
159 pass 31 questionnaire [22]. This is a self-assessment
160 instrument exploring six domains of autonomic
161 function: orthostatic intolerance, vasomotor, secre-
162 tomotor, gastrointestinal, bladder and pupillomotor
163 function. Altogether, the questionnaire consists of
164 31 items, 12 of which pertain to the gastrointesti-
165 nal domain. Score in the latter domain can range
166 between 0 and 24. The final Compass 31 score derives
167 from the sum of the scores of the six domains, and
168 can range between 0 and 100. Higher scores indicate
169 worse autonomic symptoms.

170 *Upper limbs muscular function assessment*

171 Muscular function of the upper limbs was eval-
172 uated by the Brooke Upper Extremity Scale. This
173 is a 6-point scale that allows classification of upper
174 extremity muscular function. One is the best score,
175 indicating that the patient is able to start with arms
176 at the sides and can abduct the arms in a full circle
177 until they touch above the head, while 6 corresponds
178 to the worst score, indicating inability to raise hands
179 to the mouth and absence of any useful function of
180 the hands [23].

181 *Respiratory function assessment*

182 Respiratory muscle strength was assessed by max-
183 imal static inspiratory pressure (MIP), maximal
184 expiratory pressure (MEP) and sniff nasal inspira-
185 tory pressure (SNIP). Prior to each test, participants
186 were given detailed instructions and a demonstra-
187 tion of the procedure by the examiner. MIP was
188 measured following maximal inspiration from resid-
189 ual volume. MEP was obtained through maximal
190 expiratory effort from total lung capacity. For both
191 measurements, the highest value obtained with three
192 acceptable manoeuvres from at least five attempts
193 was selected [24]. SNIP was evaluated according
194 to standardized methodology [25]. Spirometry was
195 performed in a sitting position with a flow meter
196 attached to a flanged rubber mouthpiece with the
197 nose occluded in accordance with American Thoracic
198 Society/ European Respiratory Society recommenda-
199 tions [26]. Arterial blood gases were measured early
200 in the morning in the supine position during admin-
201 istration of noninvasive ventilation (NIV).

202 To complete the follow-up evaluation, patients
203 were submitted to in-hospital nocturnal polysomnog-
204 raphy (PSG) (SomnoLab 2 AASM, Weinmann, Ham-
205 burg, Germany) with simultaneous transcutaneous
206 CO₂ (PtcCO₂) monitoring during administration of
207 NIV as previously prescribed [4]. Sleep was scored
208 according to AASM rules [27].

209 *Statistics*

210 Data are presented as mean \pm standard deviation,
211 or median (interquartile range). The Kolmogorov-
212 Smirnov test was used to test the data for normal
213 distribution.

214 Internal consistency of the SWAL-QOL was
215 determined by Cronbach's α coefficient. A coef-
216 ficient > 0.70 was taken as acceptable. Test-retest
217 reproducibility was assessed by intraclass correlation
218 coefficient (ICC) using a 2-way random effect model
219 with 95% confidence intervals (C.I.). An ICC > 0.70
220 indicated sufficient test-retest reproducibility.

221 Univariate correlations were analyzed using Pear-
222 son's correlation coefficient. To identify potential
223 independent predictors of the composite SWAL-
224 QOL score, a stepwise regression model was used.
225 In this regression, all variables that were corre-
226 lated with the composite score with a p -value < 0.10
227 were entered. The optimal cut-off value to pre-
228 dict an altered dysphagia-related QoL (composite
229 SWAL-QOL ≤ 86) and its diagnostic accuracy were

230 evaluated by receiver operating characteristics (ROC)
231 curve analysis.

232 The sample was divided according to age $< \geq 30$
233 years. Unpaired t-test and U-Mann-Whitney test were
234 used for comparisons between normally and non-
235 normally distributed data, respectively.

236 A $p < 0.05$ was considered significant. Statistical
237 analysis was performed using a commercial software
238 package (IBM SPSS v. 22 and MedCal v. 20.115).

239 RESULTS

240 Forty-eight subjects met the inclusion criteria. In
241 these patients, all items of the questionnaires were
242 completed without missing data. Mean age of the
243 patients was 30.0 ± 6.6 years. Body mass index was
244 $19.7 \pm 5.8 \text{ kg/m}^2$.

245 The average composite SWAL-QOL score in the
246 sample was 71.1 ± 18.5 . It was below the threshold of
247 86 in 33/48 patients. The mean DSB in the sample was
248 72.3 ± 19.6 . The Compass 31 score was 12.5 ± 10.5 ,
249 while gastrointestinal symptoms score was 5.8 ± 3.9 .
250 The Brooke UES score was 5.4 ± 0.5 .

251 Characteristics of muscular function, diurnal and
252 nocturnal respiratory function and sleep structure of
253 the patients are shown in Table 1. Twelve patients
254 used NIV only at night (≤ 12 hours/day), while the
255 remaining 36 patients used it also during the day (> 12
256 hours/day). All patients made use of a wheelchair and
257 of a cough assist device.

258 All participants completed the test-retest assess-
259 ment of the composite SWAL-QOL. The Cronbach's
260 α coefficient was 0.87 (95% lower CI 0.82) and ICC
261 was 0.99 (95% lower CI: 0.98), indicating good internal
262 consistency and reproducibility.

263 Table 2 shows univariate correlations between
264 the composite score of the SWAL-QOL and other
265 variables. Age, spirometry and respiratory muscle
266 function indices, as well as the Compass 31 score,
267 were significantly correlated to the composite SWAL-
268 QOL score, whereas arterial blood gases and PSG
269 indices were not.

270 Table 3 shows results of multiple regression with
271 the composite SWAL-QOL as dependent variable.
272 We identified MIP, age and Compass 31 as indepen-
273 dent predictors.

274 Figure 1 shows the ROC curve for MIP. A MIP
275 value $< 22 \text{ cmH}_2\text{O}$ was associated with the largest
276 AUC (0.917) with good sensitivity and specificity
277 (88.2% and 85.7% respectively).

Table 1
Respiratory function and sleep structure*

FVC (% predicted)	20.4 \pm 14.3
MIP (cmH ₂ O)	17.9 \pm 12.6
MEP (cmH ₂ O)	15.1 \pm 10.1
SNIP (cmH ₂ O)	21.0 \pm 11.1
PCF (L/min)	134.8 \pm 61.6
pH	7.40 \pm 0.04
PaO ₂ (mmHg)	93.4 \pm 18.7
PaCO ₂ (mmHg)	42.6 \pm 7.5
HCO ₃ ⁻ (mmol/L)	26.5 \pm 3.7
BE (mmol/L)	2.1 [0.2-4.3]
Mean SpO ₂ (%)	97.2 \pm 1.0
ODI (n/h)	0.2 [0.0-1.0]
Nadir (%)	88.8 \pm 3.2
T 90 (min)	0.0 [0.0-0.7]
mean nocturnal PtcCO ₂ (mmHg)	38.0 \pm 6.2
peak nocturnal PtcCO ₂ (mmHg)	44.4 \pm 5.3
TST (min)	349.4 \pm 68.4
SE (% time in bed)	73.6 \pm 14.5
SL (min)	36.1 \pm 24.6
WASO (min)	48.7 \pm 31.7
N1 (% TST)	15.5 \pm 8.4
N2 (% TST)	50.3 \pm 9.0
N3 (% TST)	17.6 \pm 7.8
R (% TST)	16.6 \pm 7.3
Arousals (n/h)	17.0 \pm 6.2

FVC, forced vital capacity; MIP, maximal inspiratory pressure; SNIP, sniff nasal pressure; MEP, maximal expiratory pressure; PCF, peak cough flow; PaO₂, arterial partial pressure of oxygen; PaCO₂, arterial partial pressure of CO₂; HCO₃⁻, bicarbonates; BE, base excess; SpO₂, pulse oxygen saturation; ODI, number of oxygen desaturation $\geq 3\%$ per hour of sleep; Nadir, lowest oxygen saturation; T90, time spent with oxygen saturation below 90%; PtcCO₂, transcutaneous PCO₂; TST, total sleep time; SE%, sleep efficiency; SL, sleep latency; WASO, wake after sleep onset; N1, NREM stage 1; N2, NREM stage 2; N3, NREM stage 3; R, REM stage. *Arterial blood gases and polysomnography were performed in 45 subjects.

278 Twenty-six patients were < 30 and 22 were ≥ 30
279 years old. Results of respiratory and muscular func-
280 tion tests were worse in the older subjects, but no
281 significant difference between groups was found in
282 arterial blood gases, PSG indices and autonomic
283 symptoms (Table S1). The composite SWAL-QOL
284 was worse in the older subjects. However, not all
285 items differed significantly between groups: eating
286 duration and food selection, that were already heavily
287 compromised in the younger subjects, marginally dif-
288 ferred between younger and older subjects, while other
289 items, especially burden and mental health, were sig-
290 nificantly worse in the older patients (Table 4).

291 Twenty-six of the 36 patients using NIV > 12 hours
292 applied NIV also during their meals. We re-evaluated
293 the composite SWAL-QOL and its predictors in the
294 22 patients who did not use NIV during mealtime

Table 2

Univariate correlations between composite SWAL-QOL score and other variables

	Composite score	<i>p</i>
Age	-0.50	0.0003
FVC (% predicted)	0.60	<0.0001
MIP (cmH ₂ O)	0.71	<0.0001
MEP (cmH ₂ O)	0.65	<0.0001
SNIP (cmH ₂ O)	0.44	0.006
PCF (L/min)	0.31	0.03
PaO ₂ (mmHg)	0.14	0.35
PCO ₂ mmHg	-0.20	0.17
HCO ₃ ⁻ (mmol/L)	-0.15	0.32
BE (mmol/L)	-0.15	0.31
Mean SpO ₂ (%)	0.20	0.18
ODI	0.14	0.34
Nadir (%)	-0.18	0.21
T90 (min)	0.23	0.12
mean nocturnal PtcCO ₂ mmHg	-0.31	0.03
peak nocturnal PtcCO ₂ mmHg	-0.16	0.26
TST (min)*	-0.11	0.46
SE (%)	-0.15	0.30
SL (min)	0.19	0.19
WASO (min)	-0.10	0.50
N1 (%)	0.11	0.46
N2 (%)	-0.15	0.29
N3 (%)	0.08	0.59
R (%)	-0.14	0.34
Arousals (n/h)	-0.17	0.25
Compass 31	-0.51	0.0002
Gastrointestinal domain	-0.36	0.01

FCV, forced vital capacity; MIP, maximal inspiratory pressure; SNIP, sniff nasal pressure; MEP, maximal expiratory pressure; PCF, peak cough flow; PaO₂, arterial partial pressure of oxygen; PaCO₂, arterial partial pressure of CO₂; HCO₃⁻, bicarbonates; BE, base excess; SpO₂, pulse oxygen saturation; ODI, number of oxygen desaturation $\geq 3\%$ per hour of sleep; Nadir, lowest oxygen saturation; T90, time spent with oxygen saturation below 90%; PtcCO₂, transcutaneous PCO₂; PtCO₂, transcutaneous PCO₂; TST, total sleep time; SE%, sleep efficiency; SL, sleep latency; WASO, wake after sleep onset; N1, NREM stage 1; N2 NREM stage2; N3, NREM stage 3; R, stage REM.

Table 3

Multiple regression for predictors of composite SWAL-QOL score

Independent variable	Coefficient	Std Error	t	<i>p</i>
(Constant)	89.1			
MIP	0.8006	0.1347	5.945	<0.0001
Age	-0.8712	0.2422	-3.597	0.0008
Compass 31	-0.5003	0.1569	-3.189	0.002

MIP, maximal inspiratory pressure.

to avoid the possible confounding effect of this therapy. As compared to patients using NIV during their meals, these patients were younger and had better respiratory and muscular function (Table S2). In this group, age no longer predicted the composite

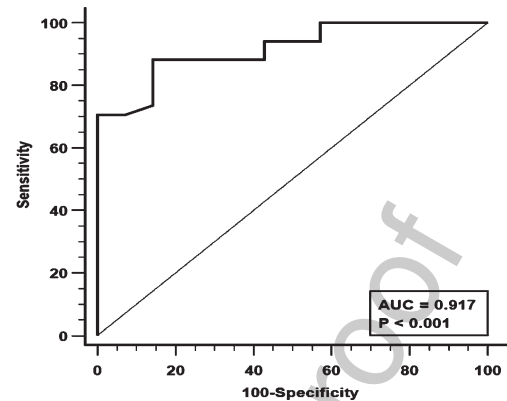


Fig. 1. Receiver Operating Characteristics (ROC) analysis for Maximal Inspiratory Pressure (MIP) and its diagnostic performance. AUC = area under the curve.

Table 4
SWAL-QOL scores in patients <30 and ≥ 30 years old

	Age<30 (n=26)	Age ≥ 30 (n=22)	<i>p</i>
Burden	82.2 \pm 26.9	55.6 \pm 35.7	0.005
Eating duration	41.3 \pm 40.5	47.7 \pm 46.2	0.61
Eating desire	74.9 \pm 15.7	74.7 \pm 23.1	0.96
Food selection	66.8 \pm 34.4	54.5 \pm 31.9	0.20
Fear of eating	79.3 \pm 20.4	61.8 \pm 25.8	0.01
Communication	82.6 \pm 28.9	72.7 \pm 31.2	0.25
Mental health	89.8 \pm 19.6	67.9 \pm 27.3	0.002
Social functioning	88.6 \pm 16.9	73.4 \pm 28.5	0.02
Sleep	85.0 \pm 20.9	75.5 \pm 18.2	0.10
Fatigue	78.5 \pm 23.4	62.8 \pm 22.8	0.02
Composite score	76.6 \pm 16.3	64.5 \pm 19.2	0.02
DBS*	76.8 \pm 17.0	67.0 \pm 21.6	0.08

DBS, dysphagia battery score.

SWAL-QOL score, while MIP remained the only independent predictor (Table S3).

DISCUSSION

This study was performed on a relatively large number of adult patients with DMD, including a high proportion of subjects over the age of 30. The main findings were as follows: 1) An altered swallowing-related QoL was present in most patients; 2) Age, inspiratory muscle strength and autonomic symptoms independently predicted degree of impairment of swallowing-related QoL; 3); QoL aspects related to the mental and social sphere were significantly worse in subjects ≥ 30 years old, whereas those more closely related to physical impairment were heavily compromised already at young ages and barely differed between younger and older subjects.

316 Although dysphagia is a common symptom in
317 DMD, to our knowledge the SWAL-QOL question-
318 naire has been used in other neuromuscular diseases
319 [28], but not specifically in DMD. The analysis in
320 our patients showed a good reliability of this ques-
321 tionnaire, supporting its use to identify perturbations
322 in QoL related to the swallowing function even in
323 DMD. We found that swallowing-related QoL is often
324 altered in DMD, confirming the results obtained in
325 a previous study where another questionnaire was
326 used [15]. We identified age, MIP and Compass 31
327 score as independently related to the outcome of the
328 SWAL-QOL questionnaire.

329 Our study demonstrated a significant role of age
330 as a predictor of swallowing-related QoL. This is not
331 in agreement with a recent study that found that age
332 was not a determinant of gastrointestinal symptoms
333 in adult patients with DMD [12]. However, that study
334 included patients with a narrow range of age. By con-
335 trast, we studied patients in a broad age range and,
336 as a consequence, with highly variable functional
337 impairment, which could allow us to demonstrate
338 a relationship between age and SWAL-QOL scores.
339 Actually, symptoms of dysphagia, which hampered
340 quality of life, were previously reported in a sample
341 of DMD patients much younger than in our study
342 [15]. Hence, dysphagia may already appear in young
343 DMD patients, but its impact on patients' well-being
344 may progressively worsen with advancing age.

345 The role of MIP as a predictor of the composite
346 score may be explained considering that the degener-
347 ation of inspiratory and oropharyngeal muscle groups
348 proceeds in parallel in the course of the disease, so
349 that inspiratory muscle strength may closely reflect
350 ability in swallowing. Moreover, oropharyngeal mus-
351 cles, which are the most directly involved in the
352 swallowing process, cooperate with inspiratory mus-
353 cles when a subject swallows, so that if inspiratory
354 muscles function is compromised, swallowing is
355 affected, too. A previous study found a relationship
356 between swallowing impairment, as assessed by an
357 8-stage scale, and respiratory function, as assessed
358 by FVC, but in this study respiratory muscle strength
359 was not evaluated [14]. In our study, MIP predicted
360 swallowing impairment better than FVC. In fact, FVC
361 reflects functional properties of the respiratory sys-
362 tems, not all of which are related to swallowing.
363 Instead, MIP is only relevant to the strength of inspi-
364 ratory muscles. In agreement with our finding, in a
365 previous study MIP was found to be associated with
366 swallowing ability and specifically with the num-
367 ber of swallows per bolus and time of swallowing

368 [29]. In common clinical practice, the SWAL-QOL
369 questionnaire is rarely administered because it is con-
370 sidered burdensome. This may lead to neglect the
371 impact of swallowing-related disorders on QoL. The
372 assessment of MIP in DMD may be clinically rele-
373 vant not only to evaluate the degree of impairment
374 of inspiratory muscles function, but also to estimate
375 the possible impact of swallowing problems on QoL.
376 According to our results, a cut off of MIP < 22 cmH₂O
377 is associated with an increased risk of an impact of
378 dysphagia on QoL.

379 Autonomic impairment, as resulting from the
380 Compass 31 questionnaire, was the last independ-
381 ent predictor of composite SWAL-QOL. We and
382 other authors have already described an altered auto-
383 nomic function in DMD [4, 30, 31]. Gastrointestinal
384 and secretomotor subdomains were the most heavily
385 affected [4]. Furthermore, esophageal dysphagia and
386 early satiety may be prominent symptoms in some
387 DMD patients [32, 33], possibly as a consequence of
388 gastroparesis due to autonomic dysfunction. Through
389 these effects, autonomic impairment may consider-
390 ably contribute to harm QoL.

391 When we divided our sample into a group < 30 and
392 a group ≥ 30 years old, we found that various aspects
393 gave a different contribution to the worse QoL in
394 the older patients. The most prominent differences
395 were found in items reflecting mental and psycho-
396 logical aspects of QoL, while items more closely
397 related to physical dysfunction, like eating duration
398 and food selection, were already severely affected in
399 younger patients and did not differ between groups.
400 A longer duration of eating may be linked to an inef-
401 fective bolus propulsion, which generates frequent
402 swallows or 'piecemeal deglutition'. A long duration
403 of meals was also observed in a previous study [15]
404 where the age of the patients was lower than in our
405 study. These findings suggest that muscular and, pos-
406 sibly, autonomic dysfunction are already enough to
407 cause significant dysphagia in young adult patients
408 with DMD. However, in these subjects they mildly
409 affect the psychological and social spheres. The lat-
410 ter make a much greater contribution to worsening
411 QoL in older subjects. It remains to be established
412 to what extent the worse psychological attitudes of
413 the older patients may depend on the persistence of
414 swallowing disorders throughout their life, and how
415 much other factors may contribute.

416 It has been suggested that NIV during meals
417 may reduce dysphagia [34], as it can improve
418 breathing-and swallowing coordination. Then, we re-
419 evaluated predictors of the composite SWAL-QOL

420 after excluding patients using NIV during meals from
 421 our sample. The remaining patients had a narrow age
 422 range, so that the effect of age was no longer evi-
 423 dent. However, the independent effect of MIP was
 424 confirmed.

425 This study has several strengths. We used a ques-
 426 tionnaire that is considered the gold standard to
 427 evaluate the impact of swallowing dysfunction on
 428 QoL. Besides, the sample of DMD patients we stud-
 429 ied can be considered large proportionally to the low
 430 prevalence of the disease, and included subjects in
 431 a wide age range. Therefore, data could be general-
 432 ized to DMD patients with similar characteristics that
 433 receive the same level of healthcare. The large pro-
 434 portion of relatively old patients allowed us to assess
 435 effects of advancing age and to recognize what might
 436 make QoL worse in older DMD patients. However, a
 437 limitation of the study was that only cross-sectional
 438 data were collected so that the role of age in our find-
 439 ings was not deduced from longitudinal observations,
 440 but from comparisons between groups of patients of
 441 different ages.

442 In conclusion, swallowing-related QoL is impaired
 443 in most adult subjects with DMD. In these patients,
 444 age, degree of weakness of inspiratory muscles
 445 and symptoms of autonomic dysfunction predict
 446 swallowing-related QoL. Since MIP closely reflects
 447 discomfort associated with swallowing dysfunction,
 448 its alteration may lead to suspect deglutition prob-
 449 lems. Swallowing-related QoL is worse in older
 450 patients, mainly due to psychological and social
 451 factors. Management and specifically designed pro-
 452 grams of rehabilitation should address with greater
 453 care dysphagia to mitigate deterioration of QoL in
 454 DMD. The use of the SWAL-QOL, in addition to
 455 more commonly used tests, may lead to a more com-
 456 prehensive evaluation of QoL in patients with this
 disease.

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466 CONFLICT OF INTEREST

The authors have no conflict of interest to report.

DATA AVAILABILITY

The data supporting the findings of this study are
 available within the article and its supplementary
 material.

SUPPLEMENTARY MATERIAL

The supplementary material is available in the
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