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Could nutritional parameters predict 90-day mortality in patients with head and neck cancer?

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Abstract:	Background: Patients with Head and Neck Squamous Cell Carcinoma (HNSCC) are often at nutritional risk or even malnutrition at the time of diagnosis and it affects directly unfavorable clinical outcomes and poor prognosis. Among the methods used to assess Nutritional Status (NS), there are some tools widely used in clinical practice such as Body Mass Index (BMI), Weight Loss (% WL), Patient Generated Subjective Global Assessment (PG-SGA) and Prognostic Nutritional Index (PNI). The aim of study was to evaluate the 90-day mortality of HNSCC patients with distinct nutritional parameters. Methods: Retrospective review of the electronic clinical records (ECR) cohort study. PG - SGA records, weight, height, BMI and %WL and blood tests were included. PNI was calculated as 10 × baseline serum albumin (g/dL) + 0.005 × baseline absolute lymphocyte counts (cells/mm3). Results: The prevalence of overall 90-day mortality was 18.5%. BMI as continuous variable, PG SGA scores and lower levels of PNI (≤35,9) were associated with 90-day mortality. Conclusion: Our findings suggest that nutritional assessment tools used in clinical practice, such as PG-SGA and PNI, should be considered not only as an evaluation of nutritional status, but also as a predictor of 90-day mortality in this group of patients.
Opposed Reviewers:	

Cover letter

March 03, 2020

Editorial Department of Clinical Nutrition Espen

Dear Editor of Clinical Nutrition Espen,

I am submitting a manuscript for consideration of publication in Cancer Journal. The manuscript is entitled "Could nutritional parameters predict 90-day mortality in patients with head and neck cancer?".

It has not been published elsewhere and that it has not been submitted simultaneously for publication elsewhere. We are from a public Brazilian Institution, and despite the economic difficulties of the country.

Cancer as a consumptive disease, especially patients with head and neck squamous cell carcinoma are often at nutritional risk or even malnutrition at the time of diagnosis and it affects directly unfavorable clinical outcomes and poor prognosis. Among the methods used to assess nutritional status, there are some tools widely used in clinical practice such as Body Mass Index, weight loss (%), Patient Generated Subjective Global Assessment (PG-SGA) and Prognostic Nutritional Index (PNI). The aim of study was to evaluate the 90-day mortality of patients with head and neck squamous cell carcinoma with distinct nutritional parameters.

I am available for any question. Thank you very much for your consideration.

Yours Sincerely,

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Could nutritional parameters predict 90-day mortality in patients with head and neck cancer?

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ABSTRACT AND KEY WORDS

Background: Patients with Head and Neck Squamous Cell Carcinoma (HNSCC) are often at nutritional risk or even malnutrition at the time of diagnosis and it affects directly unfavorable clinical outcomes and poor prognosis. Among the methods used to assess Nutritional Status (NS), there are some tools widely used in clinical practice such as Body Mass Index (BMI), Weight Loss (% WL), Patient Generated Subjective Global Assessment (PG-SGA) and Prognostic Nutritional Index (PNI). The aim of study was to evaluate the 90-day mortality of HNSCC patients with distinct nutritional parameters. **Methods:** Retrospective review of the electronic clinical records (ECR) cohort study. PG - SGA records, weight, height, BMI and %WL and blood tests were included. PNI was calculated as 10 × baseline serum albumin (g/dL) + 0.005 × baseline absolute lymphocyte counts (cells/mm3). **Results:** The prevalence of overall 90-day mortality was 18.5%. BMI as continuous variable, PG SGA scores and lower levels of PNI (≤35,9) were associated with 90-day mortality. **Conclusion:** Our findings suggest that nutritional assessment tools used in clinical practice, such as PG-SGA and PNI, should be considered not only as an evaluation of nutritional status, but also as a predictor of 90-day mortality in this group of patients.

KEY WORDS: Head and Neck squamous Cell Carcinoma;90-day Mortality; Nutritional Assessment; Prognostic Nutritional Index

INTRODUCTION

Head and Neck squamous Cell Carcinoma (HNSCC) comprises a class of malignant neoplasms which originate from anatomical structures such as oral cavity, oropharynx, hypopharynx and larynx. Patients with HNSCC are often on nutritional risk or even malnutrition at the time of diagnosis and it affects directly unfavorable clinical outcomes and poor prognosis. (De Pinho et.al, 2019; van Deudekom, 2019; Bruixola et.al, 2018).

For the purpose of nutritional assessment, some tools are used in order to guide an appropriate therapeutic approach, in relation to dietary prescription, it could be plausible to intervene as early as possible in cases of nutritional risk or malnutrition. (Müller-Richter et. al, 2017). These nutritional assessment tools should be used by health professionals, due to their facility, low cost and reproducibility, which allows an effective classification of Nutritional Status (NS) and ensure a better Nutritional Therapy (NT) (Castillo-Martínez et al.2018).

In cancer patients, the best methods used for nutritional assessment in clinical practice are still not well established due to the complexity of the disease, the location of the tumor, changes in body compartments and fluids and the availability of financial resources to fund more accurate methods. (Cederholm et. al, 2019; Gonzalez, Correia, Heymsfield, 2017). Among the methods used to assess Nutritional Status (NS), there are some tools widely used such as Body Mass Index (BMI), Weight Loss (% WL), Patient Generated Subjective Global Assessment (PG-SGA) and Prognostic Nutritional Index (PNI).

Emerging evidences are trying to establish criteria for prognostic evaluation, considering the association of NS with possible clinical outcomes such as early mortality in cancer patients. (Bruixola et.al, 2018; van Deudekom, 2019; Peng et.al, 2018; Li et.al, 2019 DIXON et al., 2017; HAMILTON et al., 2018). However, studies in this field are still lacking in the literature therefore, the aim of study was to evaluate the 90-day mortality of HNSCC patients with distinct nutritional parameters.

PATIENTS AND METHODS

Study design

We conducted a retrospective review of the electronic clinical records (ECR) cohort study which included all new patients referred to a cancer treatment institute in Brazil between 1 March 2018 and 31 June 2019, who had a confirmed diagnosis of HNSCC, with curative intention. This study was approved by the Ethics and Research Committee of the Brazilian National Cancer Institute (Protocol number: 19255519.8.0000.5274).

Patients and variables

Clinical data included, sex, age, date of diagnosis, complete blood lymphocyte counts, albumin, staging of the tumour (according to the American Joint Committee on Cancer (AJCC) Cancer Staging Manual Seventh Edition) (EDGE; COMPTON, 2010), PG - SGA records (in our institution we use an electronic form version, which contains nutritional data of all patients, such as weight, height, BMI and %WL, collected within 24-48h after admission). PNI was calculated as 10 × baseline serum albumin (g/dL) + 0.005 × baseline absolute lymphocyte counts (cells/mm3). Patients diagnosed with some type of inflammatory disease, active infections, metastases at diagnosis, in palliative care, history of cancer in the last 5 years or with no results of blood tests were excluded.

Statistical Analysis

Categorical data were compared using the χ^2 test. Non-normally distributed continuous data were presented as median and interquartile range (IQR) and compared by the Mann–Whitney U-test. Because there is no established cut-off point for PNI variables, they were categorized according to the population distribution tertiles. Receiver operating characteristic (ROC) curve was used to determine the sensitivity and specificity of continuous variables of each nutritional assessment tool to predict 90-day mortality. Data were analysed using SPSS statistics version 20.0 (IBM, Armonk, New York, USA).

Table 1 Clinical Characteristics of all patients (n=108)

	N	%
Sex		
Male	79	73.1
Female	29	26.9
Age		
20-59	39	36.1
≥60	69	63.9
Primary Tumor Site		
Oral Cavity	52	48.1
Oropharynx	26	24.1
Larynx	22	20.4
Hipopharynx	4	3.7
Other	4	3.7
T (TNM Stage)		
T1-T3	58	53.7
T4	50	46.3
N (TNM Stage)		
N0-N1	73	67.6
N2-N3	35	32.4
Current Treatment Modality		
Chemotherapy and/or Radiotherapy	25	23.1
Surgery	41	38.0
Both	42	38.9

6 RESULTS

A total of 1021 electronic medical records were analysed, which 108 meet the inclusion criteria for the analyses .Most of patients were Male (73.1%) and had Oral Cavity as a primary tumor site (48.1%). In another manner, there were more patients on T1-T3 stage (53.7%) than locally advanced tumours (46.3%) and only 32.5% had advanced lymph node disease. Surgery plus Chemotherapy/ Radiotherapy were the main treatment choices used for curative intention (38.9%) (Table 1).

Nutritional parameters from each nutritional assessment and PNI terciles classifications can be visualized in Table 2. According to BMI, most of patients were considered on normal weight (39.8%), while according to PG-SGA, most patients were classified as moderate/suspected of malnutrition or severely malnourished (PG-SGA B or C) (67.6%). The prevalence of severe weight loss (>5% in a month or >10% in six months)

(BLACKBURN et al., 1977) was the most common, comprising about 60.2% of cases. The PG-SGA score ≥ 9 represented 49.1%, in the other hand, according to PNI, 50% of patients were classified in the third tercile (≥45.9).

Table 2 Nutritional Parameters of all population (n=108)

	N	%	p[(b)]
BMI [(a)]			0.076
Underweight	40	37.0	
Normal Weight	43	39.8	
Overweight	25	23.1	
PG-SGA			**0.013**
PG-SGA A	35	32.4	
PG-SGA B	49	45.4	
PG-SGA C	24	22,1	
PG-SGA (score)			**0.000**
0-1	11	10.2	
2-3	17	15.7	
4-8	27	25.0	
≥9	53	49,1	
% Weight Loss			**0.000**
5% (1 month) or 10%(six months)	4	3.7	
>5% (1 month) or >10%(six months)	65	60.2	
No relevant weight loss	39	36.1	
PNI Terciles (range values)			**0.001**
1st tercile (≤ 35.9)	27	25	
2nd tercile (36.0 – 45.8)	27	25	
3rd tercile (≥45.9)	54	50	

[a] WHO,1995;OPAS 2002 classification according to age [b] chi-square test

Table 3: Prevalence of 90-day mortality according to different nutritional parameters (n=20)

	N	(%)	p[(b)]
BMI[(a)]			**0.011**
Underweight	12	30.0	
Normal Weight	7	16.3	
Overweight	1	4.0	
PG-SGA			**< 0.001**
PG-SGA A	2	5.7	
PG-SGA B	4	8.2	
PG-SGA C	14	58.3	
PG-SGA (score)			**< 0.001**
0-1	1	9.1	
2-3	1	5.9	
4-8	4	14.8	
≥9	14	26.4	
% Weight Loss			**0.025**
5% (1 month) or 10%(six months)	0	0	
>5% (1 month) or >10%(six months)	15	23.1	
No relevant weight loss	5	12.8	
PNI Terciles (range values)			**< 0.001**
1st tertile (≤ 35,9)	19	70.4	
2nd tertile (36,0 - 45,8)	1	3.7	
3rd tertile (≥45,9)	0	0	

[a] WHO,1995;OPAS 2002 classification according to age [b,] chi-square test

The prevalence of overall 90-day mortality was 18.5% (n=20). There was no difference of death cases between patients classified as “Normal Weight” and “Underweight” on BMI category parameters (p=0.251). However, 90-day mortality was more prevalent in patients classified as PG-SGA C (58.3%), followed by PG-SGA B (8.2%) and PG-SGA A (5.7%). Likewise, there was more cases of 90-day mortality in patients who presented PG-SGA scores ≥ 9 and in patients with severe weight loss . There was no cases of 90-day mortality in patients above the 3rd PNI tercile values (≥45.9), and only one case (n=1) in the 2nd PNI tercile. In the other hand, 90-day mortality cases were more prevalent in the 1st tercile which had lower PNI scores (p=0.000) (Table 3). Furthermore, lower scores of PNI were associated with 90-day mortality (p=0.000), such as higher PG-SGA scores (p=0.008) (Table 4).

Table 4: Different 90-day mortality according to each nutritional assessment tool.

	90-day Mortality		
Variable	Yes	No	*p value*[(b)]
PG SGA Score[(a)]	11,5(8-13)	8(3-11)	0.008
BMI[(a)]	19,0 (17,0-24,2)	23,9 (21,0-27,0)	0.001
PNI[(a)]	28,1(22,2-31,9)	48,4(41,7-59,9)	0.000

[a] Values Expressed as Median (IQR) [b] Mann-Whitney test

The receiver operating characteristic curve (ROC) was performed to identify the cut-off point with the best sensitivity and specificity, for PNI and PG SGA scores for 90-day mortality, respectively. For the PNI, an area of 0.97 with a 95% confidence interval (CI) of 0.94 to 1.0 was observed, expressing a “very good” discriminatory power, with significant value (p <0.0001). In addition, the best cut-off point for 90-day mortality can be identified, which according to the ROC curve, in this study sample, was the PNI on the first tertile (≤ 35,9), with sensitivity of 95.0% and specificity of 91.0% (Figure 1). Whereas for PG-SGA scores, an area of 0.68 was observed with a 95% CI of 0.56 to 0.81, expressing a “regular” discriminatory power with significant value (p

<0.001). It was identified that the best cut-off point for 90-day mortality in this study sample was PG SGA Score ≥ 6 , with sensitivity of 85 % and specificity of 58% (Figure 2).

Figure 1: PNI sensitivity and specificity as a 90-day mortality prognostic factor.

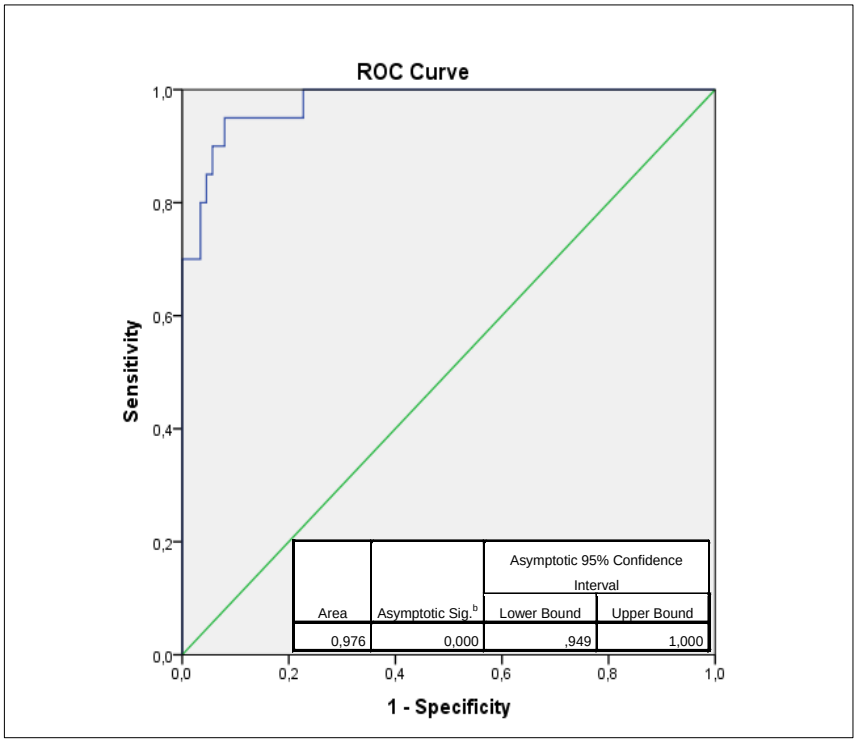
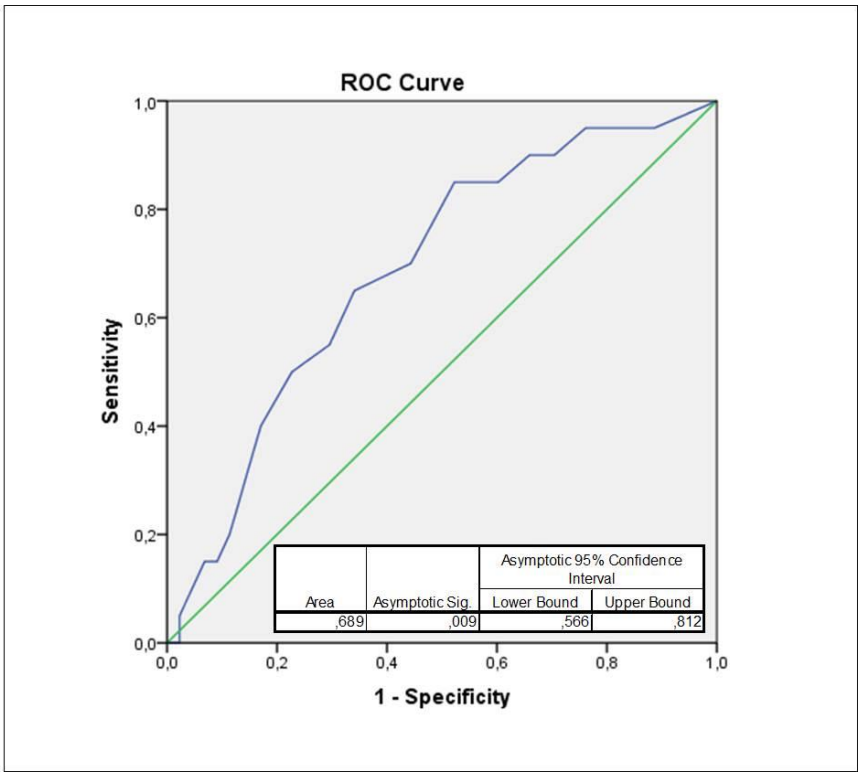


Figure 2: PG SGA scores sensitivity and specificity as a 90-day mortality prognostic factor.



6 DISCUSSION

To our knowledge, no study aimed to investigate the difference between nutritional assessment tools to assess 90-day mortality in patients with HNSCC. The prevalence of overall 90-day mortality was high (18.5%) compared to the study by GAUBATZ et al., 2019, where of the 9771 cases of death, only 3.8% occurred within a 90-day interval. This fact was already expected, since the majority of individuals in this study were elder male people. Both prevalence of HNSCC and mortality rates in elderly patients with this cancer type is common (VAN DEUDEKOM et al., 2019; TIWANA et al., 2014).

Otherwise, oral cavity and oropharynx tumours were the most prevalent and there was a less number of patients with locally advanced disease compared to the early stages. A study conducted in the USA, involving 22,162 patients, also identified a largest number of male patients affected by these tumors (OSAZUWA-PETERS et al., 2016) however, most patients with HNSCC are known to be diagnosed at advanced stages of the disease (OSAZUWA-PETERS et al., 2016;SEIWERT; COHEN, 2005; LIU; LIU, 2010; BRESSAN et al., 2016; SOUZA et al., 2018; TOPKAN et al., 2019).

Regarding to the Nutritional Status, there was a greater distribution of patients diagnosed as "Normal Weight", according to the BMI, however the majority of the population was classified as risk of malnutrition or severely malnourished according to the PG SGA (Table 2). In addition, 60.2% of the studied patients had severe weight loss. In another study conducted by SAROUL et al., 2018, they also identified that all patients identified as malnourished by BMI were considered as such by the other assessment methods, however, many malnourished patients had normal or high BMI. It's well known that BMI has little accuracy for the nutritional diagnosis of the population with cancer, as this measure does not correlate well with the body composition of these individuals an essential factor that contribute to the prognosis of the disease(GONZALEZ; CORREIA; HEYMSFIELD, 2017).

Likewise, there was no difference in 90-day mortality between BMI classifications as a

categorical variable (Table 3). Nevertheless, in this study, lower BMI values were associated with 90-day mortality (Table 4), suggesting that there may be clinical significance in using this tool as a continuous variable. Despite this, there are still no specific cut-off points that associate BMI values with clinical outcomes in patients with HNSCC.

Patients with severe weight loss had higher mortality rates in 90 days. Other studies have also shown that in patients with HNSCC, both BMI and weight loss are independent prognostic factor for worse clinical outcomes (ARRIBAS et al., 2013; TAKENAKA et al., 2015; DELLA VALLE et al., 2018). In contrast, the use of PG SGA or PGA SGA scores are more sensitive to identify cancer patients with degrees of malnutrition, which is associated with worse clinical outcomes (ARRIBAS et al., 2017; DE PINHO et al., 2019). In this study, there was a higher prevalence of patients classified as nutritional risk or severely malnourished. In addition PG SGA score ≥9 was more frequent, as was the percentage of cases of 90-day mortality in this group.

Otherwise, there was also an association between higher PG SGA scores and 90-day mortality ($p = 0.008$), indicating a population more prone to clinical complications. Nevertheless, there was a higher 90-day mortality in patients severely malnourished (Table 2). Similar findings were found in the study by CAVALCANTE MARTINS et al., 2019 , where there was higher mortality in patients with HNSCC classified as PG-SGA C.

Mortality among older patients with HNSCC may be predicted by several clinical and haematological data (MOON et al., 2016; KU et al., 2019). In this context, PNI have been studied as an easy and reproducible tool and it could be considered as a marker both of nutritional status and systemic inflammation (BOSSI, 2018). Several studies have shown the independent prognostic value of PNI levels in head and neck cancer (TAKENAKA et al., 2015; FRANCESCHINI et al., 2016; CHANG et al., 2018; QIN et al., 2018; IMAI et al., 2019; VAN DEUDEKOM et al., 2019).

In this study, most of patients classified at the first tertile (≤35.9) which were considered the lowest PNI levels presented the highest rates of 90-day mortality (70.4%). Besides, there was a higher rate of 90-day mortality compared with 2^{nd} an 3^{rd} tertiles ($p<0.0001$) (Table 3) and lower PNI levels

were associated with cases of 90-day mortality than no cases of 90-day mortality (Table 4). These data suggest that PNI could play a significant roll in the assessment and prognostic value in 90-day mortality of HNSCC patients.

Due to these results, we have performed the receiver operating characteristic curve (ROC) and PNI was the assessment tool which presented best sensitivity and specificity compared to PG SGA scores and BMI (as a continuous data) to predict 90-day mortality (Figures1 and 2). Sensitivity differences between these assessment tools, may be associated to the time which they are performed. In our institution, PG SGA is filled within 24-48h after admission, while blood tests could take an average of 7 days to be executed during hospital stay or after medical consultation. Thus, acute health changes in patients with HNSCC may be rapidly detected on blood tests, unlike PG SGA and BMI.

This study have some limitations. Despite high 90-day mortality rates, we could not perform multivariate analysis to evaluate the risk of mortality according to each nutritional assessment tool. Likewise, it was a retrospective review of electronic medical records which may be incorrectly filled, however exclusion criteria was applied as precisely as possible to correct these bias. The strength of this study consist in a new perspective of nutritional assessment tools as markers of 90-day mortality in patients with HNSCC, which could be inexpensive and easily conducted in clinical practice allowing a better planning of health actions by the multi-professional team.

7 CONCLUSION

Our findings suggest that nutritional assessment tools used in clinical practice, should be considered not only as an evaluation of nutritional status, but also as a predictor of 90-day mortality in this group of patients. More studies are needed, with this objective, to confirm these tools effectiveness as predictive factor of 90-day mortality.

8 REFERENCES

ARRIBAS, L. et al. Factores pronóstico de desnutrición a partir de la valoración global subjetiva generada por el paciente (VGS-GP) en pacientes con cáncer de cabeza y cuello. **Nutricion Hospitalaria**, v. 28, n. 1, p. 155–163, 2013.

ARRIBAS, L. et al. Nutritional changes in patients with locally advanced head and neck cancer during treatment. **Oral Oncology**, v. 71, p. 67–74, 1 ago. 2017.

BLACKBURN, G. L. et al. Nutritional and metabolic assessment of the hospitalized patient. **Journal of Parenteral and Enteral Nutrition**, v. 1, n. 1, p. 11–21, 2 jan. 1977.

BOSSI, P. Prognostic Nutritional Index: an easy nutritional screening for patients with head and neck cancer? **Bossi P. ESMO Open**, v. 3, p. 449, 2018.

BRESSAN, V. et al. **The effects of swallowing disorders, dysgeusia, oral mucositis and xerostomia on nutritional status, oral intake and weight loss in head and neck cancer patients: A systematic reviewCancer Treatment Reviews**W.B. Saunders Ltd, , 1 abr. 2016.

CASTILLO-MARTÍNEZ, L. et al. Nutritional Assessment Tools for the Identification of Malnutrition and Nutritional Risk Associated with Cancer Treatment. **Revista de investigación Clínica**, v. 70, n. 3, p. 121–125, 5 jun. 2018

CAVALCANTE MARTINS, F. F. et al. Patient-generated subjective global assessment predicts cachexia and death in patients with head, neck and abdominal cancer: A retrospective longitudinal study. **Clinical nutrition ESPEN**, v. 31, p. 17–22, jun.

CEDERHOLM, T. et al. GLIM criteria for the diagnosis of malnutrition – A consensus report from the global clinical nutrition community. **Clinical Nutrition**, v. 38, n. 1, p. 1–9, fev. 2019

CHANG, P. H. et al. Prognostic nutritional index relevance in chemoradiotherapy for advanced oral cavity, oropharyngeal and hypopharyngeal cancer. **Asia Pacific Journal of Clinical Nutrition**, v. 27, n. 5, p. 996–1001, 1 set. 2018.

DE PINHO, N. B. et al. Malnutrition associated with nutrition impact symptoms and localization of the disease: Results of a multicentric research on oncological nutrition. **Clinical Nutrition**, v. 38, n.

3, p. 1274–1279, jun. 2019.

DELLA VALLE, S. et al. Nutritional intervention in head and neck cancer patients during chemo-radiotherapy. **Nutrition**, v. 51–52, p. 95–97, 1 jul. 2018.

EDGE, S. B.; COMPTON, C. C. **The american joint committee on cancer: The 7th edition of the AJCC cancer staging manual and the future of TNMAnnals of Surgical Oncology**Springer, , 24 jun. 2010

FRANCESCHINI, D. et al. Prognostic factors in patients with locally advanced head and neck cancer treated with concurrent radiochemotherapy. **Radiologia Medica**, v. 121, n. 3, p. 229–237, 1 mar. 2016.

GAUBATZ, M. E. et al. Racial and socioeconomic disparities associated with 90-day mortality among patients with head and neck cancer in the United States. **Oral Oncology**, v. 89, p. 95–101, 1 fev. 2019.

GONZALEZ, M. C.; CORREIA, M. I. T. D.; HEYMSFIELD, S. B. A requiem for BMI in the clinical setting. **Current opinion in clinical nutrition and metabolic care**, v. 20, n. 5, p. 314–321, set. 2017.

IMAI, T. et al. Preoperative prognostic nutritional index as a method to predict postoperative complications after major head and neck surgery with free tissue transfer reconstruction. **Japanese Journal of Clinical Oncology**, 15 out. 2019.

KU, J. Y. et al. Prognostic value of neutrophil-to-lymphocyte ratio in older patients with head and neck cancer. **Journal of Geriatric Oncology**, 2019.

LIU, M.; LIU, F. Transcriptional and post-translational regulation of adiponectin. **Biochemical Journal**, v. 425, n. 1, p. 41–52, 1 jan. 2010.

MOON, H. et al. Prognostic value of nutritional and hematologic markers in head and neck squamous cell carcinoma treated by chemoradiotherapy. **Radiotherapy and Oncology**, v. 118, n. 2, p. 330–334, 1 fev. 2016.

MÜLLER-RICHTER, U. et al. Nutrition management for head and neck cancer patients improves clinical outcome and survival. **Nutrition Research**, v. 48, p. 1–8, 1 dez. 2017

OPAS OPA. XXXVI Reunión Del Comitê Asesor de Investigaciones En Salud – Encuestra Multicêntrica – Salud Beinestar Y Envejecimeiento (SABE) En América Latina E El Caribe-Informe Preliminar. 2002.

OSAZUWA-PETERS, N. et al. Race and sex disparities in long-term survival of oral and oropharyngeal cancer in the United States. **Journal of cancer research and clinical oncology**, v. 142, n. 2, p. 521–8, fev. 2016.

QIN, L. et al. Predicting 90-day mortality in locoregionally advanced head and neck squamous cell carcinoma after curative surgery. **Cancers**, v. 10, n. 10, 22 out. 2018.

SAROUL, N. et al. Which Assessment Method of Malnutrition in Head and Neck Cancer? **Otolaryngology - Head and Neck Surgery (United States)**, v. 158, n. 6, p. 1065–1071, 1 jun. 2018.

SEIWERT, T. Y.; COHEN, E. E. W. **State-of-the-art management of locally advanced head and neck cancerBritish Journal of Cancer**, 25 abr. 2005. .

SOUZA, M. T. P. et al. Resting energy expenditure and body composition in patients with head and neck cancer: An observational study leading to a new predictive equation. **Nutrition**, v. 51–52, p. 60–65, 1 jul. 2018.

TAKENAKA, Y. et al. Prognostic significance of body mass index before treatment for head and neck cancer. **Head & Neck**, v. 37, n. 10, p. 1518–1523, out. 2015.

TIWANA, M. S. et al. 25 Year survival outcomes for squamous cell carcinomas of the head and neck: Population-based outcomes from a Canadian province. **Oral Oncology**, v. 50, n. 7, p. 651–656, 2014.

TOPKAN, E. et al. Baseline Low Prognostic Nutritional Index Predicts Poor Survival in Locally Advanced Nasopharyngeal Carcinomas Treated With Radical Concurrent Chemoradiotherapy. **Ear, Nose and Throat Journal**, 2019.

VAN DEUDEKOM, F. J. et al. Geriatric assessment and 1-year mortality in older patients with cancer in the head and neck region: A cohort study. **Head and Neck**, n. February, p. 1–7, 2019.

World Health Organization. **Report of a WHO Expert Consultation**: **World Health Organization Technical Report, Series number 854. Physical status: the use and interpretation of anthropometry.** 1995.