Pre- and post-treatment malnutrition in head and neck cancer patients
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Malnutrition and quality of life in patients treated for oral or oropharyngeal cancer

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Head Neck: in press
ABSTRACT

Background & Aims
This study assessed whether malnourished patients score lower on quality of life after treatment for oral/oropharyngeal cancer.

Methods
Malnutrition (weight loss $\geq 10\%$ in 6 months/$\geq 5\%$ in 1 month) and quality of life (European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 questionnaire) were assessed cross-sectionally in patients treated for oral/oropharyngeal cancer. Interval after treatment varied from 1 day to 3 years. The relationship between malnutrition and quality of life was analyzed univariately (Mann-Whitney U test) and multivariately (linear regression analyses). Statistical significance was set at $p<0.05$.

Results
Prevalence of post-treatment malnutrition was $16\%$ ($18/115$, 95%CI: 9-23%). Analyzed univariately, malnourished patients scored significantly worse on physical functioning ($p=0.007$) and fatigue ($p=0.034$) than well-nourished patients. Multivariate analysis revealed that malnutrition was significantly related to physical functioning ($p=0.015$).

Conclusion
Malnourished patients treated for oral/oropharyngeal cancer score lower on quality of life scales related to physical fitness.
INTRODUCTION

Malnutrition has been defined as a subacute or chronic state of nutrition, in which a combination of undernutrition (insufficient food intake) and inflammation leads to a decrease in muscle mass, fat mass, and diminished body function.¹ In this definition, body function includes muscle function, cognitive function and immune function. In the period before treatment, prevalence of malnutrition in head and neck cancer patients ranges from 19% to 57%.²⁻⁴ Patients with oral or oropharyngeal cancer are at risk for malnutrition, due to oral symptoms caused by either the tumor localization or sequelae of treatment (Figure 1). Furthermore, inflammatory activity may contribute to malnutrition, either indirectly as a result of undernutrition, or directly mediated by the tumor or treatment.¹⁻³

Malnutrition is associated with increased morbidity and mortality. Malnutrition may result in an increased complication rate, including impaired wound healing, reduced immune function and decreased tolerance

Figure 1. Causes and consequences of malnutrition in head and neck cancer patients. Modified after Soeters et al.¹
Malnutrition in head and neck cancer patients may be caused by both cancer itself and its treatment. Cancer may be accompanied by disturbed metabolism, inflammatory activity and loss of appetite. These factors combined may cause cachexia, a subtype of malnutrition. Furthermore, the localization of the tumor may cause oral symptoms that hamper food intake. Treatment related oral symptoms, such as swallowing problems, chewing problems, dry mouth and changes in smell and taste may hinder food intake as well, possibly resulting in insufficient food intake. Malnutrition may result in decreased quality of life.
to surgery, radiotherapy and chemotherapy. Additionally, malnutrition has a negative impact on disease-related quality of life. Although cancer stage is the major determinant of patients’ overall quality of life, the impact of malnutrition combined with insufficient food intake on quality of life has been shown to be more important than the stage of the disease process.

The negative influence of malnutrition on quality of life has already been demonstrated in head and neck cancer patients in the period before, during and shortly after treatment. However, heterogeneous populations regarding tumor localization were studied and follow up was limited to 6 months after treatment. Consequently, the relationship between malnutrition and quality of life in the long-term period after treatment for oral or oropharyngeal cancer remains unclear. Therefore, the aim of our study was to test the hypothesis that in the period after treatment for oral or oropharyngeal cancer, malnourished patients experience a lower quality of life than well-nourished patients.

PATIENTS AND METHODS

A convenience sample of 185 consecutive adult patients was asked to participate in the study between October 2004 and February 2006. These patients had been treated for oral or oropharyngeal cancer within the setting of the multidisciplinary head and neck cancer group of the University Medical Center Groningen (UMCG), the Netherlands. Patients willing to participate underwent assessment after their scheduled visit to the physician. The study was approved by the Ethics Committee of the UMCG. Informed consent was obtained from all participants.

In this cross-sectional study, nutritional status and quality of life were assessed once after head and neck cancer treatment. Interval between day of assessment and last day of head and neck cancer treatment varied from 1 day to 3 years. Patients were classified into 3 groups in accordance with interval between end of treatment and time of study measurement: 0-3 months after treatment; >3-12 months after treatment; and >12-36 months after treatment.

Inclusion criteria were a completed head and neck cancer treatment, speaking Dutch language, and capable of completing a questionnaire. Treatment modalities were surgery (local tumor excision and/or neck dissection), surgery followed by radiotherapy, radiotherapy alone (either a conventional fractionated or accelerated scheme) or radiotherapy with concomitant chemotherapy (carboplatin and 5-fluorouracil). Exclusion criteria were patients with a recurrent, residual or newly diagnosed tumor within 3 months after study measurement, patients with edema due to liver, kidney or cardiac disease, to prevent influence of co-morbidities on hydration status, and patients with uncontrolled diabetes mellitus to prevent possible confounding in risk factors for weight loss.

All patients were routinely referred to a dietitian working at the UMCG. Patients received dietary counseling at time of diagnosis, during admission for surgery and weekly during radiotherapy. Duration of dietary counseling after treatment was generally limited to the first half year after treatment. During dietary counseling, nutritional requirements were estimated: 30 or 35 kcal and 1.0 or 1.5 gram protein per kg actual body weight for well-nourished and malnourished patients respectively. For patients with a Body Mass Index...
Malnutrition and quality of life

(BMI)>27 (n=37), a body weight equivalent to BMI=27 was calculated and used in the calculations, to correct for the relatively lower metabolic active muscle mass in overweight patients.\textsuperscript{14}

Diagnosis and treatment information were retrieved from medical records and included the number of primary tumors, localization of each primary tumor, size of each primary tumor, tumor type of the last primary tumor, number and type of head and neck cancer treatment(s) the patient had undergone, and dates of start and ending of each treatment. Pretreatment body weight (i.e. body weight at start of treatment) was retrieved from the medical records as well.

**Assessment of nutritional status**

Actual body weight (kilogram) was measured on a calibrated Seca 701 scale (Medical scales & Measuring Systems Seca Limited, United Kingdom). Patients were allowed to eat and drink before assessment. Patients were measured in indoor clothing without shoes, after voiding the bladder. Either 1 kg (for light clothes) or 1.5 kg (for jeans and sweater) was deducted from the measured weight and this corrected weight was used for further analysis. This weight is referred to as post-treatment body weight. Patients were asked for their normal body weight (without clothes and shoes), i.e. body weight of 1 and 6 months before study measurement. Height was measured by a stadiometer (Seca 222, Medical scales & Measuring Systems Seca Limited, United Kingdom).

Percentage weight loss was calculated as: [(normal body weight - actual body weight) / normal body weight] x 100. Malnutrition was defined as weight loss ≥10% in 6 months or ≥5% in 1 month.\textsuperscript{4-6,15-17} BMI (kg/m\textsuperscript{2}) was calculated as actual body weight / (body height\textsuperscript{2}).

**Quality of life assessment**

Quality of life was assessed by the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 questionnaire (EORTC QLQ-C30).\textsuperscript{18} This self-rating questionnaire contains 30 items, including 5 functional scales (physical, role, emotional, cognitive, and social functioning), 3 symptom scales (fatigue, nausea/vomiting, and pain), a global health scale, and 6 single items (dyspnea, insomnia, loss of appetite, constipation, diarrhoea, and financial difficulties). In addition, the EORTC head and neck module (EORTC QLQ-H&N35) was used to assess pain in mouth or throat, swallowing problems, senses problems, dry mouth, sticky saliva, trouble with social eating and trouble with social contact. Missing data were imputed in accordance with the guidelines in the manual.\textsuperscript{19} Linear transformation to '0–100' scales were carried out in accordance with the EORTC QLQ-C30 scoring manual.\textsuperscript{19} For the functioning scales and the global quality of life scale a high score represents a better level of functioning. For the symptom scales and the single item questions a high score represents a high level of problems.

In addition, 3 questions regarding chewing problems were asked: 1) How much difficulty did you experience while eating solid food (like meat/hard 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’. The time frame for all questions was the week prior to assessment.

Dental status was considered poor if: patients were edentate without prosthesis or edentate plus prosthesis in upper or lower jaw, or had 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.\(^{20,21}\)

**Statistical analysis**

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) 16.0 for Windows software (SPSS Incorporated, Chicago, Illinois). Interval after treatment (months) was categorized into 0-3 months after treatment, >3-12 months after treatment, and >12-36 months after treatment. Differences in gender, tumor size and type of treatment (surgery alone versus radiotherapy, surgery and radiotherapy, or chemoradiation) and interval after treatment (0-3 months after treatment, >3-12 months after treatment, and >12-36 months after treatment) between malnourished and well-nourished patients were univariately analyzed by chi-square test. Differences in age between malnourished and well-nourished patients were analyzed by independent samples Student’s t-test. Scores on the EORTC scales and items were compared between malnourished and well nourished patients by Mann-Whitney U test.

The relationship between malnutrition and quality of life was analyzed in linear regression analyses. Scales of the EORTC QLQ-C30 that were related to malnutrition were entered as outcome variables. The relationship between the EORTC scales and cancer treatment was explored in a regression analysis using 3 dummy variables: (1) chemoradiation (yes, no); (2) radiotherapy (yes, no); and (3) surgery and radiotherapy (yes, no). In this way surgery alone was the ‘reference’ therapy. Cancer treatment did not contribute significantly to the regression equation. Therefore type of cancer treatment was dichotomized into: radiotherapy, yes (including radiotherapy, surgery and radiotherapy, or chemoradiation) and no (surgery).

In the final regression analyses, malnutrition (malnutrition versus no malnutrition), gender (male versus female), age (years), tumor size (T1/T2 versus T3/T4), radiotherapy (yes, no), interval after treatment (months), pain in mouth or throat, swallowing problems, senses problems, dry mouth, sticky saliva, trouble with social eating, trouble with social contact, chewing problems (yes, no), poor dental status (yes, no) and trismus (yes, no) were entered as predictors in the linear regression analyses (method stepwise backward), entry criterion \(p \leq 0.05\), removal criterion \(p > 0.10\). In all analyses, statistical significance was set at \(p < 0.05\).

**RESULTS**

**Patients**

Of the 185 eligible patients, 63 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), or unknown reason (32%, 20/63). In total, 121 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 malnutrition and quality of life were complete in 115 patients. Characteristics of these 115 patients are shown in Table 1. Data of the 115 patients were used in the various analyses, unless stated otherwise. Twenty-three percent (26/115) of the patients had previously been treated for a primary tumor in the head and neck region.

**Table 1. Patient characteristics.**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>%</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean±SD</td>
<td>59.5±11.6</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>62</td>
<td>71</td>
</tr>
<tr>
<td>Female</td>
<td>38</td>
<td>44</td>
</tr>
<tr>
<td>Last treated tumor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>89</td>
<td>102</td>
</tr>
<tr>
<td>Salivary gland tumor</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>Other</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>T classification of last treated tumor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>46</td>
<td>53</td>
</tr>
<tr>
<td>T2</td>
<td>29</td>
<td>33</td>
</tr>
<tr>
<td>T3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>T4</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td>Unknown</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td>Site of last treated tumor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral cavity</td>
<td>70</td>
<td>81</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>26</td>
<td>30</td>
</tr>
<tr>
<td>Otherb</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Treatment of last tumor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgery</td>
<td>53</td>
<td>61</td>
</tr>
<tr>
<td>Surgery + radiotherapy</td>
<td>30</td>
<td>35</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>Chemoradiation</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Interval between end of treatment and assessment (months), median (IQRc)</td>
<td>4.2 (1.4; 12.6)</td>
<td></td>
</tr>
</tbody>
</table>

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

b. Neck metastasis, maxillary sinus, unknown primary.

c. IQR: Interquartile range.

**Nutritional assessment**

Overall, prevalence of post-treatment malnutrition was 16% (18/115, 95%CI: 9-23%). In the periods 0-3 months, >3-12 months and >12-36 months after treatment prevalence of malnutrition reduced from 25% (13/53) to 13% (4/32) and 3% (1/30) respectively (p=0.009). Prevalence of malnutrition was significantly
Table 2. Scores on EORTC QLQ-C30 of malnourished and well-nourished patients.

<table>
<thead>
<tr>
<th>Scale or item (n)</th>
<th>Malnourished patients (n=18)</th>
<th>Well-nourished patients (n=97)</th>
<th>p&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>median IQR&lt;sup&gt;a&lt;/sup&gt;</td>
<td>median IQR&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>GHSQOL (113)</td>
<td>66.7 50.0; 83.3</td>
<td>83.3 66.7; 91.7</td>
<td>0.061</td>
</tr>
<tr>
<td>Physical functioning (115)</td>
<td>60.0 40.0; 80.0</td>
<td>100.0 60.0; 100.0</td>
<td><strong>0.007</strong></td>
</tr>
<tr>
<td>Role functioning (115)</td>
<td>66.7 50.0; 100.0</td>
<td>100.0 66.7; 100.0</td>
<td>0.106</td>
</tr>
<tr>
<td>Emotional functioning (114)</td>
<td>83.3 64.6; 100.0</td>
<td>91.7 75.0; 100.0</td>
<td>0.221</td>
</tr>
<tr>
<td>Cognitive functioning (114)</td>
<td>83.3 62.5; 100.0</td>
<td>100.0 83.3; 100.0</td>
<td>0.079</td>
</tr>
<tr>
<td>Social functioning (113)</td>
<td>91.7 62.5; 100.0</td>
<td>100.0 83.3; 100.0</td>
<td>0.326</td>
</tr>
<tr>
<td>Fatigue (115)</td>
<td>33.3 19.4; 55.6</td>
<td>22.2 0.0; 33.3</td>
<td><strong>0.034</strong></td>
</tr>
<tr>
<td>Nausea/vomiting (115)</td>
<td>0.0 0.0; 4.2</td>
<td>0.0 0.0; 0.0</td>
<td>0.354</td>
</tr>
<tr>
<td>Pain (115)</td>
<td>25.0 0.0; 50.0</td>
<td>0.0 0.0; 33.3</td>
<td>0.062</td>
</tr>
<tr>
<td>Dyspnoea (115)</td>
<td>0.0 0.0; 33.3</td>
<td>0.0 0.0; 8.3</td>
<td>0.219</td>
</tr>
<tr>
<td>Insomnia (115)</td>
<td>0.0 0.0; 41.7</td>
<td>0.0 0.0; 33.3</td>
<td>0.630</td>
</tr>
<tr>
<td>Loss of appetite (115)</td>
<td>0.0 0.0; 41.7</td>
<td>0.0 0.0; 0.0</td>
<td>0.236</td>
</tr>
<tr>
<td>Constipation (115)</td>
<td>0.0 0.0; 33.3</td>
<td>0.0 0.0; 0.0</td>
<td>0.245</td>
</tr>
<tr>
<td>Diarrhoea (115)</td>
<td>0.0 0.0; 0.0</td>
<td>0.0 0.0; 0.0</td>
<td>0.251</td>
</tr>
<tr>
<td>Financial difficulties (112)</td>
<td>0.0 0.0; 8.3</td>
<td>0.0 0.0; 0.0</td>
<td>0.449</td>
</tr>
</tbody>
</table>

(n) number of valid observations.

**a.** Interquartile range.
**b.** Analyzed by Mann-Whitney U test.

Table 3. Results of multivariate linear regression analysis (stepwise backward) to predict scores on EORTC QLQ-C30 scales.

<table>
<thead>
<tr>
<th>EORTC scale</th>
<th>Predictor</th>
<th>ß</th>
<th>SE ß</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical functioning</td>
<td>Malnutrition&lt;sup&gt;a&lt;/sup&gt;</td>
<td>-15.0</td>
<td>6.1</td>
<td>-27.1 to -3.0</td>
<td><strong>0.015</strong></td>
</tr>
<tr>
<td></td>
<td>Treatment including radiotherapy&lt;sup&gt;b&lt;/sup&gt;</td>
<td>14.6</td>
<td>4.9</td>
<td>4.9 to 24.3</td>
<td><strong>0.004</strong></td>
</tr>
<tr>
<td></td>
<td>Dry mouth</td>
<td>-0.2</td>
<td>0.1</td>
<td>-0.3 to -0.03</td>
<td><strong>0.021</strong></td>
</tr>
<tr>
<td></td>
<td>Trouble with social eating</td>
<td>-0.3</td>
<td>0.1</td>
<td>-0.6 to -0.1</td>
<td><strong>0.003</strong></td>
</tr>
<tr>
<td></td>
<td>Constant</td>
<td>86.8</td>
<td>3.4</td>
<td>80.1 to 93.6</td>
<td>&lt;<strong>0.001</strong></td>
</tr>
<tr>
<td>Fatigue</td>
<td>Dry mouth</td>
<td>0.2</td>
<td>0.1</td>
<td>0.09 to 0.3</td>
<td><strong>0.001</strong></td>
</tr>
<tr>
<td></td>
<td>Pain in mouth or throat</td>
<td>0.4</td>
<td>0.1</td>
<td>0.2 to 0.6</td>
<td>&lt;<strong>0.001</strong></td>
</tr>
<tr>
<td></td>
<td>Trouble with social contact</td>
<td>0.6</td>
<td>0.1</td>
<td>0.03 to 0.9</td>
<td>&lt;<strong>0.001</strong></td>
</tr>
<tr>
<td></td>
<td>Constant</td>
<td>4.0</td>
<td>3.1</td>
<td>-2.2 to 10.2</td>
<td>0.203</td>
</tr>
</tbody>
</table>

ß = Regression Coefficient; SE ß = Standard Error of ß; 95% CI = 95% Confidence Interval.

**a.** Yes = 1; no = 0.
 **b.** Yes (including radiotherapy, surgery and radiotherapy, or chemoradiation) = 1; no (surgery) = 0.
higher in patients treated with primary radiotherapy, surgery plus radiotherapy, or chemoradiation (24%, 13/54), when compared to patients treated with surgery alone (8%, 5/61, \( p = 0.037 \)).

Pretreatment body weight and BMI data were available for all patients. Body weight declined from 78.7±13.4 kg pretreatment to 76.0±14.0 kg post-treatment (mean difference -2.8±5.9 kg, \( p < 0.001 \)). Mean percentual decline in pre- and post-treatment body weight was 3.4±7.3% and no significant differences in percentual decline in pretreatment body weight between the 3 intervals after treatment were found (\( p = 0.220 \)). Pretreatment BMI declined from 26.3±4.0 kg/m² to 25.4±4.0 kg/m² post-treatment (\( p < 0.001 \)).

No significant differences were found in age, gender and tumor size (T1/T2 versus T3/T4) between malnourished and well-nourished patients.

Quality of life
Analyzed univariately, median score of malnourished patients on global health status / quality of life was lower (66.7) than that of well-nourished patients (83.4), but this difference did not reach statistical significance (\( p = 0.061 \)). Median scores of malnourished patients on physical functioning (\( p = 0.007 \)) and fatigue (\( p = 0.034 \)) were significantly lower than those of well-nourished patients. Median scores, interquartile ranges and \( p \)-values on the EORTC QLQ-C30 of malnourished and well-nourished patients are presented in Table 2.

Analyzed multivariately, malnutrition, treatment with radiotherapy, dry mouth and trouble with social eating were significantly related to physical functioning (\( p < 0.05 \); Table 3). Malnutrition was not significantly related to fatigue in the multivariate linear regression analysis.

DISCUSSION
Our study is the first to assess the relationship between malnutrition and quality of life, assessing both the short-term and long-term period after treatment for oral or oropharyngeal cancer. Whereas malnutrition was already established as important determinant of quality of life in head and neck cancer patients in the period before, during and shortly after treatment\(^9\)\(^-\)\(^12\), it was still unclear how malnutrition relates to quality of life in the long-term period after head and neck cancer treatment. Furthermore, the relationship between malnutrition and quality of life in patients treated for oral or oropharyngeal cancer in particular was unknown, given that previous studies were performed in heterogeneous head and neck cancer populations in which only a small number of patients with oral or oropharyngeal cancer were included.\(^11\)\(^-\)\(^12\) The current study showed that malnutrition significantly pointed towards a worse physical functioning in patients treated for oral or oropharyngeal cancer.

The lower score of malnourished patients on physical functioning in our study is considered clinically relevant, because the difference in score on physical functioning between malnourished and well-nourished patients was \( \geq 10 \) points.\(^22\) The relationship between malnutrition and physical functioning has been previously reported in other studies with respect to patients with head and neck cancer. In a prospective observational study in head and neck cancer patients treated with surgery, surgery and radiotherapy, radiotherapy or chemoradiation, malnourished patients scored clinically relevant, but not significantly worse on physical
functioning compared to well-nourished patients, 6 months after end of treatment. Another study in head and neck cancer patients treated with radiotherapy demonstrated a significant positive effect of intensive dietary counseling on physical function, whereas in patients not receiving intensive dietary counseling physical functioning deteriorated significantly. The relationship between malnutrition and physical functioning can be ascribed to decreased muscle mass and muscle function. In malnourished patients, atrophy of mainly type II muscle fibres results in muscle fatigue and an altered pattern of muscle contraction and relaxation.

Although in our study prevalence of malnutrition was significantly higher in the period 0-3 months after treatment compared to longer periods after treatment, the relationship between malnutrition and physical functioning was not confounded by interval after treatment. Interval after treatment was not significantly related to physical functioning in the multivariate linear regression analysis. However, the low prevalence of malnutrition in the long-term period after treatment indicates that malnutrition is not a factor affecting quality of life in the long-term period after treatment for oral or oropharyngeal cancer.

Besides malnutrition, treatment with radiotherapy, dry mouth and trouble with social eating were shown to be related to physical functioning in the multivariate linear regression analysis as well. Unfortunately, dry mouth and trouble with social eating are direct and usually long lasting sequelae of head and neck cancer treatment and are difficult to treat. However, in contrast to these problems, malnutrition can be treated effectively, for example by intensive dietary counseling including advice on liquid dietary supplements and/or tube feeding by a percutaneous endoscopic gastrostomy.

Analyzed univariately, malnutrition was significantly related to fatigue. However, when analyzed multivariately, no significant relationship between these variables was found. Dry mouth, pain in the mouth or throat, and trouble with social contact appeared to be more strongly related to fatigue than malnutrition was.

Although we found a clinically relevant worse score of malnourished patients on global health status / quality of life, this difference did not reach statistical significance. One study found a significant relationship between malnutrition and global health status / quality of life, both during and after treatment for head and neck cancer. Other studies in this patient group focused on the impact of intensive dietary counseling during radiotherapy on quality of life. These studies demonstrated a positive effect of intensive dietary counseling on global health status / quality of life. As in our study prevalence of malnutrition was highest shortly after treatment, it is unlikely that coping strategies have played a role in the lack of a significant relationship between malnutrition and global health status / quality of life. The lack of statistical significance may be the result of insufficient power, due to the relatively low prevalence of malnutrition.

The results of our study indicate that a subgroup of patients does not sufficiently gain weight to pretreatment level, given the 3.4±7.3% decline in pre- and posttreatment body weight. Prospective studies are needed to examine if such a failure to gain weight in the long-term period after treatment for oral or oropharyngeal cancer affects quality of life and increases the risk for late complications.

Unfortunately, currently a gold standard for the assessment of malnutrition does not exist. Weight loss is one of the criteria commonly used for assessment of malnutrition. Weight loss of ≥10% in 6 months or ≥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. Besides that, weight
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loss of ≥10% in 6 months or ≥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.4-6,27,29,30 The cutoff point used was adopted by the American Society for Parenteral and Enteral Nutrition to define ‘nutritionally at risk adults’.15

Health-related quality of life is a complex, multidimensional concept that reflects the psychological, physical and social effects of disease and its therapy.31 Besides age, gender, tumor localization, tumor size and treatment modality, also emotional status, smoking and alcohol consumption, marital status and income are known to influence overall health related quality of life in patients with oral or oropharyngeal cancer.32 In the current study we did not measure lifestyle and socioeconomic variables, which may have acted as confounders in the relationship between malnutrition and quality of life. As a result, the relationship between malnutrition and quality of life might be overestimated.

The current study has some limitations. The first one is the modest participation rate of 66%. In 14% of the patients not willing to participate in this study, fatigue played a major role. For this reason it cannot be excluded that fatigue was the result of malnutrition. Furthermore, 32% of non-participants did not report a reason for no participation. Since patients in the current study were informed and recruited after they had finished treatment, we speculate that patients in this phase of treatment are less motivated to participate in studies that they deemed no longer had a clear benefit for themselves. Furthermore, there is still a general belief among patients that only underweight patients may suffer from malnutrition. Because most of the patients were not underweight, these patients may have believed that participation in the current study was not relevant. Consequently, the modest participation rate may have resulted in underestimation of prevalence of malnutrition.

The second limitation is the use of a cross-sectional study design. As patients were assessed only once after treatment, individual pre-illness scores on quality of life are unknown. Therefore, in the chosen study design we limited our analysis to test interindividual differences after treatment. Prospective studies are needed to confirm or to refute our findings. In addition, the use of a cross-sectional study design did not allow us to identify cause-effect relationships. Previous prospective studies have demonstrated a positive relationship between deterioration of nutritional status and impairment of quality of life.11,12 Thus, we assume that malnutrition is more likely to be the cause than consequence.

In conclusion, the results of our study indicate that malnourished patients score lower on quality of life scales related to physical fitness, especially in the period shortly after treatment.

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REFERENCES


