Published in final edited form as:

Int J Radiat Oncol Biol Phys. 2017 March 15; 97(4): 700–708. doi:10.1016/j.ijrobp.2016.06.010.

Long-term, Prospective Performance of the M.D. Anderson Dysphagia Inventory in “Low-Intermediate Risk” Oropharyngeal Carcinoma after Intensity Modulated Radiation Therapy

Ryan P. Goepfert, MD¹, Jan S. Lewin, PhD¹, Martha P. Barrow, MPH¹, G. Brandon Gunn, MD², C. David Fuller, MD, PhD², Beth Beadle, MD, PhD², Adam S. Garden, MD², David I. Rosenthal, MD², Merrill S. Kies, MD³, Vassiliki Papadimitrakopoulou, MD³, Stephen Y. Lai, MD, PhD¹, Neil Gross, MD¹, David L. Schwartz, MD⁴, and Katherine A. Hutcheson, PhD¹

¹Department of Head and Neck Surgery, The University of Texas M.D. Anderson Cancer Center, Houston, Texas, 77030

²Department of Radiation Oncology, The University of Texas M.D. Anderson Cancer Center, Houston, Texas, 77030

³Department of Medical Oncology, The University of Texas M.D. Anderson Cancer Center, Houston, Texas, 77030

⁴Department of Radiation Oncology, The University of Texas Southwestern Medical Center, Dallas, Texas, 75390

Abstract

Purpose—Our objective was to characterize long-term M.D. Anderson Dysphagia Inventory (MDADI) results after primary intensity modulated radiation therapy (IMRT) for oropharyngeal carcinoma (OPC) among patients with “low-intermediate risk” OPC who would be eligible for current trials (e.g. ECOG 3311, NRG HN002, CRUK PATHOS).

Methods—A retrospective pooled analysis combined data from three single-institution clinical trials for advanced stage head and neck carcinoma. Inclusion criteria were clinical stage III/IV OPC (T1-2/N1-2b, T3/N0-2b) treated with definitive split-field IMRT and prospectively-collected MDADI at baseline and at least one post-treatment interval available in trial databases. Patients were sampled to represent likely HPV-associated disease (HPV+/p16+ or <10 pack-years if HPV/p16 unknown). MDADI composite scores were collected at baseline, 6, 12, and 24 months after treatment. Pairwise tests were Bonferroni corrected for multiple comparisons.

Results—Forty-six patients were included. All received bilateral neck irradiation with a median dose of 70Gy and systemic therapy (57% concurrent, 43% induction only). Overall, the mean

Corresponding Author: Katherine A. Hutcheson, PhD, 1515 Holcombe Blvd, Unit 1445, Houston, TX 77030, karnold@mdanderson.org.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Disclosure: The authors have no relevant conflicts of interest to disclose.

baseline MDADI composite score was 90.1, dropping to 74.6 at 6 months ($p<0.0001$) and rising to 78.5 ($p<0.0001$) and 83.1 ($p=0.002$) by 12 and 24 months relative to baseline, respectively, representing a clinically meaningful drop in MDADI scores at 6-months that partially recovers by 24 months (6 v 24-months, $p=0.05$). Poor MDADI scores (composite <60) were reported in 4, 11, 15 and 9% of patients at baseline, 6-, 12-, and 24-months, respectively. 15% of patients had a persistently depressed composite score by at least 20 points at the 24-month interval.

Conclusion—“Low-intermediate risk” patients with OPC treated with laryngeal/esophageal inlet dose-optimized split-field IMRT are highly likely to report recovery of acceptable swallowing function in long-term follow-up. Only 15% report poor swallowing function and/or persistently depressed MDADI at 12 months or more after IMRT. These data serve as a benchmark future trial design and endpoint interpretation.

Summary

This study sought to characterize long-term MDADI results after primary IMRT and systemic therapy for oropharyngeal carcinoma among patients with “low-intermediate risk” disease. Most patients reported “optimal” swallowing (composite >80) at baseline (mean 90.1), which dropped to 74.6, 78.5, and 83.1 at 6, 12, and 24 months after treatment, respectively. Up to 15% reported “poor” swallowing (composite <60) and/or persistently depressed MDADI by 20 points at 12 months or more after treatment.

Introduction

The human papilloma virus (HPV) has transformed our understanding of oropharyngeal carcinogenesis in an increasing number of patients, recognized as a distinct entity from other cancers of the upper aerodigestive tract, particularly those evolving from traditional exposure to tobacco and alcohol [1, 2]. Ang et al first described risk subgroups of oropharyngeal carcinoma (OPC) in 2010, defining “low-risk” as HPV+ with less than 10 pack-years of smoking *or* greater than 10 pack-years with N2a or less nodal disease [3]. “Intermediate risk” included HPV+ disease with greater than 10 pack years of smoking and N2b-N3 disease *or* HPV– disease with less than 10 pack-years of smoking and T3 or smaller primary tumors [3]. Subsequent reports based on single institution series validated this notion of HPV risk stratification and gradually fueled discussions and trial designs to evaluate new therapeutic regimens for these “low-intermediate risk” patients given the increasing recognition that HPV-associated OPC was correlated with improved treatment outcomes and frequently occurred in younger, non-smoking patients [4–7]. Using HPV-associated OPC as the principal eligibility criteria, many active trials seek to overtly *deintensify* treatment through means such as reduced radiation dosing, use of induction chemotherapy or systemic biologic agents rather than concurrent, cytotoxic chemotherapy, and/or primary trans-oral surgical techniques [4, 8]. Their collective aim is to preserve high rates of locoregional control and disease-specific survival while minimizing short and long-term toxicities from therapy.

Though swallowing outcomes after trans-oral surgical management of OPC rarely reflect measures beyond rates of gastrostomy tube dependence and frank aspiration, the radiation oncology literature (specifically IMRT) is much more developed and refined in its

characterization of dysphagia and xerostomia as the most significant long-term toxicities among OPC survivors [9–14]. Dysphagia in particular appears most highly correlated with long-term functional and quality of life outcomes [15–17]. A recent SEER analysis provided population-level evidence that an alarmingly large proportion of head and neck cancer patients develop aspiration pneumonia (i.e., 23.8% 5-year aspiration pneumonia risk after chemoradiation) resulting in substantial morbidity and excess mortality [18]. Due in part to these toxicity and quality of life concerns, it is clear that prospective collection of both functional and patient-reported outcomes (PROs) is imperative if valid comparisons are to be made between treatment algorithms and patients are to be counseled appropriately on their therapeutic options [19–22].

Many of the open and planned clinical trials for treatment of HPV-associated OPC patients (irrespective of those involving de-intensified treatments) include longitudinal measures of patient-reported swallowing function, the most common being the M.D. Anderson Dysphagia Inventory (MDADI). In an effort to support interpretation of these swallowing outcomes and power future studies, presented here are prospectively-collected, longitudinal MDADI data for patients with “low-intermediate risk” OPC after treatment with split-field IMRT along with induction and/or concurrent chemotherapy. Note that this report presents only patient-reported MDADI results so when swallowing function is discussed, this refers to *patient-reported* swallowing function rather than other measures such as modified barium swallow (MBS) results, diet, or gastrostomy tube dependence.

Methods

Eligibility and design

A pooled analysis of three institutional trials for advanced head and neck carcinoma was conducted to evaluate patient-reported swallowing outcomes in patients with “low-intermediate risk” OPC. Inclusion criteria were: (1) biopsy-proven oropharyngeal squamous cell carcinoma in patients receiving definitive treatment on an institutional trial for advanced head and neck carcinoma; (2) stage III/IV disease; (3) split-field IMRT with laryngeal shielding and systemic therapy; (4) likely HPV-associated disease (as defined by p16 positive through immunohistochemistry and/or HPV positive by in situ hybridization, or a smoking history of less than 10 pack-years where p16 and HPV status were unknown); and (5) completion of baseline and at least one post-treatment MDADI completed prospectively as dictated by individual study protocols. See figure 1 for patient selection flowchart. Patients with T4 tumors, evidence of disease recurrence within the follow-up interval, or primary surgical management (in excess of diagnostic biopsy or tonsillectomy) were excluded. As such, the overall cohort represented “low-intermediate risk” OPC (T1-2N1-2b and T3N0-2b patients with likely HPV-associated OPC) treated definitively with IMRT and systemic therapy. All MDADI were collected prospectively using identical procedures and time points in all three trials, and all patients received bilateral, split-field IMRT prescribed using institutional standards based on TNM staging and location of primary. See Table 1 for summary of Consolidated Standards for Reporting Trials (CONSORT) – PRO objective and methods.

MDADI

The MDADI is a 20-item questionnaire designed to assess patient-reported swallowing quality of life with one question pertaining to global function and 19 additional questions representing emotional, functional, and physical subscale domains of swallowing. Responses are categorized by a 5-point Likert scale (strongly agree, agree, no opinion, disagree, strongly disagree) and converted to an ordinal scale with 1 anchored at strongly agree and 5 at strongly disagree. Global, composite, or subscale summary scores are then tabulated by taking the global score, average of the remaining 19 items, or average of the subscale items, respectively, and multiplying by 20. This normalizes the scores on a scale from 20 (worst patient-reported function) to 100 (best patient-reported function). The MDADI was initially developed and validated in a diverse group of head and neck cancer patients with reliable test-retest correlations (0.69–0.88) and internal consistency (Cronbach's alpha 0.96) [23]. For this analysis, composite and subscale scores were analyzed to provide a representation of both overall and domain-specific swallowing, respectively.

Study variables

Demographic, tumor, and treatment variables were queried from trial databases. HPV/p16 status and smoking history were collected from the electronic medical record. MDADI domain scores were retrieved from the institutional MBS tracking database and assigned to baseline or post-treatment (6-, 12-, or 24-months) intervals according to date of radiation completion and with an allowable window of ± 2 months at 6- and 12-month follow-up intervals and ± 6 months at 24 months. The 19-item MDADI composite scores were calculated according to established criteria as a weighted average of subscale scores from the physical, functional, and emotional domain questions. Composite scores were categorized for ease of interpretation such that a score of at least 80 represented "optimal" patient-reported swallowing function, between 60 and 80 was "adequate", and less than 60 was "poor". These cut-points were selected to correspond with classification of MDADI scores in current clinical trials and the Likert scaling of responses.

Statistical methods

Descriptive statistics were calculated to summarize demographics, tumor staging and HPV/p16 status, and treatment history of all patients. Pairwise comparisons between MDADI results over time (each time point compared to baseline as well as other time points) were analyzed using paired *t*-tests while Chi-squared tests were used to compare proportions between groups. All available time points were included without imputation of missing data. Bonferroni corrections were applied to account for comparisons at four intervals; therefore, statistical significance was considered α -level 0.05/6 or 0.008. Statistical analyses were performed using the STATA data analysis software, version 14.0 (StataCorp LP, College Station, TX).

Results

Patient characteristics

Forty-six patients met criteria for inclusion in the analysis. Mean patient age was 55 years and 80% were men. Forty-one percent of primary tumors were in the tonsil and 59% were in the base of tongue. All patients had American Joint Committee on Cancer (AJCC) stage III/IV disease, specifically 34 with T1-2N1-2b disease and 12 with T3N1-2b since no patients were N0. Overall, 16 (35%) patients were current or former smokers (mean: 29.7 pack-years, range: 2–132). Patients with unknown HPV and unknown p16 status (n=13) had a mean of 1.6 pack-years (range: 0–9).

All patients received irradiation of the primary tumor and bilateral neck lymph node basins with a median dose of 70Gy (range: 66–72Gy). Seventy-two percent received induction chemotherapy, 57% received concurrent chemotherapy, and 28% of those treated with systemic therapy received both induction and concurrent therapy. Ten patients had post-treatment neck dissections for concern of persistent disease. Table 2 lists patient, tumor, and treatment specifics. Additional treatment specifications are detailed in trial publications [24–26].

MDADI composite scores

Results were available for at least 34 patients at each post-treatment interval (compliance was 46/46 at baseline, 35/46 at 6 months, and 34/46 at 12 and 24 months). Most patients had “optimal” swallowing function at baseline (mean: 90.2, median: 95.8). Mean composite scores dropped significantly at six months (−15.5 relative to baseline, $p<0.0001$) with negligible recovery by 12 months (+3.9 relative to 6-months, $p=0.95$). By 24 months, more notable partial recovery was observed (+8.5 relative to 6-month nadir, $p=0.05$) but failed to reach statistical significance. Composite scores dropped at least 20 points relative to baseline (“20”) in 37% at six months. The percentage of patients with at least a 20-point drop relative to baseline declined at subsequent follow-up intervals (32% and 15% at the 12- and 24-month intervals, respectively). At this final report, 62% of patients reported composites indicating “optimal” levels of perceived swallowing function. “Poor” levels of perceived function (MDADI<60) were low at all follow-up intervals: 4%, 11%, 15%, and 9% at baseline, 6-, 12-, and 24-months, respectively. Figure 2 depicts composite scores over time and detailed statistics. Figure 3 delineates subgroup stratification data (T1-2N1-2b and T3N1-2b).

MDADI subscale scores

At baseline, patients reported high scores in each domain as expected given high overall composites prior to treatment. By the 6-month interval, all subscale domain scores declined with the physical subscale demonstrating the greatest decrement. Subscale domain scores followed trajectories similar to longitudinal composite trends with a partial recovery over time. Subscale scores were lowest in the physical domain and highest in the functional domain at 24 months. Figure 4 depicts longitudinal subscale domain trends.

Discussion

In this highly selected sample of “low-intermediate risk” OPC patients, the vast majority of patients report acceptable (*i.e.* “optimal” MDADI>80 or “adequate” MDADI>60) swallowing function at baseline prior to initiation of treatment. After laryngeal/esophageal inlet dose-optimized IMRT, patients expectedly convey the greatest reduction in swallowing function at our initial post-treatment MDADI assessment (in our schedule, at roughly 6 months) with a mean decrease in MDADI composite of 15 points. This decrement is particularly notable as we have recently shown that mean differences of 10 points discriminate feeding tube dependence, aspiration status, and Normalcy of Diet on the Performance Status Scale for Head and Neck Cancer Patients (PSS-HN) [27]. Improvement in perceived swallowing was negligible by the 12-month interval (+3.9) but approached meaningful differences by the 24-month (+8.5 relative to the nadir in early follow-up) interval. Despite this relative recovery, mean composite scores remained depressed (approximately 7 points lower) relative to baseline in overall and subgroup analyses, correlating well with the observed phenomena of gradual partial recovery across a variety of PRO inventories in the initial years of OPC survivorship [28].

The trend of partial recovery without complete return to baseline suggests a relative negative impact on long-term swallowing over and above tumor burden caused by the current standard treatment of IMRT delivered around therapeutic doses of 70Gy. While this may be assumed to represent the necessary trade-off between disease control and toxicity, perhaps the most notable impact is best estimated by the observation that 15% of patients experienced a 20-point drop (-20) in composite scores that never recovered during the follow-up interval. Furthermore, 15% and 9% of patients reported “poor” MDADI scores (<60) 12- and 24-months after the end of radiotherapy, respectively. Because of their comparatively good baseline function and prioritization of long-term swallowing, this represents a significant long-term risk, particularly when compared to MDADI data from heterogeneous head and neck cancer populations where a more sizeable portion of patients report poor function prior to treatment and this is predictive of their post-treatment swallowing dysfunction [11, 29, 30].

Drawing conclusions from comparisons of our MDADI results among non-surgically treated patients to surgical outcomes is challenging given overt selection differences in published series. At the very least, baseline function, extent of surgical resection and technique, dosing and nature of adjuvant therapy in surgical cohorts, and differences in primary radiation and systemic therapy regimens across institutions are limiting factors that affect swallowing outcomes in these published series. Acknowledging these potential sources of bias and the lack of treatment randomization in comparative reports, published MDADI results suggest a lack of recovery at 12 months among OPC patients treated with chemoradiation in case-control comparison to trans-oral surgical patients [10]. In contrast, our study indicates continued improvement in non-surgical patients after that one-year window at least to the 24-month mark. Further comparison of our data with published MDADI results of similarly staged patients receiving primary trans-oral surgical therapy (and after approximation of composite scores based on subscale data provided) also indicate at least comparable patient-reported swallowing at 12-months with an upward trajectory thereafter [9, 10]. If nothing

else, these attempted comparisons between surgical and non-surgical MDADI results support empiric evidence that the recovery of swallowing function after primary non-surgical treatment of OPC has a distinct course compared to treatment involving primary surgical resection and that valid comparison of patient-reported swallowing may necessitate longer follow-up intervals than are currently published.

The presentation of data according to staging subgroups (Figure 3) in this study was solely intended to stratify outcomes by staging parameters that dictate eligibility for surgical and non-surgical clinical trials targeting “low-intermediate risk” OPC. Larger sample sizes are needed to power hypotheses regarding differences between staging subgroups. Evidence of associations between age, T stage, and site of disease with long-term swallowing outcomes in OPC cohorts is reported by many investigators and supports need for prospective identification of patients at higher risk for poorer swallowing outcomes [31–33].

Examining the specifics of MDADI subscale scores over time provides insight into the domain of perceived swallowing that is burdensome and likely driving persistently depressed scores. Across subscales, the physical domain scores were lowest and the functional domain scores were highest. This relationship holds throughout the post-treatment interval and suggests that patients perceive physical difficulty swallowing but are able to cope thereby achieving better functionality despite reported physical limitations. This is supported by similar reports of prospective MDADI results in a population of non-surgical head and neck cancer patients, of which almost 2/3 were of the oropharyngeal primaries, offering encouragement to both patients and providers during the challenging phases of recovery [30].

The MDADI is widely used as a PRO marker of perceived swallowing function. Acute and chronic dysphagia can be characterized in many different ways, including the Common Terminology Criteria for Adverse Events grading system, rates of gastrostomy tube dependence, MBS findings, rates of silent aspiration or aspiration pneumonia, and PROs. Numerous studies demonstrate the importance of PRO utilization to complement clinical findings from provider-determined metrics [17, 34–36]. As the complementary nature of PROs and more objective swallow measures has been robustly described, our preferred approach is also to pair the MDADI with a panel of swallow-specific measures. These include MBS as an instrumental measure of swallow safety, efficiency and physiology, and the Normalcy of Diet item from the PSS-HN as a measure of swallow-specific functional status [22, 37]. Some authors have advocated for composite indices that combine these data to obtain a more representative approximation of swallowing dysfunction in head and neck cancer patients [22, 38]. Recognizing these complexities, the sampling frame and outcome measure of this study were carefully selected. The MDADI was chosen as the focus of this paper to allow detailed profiling of the measure in the context of current standard therapy without influence from other available data that we recognize contribute to interpretation of long-term swallowing outcomes such as PSS-HN diet levels, videofluoroscopic findings, or feeding tube rates.

Eligibility were defined to represent patients who might be eligible for current or planned clinical trials for “low-intermediate risk” OPC. In particular, T1-2N1-2b patients may be

eligible for surgical trials such as Eastern Cooperative Oncology Group 3311 (E3311) while both AJCC staging subgroups would be eligible for radiotherapy trials such as NRG Oncology HN002 and Cancer Research UK Post-operative Adjuvant Therapy for HPV-positive Tumours (PATHOS) [39]. From our dataset that included MDADI as the sole PRO instrument, we cannot comment on use of the MDADI as the preferred swallowing-specific PRO in prospective trials. However, by consensus of the scientific community, the MDADI has been widely selected as the primary swallowing-related PRO in a number of currently enrolling prospective trials, including those listed previously. Regarding methodologic considerations in studies adopting MDADI as an outcome measure, our recent efforts to establish the clinical relevance of difference in MDADI scores using both anchor- and distribution-based methods suggests that a 10-point between group difference in composite MDADI is clinically relevant. The optimal time points for PRO assessment depend on the study question, but experience characterizing evolution and recovery of swallowing outcomes longitudinally suggests that at least three assessment points are needed: baseline (pretreatment), post-treatment “nadir” (herein, 3–6 months) after recovery of peak mucosal toxicity, and new baseline after initial recovery (12–24 months). This approach formed the rationale for MDADI collection in the prospective trials included in this study, realizing that it will not capture on-treatment swallowing outcomes or late swallowing-related complications that can occur many years into survivorship.

Prospective, longitudinal ascertainment of MDADI scores over two years of survivorship represents a meaningful contribution to our understanding of swallow-specific outcomes in this rapidly growing subgroup of head and neck cancer patients for whom survivorship issues take center stage. Our report is limited by a small sample size and the pooling of subjects from three institutional clinical trials for retrospective analysis that resulted in heterogeneity in systemic therapies and follow-up timing given variations in trial protocol design and implementation. Radiation therapy was uniformly bilateral, split-field IMRT and planned according to institutional standards. Differences in the timing of MDADI assessment were accounted for by broadening the periods for each interval. While these follow-up intervals may represent clinically distinct points that may truly reflect the trajectory of patient swallowing function in the post-treatment period, it does limit comparisons between intervals and makes distinctions between adjacent time points less clear. Moreover, missing MDADI in roughly one-fourth of patients during the follow-up interval introduces selection bias that cannot be accounted for in this study design. Given the rise of HPV-associated OPC and its improved survival outcomes with comparatively healthier patients combined with convincing data that dysphagia is the most important long-term outcome after contemporary non-surgical treatment of OPC, we believe this study holds great importance in presenting prospectively collected data using the most commonly used patient-reported swallowing outcome measure.

Analysis of long-term, patient-reported swallowing outcomes in a cohort of “low-intermediate risk” OPC treated with laryngeal/esophageal inlet dose-optimized IMRT indicate high rates of acceptable patient-reported swallowing function at baseline and 24 months. However, a small but significant portion of patients report persistent decline in swallowing function at clinically meaningful levels. These data add to our understanding of

treatment sequelae and serve to inform the interpretation and design of future clinical trials investigating treatment de-intensification regimens.

References

1. Paz IB, et al. Human papillomavirus (HPV) in head and neck cancer. An association of HPV 16 with squamous cell carcinoma of Waldeyer's tonsillar ring. *Cancer*. 1997; 79(3):595–604. [PubMed: 9028373]
2. Gillison ML, et al. Evidence for a causal association between human papillomavirus and a subset of head and neck cancers. *J Natl Cancer Inst*. 2000; 92(9):709–720. [PubMed: 10793107]
3. Ang KK, et al. Human papillomavirus and survival of patients with oropharyngeal cancer. *N Engl J Med*. 2010; 363(1):24–35. [PubMed: 20530316]
4. O'Sullivan B, et al. Deintensification candidate subgroups in human papillomavirus-related oropharyngeal cancer according to minimal risk of distant metastasis. *J Clin Oncol*. 2013; 31(5): 543–550. [PubMed: 23295795]
5. Huang SH, et al. Refining American Joint Committee on Cancer/Union for International Cancer Control TNM stage and prognostic groups for human papillomavirus-related oropharyngeal carcinomas. *J Clin Oncol*. 2015; 33(8):836–845. [PubMed: 25667292]
6. Fakhry C, et al. Improved survival of patients with human papillomavirus-positive head and neck squamous cell carcinoma in a prospective clinical trial. *J Natl Cancer Inst*. 2008; 100(4):261–269. [PubMed: 18270337]
7. Bhatia A, Burtneß B. Human Papillomavirus-Associated Oropharyngeal Cancer: Defining Risk Groups and Clinical Trials. *J Clin Oncol*. 2015; 33(29):3243–3250. [PubMed: 26351343]
8. Quon H, Richmon JD. Treatment Deintensification Strategies for HPV-Associated Head and Neck Carcinomas. *Otolaryngologic Clinics of North America*. 2012; 45(4):845–861. [PubMed: 22793856]
9. Sinclair CF, et al. Patient-perceived and objective functional outcomes following transoral robotic surgery for early oropharyngeal carcinoma. *Arch Otolaryngol Head Neck Surg*. 2011; 137(11): 1112–1116. [PubMed: 22106235]
10. More YI, et al. Functional swallowing outcomes following transoral robotic surgery vs primary chemoradiotherapy in patients with advanced-stage oropharynx and supraglottis cancers. *JAMA Otolaryngology - Head and Neck Surgery*. 2013; 139(1):43–48. [PubMed: 23247974]
11. Feng FY, et al. Intensity-modulated chemoradiotherapy aiming to reduce dysphagia in patients with oropharyngeal cancer: Clinical and functional results. *Journal of Clinical Oncology*. 2010; 28(16): 2732–2738. [PubMed: 20421546]
12. Schwartz DL, et al. Candidate dosimetric predictors of long-term swallowing dysfunction after oropharyngeal intensity-modulated radiotherapy. *International Journal of Radiation Oncology Biology Physics*. 2010; 78(5):1356–1365.
13. O'Hara J, et al. Transoral laser microsurgery±adjuvant therapy versus chemoradiotherapy for stage III and IVA oropharyngeal squamous cell carcinoma: Preliminary comparison of early swallowing outcomes. *Head and Neck*. 2015
14. Mercante G, et al. Quality of life and functional evaluation in patients with tongue base tumors treated exclusively with transoral robotic surgery: A 1-year follow-up study. *Journal of Cranio-Maxillofacial Surgery*. 2015
15. Langendijk JA, et al. Impact of late treatment-related toxicity on quality of life among patients with head and neck cancer treated with radiotherapy. *J Clin Oncol*. 2008; 26(22):3770–3776. [PubMed: 18669465]
16. Wilson JA, Carding PN, Patterson JM. Dysphagia after nonsurgical head and neck cancer treatment: patients' perspectives. *Otolaryngol Head Neck Surg*. 2011; 145(5):767–771. [PubMed: 21746839]
17. Hunter KU, et al. Toxicities affecting quality of life after chemo-IMRT of oropharyngeal cancer: Prospective study of patient-reported, observer-rated, and objective outcomes. *International Journal of Radiation Oncology Biology Physics*. 2013; 85(4):935–940.

18. Xu B, et al. Aspiration pneumonia after concurrent chemoradiotherapy for head and neck cancer. *Cancer*. 2015; 121(8):1303–1311. [PubMed: 25537836]
19. Gillespie MB, et al. Swallowing-related quality of life after head and neck cancer treatment. *Laryngoscope*. 2004; 114(8 I):1362–1367. [PubMed: 15280708]
20. Rosenthal DI, et al. Measuring head and neck cancer symptom burden: the development and validation of the M. D. Anderson symptom inventory, head and neck module. *Head Neck*. 2007; 29(10):923–931. [PubMed: 17358040]
21. Cartmill B, et al. Long-term functional outcomes and patient perspective following altered fractionation radiotherapy with concomitant boost for oropharyngeal cancer. *Dysphagia*. 2012; 27(4):481–490. [PubMed: 22362547]
22. Hutcheson KA, Lewin JS. Functional outcomes after chemoradiotherapy of laryngeal and pharyngeal cancers. *Curr Oncol Rep*. 2012; 14(2):158–165. [PubMed: 22249533]
23. Chen AY, et al. The development and validation of a dysphagia-specific quality-of-life questionnaire for patients with head and neck cancer: The M. D. Anderson Dysphagia Inventory. *Archives of Otolaryngology - Head and Neck Surgery*. 2001; 127(7):870–876. [PubMed: 11448365]
24. Kies MS, et al. Induction chemotherapy and cetuximab for locally advanced squamous cell carcinoma of the head and neck: results from a phase II prospective trial. *J Clin Oncol*. 2010; 28(1):8–14. [PubMed: 19917840]
25. Schwartz DL, et al. Adaptive radiotherapy for head-and-neck cancer: initial clinical outcomes from a prospective trial. *Int J Radiat Oncol Biol Phys*. 2012; 83(3):986–993. [PubMed: 22138459]
26. Massarelli E, et al. Weekly paclitaxel, carboplatin, cetuximab (PCC), and cetuximab, docetaxel, cisplatin, and fluorouracil (C-TPF), followed by risk-based local therapy in previously untreated, locally advanced head and neck squamous cell carcinoma (LAHNSCC). *J Clin Oncol*. 2015; 33(suppl; abstr 6001).
27. Hutcheson KA, et al. What is a clinically relevant difference in MDADI scores between groups of head and neck cancer patients? *Laryngoscope*. 2015
28. Vainshtein JM, et al. Long-term quality of life after swallowing and salivary-sparing chemo-intensity modulated radiation therapy in survivors of human papillomavirus-related oropharyngeal cancer. *Int J Radiat Oncol Biol Phys*. 2015; 91(5):925–933. [PubMed: 25832685]
29. Patterson JM, et al. Swallowing in the first year after chemoradiotherapy for head and neck cancer: clinician- and patient-reported outcomes. *Head Neck*. 2014; 36(3):352–358. [PubMed: 23780908]
30. Roe JW, et al. Patient-reported outcomes following parotid-sparing intensity-modulated radiotherapy for head and neck cancer. How important is dysphagia? *Oral Oncol*. 2014; 50(12):1182–1187. [PubMed: 25448227]
31. Starmer HM, et al. Swallowing outcomes in patients with oropharyngeal cancer undergoing organ-preservation treatment. *Head Neck*. 2014; 36(10):1392–1397. [PubMed: 24038454]
32. Hunter KU, et al. Aspiration pneumonia after chemo-intensity-modulated radiation therapy of oropharyngeal carcinoma and its clinical and dysphagia-related predictors. *Head and Neck*. 2014; 36(1):120–125. [PubMed: 23729173]
33. Yang CJ, et al. Pretreatment Dysphagia Inventory and videofluorographic swallowing study as prognostic indicators of early survival outcomes in head and neck cancer. *Cancer*. 2015; 121(10):1588–1598. [PubMed: 25639759]
34. Pauloski BR, et al. Swallow function and perception of dysphagia in patients with head and neck cancer. *Head and Neck*. 2002; 24(6):555–565. [PubMed: 12112553]
35. Rinkel RNPM, et al. Validity of Patient-Reported Swallowing and Speech Outcomes in Relation to Objectively Measured Oral Function Among Patients Treated for Oral or Oropharyngeal Cancer. *Dysphagia*. 2015; 30(2):196–204. [PubMed: 25622807]
36. Ding R, Logemann JA. Patient self-perceptions of swallowing difficulties as compared to expert ratings of videofluorographic studies. *Folia Phoniatrica et Logopaedica*. 2008; 60(3):142–150. [PubMed: 18334849]
37. List MA, Ritter-Sterr C, Lansky SB. A performance status scale for head and neck cancer patients. *Cancer*. 1990; 66(3):564–569. [PubMed: 2364368]

38. Caudell JJ, et al. Factors associated with long-term dysphagia after definitive radiotherapy for locally advanced head-and-neck cancer. *Int J Radiat Oncol Biol Phys.* 2009; 73(2):410–415. [PubMed: 18635320]
39. Owadally W, et al. PATHOS: a phase II/III trial of risk-stratified, reduced intensity adjuvant treatment in patients undergoing transoral surgery for Human papillomavirus (HPV) positive oropharyngeal cancer. *BMC Cancer.* 2015; 15(1):602. [PubMed: 26311526]

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Figure 1.
Patient eligibility flowchart

Figure 2.
Overall MDADI composite distribution trends and statistics over time.

Figure 3.
MDADI composite distribution trends and statistics by staging subgroups over time.

Figure 4.
MDADI subscale scores over time.

Table 1**CONSORT-PRO Objectives and Methods**

Objective	Characterize longitudinal patient-reported swallowing outcomes using the MDADI among non-surgical OPC patients
Trial Designs	Three non-surgical therapeutic clinical trials for untreated squamous cell carcinoma of the upper aerodigestive tract
Participants	OPC; stages T1–3, N0-2b, M0; HPV+/p16+ or <10pack/years; baseline and 1 post-treatment MDADI
Intervention	Primary IMRT with induction and/or concurrent chemotherapy
Outcome	MDADI composite score difference at 6, 12, and 24 months compared to baseline (*secondary outcome measures from trials)
Statistical methods	MDADI reports from all available time points (baseline, 6, 12, 24 months) were included without imputation of missing data.

Abbreviations: CONSORT-PRO, Consolidated Standards of Reporting Trials – Patient-Reported Outcomes; MDADI, MD Anderson Dysphagia Inventory; OPC, oropharyngeal carcinoma; T, tumor; N, node; HPV, human papilloma virus; IMRT, intensity modulated radiation therapy

Table 2

Patient Characteristics (n = 46)

	No. of Patients (%)
Sex	
Male	37 (80)
Female	9 (20)
Age (mean)	55
Primary Site	
Tonsil	19 (41)
Base of Tongue	27 (59)
T classification	
1	11 (24)
2	23 (50)
3	12 (26)
N classification	
0	0 (0)
1	2 (4)
2a	6 (13)
2b	38 (83)
HPV/p16 status	
HPV+, p16+	23 (50)
HPV-/unknown, p16+	7 (15)
HPV+, p16unknown	3 (7)
HPVunknown, p16unknown	13 (28)
Smoking history at diagnosis	
Never	30 (65)
Former	10 (22)
Current	6 (13)
Treatment combination	
Induction + IMRT	20 (43)
Induction + Concurrent/IMRT	13 (28)
Concurrent/IMRT	13 (28)
IMRT Dosing	
66Gy	15 (33)
70Gy	27 (59)
>70Gy	4 (8)
Post-treatment Neck Dissection	
Yes	10 (22)
No	36 (78)
Post-treatment MDADI results per patient	
3 of 3	19 (41)
2 of 3	19 (41)

No. of Patients (%)	
1 of 3	8 (17)

Abbreviations: T, tumor; N, node; HPV, human papillomavirus; IMRT, intensity modulated radiotherapy; Gy, gray; MDADI, MD Anderson Dysphagia Inventory

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript