Oral Oncology 91 (2019) 13–20

Contents lists available at ScienceDirect

Oral Oncology

journal homepage: www.elsevier.com/locate/oraloncology

Patient-reported outcomes of symptom burden in patients receiving surgical or nonsurgical treatment for low-intermediate risk oropharyngeal squamous cell carcinoma: A comparative analysis of a prospective registry

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ARTICLE INFO

Keywords:
Oropharyngeal cancer
Radiation
Transoral robotic surgery
MDASI
Patient reported outcomes

ABSTRACT

Purpose: To explore treatment-related changes in symptom burden and quality of life (QOL) in oropharyngeal squamous cell cancer (OPSCC) patients treated surgically and non-surgically.

Patients and Methods: Eighty-six patients with human papillomavirus–associated OPSCC treated at the Head and Neck Center at The University of Texas MD Anderson Cancer Center were recruited to a prospective registry study between 2014 and 2016 and completed the core, head and neck-specific, and symptom interference sections of the MD Anderson symptom inventory (MDASI) multi-symptom questionnaire and the EQ-5D health status assessment as a measure of QOL at four time points.

Results: Longitudinal improvements from post-treatment nadir were observed across all groups. For patients treated with single modality, symptom interference, but not core and head and neck specific, MDASI scores were significantly better at 6 months in patients treated with surgery than radiation ($P = 0.04$). For patients treated with multiple modalities, scores for each of the three domains (i.e., core, head and neck -specific, and interference MDASI) were significantly better in the surgical group than the nonsurgical group at treatment completion ($P = 0.0003$, $P = 0.0006$ and $P = 0.02$) and 6 weeks ($P = 0.001$, $P = 0.05$ and $P = 0.04$), but not 6 months ($P = 0.11$, $P = 0.16$ and $P = 0.040$). No significant differences in EQ5D health status were observed between groups at any time point, reflecting similar overall QOL in all groups.

Conclusion: Symptom burden and QOL improves after treatment in OPSCC survivors over time regardless of whether primary surgical or nonsurgical treatment is used, although acute symptom profiles may differ.

Introduction

The incidence of oropharyngeal squamous cell cancer (OPSCC) has risen rapidly, mainly attributable to the human papillomavirus (HPV) [1,2]. The increasing incidence of HPV-related OPSCC has now surpassed that of HPV-related cervical cancer to become the most common HPV-related cancer in the United States [3]. HPV-related OPSCC represents a distinct disease phenotype that more often affects younger patients without the traditional risk factors (tobacco, alcohol) for head and neck cancer. These patients frequently present with small or unknown primary tumors that might be favorable for primary surgical management [4]. Regardless of treatment, the prognosis for patients with HPV-related OPSCC is significantly better than that of patients with HPV-negative disease [5].

Given the favorable prognosis of HPV-related OPSCC, there is an increased focus on long-term functional outcomes and quality-of-life (QOL). Yet, comparatively little data exists to guide patients and providers in selecting among surgical and non-surgical treatment options for OPSCC. Since patients often have multiple options presented to them that offer equal chance of cure, appropriate treatment counseling largely hinges on differences in the symptom profiles of these treatments options. In the current study, we conducted secondary analysis of

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https://doi.org/10.1016/j.oraloncology.2019.01.020
Received 15 October 2018; Received in revised form 22 January 2019; Accepted 25 January 2019

prospective registry data to assess longitudinal changes in symptom burden and QOL after treatment, specifically comparing the outcomes of OPSCC patients managed surgically and non-surgically in the setting of single or multi-modality care.

Materials and Methods

Patients and procedures

The data for this study originated from the MD Anderson Cancer Center (MDACC) Oropharynx Cancer Registry Patient Reported Outcomes and Function (PROF) Core. The registry prospectively acquires data on patient and disease characteristics, treatments, and outcomes for consenting patients with cancer of the oropharynx evaluated at MDACC. For this analysis, all consecutive patients recruited into the registry who received treatment for newly diagnosed OPSCC between 2014 and 2016 were sampled. Eligibility requirements for this study included age > 21 and newly diagnosed, pathologically confirmed OPSCC (i.e., tonsil, glossopharyngeal sulcus, or base of tongue).

All participants in this study were previously untreated at consent and were evaluated by a head and neck multidisciplinary team including medical oncology, radiation oncology, surgery, dental oncology, and speech and language pathology. In each case, treatment was based on a consensus tumor board recommendation and patients were included in the analysis only if dispositioned to treatment with an intention of cure. Some patients participated in other clinical trial protocols. Participants were clinically, and pathologically (if applicable) staged using the American Joint Committee on Cancer (AJCC) criteria based on the AJCC Cancer Staging Manual, seventh edition. The study population was restricted to low-intermediate risk (clinical T1-3, N0-2b) OPSCC with > 6 months follow-up to reflect a more homogeneous group. Human papillomavirus status was determined by positive p16 immunohistochemistry in all patients. The MDACC institutional review board approved the study, and all participants provided written informed consent.

Assessments

We obtained demographic and clinical information about each participant from self-administered assessments and from the electronic medical record. Although a broad range of psychosocial factors, behaviors, and symptoms were assessed, the current study focused on symptoms relevant to patient-reported symptom burden and QOL. Functional assessments were performed by the patient-reported outcome (PRO)/function section of the MD Anderson Oropharynx Program, administered by the Section of Speech Pathology.

Four patient-reported outcomes (PRO) assessment time points were included in the analysis: i. before initiation of treatment (baseline), ii. 2 weeks post-surgery or last week of radiation therapy, iii. 6 weeks after surgery or 6 weeks after completion of definitive/adjuvant radiation, and iv. 6 months after treatment completion. Time was measured from the last day of any treatment administered, regardless of modality.

At each time point, patients completed the MD Anderson Symptom Inventory for Head and Neck Cancer (MDASI-HN), which is a PRO questionnaire designed to measure the severity or burden of systemic and head and neck cancer–specific symptoms and the interference of these symptoms on patients' daily function [6,7]. This 28-item, multiple-symptom inventory includes 13 core items ("systemic symptoms" such as pain, fatigue, and sleep), nine head and neck–specific items ("local symptoms" such as mucus, and taste), and six interference items (e.g., general activity, work, relationship). The 13 core items have been validated for use in cancer patient populations regardless of the specific diagnosis or type of therapy [7] and thus can be used to compare overall symptom burden between different types of cancer. The nine head and neck–specific items were validated internally with regard to construct and concurrent validity in a cohort of 205 patients with head and neck cancer [6]. Internal consistency reliability has been shown to be high for the core items, the nine head and neck-specific items, and the six interference items (Cronbach alphas of 0.72–0.92). In the MDASI and its supplementary modules (including MDASI-HN), the severity of each symptom (at its worst during the previous 24 h) is ranked on a scale of 0 to 10, where 0 represents "not present" and 10 represents "as bad as you can imagine." The interference items are also measured on a scale of 0 to 10, where 0 represents "did not interfere" and 10 represents "interfered completely" [6].

Patients also completed the EuroQOL-5 Dimensions-5L (EQ5D) at two time points: baseline and 3–6 months post-treatment. The EQ5D is a modified version of the widely used EuroQOL-5 Dimension [8].This 6-item questionnaire is used to measure generic QOL. In the EQ5D, patients rank five dimensions of QOL on a scale of 1 to 5: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The EQ5D also contains a visual analog scale, in which respondents grade their perceived health status on a scale ranging from 0 (worst possible health status) to 100 (best possible health status).

Statistical Methods

Pearson chi-square tests were used to compare baseline demographic and clinical variables between patients who underwent surgical and non-surgical treatment, with separate analyses for those who received single modality treatment and those who received multimodality treatment. Linear mixed models were used to compare the longitudinal trajectories of PRO variables among the treatment groups. These models included fixed effects for groups and different time points (1 week, 6 weeks and six months after treatment completion). Demographic and clinical characteristics that differed between groups at baseline were controlled for in the models. Because the full set of variables used in each model included redundant variables, this redundancy was reduced to avoid collinearity. A non-collinear set of baseline demographic and clinical variables (sex, smoking status, employment, T classification, and N classification) were also controlled for in subsequent mixed models that examined longitudinal patterns of post-treatment PROs.

For each model, we obtained P values for the overall group-by-time interaction; differences among group means at the different time points; and pairwise comparisons between the surgical and nonsurgical treatment groups at 6 weeks and 6 months after treatment completion.

To illustrate significant changes in QOL scores over time, a heat map analysis was performed with a divergent color gradient defined by blue favoring non-surgical therapy, red favoring surgical therapy and gray as neutral [9,10]. Differences in mean raw scores (relative to baseline) between treatment modality for each symptom item were shaded darker hues to represent greater difference. The heat map presents the differences in QOL scores between treatment groups retrieved at the different time points. On this scale, any difference with a P value equal or less than 0.05 was considered significant and color coded (color groups reflecting of difference as follows: 0–1, > 1 – 2, > 2 – 4 and > 4 points). To generate the map, we used hierarchical clustering of questionnaires, subscales, and individual items according to the numbers of treatment modalities used (single and multimodal treatment). Analyses were conducted using JMP pro version 12.1.0 (SAS Institute, Cary, NC).

Results

Participant characteristics

All participants completed the questionnaires at baseline. Participant flow in the study is summarized in Fig. 1. Of the 86 patients recruited, a complete dataset of all time points was available for 72 (84%) participants included.

Participant baseline demographic and clinical characteristics are

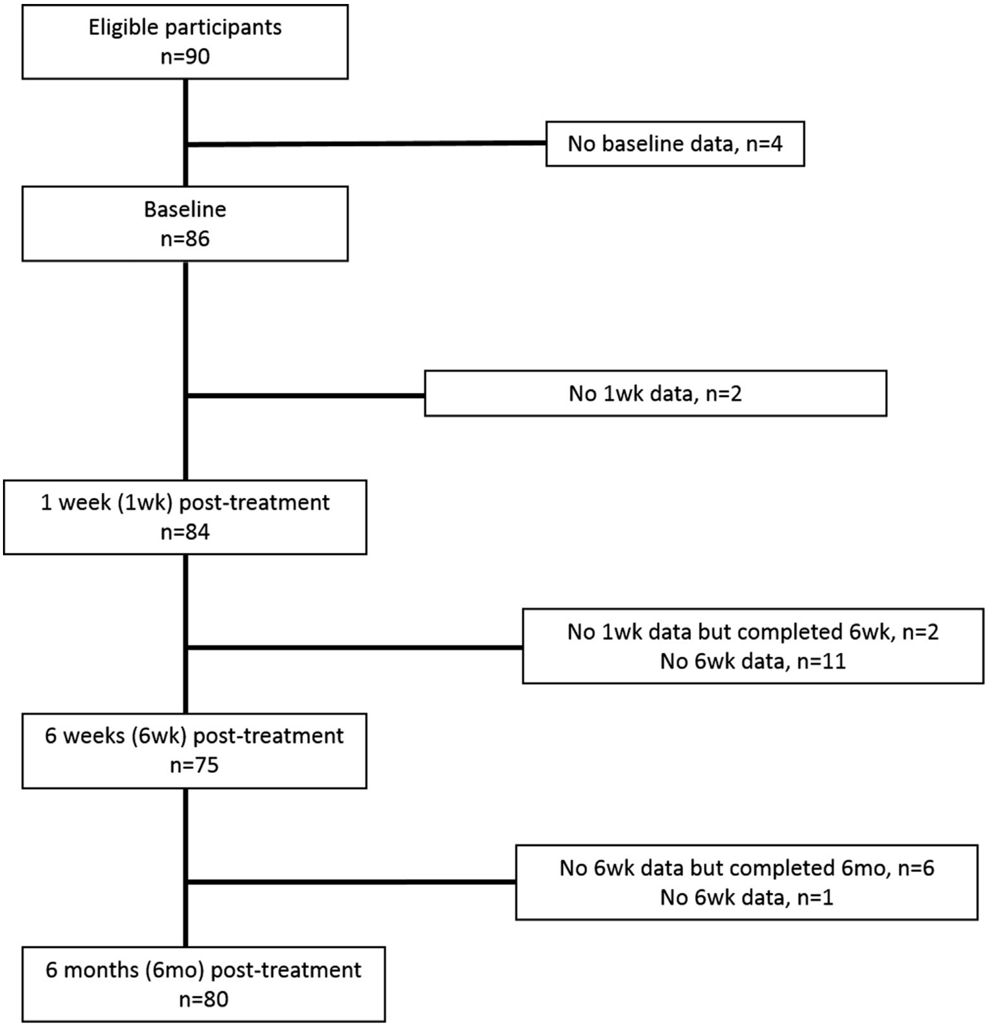

Fig. 1. Adapted CONSORT flowchart showing participant recruitment, withdrawal and questionnaire completion during the study.

summarized in Table 1. The overall mean age was 60 years, and this did not significantly differ among any of the treatment groups, nor did any other demographic variables. T classification was similar between the surgical and non-surgical cohorts. However, more participants in the radiation-only group had N2a/b class disease than in the surgery-only group ($P = 0.001$). Neck dissection was performed less frequently in the non-surgical groups than in the surgical groups ($P < 0.0001$). All patients in the surgical cohort underwent transoral robotic surgery and neck dissection. In the surgical multimodality group, seven (64%) patients were treated with post-operative radiation and four (36%) patients were treated with postoperative concurrent chemoradiation (Table 1). Treatment duration (baseline to 1 week post-treatment) differed between the surgical and non-surgical cohorts. For participants treated via single modality, treatment duration was shorter among the surgical cohort compared to the radiation only treated participants (26.2 ± 4.6 and 82.1 ± 5.2 days, respectively, $P < 0.0001$). For participants treated using multiple modalities, treatment duration was shorter among patients who had surgery compared to those who did not have surgery (80.4 ± 2.3 and 104.7 ± 5.10 days, respectively, $P < 0.0001$). In the multiple modality group, the mean (± standard deviation) overall dose of radiation administered to surgically treated patients was 60.50 ± 8.82 Gy compared to 68.12 ± 4.3 Gy in patients treated non-surgically ($P < 0.0001$). The proportion of patients treated with bilateral radiation to the neck field was significantly higher in patients treated non-surgically compared to those treated surgically with adjuvant radiation (83% and 45%, respectively, $P = 0.02$). Of note, there was no significant change in the total radiation dosage over the study period.

Single modality treatment groups

Symptom burden

At baseline, no differences were observed between the surgical and the non-surgical groups in the MDASI core, head and neck–specific, or interference scores for any specific item regardless of the number of modalities used (Supplementary Table 1). Fig. 2 shows changes in MDASI-HN subscale scores over time in the single-modality treatment groups (surgical and non-surgical). Results for significant model covariates ($P < 0.1$) for all of the longitudinal models are shown in Supplementary Table 2. All participants in the single-modality treatment groups showed rapid improvements in core scores by 6 weeks, and scores plateaued by 6 months post-treatment (Fig. 2A). The linear mixed model results indicated no group-by-time interaction ($P = 0.90$). Simple-effects analysis revealed no significant group mean differences in core scores at 6 weeks ($P = 0.99$) or 6 months post-treatment ($P = 0.08$) between the surgical and non-surgical treatment groups. Changes in head and neck–specific scores over time and at specific time points did not differ between the surgical and non-surgical treatment groups (Fig. 2B). Simple-effects analysis showed that the interference scores were significantly better (lower group mean) in the surgical group than in the nonsurgical group at 6 months ($P = 0.03$,

Table 1
Participant baseline demographic and clinical characteristics for the surgical and non-surgical treatment groups.

Characteristic	Single-modality			Multimodality		
	Surgical, no. (%)	Nonsurgical, no. (%)	P	Surgical, no. (%)	Nonsurgical, no. (%)	P
Total	14	10		11	51	
Mean ± SD age	62.6 ± 2.5 years	61.9 ± 2.9 years	0.85	57.8 ± 2.7 years	59.5 ± 1.2 years	0.56
Mean ± SD time from diagnosis to 1 week post-treatment	26.2 ± 4.6 days	82.1 ± 5.2 days	< 0.0001	104.7 ± 5.10 days	80.4 ± 2.3 days	< 0.0001
Gender			0.07			0.23
Female	3 (21)	0 (0)		2 (18)	9 (18)	
Male	11 (79)	10 (100)		9 (82)	42 (82)	
Race/ethnicity			0.21			0.82
White non-Hispanic	11 (79)	6 (60)		11 (100)	48 (94)	
Hispanic	1 (7)	2 (20)		0 (0)	0 (0)	
Black	1 (7)	0 (0)		0 (0)	0 (0)	
Asian	0 (0)	1 (10)		0 (0)	1 (2)	
Other	1 (7)	1 (10)		0 (0)	2 (4)	
Smoking status			0.31			0.49
Never	6 (43)	2 (20)		6 (55)	21 (41)	
Former	7 (50)	7 (70)		5 (45)	29 (57)	
Current	1 (7)	1 (10)		0	1 (2)	
Highest level of education			0.34			0.73
Graduate school	5 (36)	4 (40)		7 (64)	23 (45)	
College/university	6 (43)	4 (40)		3 (27)	11 (22)	
High school	3 (21)	2 (20)		1 (9)	17 (33)	
Employment status (at enrollment)			0.10			0.67
Full- or part-time	8 (57)	9 (90)		6 (55)	35 (69)	
Not employed	6 (43)	1 (10)		5 (45)	16 (31)	
Marital status			0.84			0.56
Married	9 (64)	7 (70)		10 (91)	42 (82)	
Not married	5 (36)	3 (30)		1 (9)	9 (18)	
Tumor site			0.91			0.84
Base of tongue	7 (50)	6 (60)		4 (45)	25 (49)	
Tonsil	6 (43)	3 (30)		7 (55)	24 (47)	
Glossopharyngeal sulcus	1 (7)	1 (10)		0 (0)	2 (4)	
T classification			0.10			0.23
1	6 (43)	8 (80)		7 (64)	19 (37)	
2	8 (57)	2 (20)		4 (36)	29 (57)	
3	0 (0)	0 (0)		0 (0)	3 (6)	
N classification			0.001			0.11
0	7 (50)	1 (10)		1 (9)	8 (16)	
1	7 (50)	3 (30)		3 (27)	2 (4)	
2a/b	0	6 (6)		7 (64)	41 (80)	
Neck dissection			< 0.0001			< 0.0001
Yes	14 (100)	0 (0)		11 (100)	6 (12)	
No	0 (0)	10 (100)		0 (0)	45 (88)	
Chemotherapy				4 (36%)	51 (100%)	< 0.0001
Radiation dose (Gy, mean ± SD)		67.2 ± 6.6		60.50 ± 8.8	68.12 ± 4.3	< 0.0001

SD, standard deviation.

Fig. 2C).

Symptom profiles

To better understand symptom profiles between groups, we compared the unadjusted distribution of scores for single items from the core, head and neck–specific, and interference sections of the MDASI-HN questionnaire at each time point (see Supplementary Tables 3–5). The heat map in Fig. 3 shows the extent of significant differences in specific symptoms ($P < 0.05$) between treatment groups according to the pairwise comparisons at each time point.

In the single-modality treatment groups, we did not identify a strong predominance for surgery or radiation in the core and head and neck–specific MDASI items. Voice, choking and numbness scores were significantly worse in participants treated with surgery only than in those treated with radiation alone, at 2 and 6 weeks after surgery. At 6 months post-treatment, voice, choking and numbness scores were similar between the single-modality treatment groups. Dry mouth, mucus and taste disturbances were significantly worse at 6 months post-treatment in participants treated with radiation alone than in participants treated with surgery alone.

Health status (per EQ5D)

The baseline and 6 month post-treatment health status as measured by the EQ-5D are presented in Supplementary Table 6. Health status as scored by the visual analogue scale in the EQ-5D did not differ between the surgical and non-surgical single-modality treatment groups at 6 months post-treatment. Simple-effects analysis demonstrated improvement in health status in the surgery-only group compared with the radiation-only group($P = 0.05$, 81.36 ± 6.08 at baseline and 89.90 ± 4.80 at 6 months post-treatment for the surgery-only group).

Multimodality treatment groups

Symptom burden

Fig. 3 shows the trajectories of symptom burden in patients in the surgical and non-surgical multimodality treatment groups. At the last week of radiation, 2 weeks post-surgery or 6 weeks after surgery or completion of radiation therapy, the group mean MDASI-HN scores were significantly worse in the non-surgical group than in the surgical group for core (Fig. 4A), head and neck–specific (Fig. 4B), and interference (Fig. 4C). Pairwise comparisons indicated no statistically

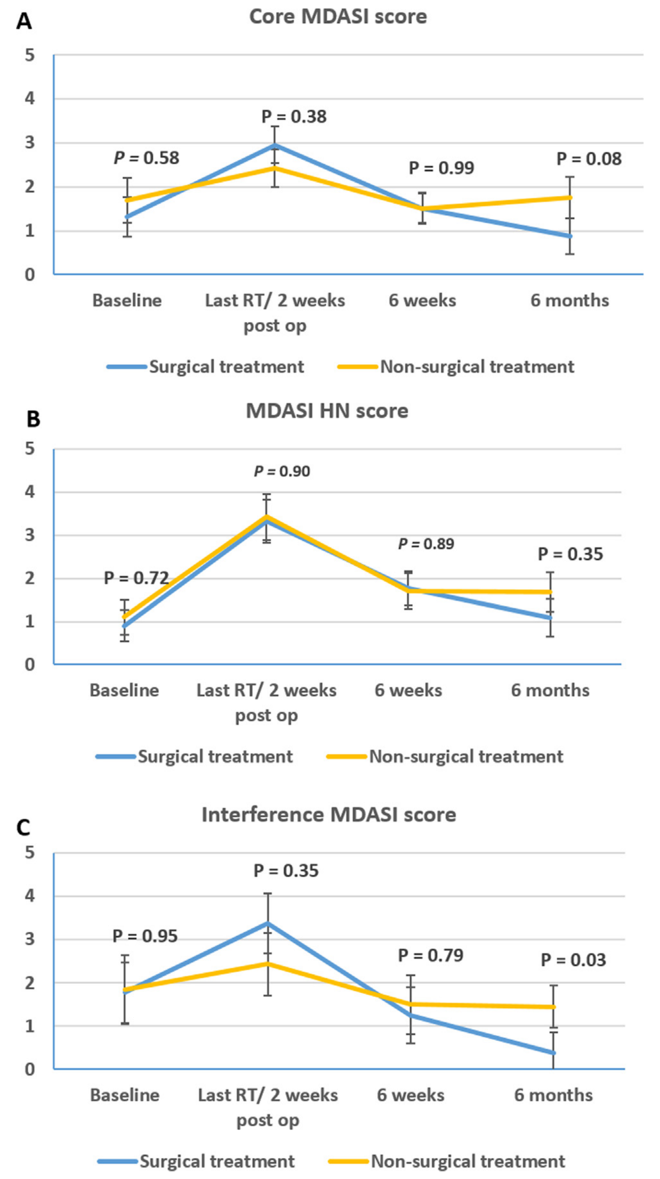

Fig. 2. Changes in MD Anderson symptom inventory (MDASI) scores over time in participants in the single-modality treatment groups (surgical or non-surgical). (A) Core MDASI scores. (B) Head and neck–specific (HN) MDASI scores. (C) MDASI interference scores.

significant differences at 6 months post-treatment between multimodality treatment groups for core ($P = 0.17$), head and neck–specific ($P = 0.22$), or interference scores ($P = 0.40$).

A comparison of change over time between the surgical and non-surgical multimodality treatment groups revealed significantly larger improvement in the non-surgical group than in the surgical group for core ($P = 0.02$) and head and neck–specific scores ($P = 0.009$), but not for interference scores ($P = 0.20$).

Symptom profiles

At the last week of radiation or 2 weeks post-surgery, most core and head and neck–specific MDASI items (15 of 22 items) were significantly better in patients who were treated with surgery in the multimodality treatment groups. Six weeks after treatment completion 9 of 22 items were significantly better in patients who were treated with surgery in the multimodality treatment groups.

In the multimodality treatment group, dry mouth was also significantly worse in the non-surgical group than in the surgical group across the 6 weeks and 6 months post-treatment time points. Non-surgical participants in the multimodality treatment group had worse mood during the last week of radiation and worse general activity and relationship interference 6 weeks after the last week of radiation than did those in the surgical multimodality group. However, no difference in interference scores was noted six months after treatment completion between surgical and non-surgical participants in the multimodality treatment group.

Health status (per EQ5D)

Pairwise comparisons between single-modality and multimodality treatment groups indicated no statistically significant differences in any of the EQ-5D items at baseline and 6 months post-treatment. Health status as scored by the visual analogue scale in the EQ-5D did not differ between the surgical and non-surgical multimodality treatment groups at 6 months post-treatment. No differences were observed in simple-effects analysis comparing multimodality treatment groups at baseline and 6 months post-treatment.

Discussion

Improved technology has led to a resurgence in primary surgical approaches to OPSCC via transoral robotic surgery (TORS). As a single-modality, TORS offers the shortest possible treatment duration and an opportunity for reduced long-term side effects associated with non-surgical management of OPSCC [11]. These results indicate that normal activities can be resumed earlier in patients treated with surgery alone than in those treated with radiation alone, as reflected by differences in MDASI symptom interference scores.

The impact of TORS on overall symptom severity and QOL is less clear when multimodality treatment is anticipated. To date, most outcomes studies including OPSCC patients treated with TORS have analyzed only indirect QOL or symptom indicators such as length of hospitalization, tracheostomy tube requirements during treatment, dysphagia assessment, and permanent gastrostomy tube requirements. Moreover, most of these studies represent post hoc analysis during the immediate post-treatment period (i.e., less than 1 month after completion of treatment), with no adjustment for the number of treatment modalities used and, often, no comparison to non-surgical strategies [12–16].

Our results showed significant improvements in PROs within the first 6 months after treatment for OPSCC. Overall, PROs for OPSCC patients improved over time regardless of whether patients were treated surgically or non-surgically. Marked improvements were observed in both core and head and neck–specific MDASI scores by 6 months after completion of treatment, reflecting improvement in the severity of both general cancer symptoms like fatigue as well as disease-specific symptoms like taste disturbance. Symptom interference scores, considered a surrogate for QOL, were also significantly better by 6 months after treatment, suggesting enhanced return to function for most patients, regardless of treatment approach. This is consistent with previous reports showing that OPSCC survivors who underwent TORS had similar overall QOL scores to those of matched OPSCC patients who were treated non-surgically two to six months after treatment [12–17].

The greatest differences in symptom burden between the surgical and non-surgical cohorts were observed at treatment completion and six weeks after treatment. By 6 months post-treatment, only dry mouth and taste disturbances appeared to be significantly worse in the non-surgical group for participants treated with single or multimodality therapy. In contrast, participants who underwent primary surgery were more likely to report numbness (i.e., 1 and 6 weeks after treatment) than those who were treated non-surgically in the single-modality group. These participants also had significantly worse voice, choking and sleep symptoms at 1 and 6 weeks post-treatment, both of which

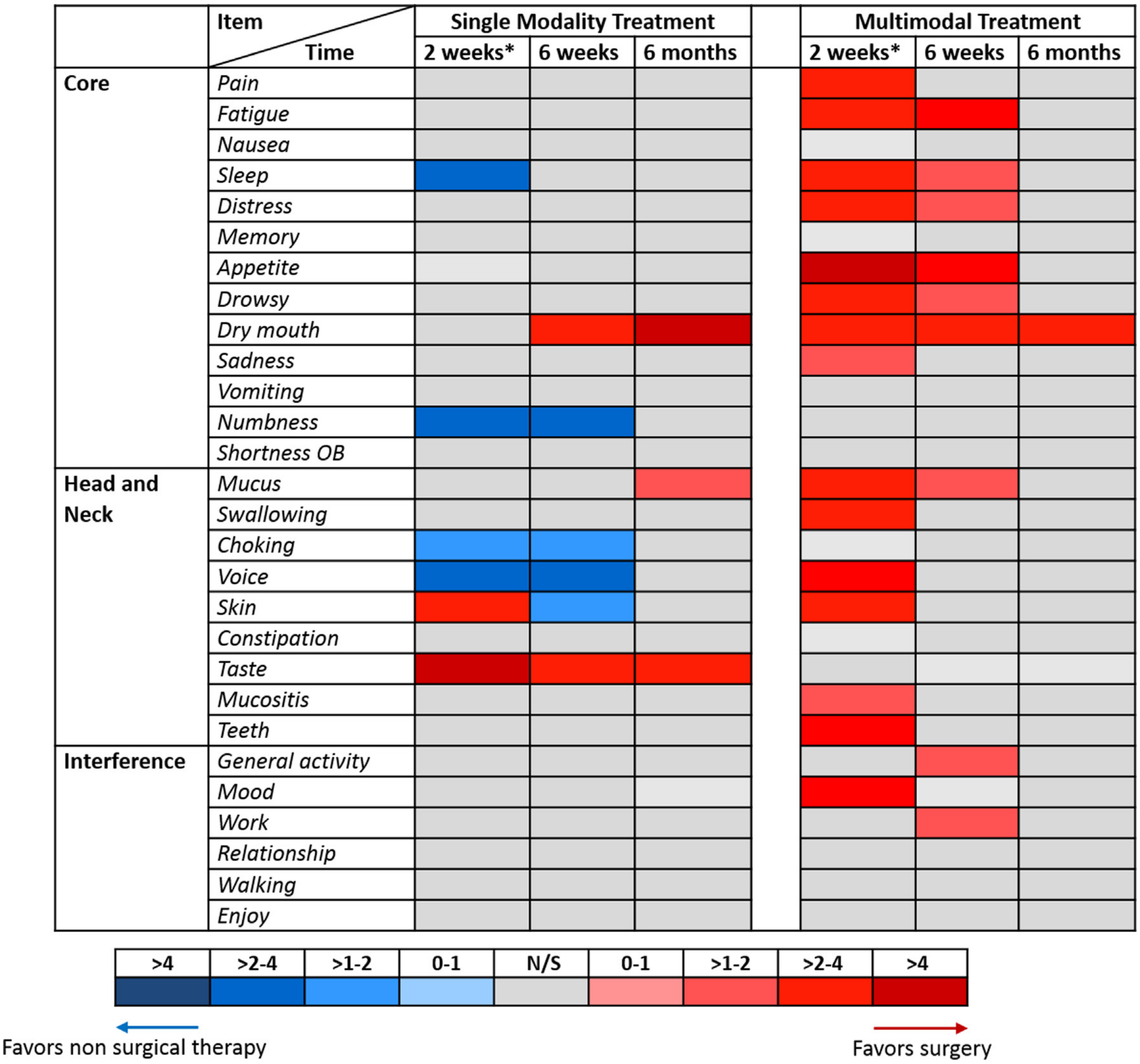

Fig. 3. Heat map showing the severity of differences in mean raw scores (range 0 to 10) between surgical and non-surgical treatment groups for specific items on the MD Anderson symptom inventory questionnaire at various time points.

could likely relate to acute alterations in pharyngeal anatomy, with differences no longer significant by 6 months. Taken together, these observations reflect a unique symptom profile for OPSCC patients treated surgically and non-surgically. Understanding the trade-off of symptoms between treatment options promises to inform shared decision-making prior to treatment. For example, in the current study, the favorable symptom profile among surgically treated patients could be therefore attributed to sparing treatment toxicities, namely a lower total dose of radiation and the avoidance of chemotherapy in the majority of patients (Table 1). So the benefits of a primary surgical approach are likely predicated on careful patient selection that allows for less intensive adjuvant treatment(s).

Health status according to EQ-5D revealed no significant differences between treatment groups at 6 months post-treatment, in accordance with the similar performance in MDASI interference scores. However, by using the EQ-5D for a weighted analysis of health status, we found a marginal but potentially clinically significant improvement in health status in survivors treated with surgery only relative to other treatment groups. We found no statistically significant differences between single-modality and multimodality treatment groups in any of the EQ-5D items at baseline and 6 month post-treatment. Similarly, other studies reported neither statistically nor clinically significant improvements in global health status in the first 6 to 12 months following completion of therapy [14,16,18–20]. Factors contributing to the possible improvement in global health status and well-being in participants who underwent surgery may include the relatively short interval to treatment completion (mean time from baseline to 1 week post-treatment was < 1 month), avoidance of radiation therapy in some participants, the avoidance of chemotherapy in other participants, and the short interval (6 months) of our global health status assessment, which may not have been an adequate period to allow significant health status improvements to occur in all groups.

The general activity and relationship disturbances we identified (per MDASI interference item) in OPSCC participants treated non-surgically, both single and multimodality, relative to those treated surgically is consistent with results from several studies suggesting that long-term survivors may have psychological distress [21–23]. These interferences may reflect short-term effects of treatment [24], or less likely could reflect acceleration of undiagnosed mood disorders initiated by alcohol and nicotine withdrawal [25,26]. The absence of longitudinal smoking and alcohol consumption data and the use of only self-reported measures of mood do not allow us to differentiate between these possible explanations in our patient population. Alternatively, early differences in mood could also be related to differences in acute pain levels [27,28], although we did not identify changes in pain scores over time. The general pain items included in our questionnaires might not have adequately captured such symptoms. All participants had less pain, on average, at 6 months post- treatment than at baseline according to the

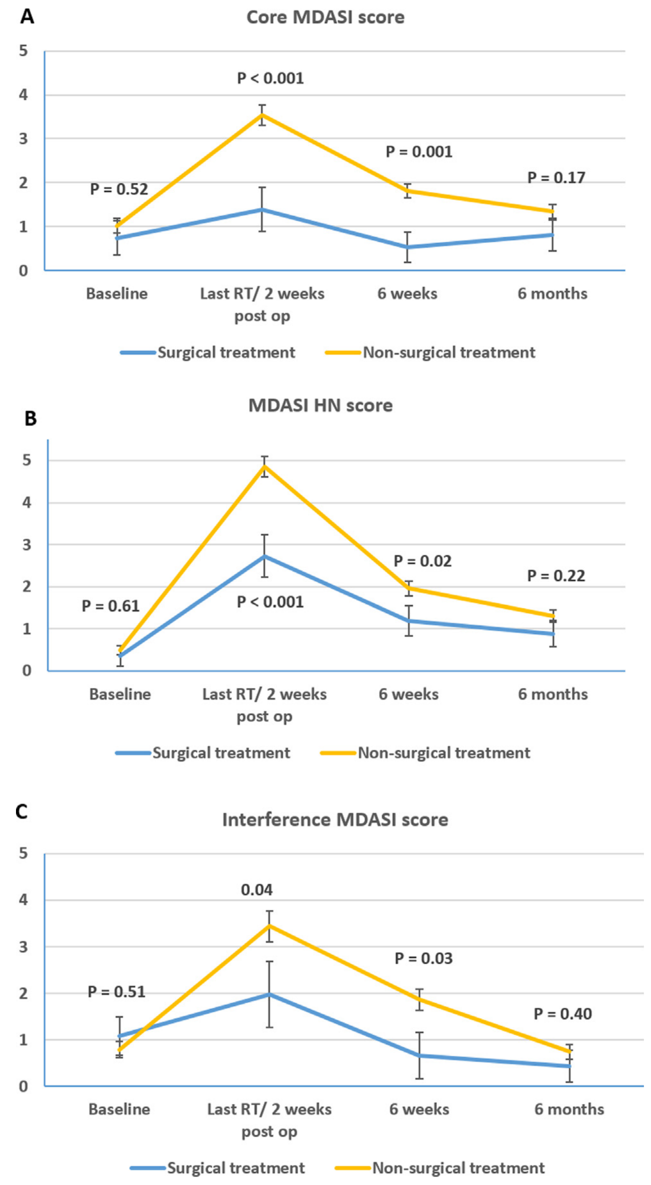

Fig. 4. Changes in MD Anderson symptom inventory (MDASI) scores over time in participants in the multimodality treatment groups (surgical or non-surgical). (A) Core MDASI scores. (B) Head and neck–specific (HN) MDASI scores. (C) MDASI interference scores.

core MDASI item for pain. Nevertheless, only one item in the MDASI-HN assessed the impact of symptoms on mood so this finding should be interpreted with caution.

This study is unique in that it follows patients from diagnosis to 6 months after completion of therapy, comparing symptom and QOL outcomes in OPSCC patients treated surgically and non-surgically, and matched by the number of treatment modalities used. A relatively small number of patients were included in each group and some of the compared groups were not balanced (i.e., multimodality groups, surgical (n = 11) and non-surgical (n = 51)); these factors precluded detailed examination of the effects of the treatment on outcomes. The registry is prospective, yet, treatment decisions are not randomized and selection bias is possible. As such, comparison of the PROs between treatment modalities is limited. We have tried to minimize the risk of bias by limiting inclusion to patients who would be eligible for either surgical or non-surgical treatment at our institution per TNM criteria. In such a scenario, patients often self-select for treatment. In addition, all surgical patients were treated with TORS and the post-operative radiation dosage and chemotherapy regimen have not changed over the time of recruitment to the prospective registry study between 2014 and 2016. These efforts have yielded the most homogeneous populations possible, thereby allowing for clinically relevant comparisons. To date, published data discuss either surgically treated patients (with or without adjuvant radiation or chemoradiation) [29] or non-surgically treated patients (i.e., different radiation doses with or without chemotherapy) [30,31]. There exist no published comparisons between surgically and non-surgically treated OPSCC patients using a multi-symptom inventory such as MDASI-HN presented here. The novelty of our analysis is the clinically relevant comparison of symptom profiles (22 unique symptom items) between treatment modalities stratified by the number of modalities. Ongoing studies (e.g., *NCT03418909*, *NCT03281499* and *NCT02984410*) and prior comparative PRO reports have focused on dysphagia solely [32,33]. These studies either used indirect measures to assess swallowing (e.g., gastrostomy tube dependence), patient reported outcome (e.g., MD Anderson Dysphagia Inventory, MDADI) or rating systems like Dynamic Imaging Grade of Swallowing Toxicity (DIGEST) or fiberoptic endoscopic evaluations of swallowing (FEES). However, our results showed a difference in swallowing only between patients in the multimodal treatment group, moreover, the difference is limited to the immediate (2 weeks) post treatment period. Our use of MDASI-HN allows us to explore difference in the severity of 22 domains of symptoms to understand where symptom profiles diverge [34,35]. This allows better counseling and selection between treatment modalities (surgery vs. radiotherapy) as well as between number of treatment modalities. We also did not include data regarding complications or adverse reactions, either of which could significantly impact PROs and QOL. Our study includes OPSCC patients treated in a multidisciplinary fashion at a high-volume, tertiary-care facility both surgically and non-surgically, which may enhance the generalizability of our results. However, as the patients in our cohort were, on average, younger (~60 years) and therefore likely had fewer comorbid conditions, our analysis was not adjusted for existing comorbidities, limiting conclusions about PROs and QOL in patients with significant baseline comorbidities.

Our results showed that PROs improved, on average, over time in low-intermediate risk OPSCC patients treated both surgically and non-surgically. PROs at 6 months post-treatment were generally similar among those undergoing the same number of treatment modalities (i.e., single and multimodality groups). Still, in patients treated with multiple modalities, symptom burden was significantly higher upon treatment completion and six weeks after in patients treated non-surgically, and dry mouth, taste disturbances, and mood disorders may persist at least until 6 months in these patients. In contrast, numbness, voice, and choking symptoms were greater upon treatment completion and 6 weeks after in patients treated surgically. The degree to which early symptom burden mirrors long-term function is unknown and remains to be defined. The results of our study warrant further research using a larger dataset, which will be available as our prospective registry grows. In the meantime, this data can help inform comprehensive patient counselling and shared decision-making regarding the unique symptom profile according to the treatment modalities used. Further research is needed to fully understand QOL deficits and to identify subgroups that may experience more extreme long-term adverse QOL effects.

Conflict of interest statement

None.

Funding sources and financial disclosures

This work is directly supported by the Charles and Daneen Steifel Oropharynx Fund; Dr. Fuller is a Sabin Family Foundation Fellow. Drs. Hutcheson, and Fuller receive (d) funding support from the National

Institutes of Health (NIH)/National Institute for Dental and Craniofacial Research (1R01DE025248-01/R56DE025248-01) and NIH/NCI Early Phase Clinical Trials in Imaging and Image-Guided Interventions Program (1R01CA218148-01).

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.oraloncology.2019.01.020.

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