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Patient reported dry mouth: Instrument comparison and model performance for correlation with quality of life in head and neck cancer survivors

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ABSTRACT

Purpose: To identify a clinically meaningful cut-point for the single item dry mouth question of the MD Anderson Symptom Inventory-Head and Neck module (MDASI-HN).

Methods: Head and neck cancer survivors who had received radiation therapy (RT) completed the MDASI-HN, the University of Michigan Hospital Xerostomia Questionnaire (XQ), and the health visual analog scale (VAS) of the EuroQol Five Dimension Questionnaire (EQ-5D). The Bayesian information criteria (BIC) were used to test the prediction power of each tool for EQ-5D VAS. The modified Breiman recursive partitioning analysis (RPA) was used to identify a cut point of the MDASI-HN dry mouth score (MDASI-HN-DM) with EQ-5D VAS, using a ROC-based approach; regression analysis was used to confirm the threshold effect size.

Results: Two-hundred seven respondents formed the cohort. Median follow-up from the end of RT to questionnaire completion was 88 months. The single item MDASI-HN-DM score showed a linear relationship with the XQ composite score ($\rho = 0.80$, $p < 0.001$). The MDASI-HN-DM displayed improved model performance for association with EQ-5D VAS as compared to XQ (BIC of 1803.7 vs. 2016.9, respectively). RPA showed that an MDASI-HN-DM score of $\geq$6 correlated with EQ-5D VAS decline (LogWorth 5.5).

Conclusion: The single item MDASI-HN-DM correlated with the multi-item XQ and performed favorably in the prediction of QOL. A MDASI-HN-DM cut point of $\geq$6 correlated with decline in QOL.

Despite significant improvements in radiation therapy (RT) treatment planning and delivery, RT-induced xerostomia still represents one of the main morbidities affecting many head and neck cancer (HNC) survivors and can result in discomfort and difficulty in chewing, swallowing, and maintaining adequate dental hygiene [1,2] and poorer quality of life (QOL) [3]. Objective measures of xerostomia (e.g. sialometry) and physician ratings (e.g. CTC-AE) are commonly used in both clinical and research settings, yet applicability of these is limited by in their reproducibility and relying solely on physician ratings may underestimate the extent of this treatment-related toxicity and the impact on a patient's function [4,5]. Furthermore, improved treatment outcomes and increasing rates of long term survival for many patients with HNC have brought to focus the importance of comprehensive assessment of patients' overall well-being [6,7].

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Given the growing focus on patients' perception of their disease [8,9], there is a need to develop, validate, and implement reliable, easily administered patient-reported outcome (PRO) assessment tools on a larger scale to allow clinicians to actively address clinically relevant cancer- and treatment-related symptoms [10]. Additionally, clinically relevant and validated thresholds for understanding the severity of specific symptoms need to be established to best guide clinicians on when, if feasible, interventions to alleviate these symptoms should be undertaken.

To address the need to define clinically relevant instrument-specific symptom severity thresholds, and as part of our larger goal to implement routine multi-symptom assessment across the HNC care continuum, this study was conducted to validate the dry mouth question of the MD Anderson Symptom Inventory-Head and Neck module (MDASI-HN) in a cohort of long term HNC survivors.

The aims of this study were to:

1. Characterize long term patient-reported dry mouth and QOL using simultaneously administered PRO tools: the MDASI-HN, the University of Michigan Hospital 8-item self-reported Xerostomia Questionnaire (XQ), and the health visual analog scale (VAS) of EuroQol five dimension questionnaire (EQ-5D);
2. Correlate and assess performance of the single item patient-reported dry mouth question of the MDASI-HN (MDASI-HN-DM) and composite XQ score with QOL (VAS score);
3. Identify a clinically meaningful cut-point for the MDASI-HN-DM in order to screen for those with long term xerostomia who may need additional assessment or intervention and to stratify patient subgroups for comparison in future studies.

Materials and methods

Study population

Following approval from our Institutional Review Board, adults (≥18 years old) previously treated for HNC without evidence of active disease and who completed initial therapy more than 6 months previous were eligible for this prospective symptom assessment study. Study-specific informed consent was provided by all participants, who completed the MDASI-HN, XQ, and VAS of the EQ-5D via telephone interview, conducted using study-specific IRB approved script and questionnaires were delivered verbatim. The PRO data analyzed in this study was cross-sectional in nature and were those collected at the time the patients entered the specific survivorship study. Patient demographic, tumor, and treatment characteristics were extracted from their medical records.

Study instruments

The MDASI-HN, is a previously validated, brief, patient-reported, diseases-site specific, multi-symptom assessment tool. It contains 13 "core symptom items" (symptoms common to all cancer types), 9 additional symptoms items specific to the MDASI-HN, and 6 items concerning how these symptoms interfere with activities of daily living. The 22 symptom items are rated on a 0-10 ordinal scale from "not present" to "as bad as you can imagine", indicating the presence and severity of the symptom in the past 24 h. The patient reported dry mouth item of the MDASI-HN asks patients to rate, "Your having a dry mouth at its worst". Likewise, the symptom interference items are rated on a 0–10 ordinal scale from "did not interfere" to "interfered completely." For this study, we analyzed only the single item patient reported dry mouth score of the MDASI-HN and symptom interference items.

The XQ is a validated patient reported xerostomia assessment tool that is frequently collected in cooperative group clinical trials. It contains 8 questions regarding dryness either during feeding or in the unstimulated state. Patients rate each item from 0 to 10, where 10 indicates the maximum dryness or discomfort due to dryness. The sum of these items produces a composite score with a maximum of 80, than can be normalized to 100 for comparative analyses [2]. Question selection had been performed after review of xerostomia-specific and overall QOL evaluation in HNC patients by investigators at the University of Michigan [11,12].

The EQ-5D is a well-established tool for general assessment of an individual's health state. The questionnaire is accompanied by a VAS, where patients provide an overall impression of their health status on the day of the assessment using a scale from 0 to 100, where 100 represents their best-imaginable health status [13]. For this study, we considered only the VAS component of the EQ-5D as a primary overall QOL outcome for correlation with xerostomia.

Statistical methods

Summary statistics were used to describe the clinical characteristics and questionnaire results. The MDASI-HN-DM and XQ scores were correlated using bivariate analysis using Spearman's correlation coefficients. Moreover, we investigated the direction of the association between xerostomia assessment tools and VAS score and the MDASI-HN-DM and MDASI-HN symptom interference items.

The Bayesian information criteria [BIC] were used to test the prediction power of each xerostomia instrument performance with QOL (VAS score). A lower BIC was considered indicative of improved model performance and parsimony when applying the BIC evidence grades presented by Raftery [14], where the posterior probability of superiority of a lower BIC model is based on the difference (BICi – BICminimum). Per Raftery, a BIC difference of <2 is considered "Weak" (representing a 50–75% posterior probability of BICminimum model being superior to BICi), 2–6 denoted "Positive" (posterior probability of 75–95%), 6–10 as "Strong" (posterior probability of >95%), and >10, "Very strong" (posterior probability >99%).

To identify the possible cutoff score of the MDASI-HN-DM at which a change in the VAS scores could be observed, we used the modified Breiman recursive partitioning analysis (RPA) with a receiver operating characteristic (ROC)-based approach. Training and validation sets for optimization of the MDASI-HN-DM score RPA were conducted using MDASI-HN-DM as a continuous variable. The RPA (decision tree-based partitioning) was performed with 20% verification "holdback" and a minimum split size of 10% per split/partition. Post hoc K-fold cross validation ($n = 10$) was performed to evaluate for over-fitting. Regression analysis was used to confirm the threshold effect size.

Results

Participants

The data from a total of 207 HNC survivors were included in this analysis. Median follow-up time from the end of RT to questionnaire completion was 88 months (range: 21–184) and 160 patients (77%) had greater than 5 years from the end of RT to questionnaire completion. Patient and previous treatment characteristics are listed in Table 1. Of the 140 patients with OPC, 50% had known HPV-association by either HPV or p16 testing. Of those tested, 91% were positive for HPV/p16. Of the 140 patients with OPC, 50% were never smokers. Intensity modulated radiation therapy (IMRT) was utilized in 90% of the patients. Median RT dose was

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