


SHORT COMMUNICATION

Predictors of malnutrition risk in neurodegenerative diseases: The role of swallowing function

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Abstract

Background and purpose: Oropharyngeal dysphagia is generally recognized to increase the risk of malnutrition; however, its role in patients with neurodegenerative disease has yet to be determined. This cross-sectional study aimed to investigate the impact of swallowing function on malnutrition risk in patients with neurodegenerative diseases.

Methods: Patients with oral nutrition and diagnosis of Huntington disease (HD), Parkinson disease (PD), or amyotrophic lateral sclerosis (ALS) were recruited. Demographic and clinical data were collected. The swallowing assessment included a fiberoptic endoscopic evaluation of swallowing, an oral phase assessment, and a meal observation scored with the Mealtime Assessment Scale (MAS). Malnutrition risk was assessed with the Mini Nutritional Assessment.

Results: Overall, 148 patients were recruited (54 HD, 33 PD, and 61 ALS). One hundred (67.6%) patients were considered at risk of malnutrition. In the multivariate analysis, age ≥ 65 years (odds ratio [OR] = 3.16, $p = 0.014$), disease severity (moderate vs mild OR = 3.89, severe vs mild OR = 9.71, $p = 0.003$), number of masticatory cycles (OR = 1.03, $p = 0.044$), and MAS safety (OR = 1.44, $p = 0.016$) were significantly associated with malnutrition risk.

Conclusions: Prolonged oral phase and signs of impaired swallowing safety during meals, together with older age and disease severity, are independent predictors of malnutrition risk in neurodegenerative diseases. This study broadens the focus on dysphagia, stressing the importance of early detection not only of pharyngeal signs, but also of oral phase impairment and meal difficulties through a multidimensional swallowing assessment.

KEYWORDS

deglutition disorders, malnutrition, neurodegenerative diseases

Gabriele Mora and Antonio Schindler equally contributed to the paper.

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INTRODUCTION

Most patients with neurodegenerative diseases suffer from oropharyngeal dysphagia along their disease progression, and alterations of the oral phase, the pharyngeal phase, and swallowing performance during meals are commonly observed [1–3]. Early identification of pharyngeal signs of dysphagia (i.e., penetration and aspiration) is the focus of clinicians to prevent aspiration pneumonia, a leading cause of mortality in neurodegenerative diseases. In addition, in patients with neurodegenerative diseases, malnutrition is a well-known condition associated with a poor prognosis, causing faster rate of disease progression, increased risk of institutionalization, morbidity, and mortality [4]. Whereas the association between dysphagia and nutritional status has been extensively investigated in stroke and elderly subjects, only few and contrasting findings are available from the literature on the risk of malnutrition in neurodegenerative diseases, mainly based on patient-reported dysphagia symptoms.

The aim of this study was to investigate the association between malnutrition risk and swallowing function in some neurodegenerative diseases. The identification of dysphagia-related risk factors can guide recognition of patients at higher risk for nutritional complications and reduce health care costs [5].

METHODS

Study design

This cross-sectional study was approved by the institutional review board of Luigi Sacco Hospital (n.2016/ST/262). All procedures performed in the study were in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. All patients provided written informed consent to study participation.

Study population

Patients affected by Huntington disease (HD), Parkinson diseases (PD), or amyotrophic lateral sclerosis (ALS) were recruited among inpatients and outpatients of three neurological centers in Northern Italy between January 2017 and June 2019. Inclusion criteria were full oral nutrition and age 18–90 years. Exclusion criteria were a history of head and neck cancer, known gastrointestinal diseases, or other concomitant neurological diseases. Age, sex, disease duration, history of aspiration pneumonia, and use of nutritional supplements were collected. Typical oral intake was recorded based on the Functional Oral Intake Scale (FOIS) [6]; patients with a FOIS score < 7 were considered on modified diet. Disease severity was assessed by a neurologist using the following disease-specific clinical scales: the Unified Huntington's Disease Rating Scale Part IV [7] for HD, the Hoehn & Yahr [8] scale for PD, and the ALS Functional Rating Scale–Revised [9] for ALS. According to these scales, patients were

stratified into three disease severity stages (mild, moderate, severe; Table 1).

Swallowing assessment

The swallowing assessment included a fiberoptic endoscopic examination of swallowing (FEES), an assessment of the oral phase efficiency using the Test of Masticating and Swallowing Solids (TOMASS) [10], and a meal observation assessed through the Mealtime Assessment Scale (MAS) [11]. FEES was conducted with liquids (5–10–20 ml of blue-dyed water × 3 trials for each volume; International Dysphagia Diet Standardisation Initiative [IDDSI] = 0 [12]; <50 mPa·s at 50 s⁻¹ and 300 s⁻¹), semisolids (5–10–20 ml of pudding × 3 trials for each volume; IDDSI = 4; 2583.3 ± 10.41 mPa·s at 50 s⁻¹ and 697.87 ± 7.84 mPa·s at 300 s⁻¹), and solids (half biscuit × 2 trials; IDDSI = 7, regular). Both FEES and TOMASS were recorded, deidentified, and independently assessed by two raters. The presence of the following signs of dysphagia was analyzed in FEES videos: penetration based on Penetration–Aspiration Scale (PAS) > 2 [13], aspiration based on PAS score > 5, and pharyngeal residue in the valleculae and in the pyriform sinus based on a Yale Pharyngeal Residue Severity Rating Scale score > 2 [14].

Nutritional assessment

Risk of malnutrition was assessed by a clinician not involved in swallowing assessment using the Mini Nutritional Assessment (MNA) [15]. Patients scoring <24 were considered at risk of malnutrition.

Statistical analysis

Statistical analysis was performed with IBM SPSS Statistics v25.0. Univariate logistic regression was performed to estimate the degree of association between nutritional status (dependent variable) and swallowing variables (independent variables). Other independent variables were age, gender, diagnosis, disease duration, disease severity, and type of oral intake. Statistically significant variables in univariate analysis were included in a multivariate logistic regression using backward elimination method of variable selection. Significance was set at $p < 0.05$. Missing values were excluded on a pairwise basis.

RESULTS

Study population

Overall, 148 patients were recruited, 54 affected by HD, 33 by PD, and 61 by ALS (Table 1).

TABLE 1 Demographic and clinical characteristics of study participants

Variable	Overall, N = 148	HD, n = 54	PD, n = 33	ALS, n = 61	p
Demographic characteristics					
Age, years	67 [56–75]	58.5 [48–67.8]	75.5 [64–79.5]	69 [61.3–75]	<0.001 ^{a,b,c,d}
Gender					
Male	79 (53.4%)	22 (40.7%)	25 (75.8%)	32 (52.5%)	0.011 ^a
Female	69 (46.6%)	32 (59.3%)	8 (24.2%)	29 (47.5%)	
Clinical characteristics					
Disease duration, years	5 [1.3–9]	7 [4–10]	9 [4–12]	2 [1–5]	<0.001 ^{a,c,d}
History of aspiration pneumonia	5 (3.4%)	2 (3.7%)	2 (6.1%)	1 (1.6%)	0.519
Oral nutritional supplements	30 (19.1%)	15 (27.7%)	1 (3%)	14 (23%)	0.016 ^a
Disease severity					
Mild	59 (39.9%)	22 (40.7%)	15 (45.5%)	22 (36.1%)	0.465
Moderate	53 (35.8%)	17 (31.5%)	9 (27.3%)	27 (44.3%)	
Severe	36 (24.3%)	15 (27.8%)	9 (27.3%)	12 (19.7%)	
Diet type					
No restriction	48 (32.4%)	23 (42.6%)	8 (24.2%)	17 (27.8%)	0.216
Modified diet	100 (67.6%)	31 (57.4%)	25 (75.8%)	44 (72.2%)	

Note: Values are presented as *n* (%) or as median [interquartile range]. Demographic and clinical variables were compared among the three diagnoses using the chi-squared test for categorical variables and the Kruskal–Wallis test with post hoc test and Bonferroni correction for continuous variables. Disease severity was categorized based on disease-specific rating scales as follows: HD, Unified Huntington's Disease Rating Scale Part IV score 13–7 = mild, 6–4 = moderate, 3–0 = severe; PD, Hoehn & Yahr stage 1–2.5 = mild, 3 = moderate, 4–5 = severe; ALS, ALS Functional Rating Scale–Revised score = 48–34 mild, 33–17 = moderate, 16–0 = severe.

Abbreviations: ALS, amyotrophic lateral sclerosis; HD, Huntington disease; PD, Parkinson disease.

^aStatistically significant *p*-values.

^bHD vs PD *p* < 0.05 at post hoc analysis.

^cHD vs ALS *p* < 0.05 at post hoc analysis.

^dPD vs ALS *p* < 0.05 at post hoc analysis.

Nutritional assessment

Based on the MNA, 100 (67.6%) patients were at risk of malnutrition. According to disease severity, risk of malnutrition was detected in 30 (50.8%) patients with mild disease, 37 (69.8%) with moderate disease, and 33 (91.7%) with severe disease.

Predictors of malnutrition risk

Univariate and multivariate analyses are reported in Table 2. At univariate analysis, age, disease severity, type of oral intake, penetration, MAS safety, number of masticatory cycles, and time at TOMASS were found to be significantly associated with risk of malnutrition. In the multivariate analysis, data from 116 patients—72 (62.1%) in the malnutrition risk group—were included because of missing data for TOMASS in 32 patients who could not safely swallow solids. Comparison between patients included and excluded from the multivariate analysis is reported in Table S1. Age ≥ 65 years (odds ratio [OR] = 3.16, *p* = 0.014), disease severity (moderate vs mild OR = 3.89, severe vs mild OR = 9.71, *p* = 0.003), number of

masticatory cycles (OR = 1.03, *p* = 0.044), and MAS safety (OR = 1.44, *p* = 0.016) were found to be independently associated with the risk of malnutrition in multivariate analysis.

DISCUSSION

In a population of three neurodegenerative diseases, two thirds of patients were at risk of malnutrition, which is a common condition since the early stages. Older age, disease severity, increased number of masticatory cycles, and signs of impaired swallowing safety during meals were found to be independent predictors of malnutrition risk.

Disease severity and age showed the strongest association with malnutrition risk, both already well-known risk factors. With regard to swallowing function, pharyngeal signs of dysphagia detected by FEES were not predictive of malnutrition risk. Our result partially contrasts from the literature on other populations with dysphagia. In a study by Oliveira and colleagues, residue but not aspiration was associated with a low body mass index (BMI) in a heterogeneous sample of patients with dysphagia referred for instrumental

TABLE 2 Demographic, clinical, and swallowing factors associated with malnutrition risk based on univariate and multivariate logistic regression analysis

Factors	Univariate analysis, N = 148		Multivariate analysis, initial model, n = 116		Multivariate analysis, final model, n = 116 ^a	
	OR (CI 95%)	p	OR (CI 95%)	p	OR (CI 95%)	p
Demographic and clinical factors						
Age, <65 vs ≥65 years	2.60 (1.28–5.27)	0.008 ^b	2.80 (1.07–7.34)	0.036 ^b	3.16 (1.26–7.89)	0.014 ^b
Gender, F vs M	1.53 (0.76–3.07)	0.236	–	–	–	–
Diagnosis		0.185	–	–	–	–
HD vs ALS	0.47 (0.21–1.05)					
PD vs ALS	0.65 (0.26–1.65)					
Disease severity		0.001 ^b		0.008 ^b		0.003 ^b
Moderate vs mild	2.24 (1.03–4.86)		3.68 (1.34–10.06)		3.89 (1.47–10.29)	
Severe vs mild	10.63 (2.94–38.53)		10.85 (1.64–71.61)		9.71 (1.83–51.56)	
Diet type, modified diet vs no restriction	4.56 (2.17–9.56)	<0.001 ^b	1.05 (0.39–2.86)	0.918	–	–
FEES findings, present vs absent						
Valleculae residue, present vs absent	2.08 (0.99–4.34)	0.053	–	–	–	–
Pyramidal sinus residue, present vs absent	1.93 (0.96–3.88)	0.064	–	–	–	–
Penetration, present vs absent	2.32 (1.10–4.90)	0.027 ^b	1.56 (0.53–4.61)	0.418	–	–
Aspiration, present vs absent	1.77 (0.76–4.12)	0.185	–	–	–	–
Oral phase efficiency, continuous						
TOMASS bites	1.26 (0.99–1.60)	0.052	–	–	–	–
TOMASS masticatory cycles	1.03 (1.01–1.06)	0.011 ^b	1.04 (1.00–1.07)	0.082	1.03 (1.01–1.06)	0.044 ^b
TOMASS swallows	1.25 (0.94–1.67)	0.131	–	–	–	–
TOMASS time	1.02 (1.01–1.04)	0.012 ^b	1.00 (0.98–1.02)	0.777	–	–
Meal observation, continuous						
MAS safety	1.41 (1.11–1.79)	0.004 ^b	1.42 (1.04–1.93)	0.028 ^b	1.44 (1.07–1.94)	0.016 ^b
MAS efficacy	1.11 (0.94–1.32)	0.205	–	–	–	–
Meal duration	0.99 (0.95–1.03)	0.731	–	–	–	–

Note: For categorical variables, OR > 1 means a higher probability of the reference group than the control group to be at risk of malnutrition. For continuous variables, OR > 1 means that an increase of 1 point in the value of the variable increases the probability of malnutrition risk.

Abbreviations: ALS, amyotrophic lateral sclerosis; CI, confidence interval; F, female; FEES, fiberoptic endoscopic evaluation of swallowing; HD, Huntington disease; M, male; MAS, Mealtime Assessment Scale; OR, odds ratio; PD, Parkinson disease; TOMASS, Test of Masticating and Swallowing Solids.

^aFinal model after using backward elimination method of variable selection.

^bSignificant *p*-values.

assessment [16]. Saito et al. found that penetration and aspiration were not associated with BMI and serum albumin but were associated with the risk of malnutrition in patients with dysphagia of different etiologies [17]. Such discrepancies can be ascribed to the differences in nutritional outcomes, bolus consistencies and volumes, and populations investigated. Interestingly, swallowing safety during meals was independently associated with malnutrition risk in our population. Swallowing safety during meals depends not only on swallowing safety assessed by instrumental assessment but also on other cognitive, motor, and behavioral aspects that can impact

on swallowing safety during meals. During meals, the patient is required to consume a greater amount of food than during swallowing trials and to devote attentional resources to eating activity for a longer period and often in the presence of distracting factors. Thus, in the case of fatigability or cognitive impairment, swallowing safety may be reduced compared to the findings of the instrumental assessment. Therefore, the meal observation may be more relevant than swallowing function per se in appraising the risk of nutritional complications. As regards the oral phase of swallowing, the association between a prolonged oral phase and malnutrition risk is not

surprising but novel. Chewing difficulties, reduced masticatory rate, and prolonged oral preparation are typical characteristics of neurodegenerative diseases and deserve a specific assessment for their association with nutritional outcome.

The study has some limitations. Only three neurodegenerative diseases were included in the study, and the sample size for each disease (especially for PD) was limited. Additionally, disease-related differences for age, sex, and disease duration were found among the three diagnoses. Future studies on larger samples are necessary to analyze whether the impact of swallowing impairments and demographic and clinical factors on malnutrition risk differs among neurodegenerative diseases. Disease severity was assessed with different disease-specific neurological scales that monitor disease progression but are not comparable to each other. Most severe patients, predominantly ALS patients, were excluded from the multivariate analysis because they could not safely complete the swallowing assessment. Thus, the association between disease severity, swallowing impairment, and malnutrition risk may have been underestimated. Additionally, future study should provide an in-depth comparison between scores of oral phase alteration and scores of pharyngeal phase alteration to enable a more precise evaluation of the impact of the different swallowing phases in determining malnutrition. The MNA is commonly used to assess nutritional status in neurodegenerative diseases. However, it provides a screening of malnutrition but does not allow diagnosis of it. Therefore, a complete nutritional assessment is advisable in future studies. Second, MNA was developed for elderly patients, although previous studies have reported good sensitivity also in young adults [18].

In conclusion, although instrumental assessment is the gold standard for diagnosis of dysphagia, our results support the need for a multidimensional assessment of swallowing in patients with neurodegenerative diseases to appraise the risk of nutritional complications. The present study broadens the focus on dysphagia, stressing the importance of early detection not only of pharyngeal phase impairment, but also of oral phase impairment and meal difficulties.

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CONFLICT OF INTEREST

None.

AUTHOR CONTRIBUTIONS

Nicole Pizzorni: Conceptualization (lead), data curation (lead), formal analysis (lead), investigation (lead), methodology (lead), project administration (equal), supervision (equal), visualization (lead), writing—original draft (lead), writing—review & editing (lead). **Andrea Ciammola:** Investigation (equal), resources (equal), writing—review & editing (equal). **Giovanni Casazza:** Data curation (supporting), formal analysis (supporting), methodology (supporting), writing—review & editing (supporting). **Daniela Ginocchio:** Investigation (equal), writing—review

& editing (supporting). **Federica Bianchi:** Investigation (equal), writing—review & editing (supporting). **Sarah Feroldi:** Methodology (equal), writing—review & editing (supporting). **Barbara Poletti:** Methodology (equal), writing—review & editing (supporting). **Lorenzo Nanetti:** Investigation (equal), writing—review & editing (supporting). **Caterina Mariotti:** Resources (equal), writing—review & editing (equal). **Gabriele Mora:** Conceptualization (equal), investigation (equal), project administration (equal), resources (equal), supervision (equal), writing—review & editing (lead). **Antonio Schindler:** Conceptualization (equal), project administration (lead), resources (equal), supervision (equal), writing—review & editing (lead).

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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