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BASIC SCIENCE SHORT REPORT

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Longitudinal dysphagia assessment in adult patients with nephropathic cystinosis using the Modified Barium Swallow Impairment Profile

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Abstract

Introduction/Aims: Nephropathic cystinosis is a lysosomal storage disorder with known myopathic features, including dysphagia. Evaluation of oropharyngeal swallowing physiology can be standardized using the Modified Barium Swallow Impairment Profile (MBSImP), a validated assessment tool used to analyze and rate swallowing across 17 distinct physiologic domains. Our objective was to better characterize swallowing impairments in nephropathic cystinosis using MBSImP analysis.

Methods: We retrospectively evaluated 40 video fluoroscopic swallowing studies performed at two time points over 1 y in patients with nephropathic cystinosis with various levels of oral and pharyngeal stage dysphagia. Patients completed two self-administered dysphagia outcome measures (the M. D. Anderson Dysphagia Inventory [MDADI] and the 10-item Eating Assessment Tool [EAT-10]).

Results: We demonstrated oral stage and pharyngeal stage dysphagia across domains that impacted bolus control, transit, and clearance through both the oral cavity and pharyngeal lumen. Also captured were deficits related to onset and completeness of laryngeal closure that impact airway protection during swallow. There were significant correlations between pharyngeal total score and EAT-10 ($r = 0.5$, $p < 0.001$) and between oral total score and EAT-10 ($r = 0.7$, $p < 0.001$), MDADI-e ($r = -0.6$, $p < 0.001$), MDADI-p ($r = -0.5$, $p < 0.001$) and MDADI-c ($r = -0.6$, $p < 0.001$). There were no differences in oral or pharyngeal total scores across the 1-y time span.

Discussion: This study identifies oral and pharyngeal stage dysphagia as crucial to patients with nephropathic cystinosis and paves the path for future studies of treatment targets.

KEYWORDS
distal myopathy, dysphagia, MBSImP, nephropathic cystinosis, videofluoroscopy

1 | INTRODUCTION

Nephropathic cystinosis is a rare lysosomal storage disorder due to autosomal recessive mutations in the cystinosin gene (*CTNS*).[1–5] Free cystine crystal deposition in muscle tissues leads to clinical

Abbreviations: EAT-10, 10-item Eating Assessment Tool; MBSImP, Modified Barium Swallow Impairment Profile; MDADI, M. D. Anderson Dysphagia Inventory; OI, overall impairment; OT, oral total; PAS, Penetration-Aspiration Scale; PT, pharyngeal total; QOL, quality of life; VFSS, Video Fluoroscopy Swallow Study.

myopathy,[6,7] characterized by distal greater than proximal muscle weakness,[8–10] prominent swallowing,[11] and breathing difficulties.[12] Dysphagia may impair quality of life and lead to other complications including aspiration pneumonia.[13]

As part of a prospective clinical trial readiness study,[14,15] we conducted video fluoroscopic swallowing studies (VFSS) at baseline and 1 y follow-up. VFSS were analyzed using the Penetration Aspiration Scale (PAS).[16] There were many patients who reported dysphagia where the PAS was not sensitive enough to capture abnormalities.[18–24] In our initial survey, 12/20 (60%) patients reported some degree of difficulty swallowing; however, PAS captured dysfunction in only 3/20 patients (15%).[14,15]

More modern techniques such as the Modified Barium Swallow Impairment Profile (MBSImP) have been applied to different neurological disorders such as myositis and have captured more subtle changes, thereby helping understand the pattern of muscle involvement implicated in dysphagia.[17] MBSImP assesses 17 specific physiologic components of swallow function, allowing the clinician to examine where disordered function correlates with patient experience. For example, difficulty with bolus transport/lingual motion may prevent an individual from eating a wide variety of foods or feeling comfortable eating around others. These complications impact quality of life and may result in difficulty maintaining adequate oral nutrition.[18]

In this retrospective study, we sought to (a) characterize oral and pharyngeal swallowing physiology using MBSImP, and (b) correlate these measures with patient-reported outcome measures.

TABLE 1 MBSImP domain items and percentage of patients with an abnormal score at each visit ($N = 20$ unless otherwise specified)

	Baseline (%)	Visit 2 (%)
Oral impairment domain		
1. Lip closure[a]	0	0
2. Tongue control during bolus hold	50	50
4. Bolus transport/lingual motion	80	85
5. Oral residue[b]	42	40
6. Initiation of the pharyngeal swallow	100	100
Pharyngeal impairment domain		
7. Soft palate elevation	5	5
8. Laryngeal elevation	40	50
9. Anterior hyoid excursion	20	25
10. Epiglottic movement	35	35
11. Laryngeal vestibular closure	35	25
12. Pharyngeal stripping wave	35	35
13. Pharyngeal contraction	20	20
14. Pharyngoesophageal segment opening	15	15
15. Tongue base retraction	35	35
16. Pharyngeal residue	30	30

Abbreviation: MBSImP, Modified Barium Swallow Impairment Profile.
[a]$N = 13$ at baseline; $N = 18$ at visit 2.
[b]$N = 19$ at baseline; $N = 20$ at visit 2.

2 | METHODS

The study was approved by the local Institutional Review Board, the Mass General Brigham Human Research Committee (MGBHRC), and written informed consent was obtained from all participants.

As part of a clinical trial readiness study, we had previously evaluated 20 patients with genetically or biochemically confirmed nephropathic cystinosis in two visits (baseline and visit 2) 1 y apart. All patients had VFSS evaluations and completed patient-reported outcome measures (the M. D. Anderson Dysphagia Inventory[19] [MDADI] and the 10-item Eating Assessment Tool[20] [EAT-10]). The MDADI is a self-administered questionnaire designed to evaluate dysphagia-related quality of life (QOL), with higher scores representing better QOL. The EAT-10 is a self-administered, functional dysphagia outcome measure, with higher scores representing more severe dysphagia. The PAS is an 8-point ordinal scale of airway safety applied to VFSS; a score of 8 indicates that material entered the airway and passed the level of the vocal cords with no effort to eject (Supporting Information Table S1, which is available online).

To gain additional insight into swallowing mechanics in this patient population, we retrospectively analyzed all VFSS data collected using the MBSImP technique. For MBSImP analysis (Table 1), each of the 17 components were rated using an ordinal scale from 0 (no impairment) to a maximum of 2, 3, or 4 depending on the specific component. These ratings are based on operational definitions representing unique observations of structural movement, bolus flow, or both. An overall impression score (OI) is generated via identification of the highest component score for each physiological component as evaluated across bolus trials.[21] The lead author (S.S.) reviewed VFSS and scored 15 domains of MBSImP, skipping items 3 (bolus preparation/mastication) and 17 (esophageal clearance) as these could not be retrospectively determined.

2.1 | Statistical analysis

MBSImP component scores were dichotomized as not impaired (score = 0) versus impaired (score ≥1) for all items except for lip closure, oral residue, tongue base retraction, and pharyngeal residue where a score ≥2 was considered impaired. These components include a score of 1 for trace appearance of barium between structures and were included to enhance visual discrimination between normal coating and signs of impairment such as collection of residue.[21] The 5 MBSImP oral and 10 pharyngeal domain items were subsequently added up to oral total (OT) scores, ranging from 0 to 22, and pharyngeal total (PT) scores, ranging from 0 to 29.[22] Wilcoxon signed-rank Test was used to compare individual item and total scores between baseline and visit 2.[23] Spearman correlation coefficient was used to assess the association between total scores and patient-reported outcomes.[24] All *p*-values of

less than 0.05 were considered significant. We used SAS Release: 3.8 (Basic Edition) (SAS Institute, Cary, NC) and GraphPad Software (GraphPad Software, Inc., San Diego, CA) for statistical analysis.

3 | RESULTS

We previously published demographics and characteristics of baseline and visit 2.[14,15] In summary, a total of 20 patients, 7 male and 13 female, ages 20-64 y (median 29, interquartile range [IQR], [27:39]) participated in the study.

Table 1 summarizes abnormal scores for individual items in the MBSImP domains. All patients had normal lip closure (item 1), and one patient had abnormal soft palate elevation (item 7). Most patients had abnormal bolus transport/lingual motion (item 4). Lip closure and oral residue could not be adequately evaluated in a few patients due to radiographic variances. There was no significant difference between OT or PT scores between baseline and visit 2 (Figure 1).

We individually explored patients with abnormal PAS scores using MBSImP. Three patients with a higher PAS score at baseline also had high PT scores. These patients were impacted by swallowing deficits across physiologic domains, including both laryngeal and pharyngeal functioning. Two patients scored normal PAS scores at baseline and demonstrated mild worsening (PAS score = 2) at visit 2.[25] These patients also had higher scores in oral residue (item 5), initiation of the pharyngeal swallow (item 6), laryngeal elevation (item 8), anterior hyoid excursion (item 9), and pharyngeal residue (item 16), physiologic markers of swallowing differences that were not captured in first pass analysis using only PAS.[24,25,30,31]

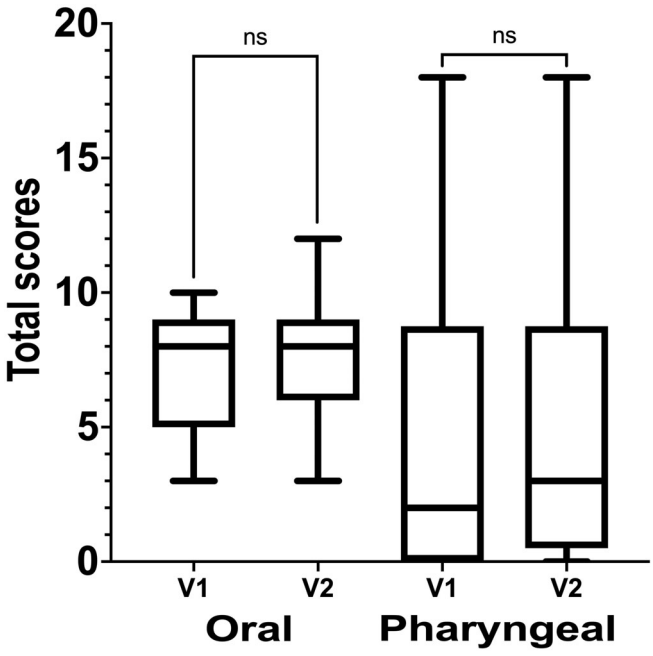

FIGURE 1 Modified Barium Swallow Impairment Profile (MBSImP) oral and pharyngeal total scores (ns, not significant)

There were significant correlations between PT score and EAT-10 ($r = 0.5$, $p < 0.001$) and between OT score and EAT-10 ($r = 0.7$, $p < 0.001$), MDADI-e ($r = -0.6$, $p < 0.001$), MDADI-p ($r = -0.5$, $p < 0.001$), and MDADI-c ($r = -0.6$, $p < 0.001$).

4 | DISCUSSION

This study sheds light on how to better characterize dysphagia across domains of swallowing in patients with nephropathic cystinosis. Our analysis highlights difficulties of tongue control during bolus hold, reduced lingual motion, presence of oral residue, reduced laryngeal elevation, reduced tongue base retraction, and presence of pharyngeal residue in ≥50% of the patients evaluated. These findings highlight the breadth of discrete physiological changes in both oral and pharyngeal phases of swallowing.

Penetration and aspiration are consequences of disordered physiology; therefore, analysis with MBSImP allows the clinician to pinpoint the source of the consequence inviting exploration of postural compensations, diet modifications, or exercise aimed at reduction or elimination of penetration or aspiration. These interventions were not trialed during this retrospective analysis but will be an interesting and important consideration for future investigations. There were subtle improvements in component scores in two patients which could not be entirely explained clinically. A larger study may highlight clinically significant differences over time. Although two patients had facial weakness in examination, none impacted function during swallowing measured by MBSImP item 1 (labial escape of contrast at any point in the swallow).[15]

Monitoring dysphagia using the MBSImP may provide further insight into the natural history of cystinosis. Clinical assessments, such as the Test of Masticating and Swallowing Solids[26] or bedside water swallow tests[27] are useful to increase index of suspicion for dysfunction in both the oral and pharyngeal phases of swallow, respectively. These screening tools are helpful when more advanced methods of evaluation are not available. However, discrete analysis of swallowing using VFSS analysis and MBSImP invites more objective, descriptive, and complete analysis of the 17 components of swallowing physiology with an ability to measure change in function over time. Use of both swallow screening tools, as above, in conjunction with instrumental measurements may provide additional useful descriptions of the swallowing function and allow us to correlate findings on screening measures with results of VFSS.

Limitations of this study include the small sample size and the retrospective nature of the VFSS analysis. As a result, we were not able to include information about mastication or esophageal clearance in this analysis. These components of swallowing are useful to describe overall function, specifically as it relates to patient experience and will be included in the planning for future investigations. Additionally, MBSImP items have not been adequately scrutinized from a psychometrics perspective. Therefore, future endeavors should include developing and validating robust scoring methods.

In summary, this swallowing analysis affords the clinician improved insight into diagnosis and management of dysphagia in

patients with nephropathic cystinosis. Sonies et al described swallowing dysfunction as a late complication of nephropathic cystinosis.[21] We learned that impairments in oral and pharyngeal stages of swallowing are present even in the absence of advanced myopathy. This may impact patient outcomes earlier in the disease process than may have been previously expected[29].

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CONFLICT OF INTEREST

None of the authors has any conflict of interest to disclose.

DATA AVAILABILITY STATEMENT

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

ETHICS STATEMENT

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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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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