

Chapter 3

Malnutrition in patients treated for
oral or oropharyngeal cancer - prevalence
and relationship with oral symptoms:
an explorative study

H. Jager-Wittenaar
P.U. Dijkstra
A. Vissink
B.F.A.M. van der Laan
R.P. van Oort
J.L.N. Roodenburg

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ABSTRACT

Background & Aims

This study aimed to assess prevalence of malnutrition after treatment for oral/oropharyngeal cancer and to explore how oral symptoms relate to malnutrition after treatment.

Methods

In this cross-sectional study, malnutrition (weight loss $\geq 10\%$ in 6 months or $\geq 5\%$ in 1 month), oral symptoms (EORTC QLQ-H&N35 questionnaire and additional questions to assess chewing problems), dental status, trismus and dietary intake were assessed in 116 adult patients treated for oral/oropharyngeal cancer.

Results

Prevalence of malnutrition was 16% (95%CI: 10% to 23%). Prevalence of malnutrition in the period 0-3 months after treatment was significantly higher (25%) than in the periods >3-12 months (13%) and >12-36 months after treatment (3%, $p=0.008$). Logistic multivariate regression analysis revealed that swallowing problems ($p=0.021$) and insufficient protein intake were significantly related to malnutrition ($p=0.016$).

Conclusion

In conclusion, malnutrition is a considerable problem in patients treated for oral/oropharyngeal cancer, shortly after treatment. Of all oral symptoms, only swallowing problems were significantly related to malnutrition in the period after treatment for oral/oropharyngeal cancer.

INTRODUCTION

Malnutrition has been defined as a subacute or chronic state of nutrition, in which a combination of undernutrition (insufficient food intake) and inflammation has led to a decrease in muscle mass, fat mass, and diminished function, i.e. immune function, cognitive function and muscle strength.¹ In the period before head and neck cancer treatment, prevalence of severe weight loss, an indicator of malnutrition, varies from 19% to 45%.²⁻⁵

Malnutrition in head and neck cancer patients may have multiple causes. In the period before treatment, a major cause of malnutrition is insufficient food intake, related to mechanical obstruction of food or pain caused by the tumor. In addition, inflammatory activity induced by the tumor or cancer treatment, leading to catabolism of body cell mass may contribute to malnutrition.¹ During and after treatment, malnutrition may develop or aggravate as a result of oral symptoms related to treatment, such as chewing and swallowing problems, pain, dry mouth, sticky saliva and taste disturbances.⁶

Although malnutrition or weight loss in the period before head and neck cancer treatment is often reported^{2,4,7}, few data are available on prevalence of malnutrition after treatment for oral/oropharyngeal cancer. Previous studies in head and neck cancer patients treated with radiotherapy reported that prevalence of malnutrition is highest during radiotherapy and declines during the first 3 months after radiotherapy.^{8,9} These studies were heterogeneous regarding tumor localization and follow-up was limited to the first 6 months after treatment. Consequently, prevalence of malnutrition in the long-term period after treatment for oral/oropharyngeal cancer is unclear.

It is well known that oral symptoms are risk factors for malnutrition.⁶ In the period before treatment, swallowing problems and pain in the mouth are identified as main risk factors for malnutrition in head and neck cancer patients.^{2,10} Besides swallowing problems, patients treated for oral/oropharyngeal cancer may also suffer from chewing problems, due to either poor dental status or trismus. Edentulous patients often cannot wear their prosthesis for about 3 months after surgery and not uncommonly even up to 6 months after radiotherapy or chemoradiation, due to either radiation-induced mucositis, oral edema, tender oral mucosal surfaces, surgically induced changes in anatomy, or time needed to manufacture a new prosthesis. Additionally, trismus may result from scar tissue formation, as a result of surgery and from radiotherapy.¹¹⁻¹³ The relationship between poor dental status and trismus and malnutrition in patients treated for oral/oropharyngeal cancer has not been studied before. Thus, it is unclear which oral symptom(s) are risk factors for malnutrition in the period after treatment for oral/oropharyngeal cancer.

The primary aim of this study was to test the hypothesis that prevalence of malnutrition in patients treated for oral/oropharyngeal cancer declines in the period after treatment. The secondary aim of the study was to test the hypothesis that swallowing problems, poor dental status and trismus are risk factors for malnutrition in the period after treatment for oral/oropharyngeal cancer.

PATIENTS AND METHODS

A convenience sample of 185 consecutive adult patients was asked to participate in this cross-sectional study between October 2004 and February 2006. These patients had been treated for oral or oropharyngeal cancer at the University Medical Center Groningen (UMCG), the Netherlands. Patients willing to participate underwent assessment after their visit to the physician. Diagnosis and treatment information were retrieved from medical records (Table 1). The study was approved by the Ethics Committee of the UMCG. Informed consent was obtained from all participants.

Inclusion criteria were: age ≥ 18 years and completed treatment for oral/oropharyngeal cancer ≤ 3 years before study measurement. Treatment modalities were: surgery (local tumor excision and/or neck dissection); surgery and radiotherapy; radiotherapy (conventional or accelerated scheme); or radiotherapy with concomitant chemotherapy (carboplatin and 5-FU). Exclusion criteria were: a recurrent, residual or newly diagnosed tumor within 3 months after study measurement; edema due to liver, kidney or cardiac disease, to eliminate confounding by edema on body weight; uncontrolled diabetes mellitus to eliminate possible confounding in risk factors for weight loss.

Patients received dietary counseling from a dietitian working at the UMCG at time of diagnosis, during admission for surgery and weekly during radiotherapy. Duration of dietary counseling was generally limited to the first half year after treatment.

Assessment of malnutrition

Actual body weight (kilogram) was measured on a calibrated Seca 701 scale (Medical scales & Measuring Systems Seca Ltd., UK). Patients were measured in indoor clothing without shoes, after voiding the bladder. Weight for clothing (1.0-1.5 kg) was deducted from measured weight and this corrected weight was used for further analysis. Patients were asked for their body weight 1 and 6 months before study measurement. Pretreatment body weight was retrieved from medical records. Height was measured by a stadiometer (Seca 222, Medical scales & Measuring Systems Seca Ltd., UK).

Percentage weight loss was calculated as: $[(\text{normal body weight} - \text{actual body weight}) / \text{normal body weight}] \times 100$. Normal body weight was defined as body weight 1 month, or 6 months ago, or prior to treatment. Malnutrition was defined as weight loss $\geq 10\%$ in 6 months or $\geq 5\%$ in 1 month.^{4,14-18} BMI (kg/m^2) was calculated as $\text{actual body weight} / \text{body height}^2$.

Assessment of oral symptoms

The EORTC QLQ-H&N35 questionnaire was used to assess pain in mouth or throat, swallowing problems, senses problems, dry mouth and sticky saliva.¹⁹ Scale scores were calculated according to the manual and range from 0 to 100.²⁰ In addition, 3 questions regarding chewing problems were asked: 1) How much difficulty did you experience while eating solid food (like meat/solid bread)?; 2) How much difficulty did you experience while eating dry food (like cookies)?; 3) How much difficulty did you experience while eating soft food (like soft bread)? Possible answers to the additional questions were: 1) no difficulty; 2) little difficulty; 3) much difficulty; and

4) so much difficulty that eating was impossible. Answers 3) and 4) were dichotomized to 'chewing problems' and answers 1) and 2) to 'no chewing problems'. Time frame for all questions was the week prior to assessment.

Dental status was assessed by number of natural teeth and/or presence or absence of a dental prosthesis. Dental status was considered poor if: edentate without prosthesis, edentate plus prosthesis in upper/lower jaw, or 1 edentulous jaw without prosthesis and 1-16 elements in the other jaw, otherwise dental status was considered acceptable.

Maximal mouth opening was measured 3 times using 2 calibrated callipers, 1 for edentates or partially dentate patients wearing their prosthesis and 1 for edentates not wearing their prosthesis. Trismus was defined as mean mouth opening ≤ 35 mm.²¹

Dietary intake and requirements

Dietary intake of the last week before measurement was assessed by means of dietary history, by a registered dietitian (HJ).²² Energy and protein intake were calculated using food calculation software (JOLE v.02r80 by iSOFT, The Netherlands). Nutritional requirements were estimated conform practical guidelines used in the UMCG: 30 or 35 kcal and 1.0 or 1.5 gram protein per kg actual body weight for well-nourished and malnourished patients respectively.²³ For patients with a BMI > 27, body weight equivalent to BMI = 27 was calculated and used in the calculations, to correct for the relatively lower metabolic active muscle mass.²⁴ Energy or protein intake < 90% of requirements was considered insufficient.

Patients were asked if they (partly) mashed or grinded their food. Patients not using oral food were able to answer with 'not applicable'.

Statistical analysis

Statistical analyses were performed using SPSS 16.0 for Windows software (SPSS Inc., Chicago, IL, USA). Interval after treatment (months) was categorized into 0-3 months after treatment, >3-12 months after treatment and >12-36 months after treatment. An independent samples Student's t-test was used to test differences in continuous variables between 2 groups. A paired sample Student's t-test was used to test differences in the mean of a continuous variable between 2 related groups. The Mann-Whitney U test was used to test differences in continuous variables between 2 groups if not distributed normally and in ordinal variables. The chi-square test was used to test differences between categorical variables. The Fisher's exact test was used for categorical variables if $\geq 20\%$ of the cells had an expected count less than 5, in 2 x 2 tables.

The relationship between oral symptoms and malnutrition was analyzed in a multivariate logistic regression analysis. Malnutrition (yes/no) was entered as outcome variable. Age (years), gender (male versus female), tumor size (T1/T2 versus T3/T4), treatment with or without radiotherapy (surgery alone versus radiotherapy, surgery and radiotherapy or chemoradiation), single or combined treatment modality (surgery alone or radiotherapy alone versus surgery and radiotherapy or chemoradiation), interval after treatment (continuous variable (months)), dental status (poor versus acceptable), chewing problems (yes versus no), trismus (yes versus no), energy intake (sufficient versus insufficient), protein intake (sufficient versus insufficient), EORTC QLQ-H&N35 scale scores on swallowing problems, sticky saliva, senses problems, dry mouth, and pain in mouth

or throat were entered in the logistic regression analysis (method stepwise backward), entry criterion $p \leq 0.05$, removal criterion $p > 0.10$.

The relationship between percentual decline in pretreatment body weight and interval after treatment (categorical variable) was analyzed by one-way analysis of variance (ANOVA).

In all analyses, statistical significance was set at $p < 0.05$.

RESULTS

Patients

Of the 185 eligible patients, 63 patients declined participation. Reasons to decline participation were: not interested in the study (33%, 23/63), fatigue (14%, 9/63), time investment too long (17%, 11/63) and unknown reasons (32%, 20/63). One-hundred and twenty-one patients were included in the study. Six patients had to be excluded because of either still being under treatment ($n=1$), tumor recurrence shortly after inclusion ($n=1$), or not being able to undergo nutritional assessment ($n=4$). Data of the remaining 116 patients (Table 1) were used in the various analyses on malnutrition, unless stated otherwise. Data on pretreatment body weight were complete in 112 patients.

Nutritional assessment

Overall prevalence of malnutrition was 16% (18/116, 95%CI: 10% to 23%). Prevalence of malnutrition in the period 0-3 months after treatment was significantly higher (25%, 13/53) than in the periods >3-12 months after treatment (13%, 4/32) and >12-36 months after treatment (3%, 1/31) ($p=0.008$). Mean pretreatment body weight significantly declined from 78.7 ± 13.4 kg to 75.9 ± 14.0 kg post-treatment ($p < 0.001$) (mean decline 2.8 ± 5.9 kg). Mean percentual decline in pretreatment body weight was $3.4 \pm 7.3\%$ and no significant differences in percentual decline in pretreatment body weight between the 3 intervals after treatment were found ($p=0.220$). Mean pretreatment BMI declined from 26.3 ± 4.0 kg/m² to 25.4 ± 4.0 kg/m² post-treatment ($p < 0.001$) (mean decline 1.0 ± 2.0 kg). Five percent (6/114) of all patients had a BMI < 18.5 kg/m².

Prevalence of malnutrition per treatment modality is presented in Table 2. Analyzed univariately, no differences in age (years), gender, tumor size (T1/T2 versus T3/T4), number of treated head and neck tumors and localization of last tumor (oral cavity versus oropharynx) were found between malnourished and well-nourished patients.

Oral symptoms

Analyzed univariately, malnourished patients scored worse on swallowing problems ($p=0.005$), dry mouth ($p=0.032$) and sticky saliva ($p=0.011$) compared to well-nourished patients (Table 3).

Dietary intake

Ninety-six percent of all patients (111/115) used an oral diet, either with (3%, 3/115) or without tube feeding (94%, 108/115) (Table 1). Of the patients using oral food (with or without tube feeding), 87% (97/111) used a

Table 1. Patient characteristics (n=116).

Age (years), mean±SD	59.7±11.7	
	<i>n</i>	% ^a
Gender		
Male	72	62
Female	44	38
Number of treated head and neck tumors		
1	90	77
2	24	21
3	2	2
Last treated tumor		
Squamous cell carcinoma	103	89
Salivary gland tumor	10	9
Other	3	3
Size of last treated tumor		
T1	53	46
T2	34	29
T3	3	3
T4	13	11
Unknown	13	11
Localization of last treated tumor		
Oral cavity	82	71
Oropharynx	30	26
Other ^b	4	3
Treatment of last tumor		
Surgery	62	53
Surgery + radiotherapy	35	30
Radiotherapy	12	10
Chemoradiation	7	6
Interval after treatment		
0 – 3 months	53	46
>3 – 12 months	32	28
>12 – 36 months	31	27
Type of diet^c		
Oral diet only	75	65
Oral diet with liquid dietary supplements	33	29
Oral diet and tube feeding	3	3
Tube feeding only	4	3
Interval between end of treatment and assessment (months), median (IQR ^d)		4.3 (1.4; 12.6)

a. Sum of percentages may be dissimilar to 100%, due to rounding.

b. Neck metastasis, maxillary sinus, unknown primary.

c. N=115.

d. IQR: Interquartile range.

solid diet and 13% (14/111) a liquid/mashed diet. Patients using a liquid/mashed diet were significantly more often malnourished (36%, 5/14) than patients using a solid diet (11%, 11/97, $p=0.003$).

Mean actual intake was 2185±699 kcal and 83±24 gram protein. No significant differences were found in intake between malnourished and well-nourished patients. Frequency of insufficient protein intake, related to

requirements, was significantly higher in malnourished patients (65%, 11/17) than in well-nourished patients (29%, 27/92 $p=0.011$).

Table 2. Prevalence of malnutrition related to last type of head and neck cancer treatment.

Type of treatment (n)	Malnutrition	
	n	% ^a
Surgery (62)	5	8
Treatment including radiotherapy (54)	13	24 ^b
Radiotherapy (12)	3	25
Surgery and radiotherapy (before or after surgery) (35)	9	26
Chemoradiation (7)	1	14

a. Percentages are row percentages.

b. Prevalence of malnutrition in patients treated with radiotherapy, surgery and radiotherapy, or chemoradiation is significantly higher than in patients treated with surgery alone ($p=0.034$), analyzed by chi-square test.

Table 3. Univariate analysis on malnutrition and oral symptoms.

Oral symptoms (n) ^a	Malnutrition		No malnutrition		p
	n	% ^b	n	% ^b	
Chewing problems (31/116)	7	23	24	77	0.248 ^c
Trismus (30/116)	7	23	23	77	0.239 ^c
Poor dental status (37/116)	9	24	28	76	0.129 ^d
	median	IQR ^e	median	IQR	p
Pain in mouth / throat (113)	25.0	14.6; 37.5	16.7	0.0; 25.0	0.092 ^f
Swallowing problems (113)	29.2	0.0; 52.1	0.0	0.0; 25.0	0.005^f
Senses problems (113)	16.7	0.0; 37.5	0.0	0.0; 16.7	0.211 ^f
Dry mouth (113)	66.7	33.3; 100.0	33.3	0.0; 66.7	0.032^f
Sticky saliva (113)	66.7	0.0; 100.0	0.0	0.0; 66.7	0.011^f

a. Number of valid observations (patients with this symptom/total number of patients).

b. Percentages are row percentages.

c. Analyzed by Fisher's exact test.

d. Analyzed by chi-square analysis, with continuity correction.

e. Interquartile range.

f. Analyzed by Mann-Whitney U test.

Multivariate logistic regression analysis

Swallowing problems and insufficient protein intake were significantly related to malnutrition in the logistic multivariate regression analysis (Table 4).

Table 4. Results of multivariate logistic regression analysis on malnutrition and oral symptoms.

Variable	β	SE β	OR	95% CI of OR	p
Swallowing problems	0.03	0.01	1.03 ^a	1.01 to 1.06	0.021
Insufficient protein intake ^b	1.60	0.66	4.93	1.35 to 18.06	0.016
Interval after treatment (months)	-0.13	0.06	0.89	0.79 to 1.00	0.057
Constant	-2.37	0.64	0.09		<0.001

β = Regression Coefficient; SE β = Standard Error of β ; OR = Odds Ratio = e^{β} ; 95% CI of OR = 95% Confidence Interval of Odds Ratio.

a. A difference, for instance of 20 points in swallowing problems assessed by EORTC QLQ-H&N35, between 2 patients results in an OR for malnutrition of 1.82.

($20 \times \beta = 20 \times 0.03 = 0.06 \rightarrow e^{0.06} = 1.82$).

b. 0 = absent; 1 = present.

DISCUSSION

The results of our study demonstrate that 1 out of 6 patients is malnourished after treatment for oral/oropharyngeal cancer, with the highest prevalence of malnutrition shortly after treatment (1 out of 4 patients). The decline in prevalence of malnutrition within the first year after treatment in our study is in accordance with results of other studies.^{8,9,25}

Very limited data are available on prevalence of malnutrition after treatment for oral/oropharyngeal cancer. In a randomized clinical trial 48% of the patients was malnourished 3 months after start of radiotherapy. If patients received dietary counseling during and shortly after radiotherapy this percentage was 24%.⁸ In a study in head and neck cancer patients, in which malnourished patients received tube feeding during and after radiotherapy, prevalence of malnutrition was 27% and 6% in the third and sixth month after start of radiotherapy, respectively.²⁵ Other studies on malnutrition in head and neck cancer patients focused on changes in nutritional status during and after treatment. In another randomized clinical controlled trial, performed in head and neck cancer patients treated with radiotherapy, nutritional status was deteriorated 3 months after treatment in all patients, but if patients received dietary counseling during radiotherapy this frequency was limited to 12%.⁹ In head and neck cancer patients not receiving dietary counseling during and after treatment, mean body weight significantly declined with 2.3 ± 4.0 kg during treatment and 2.2 ± 5.5 kg in the period after treatment.⁵ In all of these studies prevalence of malnutrition declined in the first 6 months after treatment in patients receiving dietary intervention.^{8,9,25}

Of all oral symptoms, swallowing problems was the only one related to malnutrition in the logistic multivariate regression analysis. Although swallowing problems may be present in the long-term period after treatment for oral or oropharyngeal cancer²⁶, swallowing problems are most severe during and shortly after treatment, due to radiation-induced mucositis and reduced mobility of the tongue due to surgery.^{6,27} Probably swallowing problems will cause malnutrition predominantly during treatment, and to a lesser extent in the period after treatment.

Poor dental status, trismus and chewing problems were no risk factors for malnutrition in the multivariate

regression analysis. The multiple regression analysis corrected for confounders like change in diet and dietary treatment. Patients having chewing problems often change their diet into a soft, mashed or liquid diet. As nutritional density of a mashed or liquid diet is lower than that of a solid diet, these patients also are advised to use energy- and protein enriched liquid dietary supplements. Use of these supplements increases energy and protein intake and in turn decreases the risk for malnutrition. Only 1 other study assessed the relationship between dental status and malnutrition, but this study was performed in the period before treatment.¹⁰ In the latter study also no significant relationship between these variables was found.¹⁰

No significant relationship was found between percental decline in body weight and interval after treatment. Mean decline in pretreatment body weight was limited to 3%. However, this 3% weight loss may be additional to weight loss that already may have developed before start of treatment. At time of diagnosis, 34% of patients with oral/oropharyngeal cancer have already lost $\geq 10\%$ of body weight in 6 months or $\geq 5\%$ in 1 month.² Additionally, in the current study difference between pretreatment and actual body weight ranged widely, indicating that a subgroup of patients fails to regain body weight to pre-illness or even pretreatment level.

Although patients treated with radiotherapy were significantly more frequently malnourished than patients treated with surgery alone in the univariate analysis, treatment with any type of radiotherapy was not significantly related to malnutrition in the multivariate logistic regression analysis. In a prospective study on weight loss in head and neck cancer patients not receiving dietary counseling, patients treated with any type of radiotherapy lost significantly more body weight than patients treated with surgery alone.⁵ In the current study, swallowing problems and insufficient intake were more strongly related to malnutrition than type of treatment, in the period after treatment.

Averagely, both malnourished and well-nourished patients seemed to have a rather adequate intake of energy and protein. However, insufficient protein intake related to requirements was significantly related to malnutrition. Energy and protein intake of our patients were similar to intake reported in other studies in head and neck cancer patients.^{5,8,9} On the other hand, mean body weight of our patients was higher than reported in 2 of these studies^{5,9}, suggesting that dietary requirements of our patients were higher as well. As the 95% confidence interval of the odds ratio of insufficient protein intake was wide, the significant relationship found between insufficient protein intake and malnutrition should be interpreted with caution. This wide confidence interval may be the result of insufficient power due to the relatively low prevalence of malnutrition. On the other hand, the effect of protein intake on malnutrition may vary per patient. As malnutrition is the result of a combination of insufficient intake and inflammatory activity¹, inflammatory activity may have continued in the period after treatment.

Unfortunately, currently a gold standard for the assessment of malnutrition does not exist.¹ Weight loss is one of the criteria commonly used for assessment of malnutrition.¹⁸ Weight loss of $\geq 10\%$ in 6 months/ $\geq 5\%$ in 1 month is a generally accepted cutoff for clinically relevant weight loss. Such a weight loss is associated with increased morbidity, such as impaired wound healing and reduced immune function.^{28,29} Besides that, weight loss of $\geq 10\%$ in 6 months/ $\geq 5\%$ in 1 month has shown to be of great prognostic value in the occurrence of major postoperative complications and has been associated with higher mortality and reduced quality of

life.^{4,14,16,17,28-31} The cutoff point used in the current study was adopted by ASPEN to define 'nutritionally at risk adults'.³²

Whereas weight loss reflects acute malnutrition, underweight reflects chronic malnutrition.^{33,34} Cutoff values for BMI varying from 18.5 to 20.0 kg/m² have been used as an indicator of chronic malnutrition.^{18,35} If a BMI < 18.5 kg/m² was added to our criteria for malnutrition, total prevalence of malnutrition would have risen to 19% (22/116). Prevalence of malnutrition in the period 0-3 months after treatment (28%, 15/53) also would have been significantly higher than in the periods >3-12 months and >12-36 months after treatment (16%, 5/32 and 7%, 2/31, $p=0.012$). If this cutoff for BMI is increased to BMI < 20 kg/m², total prevalence of malnutrition would have increased further to 22% (25/116). Prevalence of malnutrition per interval after treatment would have been 32% (17/53), 16% (5/32) and 10% (3/32) respectively ($p=0.012$). These findings indicate that the choice of the cutoff values is of the utmost importance for assessment of malnutrition. Obviously, a gold standard for the assessment of malnutrition is required.

To test the hypothesis that prevalence of malnutrition declines after treatment, we classified patients into 3 groups: 0-3 months after treatment, >3-12 months after treatment and >12-36 months after treatment. We chose these cutoff values, to distinguish between acute and late side effects of head and neck cancer treatment. Radiation induced acute side-effects, such as mucositis, will diminish in the first 3 months after treatment.^{6,36} In the period between 3 months and 1 year after treatment, existing oral symptoms may recover or may become chronic, as oral symptoms present 1 year after treatment usually do not recover in the period after that.^{27,37} Furthermore, in the short-term period after treatment, inflammatory activity related to treatment may still be present.³⁸⁻⁴⁰ One year after treatment, it is expected that patients reach a 'steady state' with regard to their nutritional problems.

A limitation of this study is the modest participation rate of 66%. In 14% of the patients not willing to participate fatigue has played a major role in the decision to refuse participation in the study. As it cannot be excluded that fatigue was the result of malnutrition, the modest participation rate may have resulted in underestimation of malnutrition.

Another limitation of the study is the use of prediction equations to estimate nutritional requirements.⁴¹⁻⁴³ Indirect calorimetry is the gold standard to assess energy requirements.⁴⁴ However, for practical reasons it was not possible to perform indirect calorimetry in the current study. Therefore, energy requirements had to be estimated. We have chosen to compare energy intake to energy recommendations conform clinical practice in the UMCG. Use of prediction equations to predict energy expenditure may lead to prediction errors.⁴¹⁻⁴³ Such prediction errors may vary from 235 to 425 kcal, which is about 15-30% of resting energy expenditure as measured by indirect calorimetry.⁴³ Therefore, evaluation of dietary intake in relation to requirements requires further research.

In conclusion, malnutrition is a considerable problem in patients treated for oral/oropharyngeal cancer, shortly after treatment. Of all oral symptoms, only swallowing problems were significantly related to malnutrition in the period after treatment for oral/oropharyngeal cancer.

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REFERENCES

1. Soeters P B, Reijven P L, van Bokhorst-de van der Schueren MA, Schols J M, Halfens R J, Meijers J M, van Gemert W G. A rational approach to nutritional assessment. *Clin Nutr* 2008; 27: 706-716.
2. Jager-Wittenaar H, Dijkstra PU, van der Laan BFAM, Vissink A, van Oort RP, Roodenburg JLN. Critical weight loss in head and neck cancer patients - prevalence and risk factors at diagnosis: an explorative study. *Supp Care Cancer* 2007; 15: 1045-1050.
3. Matthews TW, Lampe H B, Dragoszk K. Nutritional status in head and neck cancer patients. *J Otolaryngol* 1995; 24: 87-91.
4. Van Bokhorst-de van der Schueren MA, van Leeuwen P A, Sauerwein H P, Kuik D J, Snow G B, Quak J J. Assessment of malnutrition parameters in head and neck cancer and their relation to postoperative complications. *Head Neck* 1997; 19: 419-425.
5. Van den Berg M G, Rasmussen-Conrad E L, Gwasara G M, Krabbe P F, Naber A H, Merks M A. A prospective study on weight loss and energy intake in patients with head and neck cancer, during diagnosis, treatment and revalidation. *Clin Nutr* 2006; 25: 765-772.
6. Vissink A, Jansma J, Spijkervet F K, Burlage F R, Coppes R P. Oral sequelae of head and neck radiotherapy. *Crit Rev Oral Biol Med* 2003; 14: 199-212.
7. Lees J. Incidence of weight loss in head and neck cancer patients on commencing radiotherapy treatment at a regional oncology centre. *Eur J Cancer Care (Engl)* 1999; 8: 133-136.
8. Isenring E A, Bauer J D, Capra S. Nutrition support using the American Dietetic Association medical nutrition therapy protocol for radiation oncology patients improves dietary intake compared with standard practice. *J Am Diet Assoc* 2007; 107: 404-412.
9. Ravasco P, Monteiro-Grillo I, Marques V P, Camilo M E. Impact of nutrition on outcome: a prospective randomized controlled trial in patients with head and neck cancer undergoing radiotherapy. *Head Neck* 2005; 27: 659-668.
10. Kubrak C, Olson K, Jha N, Jensen L, McCargar L, Seikaly H, Harris J, Scrimger R, Parliament M, Baracos V E. Nutrition impact symptoms: key determinants of reduced dietary intake, weight loss, and reduced functional capacity of patients with head and neck cancer before treatment. *Head Neck* 2010; 32: 290-300.
11. Goldstein M, Maxymiw W G, Cummings B J, Wood R E. The effects of antitumor irradiation on mandibular opening and mobility: a prospective study of 58 patients. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1999; 88: 365-373.
12. Ichimura K, Tanaka T. Trismus in patients with malignant tumours in the head and neck. *J Laryngol Otol* 1993; 107: 1017-1020.
13. Wang C J, Huang E Y, Hsu H C, Chen H C, Fang F M, Hsiung C Y. The degree and time-course assessment of radiation-induced trismus occurring after radiotherapy for nasopharyngeal cancer. *Laryngoscope* 2005; 115: 1458-1460.
14. Barbosa-Silva M C, Barros A J. Bioelectric impedance and individual characteristics as prognostic factors for post-operative complications. *Clin Nutr* 2005; 24: 830-838.
15. Blackburn G L, Bistrain B R, Maini B S, Schlamm H T, Smith M F. Nutritional and metabolic assessment of the hospitalized patient. *JPEN J Parenter Enteral Nutr* 1977; 1: 11-22.
16. Nguyen T V, Yueh B. Weight loss predicts mortality after recurrent oral cavity and oropharyngeal carcinomas. *Cancer* 2002; 95: 553-562.
17. Seltzer M H, Slocum B A, Cataldi-Betcher E L, Fileti C, Gerson N. Instant nutritional assessment: absolute weight loss and surgical mortality. *JPEN J Parenter Enteral Nutr* 1982; 6: 218-221.
18. Stratton R J, Green C J, Elia M. Disease-related malnutrition: an evidence based approach to treatment. Wallingford: CABI Publishing, 2003.

19. Bjordal K, Hammerlid E, Ahlner-Elmqvist M, de G A, Boysen M, Evensen J F, Biorcklund A, de L, Jr., Fayers P M, Jannert M, Westin T, Kaasa S. Quality of life in head and neck cancer patients: validation of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-H&N35. *J Clin Oncol* 1999; 17: 1008-1019.
20. Fayers P, Aaronson NK, Bjordal K, Curran D and Groenvold M on behalf of the EORTC Quality of Life Study Group. EORTC QLQ-C30 Scoring Manual (Third edition). Brussels: 2001.
21. Dijkstra P U, Huisman P M, Roodenburg J L N. Criteria for trismus in head and neck oncology. *Int J Oral Maxillofac Surg* 2006; 35: 337-342.
22. Burke BS. The dietary history as a tool in research. *J Am Diet Assoc* 1947; 23: 1041-1046.
23. Sauerwein H P, Strack van Schijndel R J. Perspective: How to evaluate studies on peri-operative nutrition? Considerations about the definition of optimal nutrition for patients and its key role in the comparison of the results of studies on nutritional intervention. *Clin Nutr* 2007; 26: 154-158.
24. Dickerson R N, Boschert K J, Kudsk K A, Brown R O. Hypocaloric enteral tube feeding in critically ill obese patients. *Nutrition* 2002; 18: 241-246.
25. Unsal D, Mentes B, Akmansu M, Uner A, Oguz M, Pak Y. Evaluation of nutritional status in cancer patients receiving radiotherapy: a prospective study. *Am J Clin Oncol* 2006; 29: 183-188.
26. Rieger J M, Zalmanowitz J G, Wolfaardt J F. Functional outcomes after organ preservation treatment in head and neck cancer: a critical review of the literature. *Int J Oral Maxillofac Surg* 2006; 35: 581-587.
27. Tei K, Maekawa K, Kitada H, Ohiro Y, Yamazaki Y, Totsuka Y. Recovery from postsurgical swallowing dysfunction in patients with oral cancer. *J Oral Maxillofac Surg* 2007; 65: 1077-1083.
28. Correia M I, Waitzberg D L. The impact of malnutrition on morbidity, mortality, length of hospital stay and costs evaluated through a multivariate model analysis. *Clin Nutr* 2003; 22: 235-239.
29. Van Bokhorst-De van der Schuer MA, von Blomberg-van der Flier BM, Riezebos R K, Scholten P E, Quak J J, Snow G B, van Leeuwen P A. Differences in immune status between well-nourished and malnourished head and neck cancer patients. *Clin Nutr* 1998; 17: 107-111.
30. Van Bokhorst-de van der Schueren MA, van Leeuwen P A, Kuik D J, Klop W M, Sauerwein H P, Snow G B, Quak J J, Andrews E, Andrews E. The impact of nutritional status on the prognoses of patients with advanced head and neck cancer. *Cancer* 1999; 86: 519-527.
31. Van den Berg M G, Rasmussen-Conrad E L, van Nispen L, van Binsbergen J J, Merckx M A. A prospective study on malnutrition and quality of life in patients with head and neck cancer. *Oral Oncol* 2008; 44: 830-837.
32. ASPEN Board of Directors and Standards Committee. Definition of terms, style, and conventions used in A.S.P.E.N. Guidelines and Standards. *Nutr Clin Pract* 2005; 20: 281-285.
33. Ferro-Luzzi A, Sette S, Franklin M, James W P. A simplified approach of assessing adult chronic energy deficiency. *Eur J Clin Nutr* 1992; 46: 173-186.
34. Shetty P S, James W P. Body mass index. A measure of chronic energy deficiency in adults. *FAO Food Nutr Pap* 1994; 56: 1-57.
35. World Health Organization. Physical status: the use and interpretation of anthropometry. Report of a WHO expert committee. Technical Report Series No 854. Geneva: 1995.
36. Cheng K K, Leung S F, Liang R H, Tai J W, Yeung R M, Thompson D R. Severe oral mucositis associated with cancer therapy: impact on oral functional status and quality of life. *Support Care Cancer* 2009 Epub ahead of print.
37. Logemann J A, Pauloski B R, Rademaker A W, Lazarus C L, Gaziano J, Stachowiak L, Newman L, MacCracken E, Santa D, Mittal B. Swallowing disorders in the first year after radiation and chemoradiation. *Head Neck* 2008; 30: 148-158.
38. Ehrsson Y T, Hellstrom P M, Brismar K, Sharp L, Langius-Eklof A, Laurell G. Explorative study on the predictive value of systematic inflammatory and metabolic markers on weight loss in head and neck cancer patients undergoing radiotherapy. *Support Care Cancer* 2009 Epub ahead of print.
39. Ki Y, Kim W, Nam J, Kim D, Park D, Kim D. C-reactive protein levels and radiation-induced mucositis in patients with head-and-neck cancer. *Int J Radiat Oncol Biol Phys* 2009; 75: 393-398.
40. Silver H J, Dietrich M S, Murphy B A. Changes in body mass, energy balance, physical function, and inflammatory state in patients with locally advanced head and neck cancer treated with concurrent chemoradiation after low-dose induction chemotherapy. *Head Neck* 2007; 29: 893-900.
41. Da Rocha E E, Alves V G, Silva M H, Chiesa C A, da Fonseca R B. Can measured resting energy expenditure be estimated by formulae in daily clinical nutrition practice? *Curr Opin Clin Nutr Metab Care* 2005; 8: 319-328.

42. Reeves M M, Battistutta D, Capra S, Bauer J, Davies P S. Resting energy expenditure in patients with solid tumors undergoing anticancer therapy. *Nutrition* 2006; 22: 609-615.
43. Weijs P J, Kruizenga H M, van Dijk A E, van der Meij B S, Langius J A, Knol D L, Strack van Schijndel R J, van Bokhorst-de van der Schueren MA. Validation of predictive equations for resting energy expenditure in adult outpatients and inpatients. *Clin Nutr* 2008; 27: 150-157.
44. Da Rocha E E, Alves V G, da Fonseca R B. Indirect calorimetry: methodology, instruments and clinical application. *Curr Opin Clin Nutr Metab Care* 2006; 9: 247-256.