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ORIGINAL ARTICLE

Bulbar muscle impairment in patients with late onset Pompe disease: Insight from the French Pompe registry

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Abstract

Background and purpose: Late onset Pompe disease (LOPD) is a rare neuromuscular disorder caused by a deficit in acid alpha-glucosidase. Macroglossia and swallowing disorders have already been reported, but no study has focused yet on its frequency and functional impact on patients' daily life.

Methods: We reviewed 100 adult LOPD patients followed in 17 hospitals in France included in the French national Pompe disease registry. The Swallowing Quality of Life Questionnaire and the Sydney Swallow Questionnaire were completed by patients, and a specialist carried out a medical examination focused on swallowing and assigned a Salassa score to each patient. Respiratory and motor functions were also recorded. Subgroup analysis compared patients with and without swallowing difficulties based on Salassa score.

Results: Thirty-two percent of patients presented with swallowing difficulties, often mild but sometimes severe enough to require percutaneous endoscopic gastrostomy (1%). Daily dysphagia was reported for 20% of our patients and aspirations for 18%; 9.5% were unable to eat away from home. Macroglossia was described in 18% of our patients, and 11% had lingual atrophy. Only 15% of patients presenting with swallowing disorders were followed by a speech therapist. Swallowing difficulties were significantly associated with macroglossia ($p=0.015$), longer duration of illness ($p=0.032$), and a lower body mass index ($p=0.047$).

Swallowing difficulties are reported for 32% of adult late onset Pompe disease patients included in the French Pompe disease registry and lead to significant repercussions in the patients' quality of life.

For affiliations refer to page 9.

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Conclusions: Swallowing difficulties in LOPD are common and have significant functional impact. Increased awareness by physicians of these symptoms with systematic examination of the tongue and questions about swallowing can lead to appropriate multidisciplinary care with a speech therapist and dietitian if needed.

KEYWORDS

dysphagia, French Pompe registry, glycogenosis type II, late onset Pompe disease, macroglossia

INTRODUCTION

Pompe disease, also called glycogen storage disease type II (MIM#232300), is a rare neuromuscular disorder caused by a deficit in acid alpha-glucosidase. Phenotype range is wide, from very severe forms, with infantile onset characterized by early cardiorespiratory failure, to late onset Pompe disease (LOPD), with patients developing progressive limb girdle weakness and diaphragmatic involvement [1].

In recent years, some studies have focused on macroglossia in adult LOPD patients [2], a symptom initially described in 1968 by Hudgson et al. [3], who reported on the observation of a 44-year-old woman presenting with an enlarged tongue and mild lingual dysarthria. These swallowing difficulties are probably an undervalued symptom that can have important repercussions in patients' daily life, such as dysarthria, dysphagia, and sleep apneas [4–8].

More recent studies focusing on assessment of tongue strength in small cohorts of patients showed decreased tongue muscle strength in a majority of those patients [9], as could be expected considering the early fat replacement of these muscles in muscle magnetic resonance imaging (MRI) of patients with LOPD [10]. However, the prevalence and clinical manifestation of tongue involvement have never been studied among a large cohort of LOPD patients.

The aim of this study was to evaluate the prevalence and the clinical impact of bulbar muscle involvement in a French cohort of adult LOPD patients, which has been tracked by the French Pompe disease registry for 20 years [11, 12].

METHODS

Patient inclusion

We included all adult patients with Pompe disease followed in 17 neuromuscular and metabolic reference centers from 2 January 2023 to 1 October 2023 and included in the French national Pompe disease registry. This registry was created in 2004 and currently includes 262 adult patients, of whom 207 are still alive. It is hosted on a secure server at Montpellier Hospital. It is covered by section IX of the French Data Protection Act, and it adheres to the Recommendations for Ethics and Good Practice in Epidemiology (French version, 2007). The study was authorized by the National Commission for Information Technology and Freedoms (No. 909,139, 23.04.2009) and the Consultative Committee for the Treatment of Information

in the Field of Health (reference 08.461, 30.10.2008). All patients signed specific informed consent form for their inclusion in the registry. All neuromuscular and metabolic reference centers were asked to participate in this cross-sectional study, and 100 questionnaires were returned from the 17 centers. We excluded patients younger than 18 years or having refused to give consent or to respond to the questionnaire form.

Data collection

All patients underwent a tongue examination by a specialist in metabolic or neuromuscular disease, which evaluated the tongue morphology (macroglossia and lingual atrophy). Clinical data were collected regarding presence of dysarthria, dysphagia, aspirations, feeding habits, and potential follow-up by a speech and language therapist. The height and weight of the patients were also recorded. The Salassa score [13] was calculated. This score, described by Salassa in 1999, aims at determining severity of the dysphagia and the effectiveness of therapy for patients with oropharyngeal dysphagia, with six levels, from grade 0 corresponding to absence of dysphagia to grade 5 corresponding to impossibility of oral alimentation (Data S1). Two groups were determined by their Salassa score and the existence or absence of swallowing difficulties; patients without swallowing difficulties were defined by a Salassa score of 0, and patients with swallowing difficulties were defined by a Salassa score of ≥ 1 . The time necessary to drink 80 mL of cold water, or the Drink Test [14], was recorded and results of > 8 s were considered abnormal.

The answer to the second question of the Rasch-Built Pompe-Specific Activity Scale (R-Pact) [15]—"Are you able to eat?"—was collected. This validated functional scale was specifically designed for Pompe patients to evaluate daily life abilities.

Two questionnaires were filled in by the patients to evaluate the impact of swallowing disorders on their quality of life: the Swallowing Quality of Life Questionnaire (SWAL-QOL) [16] and the Sydney Swallow Questionnaire (SSQ) [17]. The SWAL-QOL, developed to integrate patients' perspective on the impact of dysphagia on quality of life and quality of care, derives from a 93-item tool first published by McHorney et al. in 2000. This questionnaire was separated in 2002 into two parts, one of which is the SWAL-QOL, a 44-item tool that assesses quality of life. The SSQ is a 17-question self-report inventory, developed to measure the severity of dysphagia as reported by the affected patient. The questionnaire uses a

100-mm-long visual analogue scale for all but one question about the duration of a meal. This questionnaire was first described by Wallace et al. in 2000 to evaluate the severity of dysphagia in 45 patients who had myogenic dysphagia.

Respiratory function data were collected with sitting forced vital capacity (FVC) and ventilation requirement. Motor function data were collected with ability to walk without technical assistance and the distance covered in the 6-min walk test (6MWT).

Statistical analysis

Data are expressed as number and percentage for qualitative variables, and as mean \pm SD or median and interquartile range (IQR) for quantitative variables, according to the distribution. The assumption of a normal distribution was performed using Shapiro–Wilk test. Patient groups with and without swallowing difficulties were compared using Student test or Wilcoxon test for quantitative variables according to the distribution and chi-squared test or Fisher exact test for categorical variables according to the sample size. Agreement between two classification methods, the second question of R-Pact and the Salassa score, was assessed using Cohen kappa coefficient. Cross-sectional analysis was performed with R 4.1.3 software (R Foundation for Statistical Computing). Statistical tests were carried out for a two-sided type I error at 5%. No correction for multiple testing was applied; the interpretation of these results could be carried out considering it as exploratory.

RESULTS

Demographic data

In this study, 100 patients were reviewed, 58 women and 42 men. The mean age was 56.1 ± 14.4 years. Eighty-nine patients (90.8%) were being treated with enzyme replacement therapy (ERT), 40 (56%) with alglucosidase alfa, 26 (37%) with avalglucosidase alfa, and five (7%) with cipaglucosidase alfa/miglustat. The median body mass index (BMI) was 24.4 kg/m^2 (IQR = 20.8–29.4). Main characteristics of the patients are reported in [Table 1](#).

Description of the studied population

Concerning the bulbar features, 18 patients (18.2%, $n=99$) presented with macroglossia and 11 (11.1%, $n=99$) with lingual atrophy ([Figure 1](#)); one patient presented with both. Dysarthria was reported for eight patients (8%). Twenty patients (20%) described daily dysphagia, and 18 patients (18%) complained of aspirations. The Drink Test, performed on 63 patients, was abnormal for 22 of those (38%).

We used a Venn diagram to show the correlation between macroglossia, dysphagia, and dysarthria in our cohort ([Figure 2](#)). Among the 19 patients who presented dysphagia, four patients additionally

presented macroglossia and dysarthria, three patients presented only macroglossia, and one presented only dysarthria; among the 18 patients who presented macroglossia, seven presented daily dysphagia and six presented dysarthria, four presenting both.

Concerning the ventilation and motor features, noninvasive ventilation was required for 50 patients (51%, $n=98$) and median FVC was 2.4 L (IQR = 1.6–3.2). Thirty-nine patients (40.2%, $n=97$) needed assistance with walking, and the median distance covered during 6MWT was 410 m (IQR = 226–493).

The Salassa score was evaluated for 85 patients. It was scored grade 0 for 58 patients (68.2%), grade 1 for 22 patients (25.9%), grade 2 for one patient (1.2%), grade 3 for three patients (3.5%), and grade 5 for one patient (1.2%).

Results of questionnaires

Results of the SSQ were as follows. Nineteen patients (19.2%, $n=99$) reported difficulties with swallowing liquids, 17 (17.2%, $n=99$) swallowing thicker liquids, 19 (19.6%, $n=97$) swallowing soft food, 24 (24.7%, $n=97$) swallowing solids, 25 (26%, $n=96$) swallowing dry food, and 21 (21.6%, $n=97$) swallowing their saliva. Twenty-eight patients (28.9%, $n=97$) described foods becoming trapped, and 22 (22.7%, $n=97$) reported coughing during their meals. Longer meals (>30 min) were reported for 26 patients (26.3%, $n=99$), including two (2.2%) very extended (>60 min) and one who cannot eat anything.

The SWAL-QOL results showed that three patients (3.3%, $n=91$) could not drink still water. Of those three, two could drink sparkling water, whereas the third could not drink at all. Two patients (2.2%, $n=91$) could not eat solids (one ate ground food, whereas the second one could not eat anything at all), and 13 (13.8%, $n=94$) have removed some foods from their meals. Eleven patients (11.6%, $n=95$) were sometimes afraid of choking while eating. These swallowing disorders can have repercussions on their daily life. For example, nine patients (9.5%, $n=95$) stopped eating out because of these swallowing issues, six patients (6.3%, $n=95$) felt depressed by these difficulties, and three patients (3.2%, $n=95$) changed their work or pastimes because of the swallowing disorders. Patients also reported difficulties with their saliva; 18 patients (18.9%, $n=95$) reported thick saliva, and 20 (20.6%, $n=97$) dribbled saliva. Concerning the dysarthria, 10 patients (10.5%, $n=95$) had difficulties in speaking, including seven patients (7.4%, $n=95$) who had difficulties making themselves understood.

Subgroup analysis

Patients without swallowing difficulties defined by a Salassa score of 0 ($n=58$) were compared with patients with swallowing difficulties defined by Salassa score ≥ 1 ($n=27$; [Table 1](#)). Among the patients who scored Salassa ≥ 1 , 16 patients (59.3%) reported daily dysphagia and 15 patients (55.6%) described suffering from aspirations. Patients

TABLE 1 Clinical patients' characteristics, comparing patients with and without swallowing difficulties based on Salassa score.

	All patients, n = 100	Patients without swallowing difficulties, n = 58	Patients with swallowing difficulties, n = 27	p
Patient characteristics				
Sex ratio, F/M	58/42	32/26	14/13	0.775
BMI, kg/m ²	24.4 (20.8–29.4)	25 (21.3–29.4)	22.7 (20.5–24.5)	0.047
Underweight, BMI < 18.5	10 (10.2%)	7 (12.3%)	2 (7.7%)	
Normal weight, BMI = 18.5–25	46 (46.9%)	23 (40.4%)	18 (69.2%)	
Overweight, BMI > 25	42 (42.9%)	27 (47.4%)	6 (23.1%)	
Age, years	56.1 ± 14.4	56 ± 12.1	60 ± 17.9	0.295
Age at first symptoms, years	34.4 ± 13.7	35.4 ± 12.7	33.2 ± 16.3	0.563
Disease duration, years	23 (16.9–28.0)	21.8 (16.2–26.4)	26.2 (21–32.7)	0.032
Patients treated	89 (90.8%)	48 (85.7%)	26 (96.3%)	0.259
Treatment duration, years	8.3 (3.5–13.9)	9.9 (5.1–13.2)	8.2 (3.8–15.4)	0.872
Disease duration before ERT initiation in years	13.89 (9.12–20.84)	13.42 (8.81–16.73)	15.98 (11.84–23.71)	0.12
Swallowing features				
Salassa score				
Grade 0	58 (68.2%)	58 (100%)	0 (0%)	
Grade 1	22 (25.9%)	0 (0%)	22 (81.5%)	
Grade 2	1 (1.2%)	0 (0%)	1 (3.7%)	
Grade 3	3 (3.5%)	0 (0%)	3 (11.1%)	
Grade 4	0 (0%)	0 (0%)	0 (0%)	
Grade 5	1 (1.2%)	0 (0%)	1 (3.7%)	
Macroglossia	18 (18.2%)	7 (12.1%)	9 (34.6%)	0.015
Lingual atrophy	11 (11.1%)	7 (12.1%)	3 (11.5%)	1
Dysarthria	8 (8%)	2 (3.5%)	6 (22.2%)	0.012
Daily dysphagia	20 (20%)	1 (1.7%)	16 (59.3%)	<0.001
Aspiration	18 (18%)	1 (1.7%)	15 (55.6%)	<0.001
Speech therapist	4 (4%)	0 (0%)	4 (14.8%)	0.009
Drink Test				
Duration, s	6.7 (4.2–10)	5 (3.9–8.7)	10 (6.4–14)	0.001
Abnormal results	22 (38%)	13 (32%)	9 (56%)	0.012
Respiratory features				
Ventilation requirement	50 (51.0%)	25 (44.6%)	16 (59.3%)	0.212
Forced vital capacity, L	2.4 (1.6–3.2)	2.5 (1.6–3.3)	2.0 (1.6–2.7)	0.315

TABLE 1 (Continued)

Motor features	All patients, n = 100	Patients without swallowing difficulties, n = 58	Patients with swallowing difficulties, n = 27	p
Walking ability				
No technical assistance	58 (59.8%)	36 (64.3%)	12 (46.25%)	0.121
One stick	15 (39.5%)	8 (40%)	7 (50%)	
Two sticks or rollator	12 (31.6%)	7 (35%)	4 (28.6%)	
Wheelchair	11 (29%)	5 (25%)	3 (21.4%)	
Distance in 6-min walk test, m	410 (226–493)	417.5 (227.5–483)	305 (233–397)	0.157

Note: Data are given as n (%), mean \pm SD, or median (interquartile range).

Abbreviations: BMI, body mass index; ERT, enzyme replacement therapy; F, female; M, male.

with swallowing difficulties tended to be older (60 ± 17.9 years vs. 56 ± 12.1 years), with a significant difference according to the illness duration (26.2 years vs. 21.8 years, $p=0.032$). A statistically significant difference was observed regarding the BMI among both groups, with a lower BMI in the group who scored Salassa ≥ 1 and fewer overweight patients in this group (23.1% vs. 47.4%, $p=0.047$).

As regards bulbar features (Figure 3), macroglossia was significantly more frequent in the group who scored Salassa ≥ 1 than in the group who scored Salassa = 0 ($n=9$ patients [34.6%] vs. $n=7$ patients [12.1%], $p=0.015$). No significant difference between the two groups was found concerning lingual atrophy ($n=3$ patients [11.5%] vs. $n=7$ patients [12.1%]). Dysarthria was significantly more frequent in the group who scored Salassa ≥ 1 ($n=6$ patients [22.2%] vs. $n=2$ patients [3.5%], $p=0.012$). Patients with swallowing difficulties needed significantly more time to perform the Drink Test (10 s vs. 5 s, $p=0.001$); prevalence of abnormal Drink Test was significantly different between the two groups: nine patients (56%) with swallowing difficulties versus 13 patients (32%) without swallowing issues ($p=0.012$). Only four patients (14.8%) presenting with swallowing difficulties were followed by a speech therapist.



FIGURE 1 Illustration of association of macroglossia and lingual atrophy in Late Onset Pompe disease patients. (a, b) The tongue of a 69-year-old man (P1) who presented with macroglossia and complains of dysphagia with aspirations. His Salassa score was 3. He performed the Drink Test in 7.3 s. (c, d) The tongue of a 75-year-old man who presented with macroglossia and complains of dysarthria. His Salassa score was 1. He performed the Drink Test in 5.9 s.

Analysis of the impact on quality of life, with the SSQ (Figure 4) and the SWAL-QOL (Figure 5), showed a significant association with Salassa score ≥ 1 . For example, 11 patients (42.3%, $n=26$) in the group who scored Salassa ≥ 1 noted extended meals against

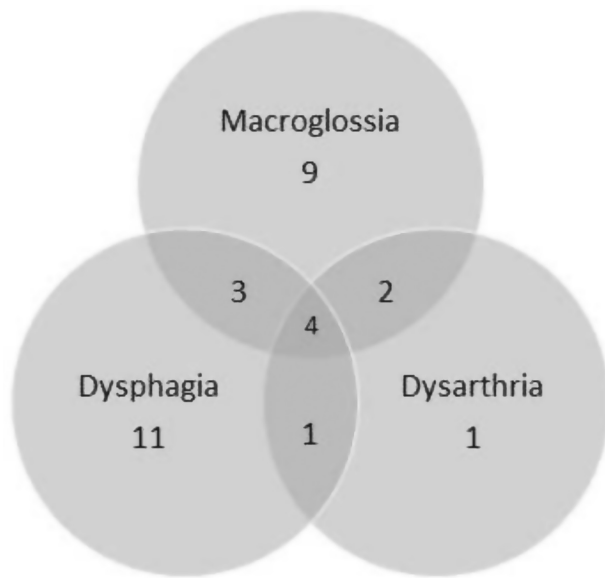


FIGURE 2 Venn diagram representing the presence of macroglossia, daily dysphagia, and dysarthria in our cohort of late onset Pompe disease.

only four (7.1%, $n=56$) in the group who scored Salassa=0; nine patients (34.6%, $n=26$) in the group who scored Salassa ≥ 1 reported difficulties in choosing their food against only two patients (3.6%, $n=57$) in the group who scored Salassa=0. Thus, nine patients (34.6%, $n=26$) in the group who scored Salassa ≥ 1 had to remove food from their diet against 1 (1.9%, $n=53$) in the group who scored Salassa=0.

No significant difference between the two groups in the respiratory and walking features was found.

Comparison with the second question of R-Pact showed that 100% of patients who scored Salassa=0 answered that they could eat without difficulty, whereas 12 patients (67%, $n=18$) who scored Salassa ≥ 1 answered that they had difficulties eating. This corresponds to a specificity of 1.0 and a sensitivity of 0.67, a positive predictive value at 1.0, and a negative predictive value at 0.85. The Kappa correlation coefficient is 0.72 ($p < 0.05$; Table 2).

DISCUSSION

Although tongue involvement is a clearly established sign of LOPD, leading to significant swallowing impairment in some patients, the prevalence and clinical impact of this manifestation has not yet been studied extensively in the population of LOPD patients. Thanks to the French neuromuscular network (FILNEMUS), we have been able to systematically collect both clinical symptoms and data extracted

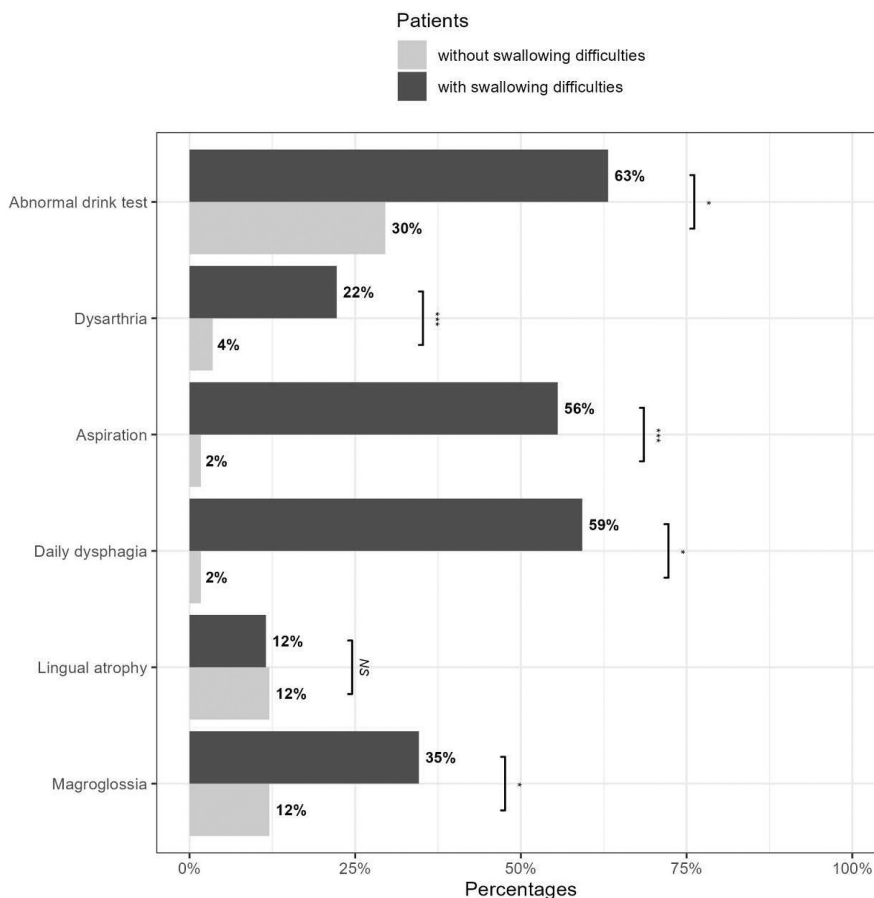


FIGURE 3 Bulbar features comparing patients without swallowing difficulties (defined by a Salassa score of 0) and patients with swallowing difficulties (defined by a Salassa score of ≥ 1). * $p < 0.05$, *** $p < 0.001$. NS, $p \geq 0.05$.

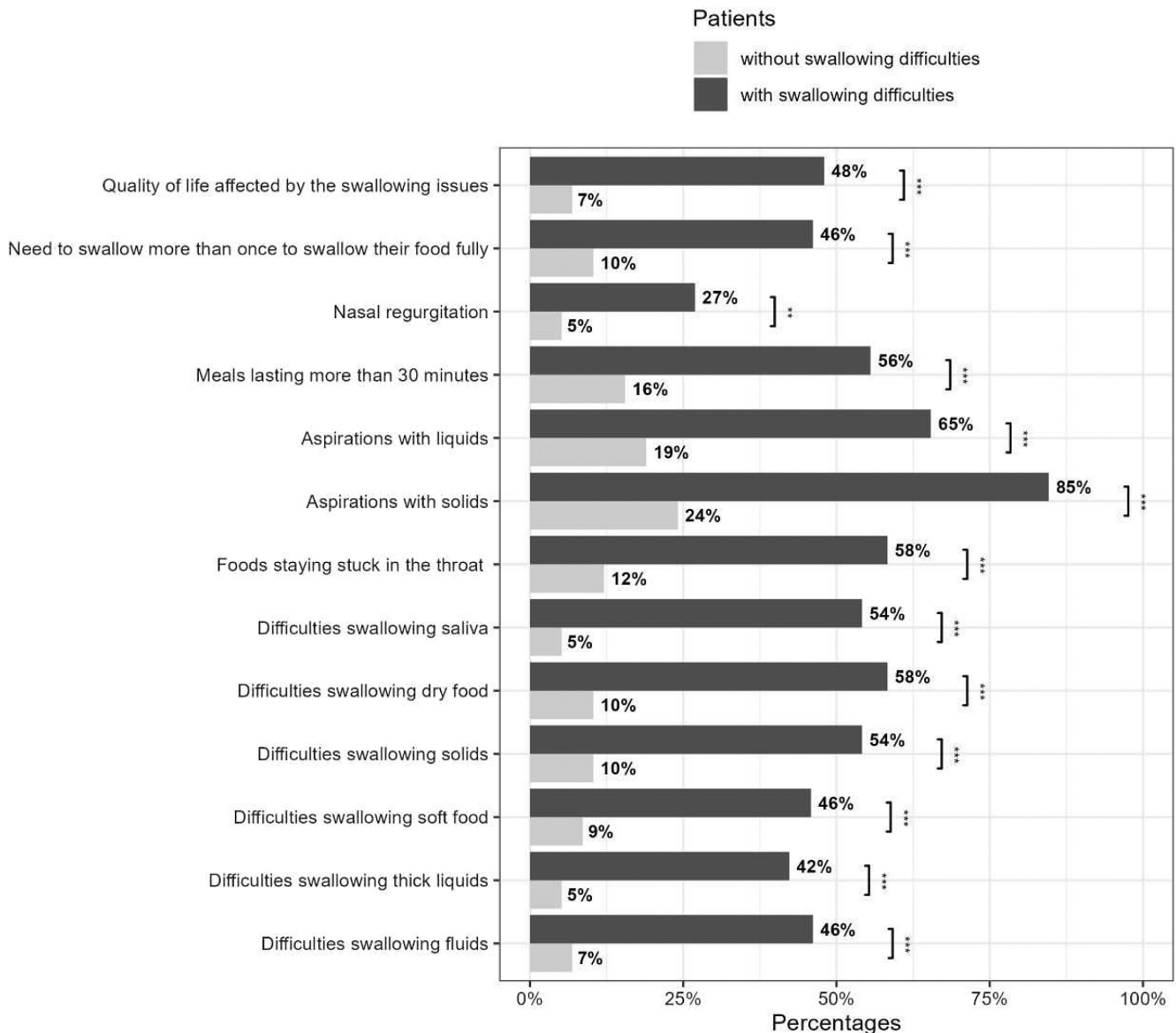


FIGURE 4 Sydney Swallow Questionnaire results comparing patients without swallowing difficulties (defined by a Salassa score of 0) and patients with swallowing difficulties (defined by a Salassa score of ≥ 1). $**p < 0.01$, $***p < 0.001$.

from questionnaires assessing bulbar muscle involvement in a large cohort of 100 patients in the French Pompe registry.

The main finding of our study through this cohort representing LOPD patients is the high frequency of bulbar muscle impairment in this population, with 32% of patients complaining of swallowing difficulties. These symptoms are often mild, but can be severe in some patients, potentially leading to percutaneous endoscopic gastrostomy and affecting patients' quality of life. These swallowing disturbances are often predominant with solids and dry food but can also affect liquids or saliva.

Although the presence of swallowing difficulty is not correlated with age in our study, we nevertheless note that the four most severe cases in our cohort were >60 years old. Several age-related pathologies can also promote the occurrence or increase of swallowing disorders, such as stroke, neurodegenerative diseases, or dental conditions. On the other hand, they are significantly correlated with

the duration of progression of the disease, with no significant result for time between first symptoms and beginning of ERT. It is interesting to emphasize that swallowing disorders are not associated with more severe respiratory dysfunction as is often the case in neuromuscular diseases. Patients with swallowing disorders do not require more ventilation assistance, and their vital capacity is no different from patients without swallowing disorders.

Furthermore, the patients with swallowing disorders present a lower BMI, and only 15% of them are followed by a speech therapist. This underlines that these difficulties are often undervalued and thus undertreated. Being proactive in the early detection of dysphagia in LOPD patients will then allow anticipation of severe consequences such as undernutrition or inhalation pneumonia.

Considering the tools available to screen swallowing disorder, we have chosen to use the Salassa score to classify patients into subgroups with or without swallowing difficulties. This simple and

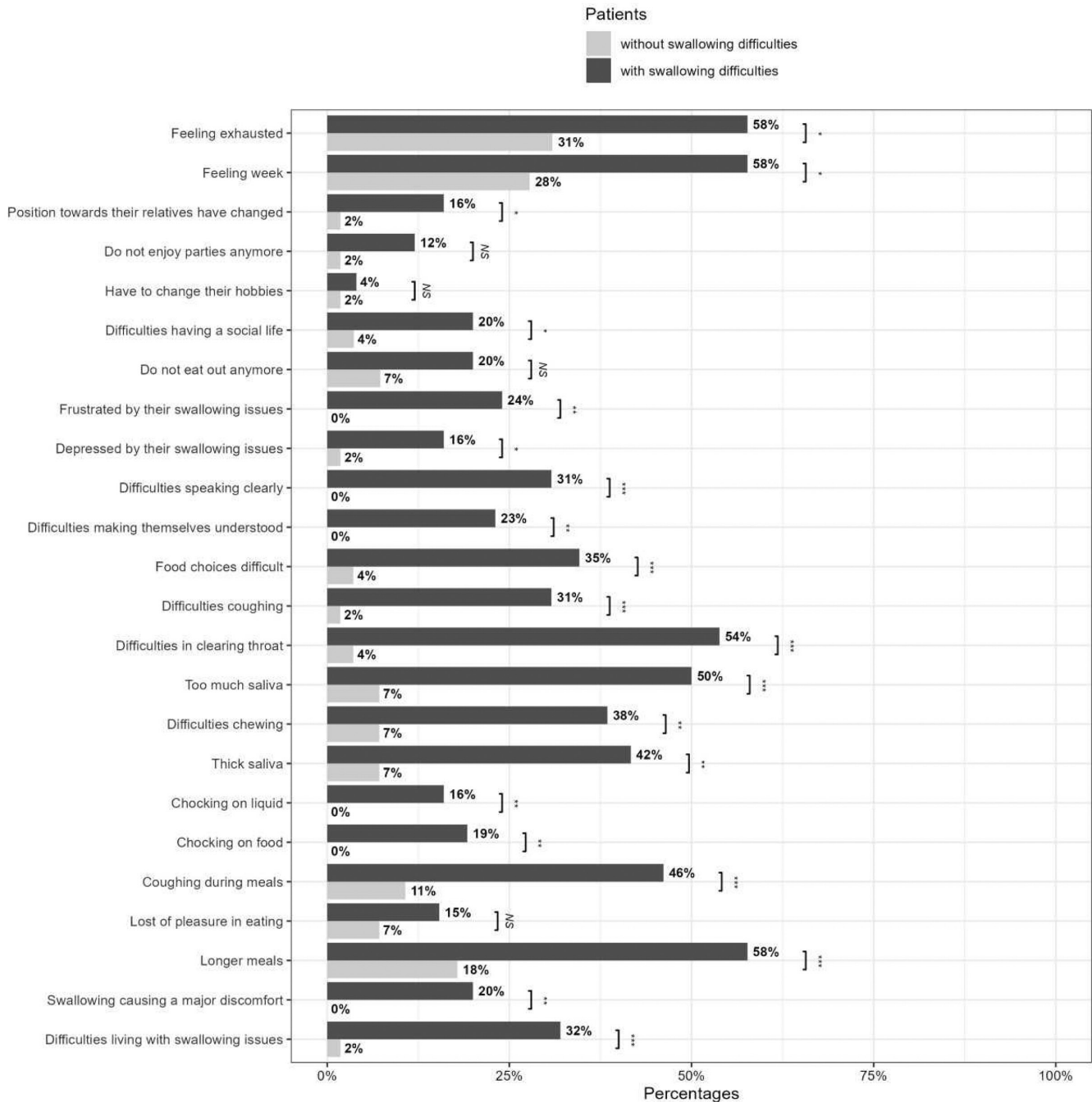


FIGURE 5 Swallowing Quality of Life Questionnaire results comparing patients without swallowing difficulties (defined by a Salassa score of 0) and patients with swallowing difficulties (defined by a Salassa score of ≥ 1). * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. NS, $p \geq 0.05$.

TABLE 2 Test of concordance between Salassa score and second question of R-Pact.

	Salassa=0	Salassa ≥ 1	Total
R-Pact no difficulty with eating	33	6	39
R-Pact eating with difficulty	0	12	12
Total	33	18	51

Abbreviations: R-Pact, Rasch-Built Pompe-Specific Activity Scale.

quick score can be carried out routinely. It has already been shown to have positive results in detecting swallowing disorders in other neuromuscular disorders, such as in oculopharyngeal muscular dystrophy by Trollet et al. [18]. This score can be used as a screening test before clinical evaluation to refer patients if necessary to specialized evaluation by a speech therapist.

The R-Pact, used routinely to evaluate Pompe patients, presents good specificity but mild sensitivity in detecting swallowing difficulties.

The results of our study extend the knowledge on tongue involvement in LOPD patients and are consistent with the study of Dubrovsky et al. [5], which assessed tongue strength in 19 consecutive LOPD patients with manual muscle testing and reported dysarthria and/or dysphagia in seven of 19 patients (37%). It should be noted that all patients examined in this study exhibited lingual weakness, even if no swallowing disorders were reported. These findings have then been confirmed by a study of quantitative assessment of lingual strength in 30 LOPD patients [9], showing tongue weakness in 80% of patients; severity was estimated as mild in 29%, moderate in 29%, and severe in 42%. In a subsequent study, Jones et al. [19] confirmed that patients diagnosed with LOPD have significantly decreased tongue strength with both manual and quantitative muscle testing and found increased echo intensity of tongue muscles and decreased muscle thickness at ultrasound. These findings strongly suggest the existence of fibrofatty replacement of lingual muscles even in asymptomatic LOPD patients. Tongue MRI was also studied in LOPD patients, and the bright tongue sign described in these patients [20] suggests as well fibrofatty replacement and could be a quite specific sign to search for when diagnosing a muscle weakness. Considering the difficulties in clinically defining macroglossia, imagery could also help to quantify precisely the volume of tongue using MRI or ultrasound imaging. The correlation between swallowing disorders and measuring of tongue volume could be explored in further dedicated studies.

Physiopathology of the swallowing disorders and the reason for specific fatty infiltration in the tongue remain for now unclear. To our knowledge, no study has yet been done on that subject. Mechanisms of these swallowing difficulties could also be clarified with fiberoptic endoscopic evaluation of swallowing.

More recently, Dupé et al. [2] reported five cases of LOPD patients who presented macroglossia, all but one suffering from symptoms related to macroglossia before the diagnosis of Pompe disease. Among these patients, two had severe dysphagia, one of whom underwent percutaneous endoscopic gastrostomy. In this latest study, swallowing difficulties seemed to be associated with macroglossia and longer duration of illness, and patients often complained of dysarthria and excessive saliva.

The strength of our study was the data collection of signs and symptoms allowing us to assess the incidence and severity of bulbar muscle involvement in a large cohort of LOPD patients, thus objectively reflecting the significance of these. Limitations of this cross-sectional study are the lack of consensus on clinical definition of macroglossia. Quantitative evaluation of the tongue volume with MRI or tongue muscle strength with dynamometry would be more accurate but unfortunately is not performed routinely. In addition, this study does not allow the assessment of the rate of progression over time of these symptoms, because the introduction of these swallowing questionnaires in the French Pompe registry is only recent. Including these clinical assessments and questionnaires in the yearly follow-up of LOPD patients will allow us to improve our knowledge of the evolution speed and severity of these symptoms. As a consequence of the cross-sectional nature of this study, we

have not been able to evaluate the effect of ERT on progression of the tongue involvement either. Considering the early fatty replacement of tongue muscle in patients with Pompe disease and its potential severity, symptoms relating to tongue weakness and changes in size should probably be taken into account in future long-term studies evaluating the benefit of innovative treatments. The collection of these data is ongoing in the French Pompe registry.

In conclusion, swallowing difficulties are reported for 32% of adult LOPD patients included in the French Pompe Disease registry and result in repercussions in patients' quality of life. Bulbar involvement is additional evidence that Pompe disease is a multisystemic disease that needs regular systemic evaluation. These symptoms require an increased awareness of physicians of the need to systematically examine the tongue and swallowing in LOPD patients, thus recognizing these symptoms can enable multidisciplinary care with a speech therapist, dietitian, and ear, nose, and throat specialist if needed. A delay in recognition of these symptoms could lead to undernutrition or inhalation pneumonia, with a potentially severe impact on vital prognosis and quality of life of LOPD patients. Future studies will be necessary to refine knowledge on the impact of ERT on swallowing disorders for adult LOPD patients.

AUTHOR CONTRIBUTIONS

Emilie Retailleau: Writing – original draft; methodology; writing – review and editing. **Claire Lefevre:** Conceptualization; methodology; validation; visualization; supervision. **Marie De Antonio:** Formal analysis. **Françoise Bouhour:** Investigation. **Celine Tard:** Investigation. **Emmanuelle Salort-Campana:** Investigation. **Emmeline Lagrange:** Investigation. **Anthony Béhin:** Investigation. **Guilhem Solé:** Investigation. **Jean-Baptiste Noury:** Investigation. **Sabrina Sacconi:** Investigation. **Armelle Magot:** Investigation. **Aleksandra Nadaj Pakleza:** Investigation. **David Orlikowski:** Investigation. **Stéphane Beltran:** Investigation. **Marco Spinazzi:** Investigation. **Pascal Cintas:** Investigation. **Maxime Fournier:** Investigation. **Fatma Bouibede:** Investigation. **Hélène Prigent:** Investigation. **Guillaume Nicolas:** Investigation. **Nadjib Taouagh:** Investigation. **Taissir El Guizani:** Investigation. **Shahram Attarian:** Investigation. **Azzeddine Arrassi:** Investigation. **Dalil Hamroun:** Investigation. **Pascal Laforêt:** Conceptualization; methodology; validation; visualization; supervision.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author; the data are not publicly available due to privacy or ethical restrictions.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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