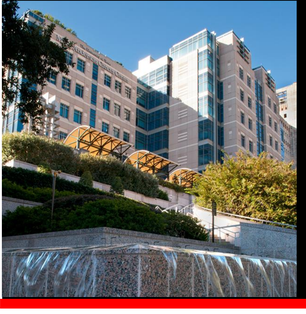

Association of Patient-Reported Outcomes with Functional Swallowing Deficits in Head and Neck Cancer Patients Receiving Radiotherapy

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Background

Patients with head and neck cancer(s) who receive radiotherapy at UTMDACC routinely complete the MD Anderson Symptom Inventory – Head & Neck (MDASI-HN) and the MD Anderson Dysphagia Inventory (MDADI). These survey inventories respectively assess patient-reported severity of symptoms and the impact of specific symptoms (specifically, the ability to swallow) on patients' daily lives. The MDASI-HN consists of 28 Likert-scale items, each asking patients to rate the severity of the symptom or its impact to daily life on a scale of 0, indicating the symptom or impact is not present, to 10, indicating the symptom or impact is as bad as can be imagined to the patient. For the purpose of this study, two specific items were chosen: Item #15 ("Your difficulty swallowing/chewing at its WORST?"; also referred to as the "chewing/swallowing" item) and item #16 ["Your choking/coughing (foods/liquids going down the wrong pipe) at its WORST?"; also referred to as the "choking/coughing" item]. The MDADI consists of 20 items with patients answering on a Likert Scale of Strongly Agree = 1, Agree = 2, No Opinion = 3, Disagree = 4, Strongly Disagree = 5 for all items but E7 ("I do not feel self-conscious when I eat.") and F2 ("I feel free to go out to eat with my friends, neighbors, and relatives."), for which the opposite is true (Strongly Agree = 5, Strongly Disagree = 1). Additionally, patients undergo modified barium swallow (MBS) testing to assess formal fluoroscopically-detected objective swallowing. Performed by diagnostic radiologists, these scans are then read by Speech Language Pathologists, with swallowing function formally graded according to the Dynamic Imaging Grade of Swallowing Toxicity (DIGEST) scale, with a grade of '0' indicating no pharyngeal dysphagia, '1' for mild pharyngeal dysphagia, '2' for moderate pharyngeal dysphagia, '3' for severe pharyngeal dysphagia, and '4' for life threatening pharyngeal dysphagia. The aim of the current project was to derive threshold values of the patient-reported outcome (PRO) measures for the MDASI-HN and MDADI in patients with matched-timepoint clinically administered MBS tests graded on the DIGEST scale to determine if the PRO measures may be used to screen patients for additional instrumental swallowing. Put simply, we wish to ascertain whether a specific patient-detected level of symptom burden may be used to stratify risk of objective swallowing injury.

Methods

Analysis was undertaken under IRB protocols PA14-0947 (PI Hutcheson) and PA-2024-0022 (PI Moreno). Two prospective cohort databases with variables derived from electronic health records were queried for the current project: The Moreno Laboratory (UTMDACC Department of Radiation Oncology – Head & Neck) provided the ePRO MDASI-HN database, which contained completed MDASI-HN items #15 and #16 for patients seen in clinic from January 2021-February 2024; the Hutcheson Laboratory (UTMDACC Department of Head & Neck Surgery) provided the ePRO DIGEST/MDADI database, containing received MDADIs from January 2021-July 2024 and MBS tests graded according to the DIGEST scale from January 2021-July 2024. To be included in the analysis, patients, all of whom were adults (>18 y.o.) with a diagnosed head/neck cancer (HNC) undergoing radiotherapy for HNC, needed to have at least one completed MDASI-HN, MDADI, and DIGEST-graded MBS test within 30 days of each other (e.g., a completed MDASI-HN on Jan. 1, 2022, DIGEST-graded MBS on Jan. 29, 2022, and MDADI on Dec. 15, 2021); any patients who did not have at least one completed series was excluded. Once all obtained data meeting the inclusion criteria were obtained, initial descriptive and frequency testing was done. Additionally, a two-tailed Spearman rank-order correlation testing of both MDASI-HN items, all MDADI subscale and overall composite scores, and DIGEST overall and subcategory grades was conducted to determine the relationship between these scores.

To derive optimum thresholding (i.e. the value of MDASI or MDADI item score(s) that best classify abnormal swallowing using the DIGEST score), we used Breiman Classification and Regression Tree (CRT) analysis (SPSS v24, IBM, NY, USA). CRT was performed with the DIGEST ordinal scale/subscale as a categorical ordinal dependent variable while the associated MDASI-HN items (MDASI *swallowing/chewing* item with the overall DIGEST grade, MDASI *choking/coughing* item with the DIGEST Safety grade) and MDADI Subscales (Physical, Emotional, and Functional and/or Composite) score were set as the independent (or predictor) variable(s). Stopping criteria consisted of a maximum depth set at five (5) levels while the parent and child nodes were respectively set to contain a minimum of 100 and 50 cases; validation was done through random assignment split-sampling into training and test samples. Gini ratio optimization was chosen as it allowed for splitting of the targeted variable in each CRT analysis into child nodes by maximizing the node homogeneity. Additionally, the independent variables were iteratively ranked on their importance to the model for each CRT analysis conducted. Upon completion of all CRT analyses, all resultant trees had three (3) nodes—a single (1) root node and two (2) terminal nodes labeled Node 1 and Node 2, respectively—for one (1) level of depth to determine the index predictor threshold value in terms of dependent variable classification.

Results

A total of 182 (n = 182) HNC patients were included in analysis. The mean age was 62 (range 32-82); the overwhelming majority (86.26%) of patients identified as Male (n = 157). 91.21% of patients (n = 166) identified as not being of Hispanic or Latino heritage, 5.49% (n = 10) self-identified as being Hispanic or Latino, and 3.30% (n = 6) declined to answer or listed their ethnicity as unknown. With regards to overall DIGEST gradings, 59.3% of patients (n = 108) were graded with No Pharyngeal Dysphagia (grade 0) or No to Mild Pharyngeal Dysphagia (grade 0-1), 28.6% (n = 52) had Mild Pharyngeal Dysphagia (grade 1), 7.1% (n = 13) had Moderate Pharyngeal Dysphagia (grade 2) or Moderate to Severe Pharyngeal Dysphagia (grade 2-3) and 4.9% (n = 9) had Severe Pharyngeal Dysphagia (grade 3). For the Safety subscale of DIGEST, 78.5% (n = 143) had No Pharyngeal Dysphagia or No to Mild Pharyngeal Dysphagia, 13.2% (n = 24) had Mild Pharyngeal Dysphagia, 5.5% (n = 10) had Moderate Pharyngeal Dysphagia, and 2.7% (n = 5) had Severe Pharyngeal Dysphagia. The Efficiency subscale of DIGEST contained 68.3% of patients (n = 124) with No Pharyngeal Dysphagia or No to Mild Pharyngeal Dysphagia, 29.3% (n = 37) having Mild Pharyngeal Dysphagia or Mild to Moderate Pharyngeal Dysphagia, 3.3 % (n = 6) with Moderate Pharyngeal Dysphagia, and 8.2% (n = 15) with Severe Pharyngeal Dysphagia. Table 1 displays the frequencies for both MDASI-HN items and all MDADI subscales.

Spearman's rank-order coefficient testing demonstrated several significant relationships. A strong positive correlation was evidenced between both MDASI items, ρ = 0.676, p = 0.001 (see Table 2). Moreover, the MDASI-HN "chewing/swallowing" item was demonstrated to have a positive correlation with the overall DIGEST grade, ρ = 0.250, p =0.001. Yet, there were relatively strong negative correlations evidenced between all the MDADI subscales and each of the MDASI items as shown in Table 2.

When the overall DIGEST grade was set as the Dependent Variable (Figure 2), the root node demonstrated that MDASI-HN "swallowing/chewing" item was the best predictor variable, with those whose item score was ≤ 6.5 corresponded to 58.1% and 62.1% in the training and test samples, respectively, of patients in the samples who were deemed to have No Pharyngeal Dysphagia (grade 0 on the DIGEST scale); yet those whose item score was > 6.5 corresponded to 66.7% with Moderate Pharyngeal Dysphagia (DIGEST grade 2) in the training sample and 40.0% with Mild Pharyngeal Dysphagia in the test sample (DIGEST grade 1). With regards to importance of the model, the item #15 score of the MDASI-HN evidenced 0.023, or 100% when importance was normalized.

When the DIGEST Safety subscale was set as the Dependent Variable (Figure 2), the root node again demonstrated the corresponding MDASI-HN item (in this case, the "choking/coughing" item) was the best predictor variable. Those with an item score ≤ 5.25 corresponded to 81.9% and 75.6% of patients graded 0 on DIGEST scale in the training and test samples, respectively; those with an item score > 5.25 corresponded to 50% of patients graded as having Mild Pharyngeal Dysphagia and 50% with Moderate Pharyngeal Dysphagia, both in the training sample (in the test sample, there were no patients whose item score > 5.25, therefore 0% of patients had any DIGEST grade). Scores for MDASI-HN item #16 demonstrated 0.021 importance, or 100% normalized importance, to the model.

When the Physical Subscale of the MDADI was listed as the first independent variable for thresholding against the overall DIGEST grade, analysis showed it to be the best predictor variable (Figure 3). In both the training and test samples, the majority of patients were graded as having No Pharyngeal Dysphagia regardless of what their MDADI Physical Subscale score was; however, of the patients with a Physical Subscale Score of ≤ 88.75, 30% had DIGEST grade 1, 15% with grade 2, and 7.5% with grade 3 in the training sample while the test sample showed 40.0% of patients had grade 1 and 9.1% had grade 3. Yet, when considering the importance to the model, the Emotional Subscale was shown to have the greatest importance at 0.036 (Graph 1), which normalized to 100% importance, while both the Physical Subscale and overall MDADI Composite Score were both shown to have a normalized importance 92.7% (0.033 importance). Listing the Functional Subscale of the MDADI first showed it to be the key important predictor variable **(Figure 4),** with those who had a score of ≤ 66.0 on the subscale corresponding to 50.0% having Severe Pharyngeal Dysphagia in the training sample while 6.7% were graded to the same level in the test sample; additionally, for those whose score was > 66.0, 69.5% and 56.4% in the training and test samples respectively were given grade 0. Yet when considering importance to the model, despite being the best predictor variable, it was of second most importance to the model at 0.046 (normalized to 97.9%)—the MDADI Composite Score had the greatest importance at 0.047 (normalized to 100%).

Relative risk estimation of the thresholding variable demonstrated patients with MDASI-HN "chewing/swallowing" > 6 demonstrated a relative risk of abnormal swallowing (DIGEST overall > 0) of 1.39 (CI0.91-1.98), while MDASI "coughing/choking" >3 showed altered Safety with an RR of 1.79 (95%CI 1.14-2.8). *Post-hoc* 10^5 bootstrap receiver operator curve (ROC) estimation demonstrated modest discriminant capacity, with a median area-under-the-curve (AUC) of 0.56 (95%CL 0.51-0.65) for MDASI-HN "chewing/swallowing" with overall DIGEST; when done for MDASI-HN "choking/coughing", an AUC of 0.58 (95%CL 0.53-0.71) was shown.

PRO Frequencies

		MDASI-HN Item 15 Score	MDASI-HN Item 16 Score	MDADI Global Subscale Score	MDADI Emotional Subscale Score	MDADI Functional Subscale Score	MDADI Physical Subscale Score	MDADI Composite Score
N	Valid	182	182	182	182	182	182	182
	Missing	0	0	0	0	0	0	0
Mean		1.959	846	84.62	83.86	85.03	81.57	83.33
Median		1.000	000	100.00	86.67	84.00	87.50	90.00
Std. Deviation		2.1816	1.3537	21.635	14.09	15.991	18.88	14.97
Range		9.0	8.0	80	66.67	91	65.00	62.11
Minimum		0	0	20	33.33	9	35.00	37.89
Maximum		9.0	8.0	100	100.00	100	100.00	100.00

Table 1. Frequencies for both MDASI-HN items and all MDADI Subscales.

Spearman Rank-Order Correlation Coefficient

			MDASI-HN Item 15 Score	MDASI-HN Item 16 Score	DIGEST Overall Grade	DIGEST Safety Grade	DIGEST Efficiency Grade	MDADI Global Subscale Score	MDADI Emotional Subscale Score	MDADI Functional Subscale Score	MDADI Physical Subscale Score	MDADI Composite Score
Spearman's rho	MDASI-HN Item 15 Score	Correlation Coefficient	1.000	.676**	.250**	.183*	.062	-.539**	-.525**	-.591**	-.596**	-.639**
		Sig. (2-tailed)		.000	.001	.014	.000	.000	.000	.000	.000	.000
		N	182	182	182	182	182	182	182	182	182	182
	MDASI-HN Item 16 Score	Correlation Coefficient	.676**	1.000	.257**	.208**	.244**	-.410**	-.384**	-.440**	-.483**	-.506**
		Sig. (2-tailed)	.000		.000	.005	.001	.000	.000	.000	.000	.000
		N	182	182	182	182	182	182	182	182	182	182
	DIGEST Overall Grade	Correlation Coefficient	.250**	.257**	1.000	.707**	.830**	-.254**	-.234**	-.285**	-.311**	-.304**
		Sig. (2-tailed)	.001	.000		.000	.000	.001	.001	.000	.000	.000
		N	182	182	182	182	182	182	182	182	182	182
	DIGEST Safety Grade	Correlation Coefficient	.183*	.208**	.707**	1.000	.374**	-.180*	-.175*	-.192**	-.240**	-.234**
		Sig. (2-tailed)	.014	.005	.000		.000	.015	.018	.010	.001	.001
		N	182	182	182	182	182	182	182	182	182	182
	DIGEST Efficiency Grade	Correlation Coefficient	.062**	.244**	.830**	.374**	1.000	-.281**	-.253**	-.265**	-.315**	-.302**
		Sig. (2-tailed)	.000	.001	.000	.000		.000	.000	.000	.000	.000
		N	182	182	182	182	182	182	182	182	182	182
	MDADI Global Subscale Score	Correlation Coefficient	-.539**	-.410**	-.254**	-.180*	-.281**	1.000	.738**	.694**	.785**	.797**
		Sig. (2-tailed)	.000	.000	.001	.015	.000		.000	.000	.000	.000
		N	182	182	182	182	182	182	182	182	182	182
	MDADI Emotional Subscale Score	Correlation Coefficient	-.525**	-.384**	-.234**	-.175*	-.253**	.738**	1.000	.731**	.704**	.881**
		Sig. (2-tailed)	.000	.000	.001	.018	.000	.000		.000	.000	.000
		N	182	182	182	182	182	182	182	182	182	182
	MDADI Functional Subscale Score	Correlation Coefficient	-.591**	-.440**	-.285**	-.192**	-.265**	.694**	.731**	1.000	.660**	.838**
		Sig. (2-tailed)	.000	.000	.000	.010	.000	.000	.000		.000	.000
		N	182	182	182	182	182	182	182	182	182	182
	MDADI Physical Subscale Score	Correlation Coefficient	-.596**	-.483**	-.311**	-.240**	-.315**	.785**	.704**	.660**	1.000	.907**
		Sig. (2-tailed)	.000	.000	.000	.001	.000	.000	.000	.000		.000
		N	182	182	182	182	182	182	182	182	182	182
	MDADI Composite Score	Correlation Coefficient	-.639**	-.506**	-.304**	-.234**	-.302**	.797**	.881**	.838**	.907**	1.000
		Sig. (2-tailed)	.000	.000	.000	.001	.000	.000	.000	.000	.000	
		N	182	182	182	182	182	182	182	182	182	182

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

Table 2. Spearman rank-order correlation coefficients and associated significance levels for both MDASI-HN items, DIGEST scale/subscales, and MDADI subscales.

Discussion

Based on our findings, we found that a positive correlation between patient-reported and instrumental swallowing assessments existed. Moreover, we determined that differential MDASI-HN PRO thresholds were associated with distinct scale/subscale performance on the DIGEST rating, providing preliminary guidance as to the correlation between severity of fluoroscopically-detected swallowing dysfunction and patient-experienced symptom. While we noted substantial differences in the relative risk of abnormal swallowing findings across the observed PRO thresholds, the discriminant capacity of PROs alone was not strong, suggesting that while PRO thresholds may be a useful metric to risk stratify patients, they are insufficient as a single-item surrogate for DIGEST-detected dysphagia, and points the way forward for further investigation of the relationship between low-cost subjective PRO screening and more intensive radiographic swallowing assessment in future efforts.

The current project did not take into consideration site, types, and severity of HNC nor types & duration of radiotherapy received, which may have provided additional context for further understanding and demonstration of significant relationships and other findings; future studies will explore the influence of these factors on Breiman CRT analysis. Additionally, the study limited the timeframe for a completed series to within 30 days, thus reducing patient eligibility and therefore power of study. Future investigations may include thresholding based on chronologic order of the PRO measures and DIGEST-rated clinical MBS test as opposed to just completion of series in a specific timeframe (future studies may wish to consider expanding the timeframe chosen past 30 days).

Conclusions

Both the MDASI-HN and MDADI are PRO measures assessing potential impairments in swallowing and its impact on the daily lives of patients receiving HNC radiotherapy treatment. Patient-reported and objective instrumental swallowing assessments were positively correlated. Additionally, distinct discrimination in DIGEST ratings were found to correspond with differential thresholds of the MDASI-HN. Based on these findings, it is reasonable to suggest future exploration into determining and better understanding the specific relationship(s) between subjective PRO measures and more objective clinical instrumental assessments.

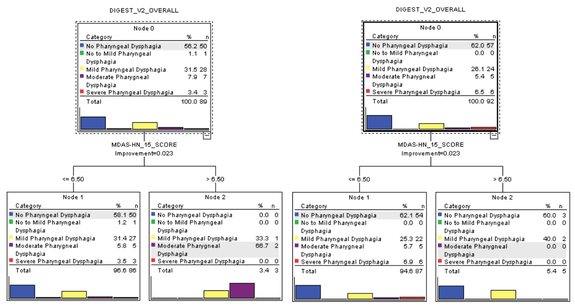


Figure 1. Training (left) and test (right) samples for MDASI-HN "choking/swallowing" (item #15) as primary predictor variable for overall DIGEST grades.

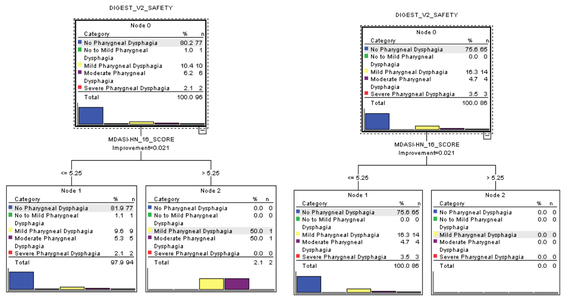


Figure 2. Training (left) and test (right) samples for MDASI-HN "choking/coughing" (item #16) as primary predictor variable for DIGEST Safety subscale grades.

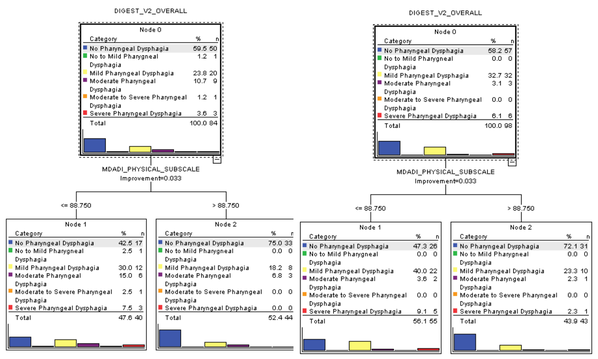


Figure 3. Training (left) and test (right) samples for MDADI Physical Subscale scores as primary predictor variable for overall DIGEST grades.

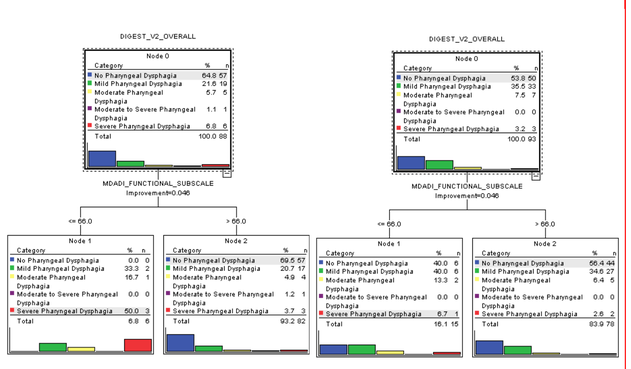
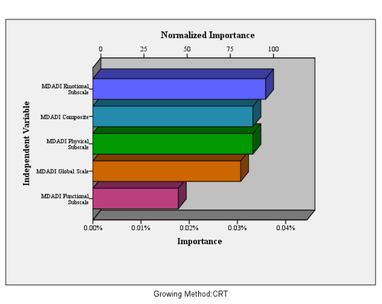
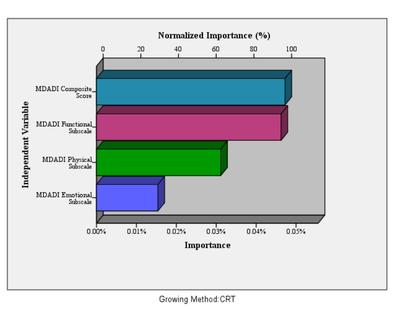


Figure 4. Training (left) and test (right) samples for MDADI Functional Subscale scores as primary predictor variable for overall DIGEST grades.



Graph 1. Ranking of independent (predictor) variables in terms of importance to model for MDADI Physical Subscale as threshold for overall DIGEST grade.



Graph 2. Ranking of independent (predictor) variables in terms of importance to model for MDADI Functional Subscale as threshold for overall DIGEST grade.

RCR

Author contribution: Conceptualization – CDF, KAH, ACM; Data Curation —TCJ, ACM, Ariana J. Sahli on behalf of KAH; Supervision – BM, CDF; Review and editing – TCJ, CDF, BM

Conflict of Interest: None

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