Frailty is associated with decline in health-related quality of life of patients treated for head and neck cancer

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ABSTRACT

Objective: To determine the effect of frailty on Health Related Quality of Life (HRQoL) after treatment for Head and Neck Cancer (HNC).

Materials and methods: Patients were prospectively included in OncoLifeS, a data-biobank. Before treatment, patients underwent geriatric screening, including the Groningen Frailty Indicator (GFI) and Geriatric 8 (G8). Patients’ HRQoL was measured using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC-QLQ-C30) at three, six, twelve and twenty four months after treatment. Linear mixed models were used for statistical analysis. All models were adjusted for baseline HRQoL values, relevant confounders at baseline and yielded estimates (β), 95% confidence intervals and p-values.

Results: 288 patients were included. The mean age was 68.4 years and 68.8% were male. During follow-up, 84 patients had tumor recurrence and 66 died. Response to EORTC-QLQ-C30 ranged from 77.3% to 87.8%. Frail patients, defined by GFI, had significantly worse Global Health Status/Quality of Life (GHS/QoL) (β = −8.70(−13.54;−3.86), p < 0.001), physical functioning (β = −4.55(−8.70;−0.40), p < 0.032), emotional functioning (β = −20.06(−25.65;−15.86), p < 0.001), and social functioning (β = −8.44(−13.91;−2.98), p < 0.003) three months after treatment compared to non-frail patients. Furthermore, frail patients had a significantly worse course of GHS/QoL (β = −7.47(−11.23;−3.70), p = 0.001) and role functioning (β = −7.27(−12.26;−2.28), p = 0.005) over time, compared to non-frail patients. When frailty was determined by G8, frailty was significantly associated with worse GHS/QoL (β = −6.68(−11.00;−2.37), p = 0.003) and emotional functioning (β = −5.08(−9.43;−0.73), p = 0.022) three months after treatment.

Conclusion: Frail patients are at increased risk for decline in HRQoL, and further deterioration during follow-up after treatment for HNC.

Introduction

With the incidence of cancer and specifically the proportion of elderly with cancer rising, oncologists may increasingly encounter the geriatric syndrome of frailty [1]. Frailty results from the heterogenic process of aging, leaving great diversity in populations with respect to physical, functional, psychological and social status, and is defined as ‘a state of increased vulnerability to poor resolution of homeostasis after a stressor event, which increases the risk of adverse outcomes’ [2]. Often, chronological age is not very representative of a patient’s biological age. One of the populations that is thought to be very frail are patients with Head and Neck Cancer (HNC). In this population, functional and cognitive impairment, depressive symptoms and social isolation have shown to be highly prevalent [3]. The burden of frailty in HNC patients
is higher than in patients with other solid malignancies [4]. Probably, general symptoms secondary to tumor extension and location, such as weight loss and malnutrition, contribute to this [5]. Additionally, patient related factors such as lifelong tobacco and alcohol abuse, which are etiological factors for HNC, increase frailty status as well [6,7].

For head and neck oncologists, this leads to a challenging clinical problem. On the one hand, intensive, often multimodal, treatment is indicated; on the other hand, patients may be vulnerable with multiple comorbidities, polypharmacy, functional and psychosocial restrictions. This makes decision making challenging. Ideally, by determining the biological age (i.e. frailty), undertreatment of fit elderly and overtreatment of frail young patients should be prevented. The gold standard to assess frailty is a Comprehensive Geriatric Assessment (CGA) by a geriatrician [8]. Because of its time consuming nature, burden for the patient and limited health care capacity, screening tools have been developed to select patients that need CGA [9].

In HNC, frailty has already been associated with increased frequency and severity of postoperative complications, prolonged length of hospital stay, increased readmission rates and worse overall survival [10]. Although these outcome measures are all clinically relevant, they do not represent the perspective of the patient. Older patients have different priorities regarding treatment outcome than their younger counterparts; e.g. Health Related Quality of Life (HRQoL) may be considered more important than survival in decision making [11–13].

Long-term HRQoL as reported by patients is increasingly considered a valuable outcome measure for cancer treatment. Previous studies showed that frailty is associated with worse HRQoL in other oncological cohorts [14–17]. However, this has never been investigated specifically in HNC patients. A more accurate prediction of patient-rated HRQoL may be of help in decision making and management of expectations. In the present prospective study, we investigated how frailty affects HRQoL shorty after treatment for HNC, and how frailty affects the course of HRQoL during long-term follow-up after treatment.

Material and methods

Study design

The present study is a prospective observational cohort study with two years of follow-up. All patients were enrolled in OncoLifeS, a prospective oncological data-biobank at the (UMCG) [18]. OncoLifeS has been approved by the local Medical Ethical Committee and the study protocol was approved by the OncoLifeS scientific board.

Study population

Between October 2014 and May 2016, all consecutive patients referred to the UMCG with a mucosal, salivary gland or complex cutaneous malignancy (giant basal cell carcinoma, squamous cell carcinoma stage II or higher, melanoma, Merkel cell carcinoma and neck metastasis of any cutaneous malignancy, requiring major surgery and/or radiotherapy) of the head and neck were asked to participate in OncoLifeS and were included after obtaining written informed consent (Fig. 1). Patients were seen at the outpatient clinics of the department of Otorhinolaryngology, Head and Neck Surgery, and the department of Oral and Maxillofacial Surgery. Patients were treated according to (inter)national guidelines and discussed within our multidisciplinary head and neck tumor board. Exclusion criteria were palliative treatment, non-standard treatment (e.g. in the scope of other clinical trials) and missing baseline data on HRQoL (Fig. 1). As the burden of frailty is expected to be relatively high in young HNC patients as well, age was not an exclusion criterion in our study, in contrast to other studies investigating frailty. Tumor recurrence or death led to exclusion from the analyses from that time point onwards (Fig. 1).

Fig. 1. Flowchart diagram with the in- and exclusion of patients and follow-up statistics of the analyzed cohort.

Data collection

Patients’ age, sex, tumor site, histopathology, cancer stage, primary treatment and comorbidities were registered at baseline. Staging was done according to the seventh edition of the Union for International Cancer Control (UICC) TNM classification of malignant tumors [19]. Comorbidities were graded using the Adult Comorbidity Evaluation (ACE-27) as none, mild, moderate or severe [20]. As part of a geriatric screening at our outpatient clinic, within the scope of OncoLifeS, frailty status of patients was assessed using two validated frailty screening instruments. The Groningen Frailty Indicator (GFI), a fifteen-item questionnaire, was completed by patients either at the outpatient clinic or at home and returned by mail. Patients with a GFI score greater than or equal to four were considered frail [21]. The Geriatric 8 (G8), an eight-item scoring instrument, was completed by one of the investigators or a nurse together with the patient at the outpatient clinic. Patients with a G8 score lower than or equal to fourteen were considered as frail [22]. Although the intention of the study was purely observational, advancing insights of patients’ frailty status might have unconsciously led to referral to a geriatrician.

As our primary measure of follow-up, patients were asked to report HRQoL using the European Organisation for Research and Treatment of
Cancer Quality of Life Questionnaire Core 30 (EORTC-QLQ-C30) before treatment and at three, six, twelve and twenty four months after treatment [23]. Global health status, functional scales, symptom scales and summary score were calculated according to the EORTC-QLQ-C30 scoring manuals [24,25].

Statistical analysis

All statistical procedures were performed with SPSS Statistics 23.0 software (IBM, Armonk, New York, United States of America). Descriptive statistics were presented as mean ± standard deviation (SD), median (interquartile range) or frequency (percentage). Differences between groups were analyzed with T-test for normally distributed continuous data and χ² test or Fisher’s exact test for categorical data.

We employed Linear Mixed-effect Models (LMMs) for the analyses of repeated continuous measures, i.e. the EORTC-QLQ-C30 scales. LMMs are a superior method for analyzing large longitudinal datasets as they allow missing data points without discarding entire cases. An online available methods paper was used as a reference [26]. Typically, HRQoL decreases steeply during treatment, and then slowly tends to get better over time (Fig. 2a) [27]. Due to this irregular shape of trajectory, we only performed analysis on the three to twenty-four month interval, treating it as being linear (Fig. 2b). Leaving out polynomial terms makes interpreting coefficients possible and thus allows for assessing clinical relevance rather than a p-value.

For the analyses, covariance type was set to unstructured. Fixed effects included the intercept and at least the variables time, frailty and frailty*time. Coefficients for frailty refer to the difference in HRQoL for frail and non-frail patients at three months after treatment. Coefficients for the interaction term frailty*time refer to the effect of frailty on change of HRQoL over time (per year). Coefficients yielded 95% confidence intervals (CIs) and p-values. All models were adjusted for baseline differences between frail and non-frail patients, by adding the baseline score of dependent EORTC-QLQ-C30 scale to the model. Furthermore, all models were adjusted for age, sex, cancer stage, treatment modality and comorbidity as well as their interaction with time (coefficients not shown in table). For random effects an intercept was included for between subject differences and covariance type was unstructured. Estimation method was set to Maximum Likelihood (ML) and predicted values and standard error of predicted values were saved for graphs. Between models, model fit was compared using likelihood ratio testing.

Results

Patient characteristics

In this study, 288 patients were included. Follow-up and drop-out statistics are shown in Fig. 1. During follow-up, 84 patients developed recurrent disease and 66 patients died. Response rates for EORTC-QLQ-C30 remained stable throughout follow-up, averaging around 80%.

Patient characteristics are presented in Table 1. The mean age was 68.4 years and approximately two-thirds of patients were male. Most patients had mucosal cancer (79.5%), followed by skin malignancy (18.8%) and malignant salivary gland tumor (1.7%). Most patients (86.1%) had squamous cell carcinoma. The most common primary mucosal sites were oral cavity (25.7%), larynx (22.9%) and oropharynx (18.1%). Patients underwent either primary surgery (56.6%), radiotherapy (28.8%) or chemoradiation (14.6%), or a combination of those. According to the GFI, 29.3% of patients were frail, while using the G8, 54.7% were considered frail. Tumor site, histopathology, stage and treatment type did not differ between frail and non-frail patients; however, frail patients (both by GFI and G8) had significantly higher age and more severe comorbidity (Table 1).

Frailty is associated with decline in quality of life

Mean EORTC-QLQ-C30 scores at baseline and during follow-up are provided in Supplementary table 1 and 2. Frailty, measured by GFI was associated with significantly worse Global Health Status/Quality of Life
Frailty is associated with decline in functioning

Frail patients, according to GFI, had worse physical (β = −4.55 (−8.70; −0.40), p = 0.032), emotional (β = −10.92 (−16.06; −5.79), p < 0.001) and social functioning (β = −8.44 (−13.91; −2.98), p = 0.003) at three months after treatment than their non-frail counterparts, adjusted for baseline and covariates (Table 2 and Fig. 3b,d,f). Moreover, these patients showed a significant further decline of physical (β = −3.28 (−6.26; −0.31), p = 0.031) and role functioning (β = −7.27 (−12.26; −2.28), p = 0.005) over time, compared to non-frail patients (Table 2 and Fig. 3b,c). When frailty was measured by G8, only emotional functioning (β = −5.02 (−9.43; −0.73), p = 0.022) was different between frail and non-frail patients at three months after treatment (Table 2 and Fig. 3j).

Frailty is associated with increased symptom burden

Frail patients, measured by GFI, showed more fatigue (β = 8.25 (2.15; 14.36), p = 0.008), pain (β = 10.09 (5.05; 15.13), p < 0.001), dyspnea (β = 8.53 (3.21; 13.85), p = 0.002), insomnia (β = 8.07 (1.35; 14.79), p = 0.019), appetite loss (β = 7.36 (2.80; 11.93), p = 0.002) and financial difficulties (β = 7.36 (14.23; 20.81), p < 0.001) than non-frail patients, in models adjusted for baseline relevant covariates, at three months after treatment (Table 2). Additionally, prolonged complaints of nausea and vomiting were seen in frail patients (β = 2.87 (0.66; 5.09), p = 0.011). Frailty, measured by the G8, was associated with more dyspnea (β = 5.02 (14.9; 9.90), p = 0.044), appetite loss (β = 7.21 (1.03; 13.39), p = 0.022), and diarrhea (β = 3.40 (0.27; 6.54), p = 0.033) at three months after treatment (Table 2).

Table 1
Patient characteristics of the included cohort (n = 288). Values given as n(%) unless otherwise specified. P-values given for a t-test b χ2 test or c Fisher’s exact test. ACE-27 = Adult Comorbidity Evaluation 27.

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Groningen Frailty Indicator</th>
<th>Geriatric 8</th>
<th>Total (n = 288)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
<td>Non-frail (n = 203)</td>
<td>Frail (n = 84)</td>
<td>p-value</td>
</tr>
<tr>
<td>Age</td>
<td>Mean ± SD</td>
<td>Median (interquartile range)</td>
<td>67.2 ± 10.6</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>Female</td>
<td>142 (70.0)</td>
</tr>
<tr>
<td>Reason for referral</td>
<td>Primary tumor</td>
<td>Recurrent tumor</td>
<td>190 (93.6)</td>
</tr>
<tr>
<td>Tumor site</td>
<td>Oral cavity</td>
<td>Nasal cavity and paranasal sinus</td>
<td>52 (25.6)</td>
</tr>
<tr>
<td>Histopathology</td>
<td>Squamous Cell Carcinoma</td>
<td>Other</td>
<td>172 (84.7)</td>
</tr>
<tr>
<td>Stage</td>
<td>I</td>
<td>II</td>
<td>51 (25.8)</td>
</tr>
<tr>
<td>Primary treatment</td>
<td>Surgery</td>
<td>Postoperative radiotherapy</td>
<td>42 (20.7)</td>
</tr>
<tr>
<td>ACE-27</td>
<td>No comorbidity</td>
<td>Mild comorbidity</td>
<td>55 (27.1)</td>
</tr>
<tr>
<td></td>
<td>Moderate comorbidity</td>
<td>Severe comorbidity</td>
<td>71 (35.0)</td>
</tr>
<tr>
<td></td>
<td>54 (26.6)</td>
<td>23 (11.3)</td>
<td>25 (19.8)</td>
</tr>
</tbody>
</table>

(GHS/QoL) at three months after treatment (β = −8.70 (−13.54; −3.86), p < 0.001), but also with a further decline of GHS/QoL during two years after treatment (β = −7.47 (−11.23; −3.70), p < 0.001), in models adjusted for baseline and relevant covariates (Table 2 and Fig. 3a). Frailty measured by G8 was associated with worse GHS/QoL at three months after treatment (β = −6.68 (−11.00; −2.37), p = 0.003) as well, but not with a worse course over time (Table 2 and Fig. 3g).
Discussion

To our knowledge, this is the first study examining the association between frailty and changes in HRQoL after treatment in HNC patients. Key findings include that frailty, identified by two different frailty screening tools, was associated with a decline in QoL, different functioning domains, and increased symptom burden after treatment for HNC, independently of other relevant factors. Moreover, frailty at baseline was also associated with further deterioration of QoL and functioning during two years of follow-up. These findings emphasize

Fig. 3. Predicted values and standard error of predicted values by linear mixed models for EORTC-QLQ-C30 scales. a-f = frailty defined by Groningen Frailty Indicator. g-l = frailty defined by Geriatric 8.
The importance of implementing frailty screening in treatment counseling and decision making.

As we expected, frail patients showed worse GHS/QoL after treatment than non-frail patients, regardless of their baseline score, and age, sex, cancer stage, treatment modality and comorbidity. This was not only the case at three months after treatment, but their trajectory increasingly diverged from non-frail patients during the two years of follow-up. This effect was most pronounced when frailty was measured by using the GFI and may roughly be interpreted in two ways: either the frail patients’ GHS/QoL trajectory deteriorates over time compared to non-frail patients, or recovery for frail patients is not as good as for non-frail patients. Plotted trajectories (Fig. 3a) reveal that this is a combination of both deterioration and worse recovery, however, this should be interpreted for each EORTC-QLQ-C30 scale independently.

Although only a minor difference (8.70 points) on the GHS/QoL scale between frail and non-frail patients was found at three months after treatment (Table 2, frail term), adding the increase per year (7.47 points, Table 2, frail*time term) resulted in a major cumulative difference (21.77 points) two years after treatment, which was adjusted for confounding factors. This is seen in plotted trajectories as well (Fig. 3a). According to classification of Osoba et al. (5–10 points difference should be interpreted as ‘little’ change, 10–20 points as ‘moderate’ change and > 20 as ‘very much’ change), the relative decrease in GHS/QoL is clinically highly relevant [28]. These findings could have a major impact on decision making: being aware of poorer outcomes for frail patients may and should be taken into account during shared decision making.

Comparing our results with published literature, a similar analysis

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**Table 2**

Results of linear mixed model analysis. Frailty measured by Groningen Frailty Indicator and Geriatric 8 alters quality of life after treatment. Frail refers to the main effect (difference in score of frail patients with respect to non-frail patients at 3 months). Frail*Time refers to the interaction of frailty and time, indicating the amount of change in Quality of Life over time (with respect to 1 year) for frail compared to non-frail patients. * All models were adjusted for baseline differences in corresponding EORTC-QLQ-C30 scale, and age, sex, stage, treatment modality and comorbidity and their interaction with time.

<table>
<thead>
<tr>
<th>EORTC-QLQ-C30</th>
<th>Groningen Frailty Indicator</th>
<th>Geriatric 8</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Parameters</td>
<td>Estimate (β)</td>
</tr>
<tr>
<td><strong>Summary score</strong></td>
<td>Frail</td>
<td>−6.12</td>
</tr>
<tr>
<td></td>
<td>Frail*Time</td>
<td>−1.70</td>
</tr>
<tr>
<td><strong>Global health status/QoL</strong></td>
<td>Frail</td>
<td>−8.70</td>
</tr>
<tr>
<td></td>
<td>Frail*Time</td>
<td>−7.47</td>
</tr>
<tr>
<td><strong>Functional scales</strong></td>
<td>Frail</td>
<td>−4.55</td>
</tr>
<tr>
<td></td>
<td>Frail*Time</td>
<td>−3.28</td>
</tr>
<tr>
<td><strong>Emotional functioning</strong></td>
<td>Frail</td>
<td>−5.70</td>
</tr>
<tr>
<td></td>
<td>Frail*Time</td>
<td>−7.27</td>
</tr>
<tr>
<td><strong>Cognitive functioning</strong></td>
<td>Frail</td>
<td>−10.92</td>
</tr>
<tr>
<td></td>
<td>Frail*Time</td>
<td>2.07</td>
</tr>
<tr>
<td><strong>Social functioning</strong></td>
<td>Frail</td>
<td>−3.88</td>
</tr>
<tr>
<td></td>
<td>Frail*Time</td>
<td>−0.89</td>
</tr>
<tr>
<td><strong>Symptom scales</strong></td>
<td>Frail</td>
<td>−10.09</td>
</tr>
<tr>
<td></td>
<td>Frail*Time</td>
<td>3.11</td>
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<tr>
<td><strong>Dyspnoea</strong></td>
<td>Frail</td>
<td>8.53</td>
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<tr>
<td></td>
<td>Frail*Time</td>
<td>0.14</td>
</tr>
<tr>
<td><strong>Insomnia</strong></td>
<td>Frail</td>
<td>8.07</td>
</tr>
<tr>
<td></td>
<td>Frail*Time</td>
<td>−3.45</td>
</tr>
<tr>
<td><strong>Appetite loss</strong></td>
<td>Frail</td>
<td>14.23</td>
</tr>
<tr>
<td></td>
<td>Frail*Time</td>
<td>−2.99</td>
</tr>
<tr>
<td><strong>Constipation</strong></td>
<td>Frail</td>
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</tr>
<tr>
<td></td>
<td>Frail*Time</td>
<td>−0.25</td>
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<tr>
<td><strong>Diarrhoea</strong></td>
<td>Frail</td>
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<td></td>
<td>Frail*Time</td>
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<td><strong>Financial difficulties</strong></td>
<td>Frail</td>
<td>7.36</td>
</tr>
<tr>
<td></td>
<td>Frail*Time</td>
<td>0.89</td>
</tr>
</tbody>
</table>
was recently performed by Kirkhus et al. in a heterogeneous oncological cohort [17]. Frailty, assessed using a modified geriatric assessment, was associated with worse GHS/QoL but not with further decline over time during twelve months follow-up [17]. However, this study did not adjust for baseline differences between frail and non-frail patients, which have been shown to be significant at baseline already [29]. This may explain the larger estimates than in our present study. Other studies that have addressed frailty with respect to GHS/QoL did not find significant differences in the breast cancer and colorectal cancer population [15,16]. Only one study included a small proportion of HNC patients (4.3%) and found within a frail population (based on G8) that several factors such as stage, pain, fatigue, nutrition and comorbidity were associated with decline in GHS/QoL [30]. Though, the study population was very heterogeneous, analyses were unadjusted for different treatment modalities and lacked long-term follow-up.

An important contributor to patients’ HRQoL is the level of functioning. Physical functioning has been demonstrated to be worse in older patients after treatment for HNC [31]. In our study, after adjusting for age, frailty was associated with worse physical functioning both shortly after treatment as well as with further deterioration during follow-up. Literature data on this issue is heterogeneous [15–17,32], but most importantly, not investigated in HNC. Differences between cohort characteristics and research methodology may largely explain differences.

Role functioning is often overlooked in literature and rarely investigated as a primary outcome measure with respect to frailty. In our study, frailty (GFI) was strongly associated with decline in role functioning over time. When reviewing the EORTC-QLQ-C30 questions involved in role functioning ‘Were you limited in doing either your work or other daily activities?’ and ‘Were you limited in pursuing your hobbies or other leisure time activities?’, these seem important matters for QoL.

Emotional functioning was significantly worse for frail (GFI and G8) patients three months after treatment. Since frailty is a multidimensional geriatric syndrome including a significant psychological domain as well, this was to be expected: patients with premorbid psychological issues have a higher risk of developing psychological problems during and after treatment [33]. Improvement of emotional functioning after treatment occurred in both frail and non-frail patients (Fig. 3d), despite the known high prevalence of fear of recurrence, depression and even high suicide risk in the HNC population in other studies [34–36].

Cognitive functioning was not significantly affected by treatment or by frailty during follow-up in our study. Another study investigating HNC patients treated with radiotherapy, however, did show significant decline of cognitive function within seven years after treatment [37]. Probably, their objective assessment of cognitive function is much more sensitive to cognitive alterations than the patient-reported cognitive functioning scale, employed in our study. These results should therefore be interpreted with care [38].

Social functioning is specifically at risk in HNC treatment due to the diseases’ relation with the organs for communication [39,40]. We found frail (GFI) patients to have worse social functioning than non-frail patients shortly after treatment, but both groups gradually improved in the following years, similar to data in literature [41].

Clearly, large differences exist between screening tools such as GFI and G8. This leads to the question: which are the most important domains of a geriatric screening with respect to changes in QoL? G8 is known as a very physically oriented screening tool with more than half of the questions related to nutrition, weight loss and comorbidities [9]. G8 is strongly associated with surgical complications as well as survival in oncological cohorts, but the relation with HRQoL has rarely been investigated [42]. In our study, G8 showed a weaker association with HRQoL than GFI. The GFI covers larger functional and psychosocial domains of frailty [9] which are, apparently, superior in long-term patient reported outcomes. Some studies have already investigated separate domains of geriatric screening in relation to QoL in more heterogeneous oncological cohorts: one found comorbidity and nutrition to be associated with decline in QoL after three months and another showed associations of malnutrition [30], depression and impaired mobility with decline in QoL after six months [43].

It has been difficult to show the objective benefit of implementing a geriatric screening in standard oncological healthcare with outcomes such as adverse events, QoL or survival [44,45]. Though, it has been shown that treatment recommendations are significantly different when an oncogeriatric multidisciplinary team is involved in decision making [12]. This does not necessarily mean that we should stop treating frail patients. After all, frail patients do not regret the decision that was made more than non-frail patients [46], but identification of vulnerabilities may open doors to pre-treatment optimization or a more patient-tailored treatment plan. Prehabilitation studies are currently being carried out, also in the field of HNC.

The main strengths of this study include the prospective inclusion of a relatively large cohort, the use of well-known validated questionnaires to address frailty and HRQoL, and a notable two years of follow-up. Solid statistical analysis was performed handling missing data well and therefore limiting bias, and also controlling for baseline differences and confounders. Some limitations may be the relative heterogeneity of the cohort, which includes mucosal, salivary gland and cutaneous tumors, and possibly underrepresentation of the frailest patients. Inclusion of frail patients remains difficult due to refusal to participate, inability (being overburdened) to undergo geriatric screening or non-responses to questionnaires [47].

Conclusion

Frailty is significantly associated with decline in QoL and functioning after treatment for HNC and even further deterioration in the long-term. Screening for frailty is highly recommended in the HNC population, as it may have implications for decision making or pre-treatment optimization.

Declaration of Competing Interest

None.

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None.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.oraloncology.2020.105020.

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