Heliyon 6 (2020) e03617

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

Dentition, nutritional status and adequacy of dietary intake in treatment naïve head and neck cancer patients

Catherine Kubrak [a,1], Arazam Farhangfar [a,1], Matthew Woynorowski [b], Naresh Jha [c], William Preshing [b], Vickie Baracos [a,*]

[a] Department of Oncology, Division of Palliative Care Medicine, University of Alberta, Cross Cancer Institute, 11560 University Avenue, Edmonton, Alberta, T6G 1Z2, Canada
[b] Faculty of Dentistry, Division of Oral Medicine, University of Alberta, Edmonton Clinic, 11400 University Avenue, Edmonton, Alberta, T6G 1Z1, Canada
[c] Department of Oncology, Division of Radiation Oncology, University of Alberta, Cross Cancer Institute, 11560 University Avenue, Edmonton, Alberta, T6G 1Z2, Canada

ARTICLE INFO

Keywords:
Diet
Oral medicine
Oncology
Nutrition
Head and neck cancer
Dietary intake
Eichner index
Weight loss
Nutrition impact symptoms
Dentition
Teeth
Occlusal support

ABSTRACT

Objectives: To examine the relationship of reduced numbers of occluding teeth and dietary intake (DI), nutrition impact symptoms (NIS), and weight loss (WL) in head and neck cancer (HNC) patients.
Methods: As a part of the standard of care, treatment-naïve HNC patients (n = 104) completed dental evaluation (number of teeth, total anterior/posterior occlusal teeth, Eichner Index (EI) classification), WL, DI questionnaire and HNC Symptom Checklist©. Descriptive statistics (Kruskal-Wallis, Fisher-exact, χ^2 tests) and (uni-) multivariable logistic regression.
Results: Overall, 42, 45 and 13% of patients were in EI-class A, B and C with a median of 8, 3, and 0 total posterior occlusal teeth. EI-class B/C patients were older, more likely to have impaired DI (OR = 3.88; 95%CI:1.63–9.26; $P = 0.002$) and reported interference with DI by 11 NIS ($p < 0.05$). DI was, however, reported as unimpaired in 77, 49 and 39% of patients in EI-class A, B and C, respectively. The subset of EI-class B/C patients with impaired DI, had more NIS interference with DI ($P < 0.05$; difficulty chewing, pain, early satiety, lack of energy); EI-class C patients additionally had dry mouth, thick saliva and dysphagia ($P < 0.05$). In logistic regression, EI-classes B/C patients with reduced (vs unimpaired) DI were more likely to have ≥5% WL (OR = 10.1; 95%CI:2.0–50.0), higher NIS interference (range OR 4.3–10.7).
Conclusions: More than half of these HNC patients had reduced numbers of occlusal teeth or were edentulous. EI-class B/C patients did not necessarily have impaired DI, however the combination of EI-class B/C and a constellation of NIS, associated with reduced DI.
Clinical significance: Treatment naïve head and neck cancer (HNC) patients with reduced occlusal and masticatory performance (Eichner Index B/C) and reduced dietary intake are at high risk for weight loss. Identifying HNC patients at risk may improve their oral health, dietary intake and reduce their risk of weight loss.

1. Introduction

Head and neck cancer (HNC) patients are at high risk of cancer-associated weight loss (WL) [1, 2, 3, 4]. Cancer-associated WL is driven by a combination of reduced dietary intake (DI) and altered metabolism [5]. Of these two factors, reduced DI is likely the predominant factor driving this WL in HNC. Pain, anxiety, nausea, and depression are but a few symptoms triggering a reduction in DI, by decreasing or eliminating the central drive to eat within the brain (appetite centre). In addition, other symptoms referred to as nutrition impact symptoms (NIS) including dysphagia, xerostomia, bowel obstruction, early satiety and dental issues may contribute to reduced DI [6].

The symptoms which can potentially impact DI in patients with HNC are legion. We previously identified 17 NIS in patients with HNC in a review of the literature [7]. One of these, dental problems, has received relatively little attention, in spite of the fact that loss or forfeiture of teeth is relatively common in patients with HNC [8]. In addition to pre-existing dental issues, surgical extraction, periodontal disease, dental caries and

* Corresponding author.
E-mail address: vickie.baracos@ualberta.ca (V. Baracos).
[1] shared first authorship.

https://doi.org/10.1016/j.heliyon.2020.e03617
Received 15 July 2019; Received in revised form 28 October 2019; Accepted 13 March 2020

osteonecrosis may occur in consequence of cancer treatments [8, 9]. Adapting to tooth loss, specifically when it affects the ability to grind and chew food can make it challenging to maintain a normal diet. Normal adults have 32 teeth, including 8 incisors, 4 canines, 8 premolars and 12 molars. Occlusion (i.e. contact between teeth) between maxillary and mandibular teeth is required for biting and chewing. Masticatory function-the ability to grind and chew food, is reduced as the number of posterior occlusal contacts (normally n = 8) decreases [10, 11]. The loss of posterior occlusal contacts has been associated with pain and decreased chewing and swallowing ability, saliva flow and quality of life (QOL) in healthy and older adults [12, 13, 14, 15, 16, 17, 18, 19].

The relationship between tooth loss, DI and nutritional status has been the subject of multiple studies, mainly in heathy and older adults [12, 13, 14, 15, 16, 17, 18, 19]. The majority of longitudinal multivariable analyses in healthy and older adults adjusted for age, sex, race, education status or socioeconomic status which measured tooth numbers through self-reported edentulism, total number of teeth or various measures of functional tooth units found a significant association between tooth loss and altered dietary choice or DI [20, 21, 22]. There has been only one study related to dentition and nutrition in patients with cancers of the head and neck [23]. In that study 34 untreated male HNC patients were stratified according tooth loss as defined by either <5/8 posterior occluding contacts, or by < 7 total pairs of occluding teeth irrespective of their anterior or posterior positions in the mouth. Neither of these definitions of tooth loss were associated with body mass index (BMI) $\leq$ 20 kg/m^2, serum albumin $\leq$2.7 g/dL, hemoglobin $\leq$11.9 g/dL and total lymphocyte count $\leq$1.449/μL [23].

We considered that there is a need for clarification of the potential impact of dentition on nutritional status in patients with cancers of the head and neck. To achieve this, we selected a series of tools to evaluate our patient population. The Eichner Index (EI) is a standardized classification of posterior occlusal contacts and a validated measure of dentition and masticatory performance [24, 25]. EI classification describes the existing posterior occlusal contacts between the maxilla and mandible in the bilateral premolar and molar area referred to as support zones and divides the occlusal status into three main classes (A, B, and C). EI-class A, have occlusal contacts in all four posterior support zones; EI-class B have occlusal contacts in one to three zones of contact or within the anterior area only; EI-class C, have no occlusal contacts at all. The Patient-Generated Subjective Global Assessment© (PG-SGA©), is a validated tool recommended by Oncology Dietitians Clinical Practice Group as a nutrition screening tool for oncology patients. PG-SGA© encompasses BMI, WL history, performance status (PS) and DI [26]. The Head and Neck Symptom Checklist© is a validated measure of seventeen specific NIS interfering with DI in patients with cancers of the head and neck [7, 27]. We previously showed that our population of HNC patients experience significant symptom burden prior to initiation of treatments and that the aggregate burden of symptoms was a significant independent predictor of reduced DI, WL and survival [28]. We aimed to clarify the relationship between posterior occlusal contacts, DI, NIS and cancer-associated WL in treatment-naive HNC patients.

2. Material and methods

2.1. Population cohort and data acquisition

This study was conducted in accordance with the Declaration of Helsinki and approved by the institutional research ethics board as a retrospective chart review of nutritional status. We studied a series of treatment-naïve patients referred to a single regional cancer treatment centre in northern Alberta, Canada. In this centre, patients are evaluated at the time of diagnosis by a team of surgeons, medical oncologists, radiation oncologists, dieticians and dental health professionals. Dental assessment is conducted in single outpatient dentistry clinic, prior to initiation of the cancer treatment plan. A full oral and dental examination was completed for all patients. Data were collected from January 2011–December 2012 on a random sample of this population. Demographic information, and cancer site and stage were obtained from the Alberta Cancer Registry, certified by the North American Association for Central Cancer Registries. Cancer stage was based on the American Joint Committee on Cancer (6th Edition) stage groupings for HNC: 0, I, II, III, and IV, unknown, primary. HNC tumor sites were based on the International Classification of Diseases for Oncology (ICD)-O-3 site codes.

2.2. Assessments

A trained dentist undertook the oral examinations to determine total number of teeth, functional anterior and posterior tooth units defined by natural, restored or fixed prosthetic teeth and define EI classification. Height and weight histories over the 6 months preceding clinic referral, performance status (PS) (a lay-language version of the Eastern Cooperative Oncology Group (ECOG) PS) and seven DI categories were collected using the Patient-Generated Subjective Global Assessment© (PG-SGA©). The PG-SGA© DI category "only tube feeding or nutrition by vein" was used as an exclusion criterion as our interest was specifically in patients capable of oral intake. Patient-reported height, weight and WL history are reliable [29, 30]. The Head and Neck Symptom Checklist© (HNSC©) a validated measure of NIS effect on energy intake and WL, was used to assess 17 NIS interference with DI [7, 27]. The patient responds to the severity of each NIS's interference with DI on a 5- point Likert scale (ranging from 1 to 5): not at all, a little bit, somewhat, quite a bit, a lot. The total NIS interference scores refer to a composite score calculated by summing the interference scores reported for all 17 NIS.

2.3. Statistical analyses

Means, medians, standard deviations (SD), cross-tabulation, frequency or percentages were used as descriptive statistics. Non-parametric statistical methods were used if data was non-normally distributed. Chi-square test, Fisher-exact test (categorical data) and Kruskall-Wallis test (continuous data) was used in statistical comparisons between EI-classes. Univariable logistic regression was undertaken to determine the odds ratio (OR) of having poor dentition *i.e* EI-class B/C vs EI-class A (reference). Univariable logistic regression was also undertaken to determine the odds ratio (OR) of having reduced DI versus normal DI (reference) in the subset of patients with dentition of EI-class B/C. Covariables in these models included: age (continuous), BMI (continuous), sex, tumor staging, stage I and II (reference) vs all other stages; ECOG PS, Normal PS (ECOG PS 0, no limitations) (reference) vs reduced PS (ECOG PS 1–4); tumor site, DI category, normal DI (DI = 0, normal food, normal amount) (reference) vs reduced DI (DI = 1 to 5, abnormal foods, reduced amount); WL, absent (reference) or present; $\leq$5% WL, absent (reference) or present. NIS interference score = 1 (reference) vs NIS scores $\geq$2. To achieve the best-fitting parsimonious multivariable logistic model, we compared it to the generalized linear modelling and used the Akaike's Information Criterion (AIC) [AIC = deviance/n + 2df deviance/n) to determine the contribution of a given variable to the model and eliminated any variable not significantly changing the AIC. For example, we evaluated tumor stage and site as confounders and found that AIC did not change and these were therefore, eliminated as a variable in the final model. A priori alpha was $p \leq 0.05$ and tests were two-tailed. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 25 (SPSS, Chicago, IL).

3. Results

Owing to lack of information on effect size and variance as well as for the demographics of EI sub-group classification in our patient population, an *a priori* sample size calculation was not attempted. This investigation can therefore be considered exploratory. Data were collected from (January 2011–December 2012), during which time a total of 295 newly diagnosed with HNC had their initial visit to the

Table 1. Demographic and clinical characteristics of treatment naïve head and neck cancer (HNC) patients and by Eichner Index classes.

Demographic or clinical characteristics	All Patients	Eichner Index Class			*P value**
	n = 104	A (*n*, %)	B (*n*, %)	C (*n*, %)	
		44 (42.3)	47 (45.1)	13 (12.5)	
Eichner Index Classification (*n*, %)					
A1	20 (19.2)				
A2	18 (17.3)				
A3	6 (5.8)				
B1	1 (1.0)				
B2	20 (19.2)				
B3	26 (25.0)				
B4	0 (0)				
C1	2 (1.9)				
C2	7 (6.7)				
C3	4 (3.8)				
Total Anterior occlusal teeth (mean, median, SD)	5, 6 (3)	7, 8 (1)	5, 5 (2)	0, 0 (1)	0.000
Total Posterior occlusal teeth (mean, median, SD)	5, 5 (3)	8, 8 (1)	4, 3 (2)	0, 0 (1)	0.000
Total number of teeth (mean, median, SD)	22, 24 (8)	28, 28 (2)	20, 21 (4)	5, 6 (4)	0.000
Age, years (mean, median, SD)	57, 57 (10.5)	54, 53 (10.6)	59, 61 (9.2)	67, 67 (8.9)	0.000
Male (*n*, %)	84 (81)	38 (86)[a]	38 (81)[a]	8 (61)[a]	0.152
Weight, kg (mean, median, SD)	80.0, 78.0 (20.0)	82.7, 81.0 (20.8)	78.7, 77.0 (20.2)	74.9, 75.0 (16.3)	0.321
Height, m (mean, median, SD)	1.7, 1.7 (0.1)	1.7, 1.7 (0.08)	1.7, 1.7 (0.09)	1.7, 1.7 (0.14)	0.868
Six month percent weight loss** (WL) (mean, median, SD)	-2.8, -1.4 (6.3)	-3.2, -1.5 (5.3)	-2.6, 0.0 (7.3)	-2.5, -2.5 (6.0)	0.615
Number of patients experiencing WL (*n*, %)	40 (38.4)	16 (36.4)[a]	17 (36.2)[a]	7 (53.8)[a]	0.543
Number of patients experiencing ≥5% WL (*n*, %)	27 (25.9)	11 (25.0)[a]	11 (23.4)[a]	5 (38.5)[a]	0.549
Body mass index (BMI) (kg/m^2) (mean, median, SD)	26.7, 26.0 (5.4)	27.2, 26.5 (5.1)	26.3, 25.9 (5.6)	26.3, 24.7 (4.7)	0.262
WHO BMI categories (*n*, %)					0.817
<18.5	3 (2.9)	0 (0)[a]	3 (6.4)[a]	0 (0)[a]	
18.5 to 24.9	38 (36.5)	15 (34.1)[a]	16 (34.0)[a]	7 (53.8)[a]	
25.0 to 29.9	40 (38.5)	19 (43.2)[a]	18 (38.3)[a]	3 (23.1)[a]	
30.0 to 34.9	13 (12.5)	5 (11.4)[a]	6 (12.8)[a]	2 (15.4)[a]	
35.0 to 39.9	8 (7.7)	4 (9.1)[a]	3 (6.4)[a]	1 (7.7)[a]	
>40.0	2 (1.9)	1 (2.3)[a]	1 (2.1)[a]	0 (0)[a]	
AJCC 6 Tumor Staging (*n*, %)					0.437
Stage I	1 (1.0)	0 (0)[a]	0 (0)[a]	1 (7.7)[a]	
Stage II	8 (7.7)	3 (6.8)[a]	4 (8.5)[a]	1 (7.7)[a]	
Stage III	22 (21.2)	11 (25.0)[a]	7 (14.9)[a]	4 (30.8)[a]	
Stage IV	66 (63.4)	25 (56.8)[a]	33 (70.2)[a]	7 (53.8)[a]	
Unknown, primary	7 (6.7)	4 (9.1)[a]	3 (6.4)[a]	0 (0)[a]	
AJCC 6 Tumor Staging Groups (*n*, %)					0.560
Stage I and II	9 (8.7)	3 (6.8)[a]	4 (8.5)[a]	2 (15.4)[a]	
Stage III, IV and unknown, primary	95 (91.3)	41 (93.2)[a]	43 (91.5)[a]	11 (84.6)[a]	
Aggregate Tumor Site (*n*, %)					0.272
Oropharynx	41 (39.4)	16 (36.4)[a]	20 (42.6)[a]	5 (38.5)[a]	
Oral cavity	17 (16.3)	5 (11.4)[a]	10 (21.3)[a]	2 (15.4)[a]	
Hypopharynx	6 (5.8)	1 (2.3)[a]	3 (6.4)[a]	2 (15.4)[a]	
Nasopharynx	14 (13.5)	9 (20.5)[a]	5 (10.6)[a]	0 (0)[a]	
Larynx	13 (12.5)	6 (13.6)[ab]	3 (6.4)[b]	4 (30.8)[a]	
Salivary Glands	6 (5.8)	4 (9.1)[a]	2 (4.3)[a]	0 (0)[a]	
Paranasal sinuses	1 (1.0)	0 (0)[a]	1 (2.1)[a]	0 (0)[a]	
Other, ill-defined sites	6 (5.8)	3 (6.8)[a]	3 (6.4)[a]	0 (0)[a]	
Planned Treatment (*n*, %)					0.136
Surgery	5 (4.8)	1 (2.3)[a]	2 (4.3)[a]	2 (15.4)[a]	
Radiotherapy (RT)	5 (4.8)	1 (2.3)[a]	1 (2.1)[a]	3 (23.1)[a]	
Chemotherapy (CT)	2 (1.9)	0 (0)[a]	2 (4.3)[a]	0 (0)[a]	
Surgery/RT	18 (17.3)	9 (20.5)[a]	9 (19.1)[a]	0 (0)[a]	
RT/CT	47 (45.2)	22 (50.0)[a]	20 (42.6)[a]	5 (38.5)[a]	
Surgery/RT/CT	23 (22.1)	9 (20.5)[a]	11 (23.4)[a]	3 (23.1)[a]	
Other (refused treatment, unknown)	4 (3.8)	2 (4.5)[a]	2 (4.3)[a]	0 (0)[a]	

(*continued on next page*)

Table 1 (*continued*)

Demographic or clinical characteristics	All Patients	Eichner Index Class			*P value*[*]
	$n = 104$	A (*n*, %)	B (*n*, %)	C (*n*, %)	
		44 (42.3)	47 (45.1)	13 (12.5)	
ECOG Performance Status (PS) (*n*, %)					0.271
ECOG PS 0, no limitations	46 (44.2)	21 (47.7)[a]	20 (42.6)[a]	5 (38.5)[a]	
ECOG PS 1, not my normal self	38 (36.5)	18 (40.9)[a]	15 (31.9)[a]	5 (38.5)[a]	
ECOG PS 2, not feeling up to most things	14 (13.5)	4 (9.1)[a]	9 (19.1)[a]	1 (7.7)[a]	
ECOG PS 3, able to do little	4 (3.8)	0 (0)[a]	2 (4.3)[ab]	2 (15.4)[b]	
ECOG PS 4, bedridden	1 (1.0)	0 (0)[a]	1 (2.1)[a]	0 (0)[a]	
Missing	1 (1.0)	1 (2.3)[a]	0 (0)[a]	0 (0)[a]	
ECOG Performance Status (PS) groups (*n*, %)					0.822
Normal PS, ECOG PS 0	46 (44.2)	21 (47.7)[a]	20 (42.6)[a]	5 (38.5)[a]	
Reduced PS, ECOG PS 1- 4	57 (54.8)	22 (50.0)[a]	27 (57.4)[a]	8 (61.5)[a]	
Dietary Intake (DI) Category (*n*, %)					0.074
DI = 0, Normal food, normal amount	62 (59.6)	34 (77.3)[a]	23 (48.9)[b]	5 (38.5)[b]	
DI = 1, Normal food, less than normal	26 (25.0)	7 (15.9)[a]	14 (28.9)[a]	5 (38.5)[a]	
DI = 2, Little solid food	11 (10.6)	3 (6.8)[a]	6 (12.8)[a]	2 (15.4)[a]	
DI = 3, Very little of anything	3 (2.9)	0 (0)[a]	2 (4.3)[a]	1 (7.7)[a]	
D1 = 4, Only liquids	1 (1.0)	0 (0)[a]	1 (2.1)[a]	0 (0)[a]	
DI = 5, Only nutritional supplements	1 (1.0)	0 (0)[a]	1 (2.1)[a]	0 (0)[a]	
DI Category (*n*, %)					0.005
Normal DI, DI = 0	62 (59.6)	34 (77.3)[a]	23 (48.9)[b]	5 (38.5)[b]	
Reduced DI, DI = 1- 5	42 (40.3)	10 (22.7)[a]	24 (51.1)[b]	8 (61.5)[b]	
Total Nutrition Impact Symptom interference score (mean, median, SD)	23, 20 (10)	18, 18 (6)[a]	26, 23 (12)[b]	25, 27 (13)[b]	0.000

Abbreviations: AJCC, American Joint Committee on Cancer; BMI, Body Mass Index; CT, Chemotherapy; DI, Dietary Intake; ECOG, Eastern Cooperative Oncology Group; EI, Eichner Index; NIS, Nutrition Impact Symptom; PS, Performance Status; RT, Radiotherapy; SD, Standard Deviation; WHO, World Health Organization; WL, Weight Loss.

Each subscript letter denotes a subset of the Eichner Index class whose column proportions significantly do not differ from each other at the 0.05 level.

[*] Kruskall-Wallis test applied.

[**] Percent weight loss (WL) was based on weight reported in previous 6 months; if missing, the one month time frame for reported percent WL was substituted where available (ie, previous 1 month). Percent WL was calculated as follows [(current weight in kg – previous six month weight in kg)/previous six month weight in kg] x 100%.

dental clinic and new patient outpatient oncology clinic at the cancer treatment center. A random sample of 132 (45% of the population) were selected and of these 28 (21%) patients were excluded due to missing data or reliance on tube feeding or nutrition by vein, leaving 104 patients in the final analysis.

Demographic and clinical characteristics are presented for all patients and by EI-class (Table 1). Overall, the population was 80% male, 91% presented with cancer stage III or IV, over half of tumors were within the oral cavity or oropharynx area, 60% were overweight or obese, 55% presented with reduced PS, 40% had a reduced DI. The entire range of the 10 EI-subclasses was represented, with the exception of sub-class B4. Overall, 42, 45 and 13% of patients were in EI-class A, B and C respectively, with a median of 8, 3, and 0 total posterior occlusal teeth. One patient was edentulous. PS and cancer stages were not significantly different between EI-classes A, B and C (Table 1). The laryngeal tumor site varied between EI-class B and C and some tumor sites were not represented in all EI-classes. Across the EI-classes, patients were increasingly likely to experience reduction in the amount of food intake and while only 6.6% of patients in EI-class A were taking “little solid food” or "only liquids", while 12% of EI-class B and 15 % of EI-class C patients had difficulty consuming "solid food". EI class C was a small group and the possibility that this group had greater nutritional impairments could not be evaluated. For this reason several planned analyses were conducted with pooled EI-class B and C patients.

Unimpaired DI, as defined by *normal food in normal amount* decreased across the EI-classes, and was reported by 77, 49 and 39% of patients in EI-class A, B and C, respectively. This was unexpected, especially for EI-class C patients, to experience no impairment of DI in spite of having zero posterior occlusal contacts and a median of only 3 teeth in total. Indeed WL and body mass index (BMI) were not significantly different across EI classes (Table 1). Patients in EI-classes B/C patients clearly included 2 subsets, those managing *normal intake in normal amounts* with a mean % WL = - 0.36 (S.D = 3.02) and those who were experiencing reduced DI with a mean % WL = - 4.51 (S.D. = 8.72).

3.1. Nutrition impact symptoms (NIS)

Aggregate NIS interference score as well as individual NIS interference scores are shown. Aggregate NIS score was significantly higher in EI-class B and C patients versus EI-class A (Table 1), so these patients had both fewer occlusal supports and a more complex symptom burden. EI-class B or C patients reported higher NIS interference compared to EI-class A ($p \leq 0.05$) for 11 of 17 symptoms evaluated (Table 2). Six NIS, diarrhea, vomiting, constipation, altered smell and other were rare and occurred in ≤6% of patients. As expected, the most prevalent symptom showing differential prevalence across EI-classes was difficulty chewing, affecting 9.1%, 42.6% and 53.8% of patients in EI-classes A, B and C, respectively. The second most prevalent NIS was dysphagia, reported by 18.2, 40.4 and 53.8% of patients in EI Classes A, B and C, respectively. Next, both dry mouth and thick saliva impaired DI in 4.5%, 17–19%, and 30.8%. Pain affected ~50% or more of patients in EI-class B and C compared to 14% in EI-class A. In many instances, EI-class C patients responses were not different from EI-class B patients. Six of the 11 NIS reported by EI-class B or C patients, specifically related to oral issues, including: dry mouth, thick saliva, sore mouth, dysphagia, and chewing difficulty. Other NIS interfering with DI of EI-class B or C patients were

Table 2. Nutrition Impact Symptoms for interference score equal to 1 vs ≥ 2 for all treatment naïve head and neck cancer patients and by Eichner Index Class.

Nutrition Impact Symptom Interference (*n*,%)	All Patients	Eichner Index (EI) Class			*P*-value*
	n = 104	A (*n* = 44)	B (*n* = 47)	C (*n* = 13)	
No Chewing Difficulty	73 (70.2)	40 (90.9)[a]	27 (57.4)[b]	6 (46.2)[b]	0.000
Chewing Difficulty	31 (29.8)	4 (9.1)	20 (42.6)	7 (53.8)	
No Dysphagia	70 (67.3)	36 (81.8)[a]	28 (59.6)[ab]	6 (46.2)[b]	0.016
Dysphagia	34 (32.7)	8 (18.2)	19 (40.4)	7 (53.8)	
No Dry Mouth	90 (86.5)	42 (95.5)[a]	39 (83.0)[ab]	9 (69.2)[b]	0.023
Dry Mouth	14 (13.5)	2 (4.5)	8 (17.0)	4 (30.8)	
No Thick Saliva	89 (85.6)	42 (95.5)[a]	38 (80.9)[ab]	9 (69.2)[b]	0.019
Thick Saliva	15 (14.4)	2 (4.5)	9 (19.1)	4 (30.8)	
No Sore Mouth	80 (76.9)	40 (90.9)[a]	30 (63.8)[b]	10 (76.9)[ab]	0.007
Sore Mouth	24 (23.1)	4 (9.1)	17 (36.2)	3 (23.1)	
No Pain	68 (65.4)	38 (86.4)[a]	24 (51.1)[b]	6 (46.2)[b]	0.000
Pain	36 (34.6)	6 (13.6)	23 (48.9)	7 (53.8)	
No Loss of Appetite	77 (74.0)	38 (86.4)[a]	29 (61.7)[b]	10 (76.9)[ab]	0.023
Loss of Appetite	27 (26.0)	6 (13.6)[b]	18 (38.3)[a]	3 (23.1)	
No Lack of Energy	82 (78.8)	43 (97.7)[a]	31 (66.0)[b]	8 (61.5)[b]	0.000
Lack of Energy	22 (21.2)	1 (2.3)	16 (34.0)	5 (38.5)	
No Depression	86 (82.7)	41 (93.2)[a]	35 (74.5)[b]	10 (76.9)[ab]	0.036
Depression	18 (17.3)	3 (6.8)	12 (25.5)	3 (23.1)	
No Feeling Full	87 (83.7)	41 (93.2)[a]	35 (74.5)[b]	11 (84.6)[ab]	0.043
Feeling Full	17 (16.3)	3 (6.8)	12 (25.5)	2 (15.4)	
No Constipation	97 (93.3)	44 (100.0)[a]	41 (87.2)[b]	12 (92.3)[ab]	0.034
Constipation	7 (6.7)	0 (0)	6 (12.8)	1 (7.7)	
No Anxiety	79 (76.0)	37 (84.1)[a]	32 (68.1)[a]	10 (76.9)[a]	0.198
Anxiety	25 (24.0)	7 (15.9)	15 (31.9)	3 (23.1)	
No Diarrhea	99 (95.2)	44 (100.0)[a]	42 (89.4)[a]	13 (100.0)[a]	0.067
Diarrhea	5 (4.8)	0 (0)	5 (10.6)	0 (0)	
No Nausea	92 (88.5)	41 (90.9)[a]	38 (80.9)[a]	13 (100.0)[a]	0.116
Nausea	12 (11.5)	4 (9.1)	9 (19.1)	0 (0)	
No Smell Bothersome	101 (97.1)	44 (100.0)[a]	44 (93.6)[a]	13 (100.0)[a]	0.347
Smell Bothersome	3 (2.9)	0 (0)	3 (6.4)	0 (0)	
No Vomiting	102 (98.1)	44 (100.0)[a]	45 (95.7)[a]	13 (100.0)[a]	0.614
Vomiting	2 (1.9)	0 (0)	2 (4.3)	0 (0)	
No Other (lack of money, etc)	98 (94.2)	43 (97.7)[a]	43 (91.5)[a]	12 (92.3)[a]	0.396
Other (lack of money, etc)	6 (5.8)	1 (2.3)	4 (8.5)	1 (7.7)	

Each subscript letter denotes a subset of the Eichner Index class whose column proportions significantly do not differ from each other at the 0.05 level.
* Fisher's Exact test or Chi-square test applied (2-sided).

pain, loss of appetite, depression, lack of energy, feeling full and constipation compared to EI-class A ($p \leq 0.05$).

3.2. Logistic regression analyses

Univariable logistic regression (Table 3) was first undertaken to determine the odds ratio (OR) of having poor dentition *i.e* EI-class B/C vs EI-class A (reference). Sex, BMI, any % WL, ≥ 5% WL, cancer stage, tumor site and reduced PS were not significantly associated with EI-classes B/C while reduced DI, 10 individual NIS and total NIS interference score were significantly associated with EI-classes B/C compared to EI-class A. Five of the 10 significant NIS were specifically related to oral symptoms interfering with DI. Not surprisingly, difficulty chewing was the oral symptom highly associated with EI-classes B/C patients compared to EI-class A. Multivariable analysis for this model (Table 4) included factors that met the Akaike's Information Criterion (see methods), however owing to restricted sample size the total NIS score was included rather than the 10 individual NIS; analysis was controlled for age and sex. In the multivariable analysis, only age (OR = 1.11; 95%CI 1.04–1.19**)** and total NIS interference score (OR = 1.10; 95%CI:1.02–1.18; $P = 0.007$) were significantly associated with having poor dentition *i.e* EI-class B/C vs EI-class A (reference).

Logistic regression was also undertaken to determine the odds ratio (OR) of having reduced dietary intake versus normal dietary intake (reference) in the subset of patients with dentition of EI-class B/C. At the univariable level (Table 3), age, sex, BMI, cancer stage, tumor site, dry mouth and depression were not significantly related to reduced DI while any %WL, ≥ 5% WL, reduced PS, eight NIS and total NIS interference score were significantly associated with EI-classes B/C with reduced DI compared to EI-classes B/C with normal DI. In the multivariable analysis (Table 4), owing to sample size considerations, a single aggregate NIS score was included in this analysis, rather than the 10 individual symptoms that were significantly more frequent in patients in EI-class B/C. The multivariable analysis demonstrates that total NIS interference score and reduced PS were significantly associated with EI-classes B/C with reduced DI compared to EI-classes B/C with normal DI.

4. Discussion

Our study shows that patients with cancers of the head and neck present with a wide range of total numbers of teeth and that they vary from a complete set of posterior occlusal surfaces, to none at all. We found that 57% of the treatment naïve HNC patients had some degree of reduced posterior occlusal contact, which is similar to that reported by

Table 3. Univariable logistic regression analysis comparing Eichner Index (EI) reference classes.

Reference Class vs	EI-class A (N = 44)	EI-classes B/C with normal Dietary Intake (DI) (N = 28)	EI-class A	EI-classes B/C with normal DI
Comparison Class	EI-classes B/C (N = 60)	EI-classes B/C with reduced DI (N = 32)	EI-class B/C	EI-classes B/C with reduced DI
Variable	OR (95%CI)	OR (95%CI)	*Overall P* value	
Age	1.07 (1.02–1.11)	0.98 (0.93–1.04)	0.002	0.656
Sex (male)	1.92 (0.67–5.50)	1.22 (0.36–4.08)	0.220	0.744
Body Mass Index (BMI)	0.96 (0.89–1.03)	1.03 (0.94–1.14)	0.356	0.424
Any % WL	1.16 (0.52–2.60)	6.72 (2.03–22.25)	0.707	0.002
≥5% WL	1.09 (0.44–2.68)	10.11 (2.04–50.02)	0.848	0.005
AJCC 6 Tumor Staging				
Stage I and II				
All other Stages	0.65 (0.15–2.79)	(0.00–0.00)	0.571	0.999
Aggregate Tumor Sub-sites				
Oral Cavity			0.445	0.461
Oropharynx	0.65 (0.19–2.20)	0.13 (0.02–0.74)	0.490	0.021
Hypopharynx	2.08 (0.19–22.67)	0.30 (0.02–3.13)	0.547	0.315
Nasopharynx	0.23 (0.05–1.04)	0.13 (0.01–1.39)	0.058	0.092
Larynx	0.48 (0.10–2.19)	0.50 (0.05–4.67)	0.349	0.543
Salivary Glands	0.20 (0.02–1.52)	0.20 (0.00–4.71)	0.123	0.318
Paranasal Sinuses	(0.00–0.00)	(0.00–0.00)	1.000	1.000
Other, ill-defined sites	0.41 (0.62–2.81)	0.99 (0.00–0.00)	0.369	0.999
Performance Status (PS) Normal PS, ECOG PS 0				
Reduced PS, ECOG PS 1- 4	1.27 (0.5–2.7)	9.14 (2.78–30.08)	0.539	0.000
Dietary Intake (DI) Category				
Normal DI, DI = 0				
Reduced DI, DI = 1-5	3.88 (1.63–9.26)		0.002	
Nutrition Impact Symptoms (NIS) (bivariate)				
CHEWING DIFFICULTY	8.18 (2.59–25.75)	7.00 (2.19–22.34)	0.000	0.001
DYSPHAGIA	3.44 (1.37–8.64)	4.38 (1.44–13.28)	0.009	0.009
THICK SALIVA	5.80 (1.23–27.25)	6.81 (1.35–34.15)	0.026	0.020
SORE MOUTH	5.00 (1.56–15.94)	9.44 (2.36–37.70)	0.007	0.001
DRY MOUTH	5.25 (1.11–24.81)	3.26 (0.78–13.54)	0.036	0.104
PAIN	6.33 (2.33–17.19)	7.66 (2.42–24.25)	0.000	0.001
LOSS of APPETITE	3.41 (1.24–9.37)	6.80 (1.91–24.11)	0.017	0.003
FEELING FULL	4.15 (1.11–15.5)	4.36 (1.07–17.74)	0.034	0.039
DEPRESSION	4.55 (1.22–16.88)	1.00 (0.31–3.22)	0.023	1.000
LACK of ENERGY	23.15 (2.97–180.28)	10.71 (2.67–42.85)	0.003	0.001
TOTAL NIS INTERFERENCE SCORE	1.10 (1.03–1.17)	1.11 (1.03–1.20)	0.003	0.003

Abbreviations: AJCC, American Joint Committee on Cancer; BMI, Body Mass Index; CI, confidence interval; DI, Dietary Intake; ECOG, Eastern Cooperative Oncology Group; EI, Eichner Index; NIS, Nutrition Impact Symptoms; OR, odds ratio; PS, Performance Status; ref, reference group; vs, versus; WL, Weight Loss.

Friedman et al. (2008) [23], in a sample of 34 male HNC patients. In our sample EI class was strongly related to the patient's subjective experience of chewing difficulty. Posterior occlusal contacts are considered essential for mastication and swallowing, thus any reduction to these contacts would be expected to make it challenging to maintain optimal DI [11, 12, 13, 14, 15]. Reduced numbers of occlusal surfaces associated overall with impairments of DI and these results concur with reports on healthy and older adult subjects [9, 10, 13, 14, 20]. However, we found that many patients experience no impairment of DI and were able to maintain their body weight in spite of having as few as five teeth in total and zero posterior occlusal surfaces. The absence of occlusal surfaces is not necessarily an absolute impairment to achieving normal DI. Patients with EI-class B/C who were nutritionally successful had a relatively limited number of additional NIS and obstacles to DI. It is possible that EI-class B/C patients over preceding years have developed dietary strategies to maintain oral intake with fewer teeth. Thus, it would be most interesting to understand what dietary strategies are adopted by persons with EI-class B/C in order to maintain their body weight. This might involve selection of foods of high energy density and high-protein density, however a prospectively conducted study of dietary habits would be required to understand this further. Patients with EI-class B/C experienced nutritional impairment, when difficulty chewing was present in combination with a burden of additional symptoms, notably dysphagia, thick saliva, dry mouth and pain. This combination of deficits in mastication and salivation, combined with difficult and painful swallowing would be particularly detrimental to ingestion of solid food.

Patients with HNC are at high risk for severe impairment of food intake. Screening and assessment for malnutrition in patients with HNC are recommended in Clinical Nutrition [31] and French Society of Otorhinolaryngology [32] clinical practice guidelines. Several validated screening tools are recommended such as the PG-SGA© used here and the Nutrition Risk Index [32]. The application of validated tools for screening

Table 4. Multivariable logistic regression analysis comparing Eichner Index (EI) classes controlling for age and sex.

Reference Class vs	EI-class A (N = 44)	EI-classes B/C with normal Dietary Intake (DI) (N = 28)	EI-class A	EI-classes B/C with normal DI
Comparison Class	EI-classes B/C (N = 60)	EI-classes B/C with reduced DI (N = 32)	EI-classes B/C	EI-classes B/C with reduced DI
Variable	OR (95%CI)	OR (95%CI)	*Overall P* value	
Age	1.11(1.04–1.19)	1.04 (0.95–1.14)	0.001	0.325
Sex (male)	2.09 (0.47–9.23)	1.17 (0.21–6.43)	0.329	0.855
≥5% WL	1.03 (0.29–3.70)	5.94 (0.81–43.25)	0.954	0.079
Performance Status (PS) Normal PS, ECOG PS 0				
Reduced PS, ECOG PS 1- 4	0.52 (0.15–1.78)	**6.20(1.33–28.84)**	0.303	**0.020**
Dietary Intake (DI) Category				
Normal DI, DI = 0				
Reduced DI, DI = 1-5	3.16 (0.84–11.78)		0.086	
TOTAL NIS INTERFERENCE SCORE	**1.10 (1.02–1.18)**	**1.10(1.01–1.19)**	**0.007**	**0.022**

Abbreviations: DI, Dietary Intake; ECOG, Eastern Cooperative Oncology Group; EI, Eichner Index; NIS, Nutrition Impact Symptom; OR, odds ratio; PS, Performance Status; ref, reference group; vs, versus; WL, Weight Loss.
Multivariable logistic regression analysis controlling for age and sex demonstrates that total NIS interference score explains as a whole between Cox & Snell R square = 31.0%; Nagelkerke R Square = 42.0%, of the variance in EI classes and correctly classified an overall percentage = 80.9% of the cases.
Multivariable logistic regression analysis controlling for age and sex demonstrates that total NIS interference score and ECOG PS explains as a whole between Cox & Snell R square = 38.5%; Nagelkerke R Square = 51.6%, of the variance in the EI class BC with reduced DI and correctly classified an overall percentage = 79.6 % of the cases. Bold in table - demonstrate significant OR(95% CI) and *P*-value.

of nutritional risk is especially important because high BMI at diagnosis as seen here and by others [33] cannot be taken to mean that nutrition risk is absent. Nutritional assessment at this tumor site is focused on symptoms impacting oral intake. It is rare for any person with HNC to have just one or two nutritionally impactful symptoms [7, 27]. Burden of NIS has been previously demonstrated to increase treatment naïve HNC patient's risk of reduced DI and in turn accelerate the rate of WL [34]. This finding suggests HNC patients may benefit from proactive symptoms management to stem WL. Here we specifically explored the impact of reduced dentition as a potential limitation. HNC patients may benefit from dental care that would prevent tooth loss, restores dentition and dietary counselling that could provide them with knowledge regarding nutrient dense foods which may include oral nutrition supplements and alternative cooking methods to take in foods that do not require intensive mastication.

Our study has strengths and limitations. This analysis was conducted on a sub sample of a much larger consecutive series [28] and can therefore be argued to be typical of this population. However, the sample size was limited and few patients (12.5% of the population) fell into EI-class C. Our sample also included a mixture of tumor sites; a much larger sample size would be required to do analysis on a tumor site-specific basis; our population-based results [35] suggest different rates of dysphagia, chewing difficulty and other NIS across the tumor sites. Even though this group appeared to be worse off in several respects than EI-class B, larger numbers would be required to determine to evaluate this. The nutritional profiling of our patients and is consistent and detailed. We used standardized validated instruments for screening of nutritional status and NIS. The 17 items on the checklist represent all the symptoms reported in the HNC literature to be associated with nutritional impairments. The degree to which the patient feels each symptom is impacting their ability to consume food is scored.

5. Conclusion

This study demonstrates that reduced occlusal support impacts NIS, DI and WL in treatment naïve HNC patients. EI-class B/C patients did not necessarily have impaired DI, however the combination of EI-class B/C and a constellation of NIS, associated with reduced DI. Optimizing the dental status and NIS management may improve DI and reduce the risk of future WL of HNC patients.

Catherine Kubrak PhD RN declares copyrights for the instrument "Head and neck symptom checklist" and reports no other conflicts of interests to declare.

We have full control of all the primary data and we agree to allow the journal to review the data if requested.

Declarations

Author contribution statement

C. Kubrak: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

A. Farhangfar: Conceived and designed the experiments; Performed the experiments; Contributed reagents, materials, analysis tools or data.

V. Baracos: Conceived and designed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

M. Woynorowski and W. Preshing: Performed the experiments; Contributed reagents, materials, analysis tools or data.

N. Jha: Contributed reagents, materials, analysis tools or data.

Funding statement

This work was supported the Canadian Institutes of Health Research.

Competing interest statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

References

[1] J.A.E. Langius, S. Bakker, D. Rietveld, H. Kruizenga, J. Langendijk, P. Weijs, C. Leemans, Critical weight loss is a major prognostic indicator for disease-specific survival in patients with head and neck cancer receiving radiotherapy, Br. J. Canc. 109 (2013) 1093–1099.

[2] G. Capuano, P.C. Gentile, F. Bianciardi, M. Tosti, A. Palladino, M. Di Palma, Prevalence and influence of malnutrition on quality of life and performance status in patients with locally advanced head and neck cancer before treatment, Support. Care Canc. 18 (2010) 433–437. Epub 2009 Jun 29.

[3] H. Jager-Wittenaar, P.T. Dijkstra, G. Dijkstra, J. Bijzet, J.A. Langendijk, B.F. van der Laan, J.L.N. Roodenburg, High prevalence of cachexia in newly diagnosed head and neck cancer patients: an exploratory study, Nutrition 35 (2017) 114–118. Epub 2016 Dec 14.

[4] U. Mulasi, D.M. Vock, A.J. Kuchnia, J. Gautam, N. Fujioka, V. Rudrapatna, M.R. Patel, L. Teigen, C.P. Earthman, Malnutrition identified by the Academy of Nutrition and Dietetics and American Society for Parenteral and Enteral Nutrition Consensus Criteria and other beside tools is highly prevalent in a sample of individuals undergoing treatment for head and neck cancer, JPEN - J. Parenter. Enter. Nutr. (2016) pii: 0148607116672264. [Epub ahead of print].

[5] K. Fearon, F. Strasser, S.D. Anker, I. Bosaeus, E. Bruera, R.L. Fainsinger, et al., Definition and classification of cancer cachexia: an international consensus framework, Lancet Oncol. 12 (5) (2011) 489–495. Epub 2011 Feb 4.

[6] V.E. Baracos, L. Martin, M. Korc, D.C. Guttridge, K.C.H. Fearon, Cancer-associated cachexia, Nat. Rev. Dis. Prim. 4 (2018) 17105.

[7] C. Kubrak, K. Olson, V.E. Baracos, The head and neck symptom checklist©: an instrument to evaluate nutrition impact symptoms effect on energy intake and weight loss, Support. Care Canc. 21 (11) (2013) 3127–3136.

[8] F. Samim, J.B. Epstein, Z.S. Zumsteg, A.S. Ho, A. Barasch, Oral and dental health in head and neck cancer survivors, Canc. Head Neck 14 (1) (2016).

[9] R. Barrios, G. Tsakos, B. García-Medina, L. Martínez-Lara, M. Bravo, Oral health-related quality of life and malnutrition in patients treated for oral cancer, Support. Care Canc. 22 (11) (2014) 2927–2933. Epub 2014 May 22.

[10] I.C. Lee, Y.H. Yang, P.S. Ho, I.C. Lee, Chewing ability: nutritional status and quality of life, J. Oral Rehabil. 41 (2014) 79–86. Epub 2013 Nov 29.

[11] O. Naka, V. Anastassiadou, A. Pissiotis, Association between functional tooth units and chewing ability in older adults: a systematic review, Gerodontology 31 (3) (2014) 166–177.

[12] J.S. Lee, R.J. Weyant, P. Corby, S.B. Kritchevsky, T.B. Harris, R. Rooks, S.M. Rubin, A.B. Newman, Edentulism and nutritional status in a biracial sample of well-functioning, community-dwelling elderly: the health, aging, and body composition study, Am. J. Clin. Nutr. 79 (2) (2004) 295–302.

[13] H. Wakabayashi, M. Matsushima, H. Ichikawa, S. Murayama, S. Yoshida, M. Kaneko, R. Mutai, Occlusal support, dysphagia, malnutrition, and activities of daily living in aged individuals needing long-term care: a path analysis, J. Nutr. Health Aging 22 (1) (2018) 53–58.

[14] F.B. de Andrade, M.L. Lebrão, Y.A. de Oliveira Duarte, J.L. Santos, Oral health and changes in weight and waist circumference among community-dwelling older adults in Brazil, J. Am. Dent. Assoc. 145 (7) (2014) 731–736.

[15] W.1 Marcenes, J.G. Steele, A. Sheiham, A.W. Walls, The relationship between dental status, food selection, nutrient intake, nutritional status, and body mass index in older people, Cad. Saúde Pública 19 (3) (2003) 809–816.

[16] K.J. Joshipura, W.C. Willett, C.W. Douglass, The impact of edentulousness on food and nutrient intake, JADA 127 (4) (1996) 459–467.

[17] A. Sheiham, J.G. Steele, W. Marcenes, C. Lowe, S. Finch, C.J. Bates, et al., The relationship among dental status nutrient intake, and nutritional status in older people, J. Dent. Res. 80 (2001) 408–413.

[18] C.S. Ritchie, K. Joshipura, R.A. Silliman, B. Miller, C.W. Douglas, Oral health problems and significant weight loss among community-dwelling older adults, J. Gerontol. A Biol. Sci. Med. Sci. 55 (7) (2000) M366–M371.

[19] R. Koodaryan, A. Hafezeqoran, A. Nourizadeh, A. Ostad, R.M. Ahmadian, The relationship between dental status, body mass index and nutrient intake, ABCmed 2 (2) (2014), 2203-1413, http://www.journals.aiac.org.au/index.php/ABCMED/article/view/655.

[20] P. Gaewkhiew, W. Sabbah, E. Bernabé, Does tooth loss affect dietary intake and nutritional status? A systematic review of longitudinal studies, J. Dent. 67 (2017) 1–8. Epub 2017 Oct 31.

[21] M. Iwasaki, A. Yoshihara, H. Ogawa, M. Sato, K. Muramatsu, R. Watanabe, T. Ansai, H. Miyazaki, Longitudinal association of dentition status with dietary intake in Japanese adults aged 75 to 80 years, J. Oral Rehabil. 43 (10) (2016) 737–744. Epub 2016 Aug 21.

[22] H.C. Hung, W. Willett, A. Ascherio, B.A. Rosner, E. Rimm, K.J. Joshipura, Tooth loss and dietary intake, J. Am. Dent. Assoc. 134 (9) (2003) 1185–1192.

[23] A.H. Friedlander, T. Tajima, K.T. Kawakami, M.B. Wang, J. Tomlinson, The relationship between measures of nutritional status and masticatory function in untreated patients with head and neck cancer, J. Oral Maxillofac. Surg. 66 (1) (2008) 85–92.

[24] K. Yoshino, I. Kikukawa, Y. Yoda, H. Watanabe, K. Fukai, N. Sugihara, Matsukubo T relationship between Eichner index and number of present teeth, Bull. Tokyo Dent. Coll. 53 (1) (2012) 37–40.

[25] K. Ikebe, K. Matsuda, S. Murai, Y. Maeda, T. Nokubi, Validation of the Eichner Index in relation to occlusal force and masticatory performance, Int. J. Prosthodont. (IJP) 23 (6) (2010) 521–524.

[26] H. Jager-Wittenaar, F.D. Ottery, H. de Bats, et al., Diagnostic accuracy of PG-SGA SF, MUST and SNAQ in patients with head and neck cancer, Clin. Nutr. 35 (S1) (2016) S103–S104. http://pt-global.org/wp-content/uploads/2016/09/Jager-Wittenaar_Diagnostic-accuracy-PG-SGA-SF_ESPEN-2016.pdf.

[27] K.N. Schmidt, K. Olson, C. Kubrak, M. Parliament, S. Ghosh, Validation of the Head and Neck Patient Symptom Checklist as a nutrition impact symptom assessment tool for head and neck cancer patients, Support. Care Canc. 21 (1) (2013) 27–34. Epub 2012 May 16.

[28] A. Farhangfar, M. Makarewicz, S. Ghosh, N. Jha, R. Scrimger, L. Gramlich, V. Baracos, Nutrition impact symptoms in a population cohort of head and neck cancer patients: multivariate regression analysis of symptoms on oral intake, weight loss and survival, Oral. Oncol. 50 (9) (2014) 877–883. Epub 2014 Jul 10.

[29] E.B. Haverkort, R.J. de Haan, J.M. Binnekade, et al., Self-reporting of height and weight: valid and reliable identification of malnutrition in preoperative patients, Am. J. Surg. 203 (2012) 700–707. Epub 2012 Feb 23.

[30] G.S. Perry, T.E. Byers, A.H. Mokdad, et al., The validity of self-reports of past body weights by U.S. adults, Epidemiology 6 (1995) 61–66. https://www.ncbi.nlm.nih.gov/pubmed/7888448.

[31] J. Arends, P. Bachmann, V. Baracos, et al., ESPEN guidelines on nutrition in cancer patients, Clin. Nutr. 36 (1) (2017) 11–48. Epub 2016 Aug 6.

[32] E. de Monès, S. Vergez, B. Barry, et al., Initial staging for squamous cell carcinoma of the mouth, larynx and pharynx (except nasopharynx). Part 3: general assessment. 2012 SFORL recommendations, Eur. Ann. Otorhinolaryngol. Head Neck Dis. 130 (3) (2013) 165–172.

[33] M. Magnano, P. Mola, G. Machetta, et al., The nutritional assessment of head and neck cancer patients, Eur Arch Otorhinolaryngol. Dec 272 (12) (2015) 3793–3799.

[34] C. Kubrak, K. Olson, N. Jha, et al., Nutrition impact symptoms: key determinants of reduced dietary intake, weight loss, and reduced functional capacity of head and neck cancer patients prior to treatment, Head Neck 32 (3) (2010) 290–300.

[35] C. Kubrak, L. Martin, L. Gramlich, R. Scrimger, N. Jha, B. Debenham, N. Chua, J. Walker, V.E. Baracos, [Epub ahead of print] Prevalence and prognostic significance of malnutrition in patients with cancers of the head and neck, Clin. Nutr. 39 (3) (2020) 901–909, pii: S0261-5614(19)30144-X.