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Impact of nutritional status at the outset of assessment on postoperative complications in head and neck cancer

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Conflicts of interest

The authors have no conflicts of interest to disclose in relation to the present article.

ABSTRACT

Objectives

Half the patients presenting with head and neck tumor are malnourished at the outset of treatment. Muscle mass loss (sarcopenia) seems to be critical. The aim of the present study was to assess the impact of nutritional status and sarcopenia on postoperative complications in head and neck cancer.

Materials and Methods

A retrospective study for the period November 2014 to May 2016 included 92 patients operated on for head and neck squamous cell carcinoma. Complications at 30 days were graded on the 5-level Clavien-Dindo classification. Nutritional status was assessed anthropometrically (weight), biologically (albuminemia and Nutrition Risk Index (NRI)), on CT (muscle mass index at 3rd lumbar vertebra) and functionally (Short Physical Performance Battery). Assessment was made at the outset of management, and nutritional treatment was initiated as appropriate. Potential risk factors for postoperative complications were assessed: performance status, prior radiation therapy, smoking and alcohol abuse.

Results

54% of patients were malnourished on the NRI. 41% had grade ≥ 2 complications. The most frequent complications were infection and healing disorder. The risk of complications was higher in case of malnutrition (62% vs. 17%; $p < 0.001$) and sarcopenia (56% vs. 22%; $p < 0.01$), with 50% longer hospital stay ($p = 0.04$).

Conclusion

Malnutrition and sarcopenia are independent risk factors for postoperative complications.

Key-words: malnutrition, sarcopenia, Clavien-Dindo classification, postoperative complications, head and neck cancer

Introduction

More than half of head and neck cancer patients present with malnutrition at diagnosis [1]. In oncology, malnutrition can be defined as a subacute or chronic state of nutritional imbalance associated with the inflammatory tumoral context, altering body composition, with diminished lean mass and muscle mass with or without diminished fat mass, and leading to organ dysfunction, with immune, muscular and cognitive deficits [2]. It is also a source of postoperative infection and delayed healing [3,4].

Despite the growth of chemoradiotherapy, surgery is still a major form of head and neck cancer treatment, about a half of patients undergoing surgery at some point. It entails, however, numerous complications and should not be undertaken without first assessing the full range of possible risk factors, either to reduce their impact or to abstain from surgery.

Risk factors for postoperative complications in oncologic head and neck surgery include: smoking, large tumor size, degree of resection, hypopharyngeal location, long operating time, high ASA (American Society of Anesthesiologists) score, and diabetes. These are all non-independent risk factors for complications or longer hospital stay in head and neck surgery. Prior radiation therapy is also a strong risk factor for complications and for healing disorder in particular [5,6].

The literature is agreed on the need for early diagnosis and management of malnutrition [7], but few studies have focused on the impact of nutritional status on postoperative complications in head and neck cancer [8]. In particular, there have been no studies on the impact of sarcopenia, although data are plentiful for other forms of cancer, associating sarcopenia with higher rates of postoperative complications, nosocomial infection and lengthened hospital stay in colorectal, esophageal and renal cancer [9, 10, 11].

The present study aimed to assess the correlation between complications and nutritional and muscle status (mass and function) at the outset of treatment (first surgical consultation) ahead of any corrective measures in head and neck oncologic surgery.

Patients and methods

A single-center retrospective observational study included all patients undergoing curative surgery for head and neck squamous cell carcinoma from September 2014 to April 2016. Cases of recurrence, relapse or second cancer and of prior radiation therapy and of salvage surgery were included.

Study data comprised:

- General characteristics: history, smoking status in pack-years, alcohol consumption, anesthesia risk on ASA score (Appendix 1), WHO Performance Status (Appendix 2) and demographics (age and gender).
- Tumor characteristics: UICC (7th edition) classification and staging, location, classification as primary, recurrent or secondary head and neck cancer, and prior radiation or chemo-therapy.

- Surgical characteristics: type of resection, type of reconstruction, any pharyngeal opening or loss of oral floor tightness. Procedures were categorized by high versus low risk of fistula, with high risk comprising total or partial laryngectomy, total pharyngolaryngectomy, oropharyngectomy with pharyngeal opening, and oral resection with intraoperative loss of oral floor tightness.

Nutritional work-up comprised anthropometric, biological and CT assessment. Anthropometric and biological assessment was performed during the first surgical consultation, and CT examination as part of the extension assessment as soon as possible afterward.

- Anthropometric measurements:

Anthropometric measurements comprised weight 3 months previously, and current weight (kg) and height (cm). Percentage weight-loss was calculated as (weight 3 months previously minus current weight) / current weight x 100; body-mass index (BMI) was calculated as current weight/height². Malnutrition was defined by BMI according to age: ≤ 70 years, <18.5 kg/m²; >70 years, < 21 kg/m² [12].

- Biological assessment:

Albuminemia and pre-albuminemia thresholds were 35g/l and 0.11 g/l respectively [12].

- Composite assessment (NRI) :

Biological data were coupled to anthropometric data to calculate a composite Nutrition Risk Index (NRI): 1.519 x albuminemia + (current weight/usual weight) x 100. NRI malnutrition threshold was <97.5, often considered a reference score in head and neck oncology [13].

- CT assessment (quantitative assessment of body composition and especially of muscle mass):

CT is a recent means of assessing body composition that has proved highly contributive in oncology [13]. Relative muscle area is determined on a 3rd lumbar vertebra slice using templates and dedicated software (Slice-O-Matic® V 4.3). It was assessed as part of the extension work-up if an abdominal slice was taken, as in most cases with our institution's nutritional assessment protocol, or else on PET-CT. L3 muscle-mass index (L3MMI) was thus calculated as the ratio between muscle area and height squared, with a threshold of < 52.4cm²/m² for males and < 38.5 cm²/m² for females [14].

- Functional nutritional assessment (qualitative assessment of muscle function)

Functional nutritional assessment used the Short Physical Performance Battery (SPPB), a 3-item test scored out of 12 (Appendix 3), with scores <8 indicating severe muscle function disorder, which is a malnutrition severity factor.

Nutritional management was adapted according to malnutrition threshold, following the guidelines of the French-speaking Society of Clinical Nutrition and Metabolism (SFNEP) [12].

Complications were assessed over a 30-day postoperative period. Quantitative and qualitative analysis used the 5-grade Clavien-Dindo classification, validated in head and neck surgery

[15] and quick and easy to implement (Table 1). It requires a definition of normal postoperative course in head and neck oncologic surgery, for which our department uses the Enhanced Recovery After Surgery (ERAS) guidelines to standardize management, and antibiotic prophylaxis in particular [16]. For analysis, only patients with grade ≥ 2 complications were counted as having complications.

Further data comprised hospital stay (days), compared to the mean for each procedure, and type of discharge (home or to follow-up unit).

Statistical analysis

Qualitative data were reported as number and percentage, and quantitative data as mean \pm standard deviation. Intergroup comparison used chi² test or Fisher exact test as appropriate for qualitative variables and Student or Mann-Whitney test for quantitative variables. Complications were analyzed by logistic regression, adjusting on the main clinically and statistically relevant criteria. Analyses used Stata 12 software. All tests were 2-tailed, with the significance threshold set at $p < 0.05$.

RESULTS

92 patients were included: 75 male, 17 female; mean age, 62.3 ± 10 years. 51% were smokers and 43% had chronic alcohol abuse. 6 were ASA 1 (6%), 59 ASA 2 (64%), 26 ASA 3 (28%), and 1 ASA 4 (2%). 11 (12%) had PS (performance status) 0, 67 PS 1 (75%), 10 PS 2 (11%), 1 PS 3 (1%) and none PS 4; in 3 cases, PS was not known. TNM stages were mainly advanced: 9% stage 1, 19% stage 2, 28% stage 3 and 44% stage 4.

Table 2 presents procedures, and Table 3 nutritional data.

91 NRI, 68 L3MMI and 92 SPPB data sets could be analyzed. There were no significant differences in tumor location, TNM stage, WHO or ASA score or type of surgery between patients with complete scoring (SPPB, NRI and L3MMI) and those lacking L3MMI.

On NRI, 49 patients (54%) were malnourished. On L3MMI, 36 showed sarcopenia (53%). 12 had SPPB < 8 (13%).

The overall grade ≥ 2 complications rate was 41.7% (38 patients) and grade ≥ 3 rate 21.5% (20 patients). The majority of complications were grade 2 (32 patients), the most frequent being surgery-site infection (15 cases: 39%) and delayed healing (18 cases: 47%). There were 11 grade 3 complications: 8 revision procedures for surgery-site infection, 2 cases of surgery-site hemorrhage, and 1 tracheotomy for respiratory distress associated with oral floor hematoma. There were 7 grade 4 complications: 3 following local or general infection (2 pneumopathies, 1 septic shock), 1 following myocardial infarction, and 2 decompensations of smoking-related lung disease. There were 2 deaths: 1 from hemorrhage, and 1 from multiple organ failure following pneumopathy. Figure 1 shows complications types and rates.

Risk of surgical complications, taking all procedures together, was significantly higher in case of malnutrition on NRI (OR: 8.5; 63% with vs. 17% without; $p < 0.001$), L3MMI (OR: 4.5; 56% vs. 22%; $p < 0.015$) and albuminemia (OR: 4.4, 31% vs. 67%; $p = 0.002$), but not on BMI (OR: 2, 40% vs. 57%; $p = 0.38$). 75% ($n = 9$) of the 12 patients with SPPB < 8 showed complications (OR: 5.27; $p = 0.018$).

Other risk factors for complications on univariate analysis were non-significant: pharynx or oral floor opening (31% (13 patients out of 41) without versus 49% (25 out of 51) with opening; OR: 2; $p = 0.09$); salvage surgery after radiation or chemo-therapy (55% (10 out of 18) with prior radiation therapy, but for a small sample of 18 patients; $p = 0.1$); tumor stage;

performance status; ASA score (16.7% (1 out of 6 patients) with ASA 1 showing complications, versus 40.6% (24 out of 59) with ASA 2, and 50% (13 out of 26) with ASA 3); advanced age >70 years; OR: 1.4; p=0.5); or active smoking or alcohol abuse.

Hospital stay was significantly longer, by 50%, in NRI-malnourished patients (p=0.042). A similar trend could be seen for L3MMI-sarcopenia, although the difference was not significant (p=0.18).

Focusing on severe surgical complications (Clavien-Dindo ≥ 3 , requiring revision surgery or intense care, there were no significantly associated parameters. However, 27% of malnourished patients (13 out of 49) had severe complications, compared to 11% of the others (5 out of 42) (OR: 2.7; p=0.08).

On multivariate analysis, NRI malnutrition, L3MMMI sarcopenia and SPPB were the only significant independent risk factors for onset of postoperative complications.

DISCUSSION

Few studies have dealt with surgical complications in head and neck oncology taking all sublocations and procedures together, most focusing rather on some particular type of surgery or, more recently, on free transplants [17,18]. Studies were mainly retrospective, focusing on the most severe complications and thus underestimating the overall rate. The present study used the Clavien-Dindo classification, recently validated in head and neck surgery; its main advantage is to allow comparison between procedures, as it is used in many other specialties. Another advantage is that it does not ignore complications liable to appear to be part of a normal postoperative course; it therefore requires a good definition of “normal” or indeed “ideal” course after a given surgery. Its main drawback is that it is not always well-adapted to head and neck pathology; for example, surgical revision of necrotic free flap is graded 3, the same as for hematoma, despite being much less serious. Nevertheless, in our opinion, lacking a better-adapted classification, surgical complications should be reported on the Clavien-Dindo classification.

The present study found an almost 42% rate of grade ≥ 2 complications. Surgery site infection and delayed healing were preponderant. The rate reflects the continuous activity of a surgery department over slightly more than 1 year. Comparison with the literature is hampered by the problems mentioned above. Eskander reported a 54% complications rate, with 15% fistula and 11% infection, in a series of 515 patients with free flap reconstruction [17]; independent risk factors comprised mucosal opening and intraoperative filling volume for delayed healing, and age, diabetes and malnutrition for infection. Comparison with the present findings is hindered by Eskander’s inclusion of salivary and cutaneous tumor and the systematic use of free flaps. Goepfert focused exclusively on complications of total pharyngolaryngectomy, with a 33% rate of complications overall and 21% for healing complications. The present series showed 26% fistula in procedures with pharyngeal opening, compared to 20-27% for other authors [5,6]. In recent reports, preoperative nutritional status was an important factor for postoperative complications, although nutritional status assessment modalities were not clearly described and some authors used only preoperative albuminemia, which has proved useful in predicting postoperative complications in both general and in head and neck surgery and also in predicting overall survival in head and neck oncology [19]. In the present series, it correlated with postoperative complications, but did not emerge as the most important

prognostic factor. It is dependent on inflammatory status, varies slowly over time and is a poor indicator of nutritional status in head and neck cancer, as our results confirmed [1]. We consider it necessary to associate weight loss by calculating NRI, to increase sensitivity. We showed NRI to correlate well with body composition, and it is an easy assessment to carry out. In the present study, NRI was the parameter correlating most closely with postoperative complications (OR: 8.5).

Interestingly, in the present retrospective study, nutritional status at the outset of treatment was the sole independent risk factor for complications on multivariate analysis. Other classical risk factors (diabetes, prior radiation therapy, smoking) showed no significant correlations. These findings are of course to be taken with caution, given the retrospective design, small study sample and failure to analyze such biological parameters as blood lymphocyte and hemoglobin levels at treatment outset. Complications generally lengthen hospital stay, and in the present study malnutrition at treatment outset was associated with 50% longer hospital stay.

The study objective was to assess the impact of sarcopenia on postoperative complications. It is now clear that sarcopenia is a major predictor of postoperative complications and overall survival in digestive, urologic and esophageal oncology [9,10,20]. The present study showed the same findings, with sarcopenia as an independent risk factor for postoperative complications (OR: 4.5) and a very high (75%) complications rate in case of impaired muscle function (SPPB<8). We find this correlation coefficient abnormally low, and difficult to interpret due to missing data in this retrospective study. Moreover, sarcopenia seems to be a risk factor for serious complications; this could not be shown from the present study, but emerges from the literature [21], and is important for patient management. Diminished muscle mass can be reversible [22]: appropriate feeding with high-quality amino acids associated to physical exercise seems to be the key to correcting sarcopenia. Two recent Japanese studies showed that elderly sarcopenic patients scheduled for gastric cancer surgery had low protein and calorie intake and incurred more severe postoperative complications [23]. The same team demonstrated that adapted nutritional therapy combined with physical activity increased protein and calorie intake in such patients, significantly improving muscle function [24]. Correlation with decreased postoperative complications, however, remains to be proven. In the present series, around 50% of patients showed sarcopenia. This is due to imbalance between muscle protein anabolism and protein catabolism. Pathophysiological hypotheses have been put forward to explain such sarcopenia, and notably muscle protein anabolism resistance in case of neoplasia: inflammation, insulin resistance [25,26], and myofibril fatty infiltration (myosteatorsis) [27]. This resistance is found even without malnutrition (pre-cachexia) [28]. Studies have confirmed that conventional diet supplements using formulae available on the market are ineffective in stimulating muscle protein synthesis in advanced cancer, and that daily protein dose and the protein and amino acid composition of meals are among the most important factors affecting anabolic response in cancer patients [29,30]. The present results thus advocate specific preoperative nutritional therapy or nutritional prehabilitation to reduce postoperative complications. Over the last 10 years, most studies of nutritional preparation for surgery have focused on the immune effects of diet. Some studies showed the contribution of pre- and peri-operative immunonutrition (arginine, nucleotides, omega-3 fatty acids) to reducing surgical complications [31,32,33,34]. We therefore consider it necessary to develop specific renutrition strategies ahead of head and neck cancer surgery, associating immunonutrition, exercise and formulae stimulating protein anabolism to optimize management of sarcopenia detected at the outset of treatment of patients with head and neck cancer.

CONCLUSION

Malnutrition emerged as an independent risk factor for surgical complications in head and neck cancer surgery. Such complications are frequent, mainly comprising infection and delayed healing. Nutritional assessment at the outset of treatment should be systematic. Particular attention should be paid to muscle tissue, impaired quantity and quality being predictive of complications. In future, muscle function should be restored preoperatively by specific nutritional formulae and physical exercise to reduce the rate of surgical complications.

Disclosure of Interest: The authors declare that they have no conflicts of interest concerning this article

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Table 1: Clavien-Dindo Classification

GRADE 1	<p>Any deviation from the normal postoperative course without pharmacological treatment (other than below) or surgical, endoscopic or radiological interventions.</p> <p>Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgesics, diuretics, electrolytes.</p>
GRADE 2	<p>Complication requiring pharmacological treatment, including blood/plasma transfusion and non-scheduled parenteral nutrition.</p>
GRADE 3	<p>Complication requiring surgical, endoscopic or radiological interventions under non-general anesthesia.</p> <p>Complication requiring surgical, endoscopic or radiological interventions under general anesthesia.</p>
GRADE 4	<p>Life-threatening complication requiring intensive care management:</p> <p>a) Single-organ dysfunction</p> <p>b) Multiorgan dysfunction</p>
GRADE 5	<p>Death of a patient.</p>

Table 2: Numbers per procedure.

Procedure	number
Isolated neck dissection	11
Extended tonsillectomy (Huet procedure) + neck dissection	12
Intraoral oropharyngectomy + neck dissection	5
Combined oral and cervical oropharyngectomy with or without transmandibular approach	9
Isolated cervical tongue-base surgery + neck dissection	2
Partial laryngectomy	10
Total laryngectomy	7
Total pharyngolaryngectomy	18
Oral resection with isolated oral approach	6
Oral resection with oral and cervical approach	5
Partial glossectomy	7

Table 3: Various nutritional parameters. Numbers of “Complications” are of patients with Clavien-Dindo grade ≥ 2 complications classification; numbers of “No complications” are of patients with no or grade 1 complications. Numbers for L3MMMI are small as many patients had extension assessment elsewhere, without abdominal CT scan.

Parameter		Number	Mean \pm standard deviation
Age (years)	Total population	92	62.3 \pm 10
	No complications	54	60.9 \pm 10.6
	Complications	38	64.3 \pm 8.8
BMI (kg/m ²)	Total population	92	25.7 \pm 5.4
	No complications	54	26.8 \pm 5.3
	Complications	38	24.3 \pm 5.2
Albuminemia (g/l)	Total population	91	37.2 \pm 5
	No complications	53	39.1 \pm 4.3
	Complications	38	34.5 \pm 4.9
NRI	Total population	91	97.4 \pm 8.9
	No complications	53	101.1 \pm 7.8
	Complications	38	92.1 \pm 7.7
SPPB (score out of 12)	Total population	92	10.5 \pm 2.2
	No complications	54	11.1 \pm 1.9
	Complications	38	9.5 \pm 2.4
L3MMMI (cm ² /m ²)	Total population	68	49.1 \pm 11
	No complications	39	51 \pm 11.5
	Complications	29	46.6 \pm 9.8

Appendix 1: American Society of Anesthesiologists (ASA) score

ASA physical status **Description**

I	Normal, healthy patient
II	Patient with mild systemic disease which does not affect daily functioning (such as controlled hypertension, stable chronic obstructive pulmonary disease (COPD), well-regulated diabetes mellitus, mild obesity)
III	Severe systemic disease which affects daily functioning (such as coronary artery disease, heart failure or COPD limiting exercise tolerance, morbid obesity)
IV	Systemic disease that is a constant threat to life (such as invalidating COPD or heart failure, unstable angina pectoris)
V	Moribund patient

Appendix 2: World Health Organization Performance index

WHO Performance index	
0	Normal activity
1	Restricted activity: ambulatory and able to carry out light work during the day
2	Activity reduced by 50%: ambulatory but unable to carry out any work
3	Confined to bed or chair for more than 50% of working hours: capable of only limited self-care
4	Totally confined to bed. Cannot carry on any self-care.

Short Physical Performance Battery

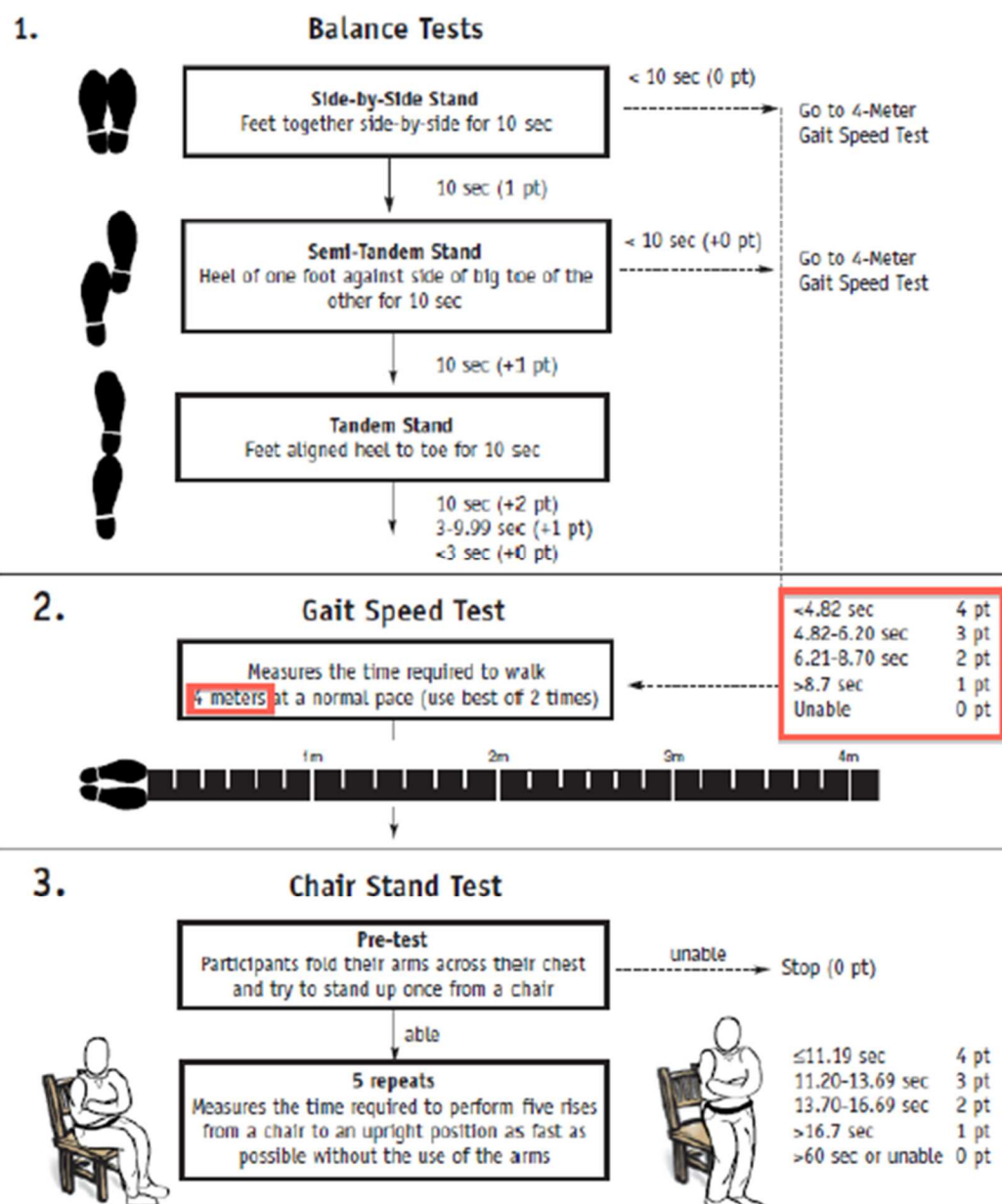


Figure 1: Type and rates of complications