Oral Oncology 49 (2013) 438–442

Contents lists available at SciVerse ScienceDirect

Oral Oncology

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

Clinical factors predicting for prolonged enteral supplementation in patients with oropharyngeal cancer treated with chemoradiation ☆

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ARTICLE INFO

Article history:
Received 11 July 2012
Received in revised form 28 November 2012
Accepted 6 December 2012
Available online 26 January 2013

Keywords:
Gastrostomy tube
G-tube
Oropharyngeal cancer
Chemoradiation
Squamous cell cancer of the head and neck
Enteral feeding

SUMMARY

Objectives: The purpose of this study is to determine the pre-treatment clinical factors associated with prolonged enteral feeding in patients with oropharyngeal cancer treated with chemoradiation.
Materials and methods: One hundred and nine patients with stage III–IVB oropharyngeal carcinoma treated with definitive chemoradiation were analyzed. Feeding tube usage was defined as the duration of active usage for nutritional purposes.
Results: Median follow-up was 4.4 years and median feeding tube usage was 2.5 months. On multivariate analysis, increasing duration of feeding tube usage was associated with narcotic use before treatment ($p = 0.04$), living alone at the time of treatment ($p = 0.04$), and larger pre-treatment decrease in body-mass index ($p = 0.01$). Prolonged feeding tube usage was associated with decreased overall survival ($p = 0.06$) and disease-free survival ($p = 0.02$) in univariate analysis.
Conclusions: By identifying patients at risk for prolonged feeding tube usage, aggressive measures can be attempted to prevent feeding tube dependence.

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Introduction

Treatments for oropharyngeal cancers include surgical options, such as transoral laser surgery or robotic surgery, and concurrent chemoradiation. The cure rate for oropharyngeal cancer is relatively high, particularly for human papilloma virus (HPV)-related tumors,[1] and many of these patients not only have normal function and performance status at baseline, but are living longer after treatment. As a result, treatment-related toxicities should play a larger role in the decision as to which treatment option to follow. For patients who undergo concurrent chemoradiation, there has been increasing recognition of acute and late toxicities, including mucositis, weight loss and malnutrition, aspiration, stricture, and xerostomia.[2–5] In order to combat some of these symptoms, nutritional support in the form of a feeding tube, such as a nasogastric (NG) tube or gastrostomy tube (g-tube), is now necessary for the majority of patients receiving chemoradiation for head and neck cancer.

It has been shown that nutritional supplementation can reduce weight loss, hospitalizations, and treatment interruptions during radiation therapy (RT).[6–8] However, these studies also show that a significant proportion of patients with feeding tubes placement will remain nutritionally dependent on them for long periods of time. Contemporary prospective trials involving concurrent chemotherapy and radiation for head and neck cancer demonstrate that of patients that receive a feeding tube, long-term dependency rates ($\geqslant$2 years) range from 14% to 51%.[9–11] This can delay the return of normal swallowing, prolong the duration for which the patient is at risk for feeding tube complications, and cause significant detriments in patients' quality of life.[12,13]

To date, there have only been a few reports of clinical factors that could predict for prolonged feeding tube usage, many of which predominantly focus on radiation doses to specific structures in the head and neck.[14–18] The purpose of this study is to identify clinical pre-treatment factors associated with prolonged feeding tube usage in patients with locally advanced oropharyngeal cancer treated definitively with radiation and chemotherapy.

Materials and methods

Patient cohort

Between 2000 and 2009, 132 patients with stage III–IVB oropharyngeal carcinoma were treated with definitive radiation and chemotherapy at the Massachusetts General Hospital. Of these,

☆ Presented at the 8th International Conference on Head and Neck Cancer, Toronto, ON, Canada.

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http://dx.doi.org/10.1016/j.oraloncology.2012.12.003

119 underwent feeding tube insertion. Four patients were excluded for persistent disease, four patients were excluded for incomplete information regarding actual feeding tube usage, and two patients were excluded due to death from intercurrent illness less than 1 month after finishing radiation, while still dependent on a feeding tube. No patients developed local or regional recurrence during the duration of feeding tube usage. The baseline characteristics of the remaining 109 patients are shown in Table 1.

Table 1
Patient, tumor, and treatment characteristics.

Characteristic	*N* (%)
Age (years)	
Median	57.4
Range	34.9–90.5
Gender	
Male	88 (80.7)
Female	21 (19.3)
Race	
White	99 (90.8)
Black	2 (1.8)
Hispanic	4 (3.7)
Others	4 (3.7)
KPS[a]	
⩾90	98 (89.9)
<90	11 (10.1)
Smoking status	
Non-smoker	37 (33.9)
Former	54 (49.5)
Current	18 (16.6)
Alcohol status	
Unknown	9 (8.3)
None (0 drinks/day)	28 (25.7)
Low (⩽1 drink/day)	53 (48.6)
Moderate (>1 and <4 drinks/day)	9 (8.3)
Heavy (⩾4 drinks/day)	10 (9.1)
Baseline dysphagia/odynophagia	
Unknown	23 (20.2)
Yes	32 (28.4)
No	56 (51.4)
T-category	
1	26 (23.9)
2	45 (41.3)
3	25 (22.9)
4	13 (11.9)
N-category	
0	9 (8.3)
1	13 (11.9)
2a	25 (22.9)
2b	36 (33.0)
2c	10 (9.2)
3	16 (14.7)
AJCC stage[b]	
III	20 (18.4)
IVA	70 (64.2)
IVB	19 (17.4)
HPV[c] *status (Negative vs. Positive)*	
Unknown	74 (67.9)
Negative	2 (1.8)
Positive	33 (30.3)
Chemotherapy	
None	3 (2.8)
Concurrent	91 (83.5)
Induction and concurrent	14 (12.8)
Adjuvant	1 (0.9)
Radiation type	
CRT[d]	38 (34.9)
IMRT[e]	71 (65.1)
Radiation dose (Gy)	
Median	70
Range	64.0–73.0
Radiation duration (days)	
Median	47
Range	31–63
Pre-RT[f] *neck dissection*	
Yes	13 (11.9)
No	96 (88.1)
Post-RT[f] *neck dissection*	
Yes	30 (27.5)
No	79 (72.5)

[a] Karnofsky performance status.
[b] American Joint Committee on Cancer.
[c] Human papilloma virus.
[d] Conventional radiation therapy.
[e] Intensity-modulated radiation therapy.
[f] Radiation therapy.

Treatment

Tumor and treatment characteristics are listed in Table 1. All patients received definitive radiation therapy using either conventional radiation with concomitant boost technique or intensity-modulated radiation therapy (IMRT). Median radiation dose to the tumor was 70 Gray (Gy).

The primary sites of tumor were tonsil (52%), base of tongue (45%), and others (3%). Ninety-nine percent of patients had concurrent chemotherapy, consisting of a platinum/taxane combination (61%), a platinum alone (18%), cetuximab alone (18%), or a platinum/taxane/cetuximab combination (3%). Twelve percent of patients had a pre-RT neck dissection and 28% of patients had a planned post-RT neck dissection.

Enteral tube placement and management

At all times before, during, and after treatment, patients were managed in a multidisciplinary manner, which included input from surgeons, medical oncologists, radiation oncologists, speech and swallow therapists, and dieticians. As such, decisions regarding feeding tube placement and usage were similarly made jointly by the treating clinicians. Our institutional policy is to see these patients at least weekly during treatment by both the radiation and medical oncology teams, and recommend feeding tube placement when the patients start experiencing significant problems with caloric intake, or are likely to have such problems in the near future. For patients with significant weight loss before treatment, feeding tubes were recommended and patients were encouraged to increase their nutritional intake before starting treatment. The decision to remove a feeding tube was made when patients were able to resume a regular oral diet and their weight had stabilized.

Predictors and outcomes

Feeding tube usage for nutritional purposes was the primary outcome, which was defined as the time during which the patients actively used their feeding tube for nutritional purposes, and not based on feeding tube insertion and removal dates. Secondary outcomes included the effect of feeding tube usage duration on overall survival (OS) and disease-free survival (DFS).

Predictors used included age, gender, race, comorbidity scores, mental health history, marital status, employment status, whether

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