Self-reported oral morbidities in long-term oropharyngeal cancer survivors: A cross-sectional survey of 906 survivors

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ABSTRACT

Objective: The purpose of this study is to estimate the prevalence and severity of late oral morbidities in disease-free oropharyngeal cancer (OPC) survivors using patient reported outcomes.

Materials and methods: Cross-sectional survivorship survey of patients who completed definitive treatment for oropharyngeal carcinoma > 12-months previously without evidence of recurrence, second primary malignancy, or distant metastasis after index cancer. Using MD Anderson Symptom Inventory- Head and Neck Module (MDASI-HN), scores for 4 self-reported oral morbidities: dry mouth, mucus secretions, mouth and throat sores, and teeth and gum issues were evaluated.

Results: Among 906 survey respondents (57% response rate), (median survival time: 7 years), "dry mouth" and "problems with my mucus" were reported moderate/severe (MDASI-HN item score ≥ 5) in 39% and 22% of respondents, while 14% reported moderate/severe "problems with teeth and gums". Smoking at the time of survey was significantly associated with the severity of oral symptoms including "mucus" (p = 0.03), "dry mouth" (p = 0.02), "problems with my teeth and gums" (p = 0.001). All the oral morbidities symptom items significantly, positively correlated with the mean interference scores reflecting adverse impact to quality of life (QOL): "mucus" (r = 0.445, p < 0.001), "problems with teeth" (r = 0.446, p < 0.001), "mouth sores" (r = 0.321, p < 0.001) and "dry mouth" (r = 0.459, p < 0.001).

Conclusion: This study showed that 45.5% reported at least one late oral morbidity at moderate/severe level which negatively correlated overall function, even years after treatment.

Introduction

With the rise in incidence of HPV-positive oropharyngeal cancer (OPC), increased treatment response and decreased recurrence rates, there is a growing population of OPC survivors who now go on to live years (often decades) with long-term effects of therapy [1–3]. Oral morbidities such as mucositis, osteoradionecrosis and xerostomia are common side effects when oral tissues such as mucosa, bone, and

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salivary glands, are within the volume of tissue irradiated. Furthermore, salivary changes affect the oral flora and overall risk of dental caries further increasing risks of osteoradionecrosis and dental/oral complications [4]. These complications are well described in the literature and can easily be evaluated by clinicians; however, at times, there is a discordance between clinician- and patient-reported measures [5–9]. The best example of this is xerostomia, in which an objective decrease in salivary production does not directly correlate to subjective perception of xerostomia despite the persistent impact of hyposalivation on oral health. This discordance does not negate the need for objective measures; however, clinicians increasing recognize the value of more subjective, patient-reported outcomes assessment to understand toxicities of modern therapy [9].

Patient-reported outcomes (PROs) are quickly becoming a part of the decision-making process for choosing the best and most effective therapy for cancers [10]. The MD Anderson Symptom Inventory- Head and Neck Module (MDASI-HN) is a validated instrument used to assess patient symptoms associated specifically with head and neck cancer and its treatment [11,12]. The MDASI-HN is completed by the patient to assess the severity of 22 common head and neck symptoms such as xerostomia, oral mucositis, challenges with mucus, and difficulty chewing/swallowing. MDASI-HN includes 4 symptom items directly reflecting oral morbidities: "dry mouth," "mucus," "problems with teeth/gums," and "mouth sores." Patient self-reporting is an opportunity to better understand the impact of treatment which then can inform practitioner decisions and research priorities. Yet, current estimates of late effects of radiation therapy are primarily derived from small or highly selective clinical studies, and often comprise heterogeneous groups of head and neck cancers for whom radiation fields and surgical impact on oral cavity vary greatly [13]. Further, there is lack of data about the association between the oral morbidities and the influence on the quality of life and functional status of survivors, particularly in homogenous groups such as OPC survivors. The purpose of this study, therefore, is to estimate the prevalence and severity of late oral morbidities using a validated PRO questionnaire in a large sample of long-term (> 1-year) disease free OPC survivors at MD Anderson Cancer Center, more specifically to evaluate and characterize the self-reported symptoms that relate to late treatment side effects to salivary glands as well as oral hard and soft tissues.

Materials and methods

This cross-sectional survivorship survey was conducted from September 2015 to July 2016 among OPC patients who received their primary treatment (radiation ± chemotherapy, ± surgery) at The University of Texas, M.D. Anderson Cancer Center (MDACC) between 01/01/2000 and 12/01/2016 were eligible for survey. The study population included adult patients greater than 18 years of age with no evidence of locoregional recurrence, second primary malignancy or distant metastasis at the time of survey. Potential subjects excluded were those having received treatment less than two years prior to the time of the survey. Approval for this study was granted by the Institutional Review Board of MDACC PA11-0936, and patients provided informed consent by survey response.

Survey administration

Participants were asked to complete the survey once. The survey was administered using an adapted version of Dillman method [14], including: (1) a letter of invitation via the US postal service to eligible patients 2–3 weeks prior to the initial contact, (2) the survey questionnaire to all eligible participants via an online server Qualtrics or US postal service; and (3) two reminders were sent to non-responders via US postal service at 2–3 weeks and 4–5 weeks after the initial contact. Participants were contacted by multiple modes of communication, including email (among those with addresses on record) via Qualtrics or

myMDAnderson (a secure, personalized patient website), and US postal service via first-class mail with a return envelope.

The MDASI-HN questionnaire

The survey included the MDASI-HN (MD Anderson Symptom Inventory-Head and Neck Module), a psychometrically validated 28-items questionnaire containing 13 "core" items representing important symptoms common to all cancer types, 9 "head and neck cancer specific" items, and 6 questions regarding the extent to which the symptoms interfere with activities of daily life [12]. The validation sample included patients along the continuum of survivorship (pre, during, and post-treatment). MDASI-HN has not, however, been validated in an exclusive sample of long-term cancer survivors. The 6 interference items are rated on numeric scales of 0–10 from" did not interfere" to "interfered completely"; interference mean score is felt to reflect a proxy for health-related quality of life and overall patient function. The MDASI-HN symptoms items are rated on numeric scales of 0–10 from" not present" to "as bad as you can imagine". MDASI-HN items pertaining to self-reported oral morbidities were the primary endpoints of interest for this analysis. These comprise 4 items including: "dry mouth", "mucus", "mouth sores", and "problems with my teeth/gums".

Statistical analysis

Mean values for each MDASI- HN oral morbidities items were plotted, and to clarify the clinical interpretation of these data, the percentage of patients with moderate to severe perceived oral symptoms (ratings of ≥ 5 on the scale of 10) were calculated for each item. Primary covariates considered in subgroup comparisons and correlations of self-reported oral morbidities included sex, age, cancer subsite, tumor classification, therapeutic combination, dental status, follow up time, and smoking at diagnosis and at time of survey, with comparisons Bonferroni corrected (p < 0.006 considered significant for 9 clinical covariates tested). The data were analyzed using one-way ANOVA (categorical covariates), with post hoc students *t*-test, and pairwise correlations for continuous covariates. Analysis was performed in Stata Data Analysis Software (Version 14.0 College Station, TX).

Selected chart review

To understand the nature of clinical correlates for the symptom item, "problems with my teeth/gums", chart review was conducted among those respondents who reported moderate to severe values for "problems with teeth/gums" to further clarify the dental challenge. Chart detected dental challenges in this subgroup were coded: as (1) periodontal disease, (2) multiple missing teeth, (3) osteonecrosis, or (4) no chart documented problem.

Results

A total 1728 participants met the inclusion criteria above in order to be eligible for survey; 989 patients responded for an initial response rate of 58%. Eighty-two subjects were excluded after further chart abstraction revealed them ineligible for this analysis yielding a total of 906 subjects included in this study.

Clinical and demographic profiles are detailed in Table 1. The mean age for patients was 65 years (SD 8.4) and 84% of the patients were male. The majority of the tumors were located in the tonsil (46%) and the base of the tongue (49%). The majority of the patients (67%) were treated by combination of radiation and chemotherapy, and 3% of the patients were treated by primary surgery. Thirty-one patients (3%) reported to be current at the time of the survey, whereas at the time of diagnosis, 60 patients (6%) were current smokers and 428 patients (47%) were former smokers. Four hundred and forty-one (49%) tumors tested positive for human papilloma virus (HPV) association (HPV