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Functional decline after surgery in older patients with head and neck cancer

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ABSTRACT

Introduction: In addition to classical endpoints such as survival and complication rates, other outcomes such as quality of life and functional status are increasingly recognized as important endpoints, especially for elderly patients. However, little is known about the long-term effect of surgery with regard to these other outcomes. Our aim is to investigate the functional status and self-reported health status of patients ≥ 70 years one year after surgery for head and neck cancer.

Methods: We present one-year follow-up data of patients ≥ 70 year who underwent surgery for HNC. During an interview by telephone, functional status was evaluated by using the Katz-15 Index of Independence questionnaire including six items covering basic Activities of Daily Living (ADL) and nine items covering Instrumental Activities of Daily Living (IADL). Measurements were compared with those obtained preoperatively.

Results: In total, 126 patients were included and eventually we collected follow-up data of 68 patients. There was a statistically significant decrease in functional status on the total Katz-15 and on the IADL questionnaire scores one year after surgery (mean 1.34 versus 2.42, p -value 0.00 and mean 1.21 versus 1.94, p- value 0.00). There was no significant change concerning ADL dependence (p -value 0.18) and cognitive status (p -value 0.11). The self-reported health status improved postoperatively, although not statistically significantly so (mean 67.36 versus 71.25, p -value 0.12).

Conclusion: Approximately-one year after surgery for HNC, there is a significant decline in functional status indicating a higher level of dependency.

Introduction

Head and neck cancer (HNC) is a heterogeneous group of cancer which includes those cancers originating in the oral cavity and lip, the pharynx, the larynx, the salivary glands, the nasal cavity, and paranasal sinuses. HNC is primarily a cancer that occurs among the older population. In the Netherlands, 40 % of the patients newly diagnosed with HNC in 2019 was older than 70 years [1]. With the increase in the aging population and the increasing cancer burden, the incidence of HNC is expected to rise even more in the following years [2].

In the past decades, there have been multiple improvements in the treatment of HNC resulting in prolonged survival and better disease control [3]. However, older patients are often considered poor candidates for multimodality treatment and are subsequently less likely to receive the standard of care treatment that younger patients receive [4,5]. As a result, previous randomized trials in HNC included relatively few older patients and, predominantly, those that were included had a good performance status and less comorbidity. This strongly limits the evidence base for the older population, where geriatric deficits and comorbidity are much more prevalent [4,5]. Thus, the outcomes of these trials may not be applicable to the older patients we encounter in our clinic.

In addition, existing oncological trials focus primarily on the classical endpoints such as overall survival and complication rates whereas other outcomes, such as health-related quality of life and retaining independence are increasingly being recognized as important. All this

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information would ideally be discussed with the patient, when personalized decisions are made concerning cancer treatment. These outcomes are particularly relevant in the discussion with older patients, since older patients generally seem to have a preference for quality of life (QoL) over length of life [6,7]. However, in elderly patients information concerning the long-term effects of HNC surgery on functionality, independence, and quality of life is lacking at this time [8]. Based on the very rare evidence, we hypothesize that HNC surgery at least impacts functionality.

Taking this into consideration, the primary aim of this study is to provide insight into the long-term effects of surgery on functionality in HNC patients older than 70 years to explore whether HNC surgery indeed impacts this. In addition to functionality, assessed by measuring the Instrumental Activities of Daily Living (IADL) and the Activities of Daily Living (ADL), the long-term effect on cognition, mood, and the quality of life by using the self-reported health status will also be assessed.

Methods

Patient selection

Between September 2015 and July 2019, patients aged 70 years or older who were scheduled for surgery and visited the pre-operative screening clinic before undergoing surgical treatment were enrolled in this prospective study at the department of Geriatrics at the University Medical Center Utrecht in Utrecht, the Netherlands.

Approximately-one year after surgical treatment, patients were approached for follow-up by telephone. If the medical record showed the patients had not been in contact with their physician for over three months, the patient's general practitioner was called first to check if the patient was still alive. Patients were excluded if they had not given informed consent for the follow-up by telephone or if they were not able to complete the follow-up by telephone due to deafness, dementia, or a terminal condition caused by progressive disease. The study was reviewed and approved by the local ethics committee.

Demographic and treatment data

Patient characteristics such as age, gender, marital status, and living situation were obtained from the medical record. Tumor and treatment characteristics involved localization, stage, type of surgery, and post-operative radiation. Treatments were grouped based on extent and duration of surgery. Comorbidity was assessed with the Charlson Comorbidity Index (CCI), excluding points for age and current malignancy [9].

Outcome measurement

Data about functional status, cognition, and mood was collected by questionnaires both preoperatively as well as at follow-up by telephone. Functional status was assessed by the Katz-15 Index of Independence that measures ADL and IADL [10,11]. This questionnaire consists of six ADL items that are also found in the Katz-6 index [12] (i.e. bathing, dressing, eating, toileting, continence, transferring), and nine IADL items adapted from the Lawton IADL index [13] (i.e. traveling, grooming, preparing a meal, use of telephone, shopping, household tasks, managing medications, managing finances and mobility). Each item was given a score of zero (no disability) or one (yes, disabled), and then all items were totaled, leading to a range of 0–15 for the Katz-15 score, with a higher score indicating a higher level of dependency. Patients were considered dependent in ADL if there was ≥ 1 disabled item in the Katz-6 index and dependent in IADL if there was ≥ 1 disabled item in the remaining nine items of the Katz-15. The Katz-15 has been demonstrated to be a reliable and valid measurement of ADL and IADL [11].

Cognition was preoperatively assessed with the mini-mental state examination (MMSE) [14]. The telephone interview for cognitive status (TICS) was used to assess cognition at the follow-up by telephone [15]. This score was converted to a score corresponding with the MMSE as validated in the study of Fong et al. [16] Mood was assessed with the Patient Health Questionnaire-2 (PHQ-2) [17]. This instrument consists of two questions: (1) "During the past month, have you often been bothered by feeling down, depressed, or hopeless?" and (2) "During the past month, have you often been bothered by little interest or pleasure in doing things?". If one or both questions were answered with "yes", the mood was considered as impaired.

To acquire insight into the quality of life by using the self-reported health status, the EuroQol Visual Analog Scale (EQ-VAS) was used developed by the EuroQoL Group [18]. With the EQ-VAS, patients were asked to indicate their health status between 0 and 100, where 0 represents their worst imaginable health status and 100 represents their best imaginable health status. The EQ-VAS was demonstrated as a valid instrument for monitoring the patients' health status in time [18–20]. Lastly, the interview by telephone included a question about weight.

Statistical analysis

Descriptive statistics were used to summarize patient and tumor characteristics. The categorical variables were described using numbers and percentages. Medians and standard deviations were used to describe continuous variables. For a comparison of patients and tumor characteristics between the patients included in the follow-up by telephone with the total population including patients excluded from follow-up by telephone, the chi-squared test was used. For continuous variables with a normal distribution the Student's *t* test was used. The Mann-Whitney *U* test was used if there was an abnormal distribution.

The primary endpoint of this study was the functional decline one year after surgery expressed as a change in the Katz-15. Second, we assessed changes in ADL impairment and IADL impairment separately. As secondary endpoints we analyzed the change in cognitive function, mood, self-reported health status, and weight. To determine changes between data collected at baseline and during follow-up by telephone, the Wilcoxon signed rank test was used for paired continuous variables without a normal distribution. To analyze paired dichotomous variables the McNemar's test was used. A p-value of ≤ 0.05 was considered as statistically significant.

The Statistical Package for the Social Sciences (SPSS) version 21.0 was used for the analyses.

Results

Baseline characteristics

In total, 126 patients were included in this study. These patients visited the pre-operative screening clinic as part of the schedule for surgery. The baseline characteristics were summarized in Table 1. The median age was 80.5 years old and 57.9 % were men. Almost half of the tumors were localized in the oral cavity (49.2 %). Twenty-five patients (20 %) died in the first year, so 101 patients were approached for follow-up by telephone as shown in Fig. 1. Finally, follow-up data from 68 patients was collected. The follow-up population was significantly younger compared with the total population, lived independently more often, and had statistically significant less comorbidity according to the CCI (Table 1). Moreover, this population had less IADL impairment, and less cognition impairment as shown in Table 2. Median time to follow-up was 13 months (range 5–24 months).

Outcome of functional status

Of the 68 patients included for follow-up, 26 patients (38.2 %) had a Katz-15 score ≥ 1 preoperatively as shown in Table 3. One year later, 51 patients (75.0 %) had a Katz-15 score ≥ 1. The mean score of the KATZ-

Table 1
Baseline characteristics.

	Total (n = 126)	Follow-up data available (n = 68)	*p*-value
Variable	**No. (%)**	**No. (%)**	
Male	73 (57.9)	42 (61.8)	0.35
Median age in years ± SD	80.5 ±	79.0 ± 5.6	*0.03*
70–79	6.35	37 (54.4)	*0.03*
80–89	56 (44.4)	26 (38.2)	
≥ 90	54 (42.9)	5 (7.4)	
	16 (12.7)		
Living situation			*0.02*
Independently	109	64 (94.1)	
Assisted	(86.4)	4 (5.9)	
	17 (13.6)		
BMI in kg/m2	25.2 ± 4.06	25.9 ± 3.75	0.25
Medication use ≥ 5	75 (59.5)	43 (63.2)	0.36
CCI ≥ 3	27 (21.6)	10 (14.7)	*0.04*
ASA ≥ 3	88 (71.5)	45 (67.2)	0.24
Tumor localization			0.22
Lip	3 (2.4)	1 (1.5)	
Oral cavity	62 (49.2)	32 (47.1)	
Pharynx	6 (4.8)	2 (2.9)	
Larynx	16 (12.7)	7 (10.3)	
Salivary glands	11 (8.7)	8 (11.8)	
Nasal cavity	2 (1.6)	0 (0.0)	
Skin	24 (19.0)	16 (23.5)	
Unknown	2 (1.6)	2 (2.9)	
Stage			0.17
0	5 (4.0)	4 (5.9)	
I	26 (20.6)	18 (26.5)	
II	34 (27.0)	18 (26.5)	
III	17 (13.5)	9 (13.2)	
IV	40 (31.8)	16 (23.6)	
Unknown	4 (3.2)	3 (4.4)	
Surgery category			0.71
Endoscopy/ examination under general anesthesia	17 (13)	8 (12)	
Excision primary tumor skin or oral cavity	41 (33)	20 (29)	
Neck dissection/ parotidectomy	27 (21)	20 (29)	
Laryngectomy with/without neck dissection / excision primary tumor, neck dissection and reconstruction with pedicle or free flap	41 (33)	20 (29)	
Postoperative radiotherapy	45 (38.1)	23 (35.9)	0.59

Number (No.); Body Mass Index (BMI); Charlson Comorbidity Index (CCI); American Society of Anesthesiologists (ASA); Comprehensive Geriatric Assessment (CGA)

15 increased statistically significantly from a mean of 1.34 to a mean of 2.42 (*p*-value 0.00). With regard to ADL, 13 patients (19.2 %) had an impaired ADL preoperatively. At follow-up, 18 patients (26.5 %) had an impaired ADL (*p*-value 0.18). The mean ADL score changed from 0.24 preoperatively to 0.47 at follow-up (*p*-value 0.18). In 25 patients (22.1 %) the IADL was preoperatively impaired and in 48 patients (70.6 %) the IADL was impaired at the one-year follow-up (*p*- value < 0.001). The mean score of the IADL increased statistically significantly from a mean of 1.21 to a mean of 1.94 (*p*-value 0.00).

Disability in activity with housekeeping, walking, travelling, and shopping most often occurred both preoperatively and at follow-up (Fig. 2).

Other outcomes

Before surgery, the mean MMSE was 28.64 ± 1.36. At follow-up by telephone, three TICS were not completed because of hearing problems. The mean MMSE of the 65 patients with completed data after one year was 28.83 ± 2.1 (*p*-value 0.11). Three patients had an impaired MMSE < 24 at follow-up compared with one patient preoperatively.

Concerning mood, there were less patients with an impaired PHQ-2 at follow-up by telephone compared to preoperatively (ten patients at baseline versus four patients after follow up, *p*-value 0.15).

The self-reported health status at the follow-up by telephone, assessed with the EQ-VAS, improved by a mean of four points (from 67.36 to 71.25), although it was not statistically significant (*p*-value 0.12).

The mean weight at follow-up by telephone decreased statistically significantly from 75.91 kg (kg) to 74.94 kg (*p*- value 0.04). The majority of patients (54.4 %) had lost weight one year after surgery (see Table 3).

Discussion

One year after surgical treatment for HNC, patients ≥ 70 year old were statistically significantly more disabled according to the Katz-15 questionnaire compared to preoperatively indicating a higher level of dependency. Approximately, 10 % (19 % versus 27 %) of the patients had lost ADL function and 37 % (38 % versus 75 %) of the patients had lost IADL function.

In contrast to ADL, IADL declined statistically significantly. It is well known that impairments in IADL normally precede impairments in ADL [21,22]. ADL consists of those activities essential for an independent life, while carrying out the IADL is more complex. Complex activities were affected to a higher degree than basic daily functions. The decline in IADL we noticed may represent a substantially clinically relevant impact on an individual's functional dependency, because it indicates that this patients will need assistance from a family member, care giver, or long-term care services [23,24]. Our results showed that these patients mainly need assistance in housekeeping, travelling, shopping, and mobility.

Our findings are overall in line with other studies investigating functional decline after oncologic surgery in older patients [25–28]. Rønning et al. found a decline in ADL in one third of the 84 patients and a decline in IADL in two third of the patients 16–28 months after surgery for colorectal cancer [29]. Another study, comprising of 1007 older patients with stage I-IIIa non-small cell lung cancer, reported a decline in ADL in 5 % of the patients one year after surgery [30]. Giannotti et al. enrolled 99 patients undergoing elective surgery for gastro-intestinal cancer and found a decline in ADL in 13 % of the patients after one year [28].

Studies specifically focusing on the effect on dependency after HNC surgery are rare. As far as we know, Silver et al. published the only study covering this subject in HNC patients so far [31]. Their findings differed from our results: six months after surgery, the need for assistance with ADL quadrupled and the need for assistance with IADL doubled in 60 Brazilian HNC patients. The applicability of these results to our patients is doubtful, since the presentation, clinical course, and outcomes of HNC in developing countries may differ from those in developed countries.

Although all abovementioned studies found a negative change in the functional status of older patients after oncological surgery, inter-study comparison of these studies is difficult, because these studies vary in study design, analyses, time to follow-up, and in measurement and definition of functional decline. A systematic review covering studies with non-oncological patients, showed that there is conceptual uniformity in the measurement of ADL with a little variability of items within Katz ADL and IADL questionnaires, but that there is far less uniformity in the definition of functional decline and the cutoff scores reflecting functional decline ranged from about 2 % to 20 % of the instruments' total score range [10]. As a result, it is unclear when we should speak of a clinical relevant decline in functioning. Therefore, further research should also focus on the patients' self-report of functioning and quality of life [32].

We also aimed to acquire insight in the quality of life of HNC patients one year after surgery. The EQ-VAS improved postoperatively, although not statistically significant, indicating that patients may rank their health status higher than preoperatively. Although an extended examination of the quality of life, for instance by using the EQ-5D

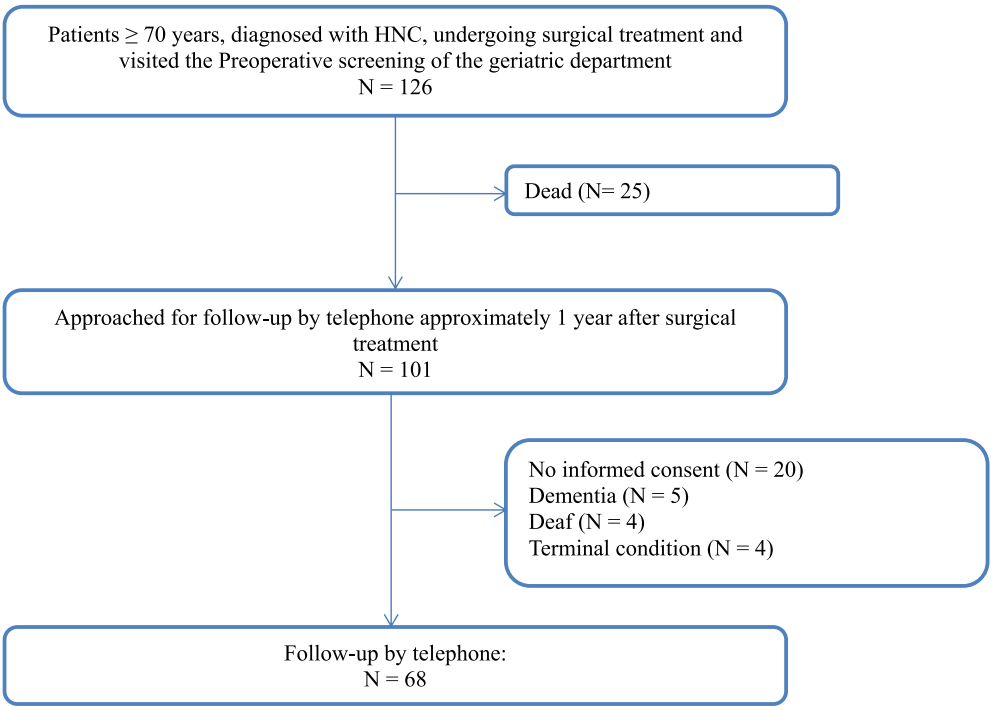

Fig. 1. Flowchart of patient inclusion.

Table 2
Differences in baseline functional status, cognition, mood, and self-reported health status between the total population and the follow-up population.

	Total (n = 126)	Follow-up data available (n = 68)	*p*-value
Variable	**No. (%)**	**No. (%)**	
Functional status:			
Impaired Katz-15	60 (47.6)	26 (38.2)	*0.02*
ADL impairment	31 (24.6)	13 (19.1)	0.16
IADL impairment	58 (46.0)	25 (36.8)	*0.02*
Cognition:			
MMSE < 24	6 (5.0)	1 (1.5)	*0.05*
Mood:			
PHQ-2 impaired	16 (12.7)	10 (14.7)	0.46
Self-reported health status: Mean EQ-5D VAS ± SD	66.90 ± 15.58	67.70 ± 15.92	0.64

Activity of Daily Living (ADL); Instrumental Activities of Daily Living (IADL); Minimal Mental State Examination (MMSE); Patient Health Questionnaire-2 (PHQ-2); EQ-5D Visual Analog Scale (EQ-5D VAS).

questionnaire, was lacking, the results of the EQ-VAS might suggest that patients do at least not experienced a decline in their quality of life at one year follow-up. In contrast, the quality of life might be improved by the fact that postoperatively the fear and the insecurity about their diagnosis and treatment had been resolved. This finding may also be taken into account in counselling our older patient.

In addition to functional status, we also investigated the effect on cognitive status. We did not find a significant difference in the MMSE before and one year after surgery. However, we have to take selection bias into account. Preoperatively, hardly any patient was not cognitively impaired. Additionally, at follow-up by telephone we excluded five patients because their cognitive status hindered an interview by telephone. As a result, all patients analyzed were functioning well cognitively.

Also, we did not find a significant decrease in mood. On the contrary, we may note a carefully improving trend of the PHQ-2. Patients themselves explained their improved mood due to the fact that fear for the cancer diagnosis and the upcoming surgery could have impacted their mood preoperatively. In a study on stepped care targeting psychological distress, recovery was observed after 2 weeks of watchful waiting in 30 % of distressed HNC and lung cancer patients [33]. Although the PHQ-2 could be seen as a rough scale for depression, the validation study showed that a "no" response to both questions made depression very unlikely [17]. Thus, in 94 % of our patients, depression was very unlikely-one year after surgery. This may be different from other studies which report on depression symptoms at follow-up in 20–37 % of HNC patients of all ages [34–36].

In a systematic review the pooled prevalence of depression in cancer patients ranged from 8 % to 24 % and differed according to the type of instrument, type of cancer and treatment phase [35]. In a study on (mainly surgically treated) oral cancer patients, the situation most frequently involved in our study, age did not contribute to the presence of depression [34].

Lastly, we noticed a statistically significant weight decrease postoperatively, although the difference was small (1 kg). In a study on post-treatment weight change in oral cavity and oropharyngeal squamous cell carcinoma patients (mean age 60.0 ± 12.0 years old), the mean weight loss from pre-treatment to 0–6 months post-treatment was 5 kg (6 % of baseline mean body weight), and the mean weight gain from the 0–6 month-follow-up period to the 18–24-month follow-up period was 2 kg (2 % of baseline mean body weight) [37]. In addition, the patients with primary surgery with or without adjuvant therapy had significantly more weight gain from baseline to 12–18-month follow-up as compared to the patients with primary radiation and/or chemotherapy. Therefore, the point of timeweighing post treatment seems important in determining if weight decrease or increase is present. In the present study the median follow-up weight measurement was 13 months.

Maintaining independence and quality of life has been shown to be an important treatment outcome in older patients. In one study of patient preferences, including 226 patients over 60 years old with a diagnosis of cancer, heart failure, or chronic obstructive pulmonary disease, 74 % stated that they would refuse to, or be reluctant to receive

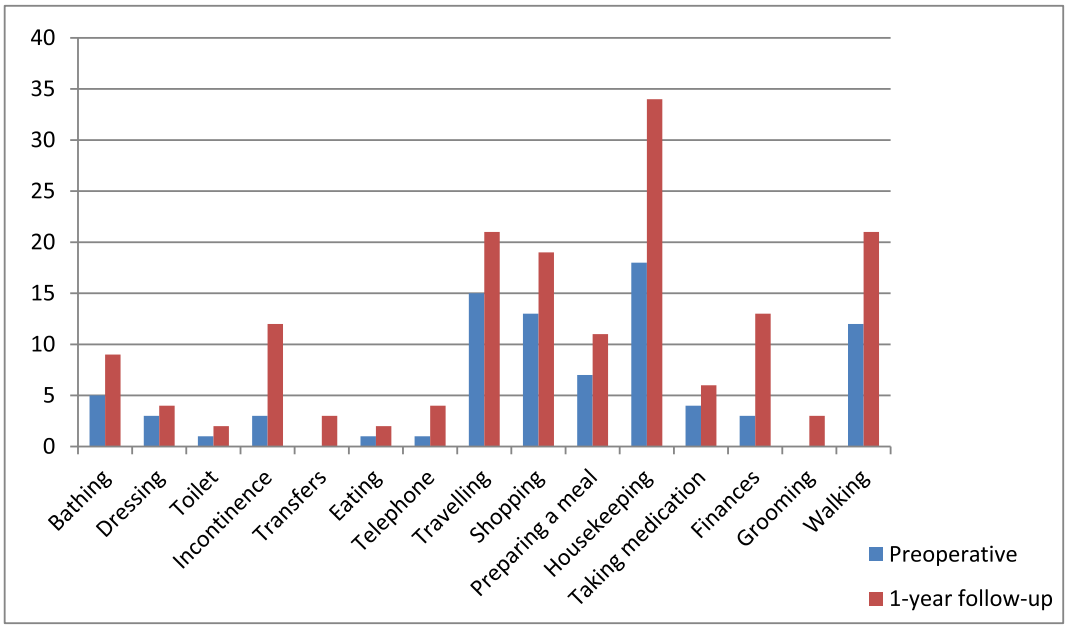

Fig. 2. Dependence Katz-15 per item preoperatively and at follow-up.

Table 3
Preoperative outcomes compared with one-year follow-up.

	Preoperatively (n = 68)	**Follow-up (n = 68)**	***p*-value**
Variable	**No. (%)**	**No. (%)**	
Dependency by Katz-15	42 (61.8)	17 (25.0)	*0.00*
0	26 (38.2)	51 (75.0)	
≥ 1	1.34 ± 2.16	2.42 ± 2.75	
Mean ± SD			
ADL by Katz-6			
0	55 (80.8)	50 (73.5)	0.18
≥ 1	13 (19.2)	18 (26.5)	
Mean	0.24 ± 0.55	0.47 ± 1.00	
IADL bij Katz-9			*< 0.001*
0	53 (77.9)	20 (29.4)	
≥ 1	25 (22.1)	48 (70.6)	
Mean ± SD	1.21 ± 1.84	1.94 ± 2.06	
MMSE, mean ± SD	28.64 ± 1.36	28.83 ± 2.1	0.11
PHQ-2			0.15
0	58 (85.3)	64 (94.1)	
≥ 1	10 (14.7)	4 (5.9)	
EQ-VAS, mean ± SD	67.36 ± 16.01	71.25 ± 13.49	0.12
Mean weight ± SD	75.91 ± 13.12	74.94 ± 13.39	*0.04*
Gain weight		20 (29.4)	
Lost weight		37 (54.4)	
No weight change		10 (14.7)	

Number (No.); Activity of Daily Living (ADL); Instrumental Activities of Daily Living (IADL); Minimal Mental State Examination (MMSE) ; Patient Health Questionnaire-2 (PHQ-2); EuroQoL Visual Analog Scale (EQ-VAS).

treatment resulting in severe functional impairment [7]. Of course, HNC is a lethal disease when left untreated, so there is little doubt that surgery is a proper course of action not only to achieve oncological cure, but also to minimize the functional, cosmetic, and psychosocial impact of the disease [38]. Besides discussing the prognosis and complication rates of a surgical procedure for HNC, it is important to discuss the long-term effect on functionality. Based on our findings, we could now inform our patients about the fact that a surgical procedure may lead to a decline in functional status, specifically more dependency in IADL activities. However, we can also reassure our patients, it does not influence their self-reported health status negatively. Indeed, we noticed an improvement in self-reported health status in contrast to other studies in which a functional decline was correlated to a decreased quality of life [39].

The strength of our study lies in the fact that this is, as far as we know, the first study prospectively assessing the functional status, quality of life by using the self-reported health status, mood, and cognition status in older HNC patients one year after surgery in a Western population.

Our study also had some limitations. First of all, the size of our study population was limited. Our sample size limited the use of a statistical analyses for identifying predictive factors of functional decline. For instance, it is possible that postoperative radiation therapy further impacts functional outcome. In the future, more research like this study should be conducted, possibly with the goal of developing a prediction model for functional decline after surgery in elderly HNC patients which could then be used to counsel these patients better in their choice of therapy. Thereby, adequate detection of risk factors of functional decline and the implementation of recommendation to address them could lead to interventions which may prevent or delay functional decline [40]. The sample size also limited the performance of a subgroup analyses by surgical procedures. Our population was treated with different surgical treatments. It is possible that the functionality may decline more in patients treated with major surgery. Using a larger study population should therefore be considered. When determining the size of the study population, the high mortality rates of HNC in elderly patients should be taken into account. In this study, 25 of the 126 patients (20 %) died: seven patients were deceased within the first three months and 18 were deceased within 12 months after surgery. Another five patients were deceased more than a year after surgery but before they were approached for follow-up. On the other hand, despite the limited size of our sample we found a statistically significant decrease in the Katz-15 and in IADL scores.

Another limitation is the risk of selection bias. It is possible that the fittest patients participated in the follow-up by telephone, because the follow-up population was significantly younger than the non-follow-up population and had statistically significant less comorbidity according to the CCI, less IADL impairment, and less cognition impairment. This means that patients with cognitive disorders or with a terminal condition due to progressive disease were excluded from follow-up by telephone. As a result, the functional decline could be underestimated with this study. Third, objective physical performance measurements such as hand grip strength and gait speed could have given some additional

information about functional status. In addition, to acquire more insight into the quality of life, a questionnaire that is more extensive than the EQ-VAS should be utilized.

In conclusion, a statistically significant decline in functional status was found in older patients with HNC one year after surgery indicating a higher level of dependency. The impact of surgical treatment on patient-centered outcomes such as functional status and quality of life should be part of the discussion in counselling older patients in treatment-decision making.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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