PRE-SURGICAL NUTRITIONAL STATUS AND SURGICAL COMPLICATIONS IN PATIENTS WITH DIGESTIVE AND HEAD AND NECK CANCER

ESTADO NUTRICIONAL PRÉ-OPERATÓRIO E COMPLICAÇÕES CIRÚRGICAS EM DOENTES COM CANCRO DIGESTIVO E DA CABEÇA E PESCOÇO

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ABSTRACT

Introduction: Malnutrition is present in 40-50% of surgical patients upon hospital admission and is one of the most important factors influencing post-surgical morbidity and mortality. It is important to establish routines to identify and monitor patients at nutritional risk nutritional, to start early nutritional therapy, ideally in the pre-surgical phase. The aim of this study was to evaluate the association between pre-surgical nutritional status and postoperative complications and assess the nutritional assessment tool with the best prognostic value for post-surgical complications, in patients referred to surveillance in intermediate and intensive care units during surgical planning. **Methods:** We recruited patients at the Digestive Pathology and Head and Neck Units, referred for surgery and signaled at the anesthesia consultation for post-surgical surveillance in Intermediate or Intensive Care, from August to December 2016, at the Portuguese Institute of Oncology of Porto, Francisco Gentil, EPE. Clinical and demographic data were collected from the clinical process of the patients. Risk and nutritional status assessment was performed in the first 24 hours of patient's admission to hospital using the PG-SGA and NRI. Data analysis was performed using the SPSS 23.0 statistical program. **Results:** We included 97 patients, 62 with digestive malignancies and 35 with head and neck malignant tumors. The prevalence of pre-surgical malnutrition was 51.2% and 33%, as assessed by NRI and PG-SGA, respectively. Nutritional status, as assessed by NRI was associated with postoperative complications and length of hospital stay. Nutritional status and lack of nutritional support were also associated with greater odds of prolonged hospitalizations (>10 days). **Conclusion:** The odds of developing post-surgical complications was about 3 times higher if the patient is malnourished or at risk of malnutrition, as assessed by NRI.

Keywords: *Malnutrition; Cancer; NRI; Post-surgical outcomes.*

RESUMO

Introdução: A desnutrição está presente em 40-50% dos doentes cirúrgicos no momento da admissão hospitalar, sendo considerada um dos fatores que mais influencia a morbimortalidade pós-cirúrgica. É importante estabelecer rotinas para identificar e

monitorizar os doentes em risco nutricional, para iniciar a terapia nutricional precocemente, idealmente na fase pré-cirúrgica. O objetivo do presente trabalho foi avaliar a associação entre estado nutricional pré-cirúrgico e as complicações pós-cirúrgicas e verificar qual o instrumento de avaliação nutricional com melhor valor prognóstico para complicações pós-cirúrgicas, em doentes encaminhados para vigilância para as unidades de cuidados intermédios e intensivos durante o planeamento cirúrgico. **Métodos:** Foram recrutados doentes nas Unidades de Patologia Digestiva e de Cabeça e Pescoço, que tinham sido encaminhados para cirurgia e sinalizados na consulta de anestesia para vigilância pós-cirúrgica em Terapia Intermediária ou Intensiva, de agosto a dezembro de 2016, no Instituto Português de Oncologia do Porto, Francisco Gentil, EPE. Dados clínicos e demográficos foram recolhidos através de consulta ao processo clínico. A avaliação do risco e do estado nutricional foi realizada através do PG-SGA e do NRI, nas primeiras 24 horas da admissão do doente para internamento hospitalar. A análise dos dados foi realizada através do programa estatístico SPSS 23.0. **Resultados:** Foram incluídos 97 doentes, 62 com neoplasias digestivas e 35 com neoplasias malignas de cabeça e pescoço. A prevalência de desnutrição pré-cirúrgica avaliada foi de 51,2% e 33%, avaliada pelo NRI e PG-SGA, respetivamente. O estado nutricional, avaliado pelo NRI, foi associado a complicações pós-operatórias e maior tempo de hospitalização. O estado nutricional e a falta de suporte nutricional também foram associados a maior risco de hospitalização prolongada (> 10 dias). **Conclusão:** O risco de desenvolver complicações pós-cirúrgicas foi cerca de 3 vezes maior em doentes desnutridos ou em risco de desnutrição avaliados pelo NRI.

Palavras-chave: *Desnutrição; cancro; NRI; prognóstico pós-cirúrgico.*

INTRODUCTION

Malnutrition and its underlying complications are responsible for about 20% of deaths in cancer patients[1] and is one of the main causes of morbidity and mortality among those at advanced stages[2] =. The prevalence of malnutrition in cancer patients, at the time of diagnosis, is thought to be in the range of 15% to 40%, and this value may rise to 80% as the disease progresses[3,4]. Patients with digestive or head and neck (HN) neoplasms are particularly susceptible to developing malnutrition and cachexia[5]. These are among the types of cancer with the highest prevalence of malnutrition[2,6], namely cancer of the pancreas (80-85%), stomach (65-85%), HN (65-75%), esophagus (60-80%), and colorectal (30-60%)[6].

Nutritional status is one of the most important factors influencing post-surgical outcomes. Numerous studies confirm the negative impact of malnutrition or lack of nutritional support on postoperative complications (POC)[7-12]. Malnourished patients or those at risk of malnutrition often have an impaired immune system, increasing the susceptibility to infections in the postoperative period[13]. The organic response to surgical trauma, namely the acute catabolic effects, has also greater negative repercussions in those patients[10]. Despite that, it is also recognized that early detection of malnutrition and proper intervention in the preoperative period, could potentially mitigate postoperative burden, including POC[14,15].

The primary objective of nutritional screening and assessment is the unambiguous early identification of patients with malnutrition or who are at risk of malnutrition, and who would benefit from nutritional support and monitoring. Ideally, this should be possible by using a fast, simple and easy to use nutritional screening tool, that should also be sensitive. However, such tool does not currently exist, and the choice is further difficulted by the varied number of nutritional screening tools available from the literature[16,17]. Thus, the comparison of different tools within the same patient population are required if we want to draw any conclusions on defining the best tool for a certain patient population, age group or clinical setting. The objectives of the present work are to compare 2 risk/nutritional status assessment tools (PG-SGA and NRI) and to identify which one has the best prognostic value in surgical patients with digestive and HN cancer.

METHODS

The current study was conducted in accordance with the Declaration of Helsinki and was approved the IPOP Ethics Committee for Scientific Research. The authors declare that they have no conflict of interest.

We conducted a prospective longitudinal descriptive study from August to December 2016, at the *Instituto Português de Oncologia do Porto* (IPOP). Inclusion criteria were: i) patients from the Digestive and HN Pathology Units (UP), referred for surgery and signaled at the General Anesthesia consultation for post-surgical surveillance at the Surgical Intermediate Care Unit (SICU) and the Intensive Care Service (ICS); ii) who consented to participate in the present study and signed the informed consent; iii) to whom it was possible to apply the questionnaire to collect information for nutritional status assessment. We excluded patients with surgery scheduled on Mondays as these patients were admitted to the hospital on Sundays, and it was not feasible for the research team members to assess the nutritional status.

The patient's clinical file was accessed, and the following data were collected: sex, age, length of stay (LOS), LOS at the SICU / ICS, location of the primary tumor, primary, secondary, or recurrent neoplasia, staging (TNM classification), previous oncological treatments, oncological history, co-morbidities, physical status as assessed by the criteria of the American Society of Anesthesiologists (ASA)[18] and POC during hospitalization. Anthropometric data (weight, height, and body mass index (BMI) were also evaluated.

The following strategies were used to evaluate the nutritional status / risk: i) applying the Portuguese version of PG-SGA tool[19]. This was applied before surgery, during the first 24 hours of hospitalization; ii) using the NRI tool[20]. Table 1 describes the different criteria used in the present study for the diagnosis of malnutrition (or risk of malnutrition), according to the different tools.

Table 1 – **Criteria for nutritional status / risk assessment**

Tool	Criteria	Diagnostic
PG-SGA	A	No malnutrition
	B + C	Malnutrition
NRI	< 100	No malnutrition
	≤ 100	Malnutrition

Statistical analysis

Data analysis was performed using the SPSS 23.0 software (SPSS INC. 2011, Chicago, Illinois, USA). A significance level of $p< 0.05$ was considered.

Categorical variables were described as absolute or relative frequencies and comparisons between groups were performed using the chi-square test or *Fisher's* exact test. Continuous variables with normal distribution were described using mean and standard deviation and variables with non-normal distribution were described using median and 25th and 75th percentiles (P25-P75), and comparisons between groups were made using the t test for two independent samples or the *Mann-Whitney* test, respectively.

The association between nutritional status, and the presence of postoperative complications and longer hospital stay, were assessed using logistic regression models, with data presented as *odds ratios* and its 95% confidence intervals [OR (CI95)].

RESULTS

Characterization of the sample

General features of the sample are presented in Table 2. A total of 97 patients were included, mostly male (72.2%), with an average age of 64±12.1 years. Sixty-two patients (64%) had digestive cancer and 35 (36%) had HN cancer. The most frequent locations were colon, rectum and stomach for digestive tumors, and oral cavity, pharynx, and

Table 2 – **General characterization of the sample**

	Total (n=97)	**Digestive** (n=62)	**HN** (n=35)
Gender, n (%) female	27 (27.8)	22 (35.5)	5 (14.3)
Age (years), average (SD)	64 (12,1)	64 (12.1)	65 (13.6)
IMC, n (%)			
Underweight	6 (6.3)	2 (3.3)	4 (11.4)
Normal weight	46 (47.9)	27 (44.3)	19 (54.3)
Overweight/Obese	44 (45.8)	32 (52.5)	12 (34.3)
Diagnostic, n (%)			
Primary neoplasia	70 (72.2)	47 (75.8)	23 (65.7)
Secondary neoplasia	11 (11.3)	4 (6.5)	7 (20.0)
Recurrence	16 (16.5)	11 (17.7)	5 (14.3)
Metastatic disease, n (%)	40 (41,2)	40 (41.2)	32 (51.6)
Neoadjuvant treatment, n (%)			
CT	14 (15.4)	12 (20.7)	2 (6.1)
RT	0	0	0
CT+RT	6 (6.2)	4 (6.5)	2 (5.7)
none	77 (79.4)	46 (74.2)	31 (88.6)
Co-morbidities and risk factors, n (%)			
Diabetes *Mellitus*	23 (23.7)	16 (25.8)	7 (20.0)
Hypertension	50 (51.5)	27 (43.5)	23 (65.7)
Dyslipidemia	33 (34.0)	22 (35.5)	11 (31.4)
Stroke	1 (1.0)	1 (1.6)	0 (0.0)
Cardiovascular disease	31 (32.0)	22 (35.5)	9 (25.7)
Respiratory disease	19 (19.6)	11 (17.7)	8 (22.9)
Kidney disease	11 (11.3)	8 (12.9)	3 (8.6)
Hepatic disease	9 (9.3)	7 (11.3)	2 (5.7)
Smoker/former smoker	52 (53.6)	21 (33.9)	31 (88.6)
Alcohol consumption	23 (23.7)	7 (11.3)	16 (45.7)
Anemia	9 (9.3)	7 (11.3)	2 (5.7)
Neurologic	8 (8.2)	5 (8.1)	3 (8.6)

CT, chemotherapy; RT, radiotherapy; CT/RT, chemoradiotherapy

larynx for HN tumors (table 3). The most prevalent diagnosis was primary neoplasia (72.2%) and about 38% of the patients had metastatic disease (Table 3). In most patients (75%), there was no neoadjuvant treatment, while the remains had isolated treatment with chemotherapy (15%) or concomitant with radiotherapy (6%). Most patients (90.7%) had one or more co-morbidities, with hypertension (51.5%)

and dyslipidemia (34.0 %) as the more prevailing ones (Table 3). A significant proportion of the sample was smoker / former smoker (53.6%).

Table 3 – **Tumor location**

Digestive cancer		HN cancer	
Total, n (%)	**62 (100)**	**Total, n (%)**	**35 (100)**
Colon	19 (30.6)	Oral cavity	9 (25.7)
Rectum	17 (27.4)	Pharynx	9 (25.7)
Stomach	12 (19.4)	Larynx	8 (22.9)
Appendix	5 (8.1)	Tongue	3 (8.6)
Pancreas	3 (4.8)	Vocal chords	2 (5.7)
Liver	2 (3.2)	Amygdala	1 (2.9)
Peritoneum	2 (3.2)	Epiglottis	1 (2.9)
Gastroesophageal junction	1 (1.6)	Jaw	1 (2.9)
Gallbladder	1 (1.6)	occult	1 (2.9)

Characterization of the nutritional status

Table 4 shows the results of nutritional status as assessed by PG-SGA or NRI. The prevalence of malnutrition was 33% if using PG-SGA (B + C), and 51.2% if using the NRI (≤100), which contrasts with the 6% if using the BMI (BMI <18.5 kg/m2) (table 2). From the final sample, 48.5% of the patients did not receive nutritional monitoring. Of the 50 patients who were followed by the nutrition service, the majority (74%) were only seen after surgery.

Characterization of postoperative outcomes

Despite the pre-surgical indication, 35.2% of the patients were not admitted to the ICS / SICU. Regarding POC, 28% of patients had at least one complication, the most prevalent being general infection (14%). There were two deaths. The median length of hospital stay was 10 days, and the median length of stay in ICS / SICU was 1 day (table 5).

Table 4 – **Nutritional status and nutritional follow-up**

	Total (n=97)	**Digestive** (n=62)	**HN** (n=35)
Nutritional status			
PG-SGA, score, median (P25-P75)	3.00 (2.00-9.00)	3.00 (2.00-7.25)	5.00 (2.00-10.00)
PG-SGA, n (%)			
A – well-nourished	65 (67.0)	45 (72.6)	20 (57.1)
B – Moderately nourished or suspected malnutrition	26 (26.8)	14 (22.6)	12 (34.3)
C – Severely malnourished	6 (6.2)	3 (4.8)	3 (8.6)
NRI			
Well-nourished (>100)	27 (48.8)	21 (40.0)	6 (46.6)
Malnourished (≤100)	31 (51.2)	22 (60.0)	9 (53.4)
Nutritional follow-up			
No	47 (48.5)	39 (62.9)	8 (22.9)
Yes, Preoperative	13 (13.4)	6 (9.7)	7 (20.0)
Yes, Postoperative	37 (38.1)	17 (27.4)	20 (57.1)

Table 5 – **Postoperative complications and length of hospital stay**

	Total (n=97)	Digestive (n=62)	HN (n=35)
Postoperative complications, n (%)			
Surgical site infection	7 (7.2)	6 (9.7)	1 (2.9)
Dehiscence	6 (6.2)	5 (8.1)	1 (2.9)
Fistula	8 (8.2)	6 (9.7)	2 (5.7)
Respiratory complications	7 (7.2)	3 (4.8)	4 (11.4)
Cardiac complications	0	0	0
General infection	14 (14.4)	8 (12.9)	6 (17.1)
Neutropenia	0	0	0
Neurologic complications	4 (4.1)	3 (4.8)	1 (2.9)
Death	2 (2.1)	0	2 (5.7)
Length of hospital stay, median (P25-P75)			
Total days	10 (7-18)	10 (7-15)	12 (4-25)
Days at SCI/UCI	1 (0-3)	1 (0-2)	2 (0-3)

Characterization of postoperative outcomes by nutritional status

Table 6 shows the prevalence of POC and the LOS of patients classified as "malnourished" or "well-nourished". The results show that malnourished patients, as assessed by PG-SGA had longer LOS. There was no difference in the length of stay in the ICS / SUCI. Regarding the prevalence of POC, patients classified as malnourished had significantly more POC, namely, surgical site infection and dehiscence. Patients classified as malnourished by NRI, had a higher prevalence of fistula. No significant changes were found in the prevalence of postoperative burden when patients were classified by PG-SGA.

Association between nutritional status and postoperative outcomes

The crude associations between nutritional status, POC and LOS are shown in table 7. Postoperative complications were more likely to occur in malnourished patients as assessed by NRI [OR = 3.42 (95% CI: 1.27-11.32)]. Longer hospital stay (>10 days) was also associated with malnutrition status as assessed by PG-SGA [OR = 3.17 (95% CI: 1.27-7.90)], and NRI [OR = 3.06 (95% CI: 1.03-9.04)]. Patients who received nutritional monitoring were less likely to have a hospital stay of more than 10 days.

Table 6 – **Prevalence of POC, LOS and days at SCI/SICU among well-nourished and malnourished**

PG-SGA	Total (n = 97)	Well-nourished (n = 65)	Malnourished (n = 32)	p
POC, n (%)	27 (28.1)	16 (24.6)	11 (34.4)	0.313[a]
LOS, median (P25-P75)	10 (7-18)	9 (6-13.5)	15 (9-25)	**0.004**[b]
Days at SCI/UCI, median (P25-P75)	1.00 (0.00-3.00)	1.00 (0.00-2.75)	2.00 (0.00-3.00)	0.53[b]
NRI	**Total** (n = 58)	**Well-nourished** (n = 27)	**Malnourished** (n = 31)	**p**
POC, n (%)	18 (31.0)	5 (18.5)	13 (41.9)	0.055[a]
Fistula	6 (10.3)	0 (0.0)	6 (19.4)	**0.026**[c]
LOS, median (P25-P75)	11.00 (8.00-19.00)	9.00 (7.00-13.00)	13.00 (8.00-20.00)	0.054[b]
Days at SCI/UCI, median (P25-P75)	2.00 (0.00-2.00)	1.50 (0.00-2.20)	2.00 (1.00-3.00)	0.401[b]

[a] Chi-square test, [b] Mann-Whitney test, [c] Fisher test

Table 7 – **Association of nutritional status with POC and LOS**

	POC	LOS
	OR (IC 95%)	OR (IC 95%)
Nutritional follow-up		
No	1	1
Yes	0.19 (0.02-1.51)	**0.24 (0.10-0.57)**
Nutritional status		
PG-SGA		
Well-nourished (A)	1	1
Malnourished (B+C)	1.60 (0.64-4.04)	**3.17 (1.27-7.9)**
NRI		
Well-nourished (>100)	1	1
Malnourished (≤100)	**3.42 (1.04-11.32)**	**3.06 (1.03-9.04)**

DISCUSSION

The main purpose of the present work was to assess the prevalence of malnutrition according to NRI and PG-SGA, and explore the association between the pre-surgical nutritional status, as assessed by the different methods, and the occurrence of POC and LOS in surgical patients with digestive or HN cancer. Our data suggests that the prevalence of preoperative malnutrition ranged among different tools. The risk of developing POC was higher among malnourished patients defined by the NRI. The length of hospital stay was higher among malnourished patients as defined by PG-SGA, and NRI.

The association between pre-surgical nutritional status and the risk of POC has been shown in the literature for several years for different groups of pathologies[14,21-23]. However, there is a lack of consensus about which tool has the best prognostic value. As supported by the data of the current study, this is a very important concern that must be clarified, as the patients selected for nutritional intervention will differ according to the method used to assess malnutrition status (33% if using PG-SGA (B + C), and 51.2% if using the NRI (≤100)). In addition to that, our data showed that malnutrition was associated with the risk of POC, but only when diagnosed by NRI. The univariate logistic regression also showed that the nutritional status as assessed by NRI (≤ 100) could influence the "risk" to develop POC. Shinkawa *et al*[24] assessed the nutritional risk of 64 patients undergoing pancreatoduodectomy using the NRI and NRS 2002 and demonstrated the NRI was an independent risk factor for the development of infection at the surgical site. *Bo et al.*[25] also demonstrated that NRI was capable to identify liver cancer surgical patients at risk of developing POC and death. Thieme *et al.*[26] showed a positive association between NRI and non-infectious complications in patients undergoing digestive surgery.

PG-SGA is a validated tool for the assessment of nutritional status and recommended by several authors as the reference tool to be used in cancer patients. However, few studies have analyzed its prognostic validity for the development of POC in cancer patients. In our study, the association between nutritional status and the presence of POC was not demonstrated when malnutrition was diagnosed by PG-SGA. This can be explained by the reduced prevalence of POC in the present sample, mainly in the case of patients with pre-surgical indication for post-surgical surveillance in the SICU or ICS, which may have weakened the possibility of proving these associations. *Harter et al.* found a significant association between PG-SGA and POC in cancer patients, however the percentage of POC was higher (53.3%) than in the present study (28.1%)[22]. *Auntoun et al.* in a sample of 275 cancer patients, described a prevalence of malnutrition (34%) and POC (28.4%)[27] very similar to the one found in the present study and, similarly to *Harter et al*[22], those authors also showed that malnourished patients assessed by PG-SGA had a significantly higher prevalence of major complications when compared to well-nourished patients. However, in the study by *Auntoun et al.*[27], this association was not found for infectious complications, and in the multivariate analysis, only malnutrition diagnosed by serum albumin values was considered a risk factor for POC.

LOS was significantly higher in malnourished patients, regardless of the parameters used to assess nutritional status. These results are in line with the findings of other authors, who demonstrated a significant association between LOS and malnutrition diagnosed by various tools such as PG-SGA[22], SGA[28], NRS 2002[8]. In the analysis made through logistic regression, only malnutrition and nutritional monitoring were found to influence the risk of prolonged LOS (>10 days). These findings are clinically relevant because, as demonstrated in the literature, long periods of hospitalization, in addition to increasing hospital costs, increase the likelihood of inter-occurrences,[29] as has been shown in the present study. It is also important to emphasize the importance of nutritional support throughout the treatment pathway. Our data suggest that nutritional follow-up reduces the risk of having LOS for more than 10 days. In the literature, several authors prove that patients who had nutritional monitoring during hospitalization when compared to those who are not followed by the nutrition team, have significantly fewer complications and a shorter hospital stay[23,30,31], and that insufficient energy intake during the period of hospitalization and the lack of nutritional monitoring are associated with an increased rate of infections, the risk of complications and an increase in the length of stay in intensive care[12,32].

Limitations

In this study, information was only collected from the patients' files during the hospitalization period, which is why the presence of late postoperative complications may have been underestimated. Another important limitation of the present study was the fact that some important risk factors for the presence of POC were not evaluated, namely the time of surgery, type of surgery, type of anesthesia, post-surgical medication, and whether there were recent hospitalization or surgeries.

It was not considered how many patients with surgical indication, did not perform the surgery because they did not meet conditions, namely because they are malnourished. Thus, a selection bias may have occurred.

CONCLUSION

From the present study, it can be concluded that the prevalence of preoperative malnutrition ranged among two widely used tools (PG-SGA and NRI). The risk of developing POC or having a prolonged LOS was about 3 times higher in malnourished patients or at risk of malnutrition by the NRI.

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