

Nutritional Risk versus Risk of Sarcopenia Associated to Postoperative Complications and Mortality in Cancer Patients Undergoing Major Surgery

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Risco Nutricional versus Risco de Sarcopenia Associado a Complicações Pós-Operatórias e Mortalidade em Pacientes Oncológicos Submetidos a Cirurgias de Grande Porte

Riesgo Nutricional versus Riesgo de Sarcopenia Asociado con Complicaciones Postoperatorias y Mortalidad en Pacientes con Cáncer Sometidos a Cirugía Mayor

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ABSTRACT

Introduction: Surgical patients who are at either nutritional or sarcopenia risk may have worst outcomes in the postoperative period.

Objective: To investigate whether nutritional or sarcopenia risk is associated with mortality and postoperative complications in cancer patients undergoing major operations. **Method:** Prospective cohort bicentric study enrolling 220 adult oncological patients submitted to major surgeries at Cancer Hospital and Santa Casa de Misericórdia in Cuiabá-MT. Patients were classified with or without nutritional risk per the Nutritional Risk Screening 2002 and sarcopenia risk according to the Strength, Assistance with walking, Rise from a chair, Climb stairs - and Falls questionnaire preoperatively. The outcomes variables were postoperative infectious complications and death.

Results: Patients with nutritional risk showed higher risk of infectious complications (24.6 vs. 5.1%; RR=4.8 CI95% 1.94-12; p<0.001) or die (11.5 vs. 1.0%; RR=11.2 CI95% 1.5-84.0; p=0.002) in post-operation when compared to patients without nutritional risk. There was no association between sarcopenia risk with infectious complications or mortality during post-operation (p>0.05). **Conclusion:** Oncological patients with nutritional risk have higher risk of developing postoperative infectious complications or die when compared with patients without nutritional risk or in risk of sarcopenia.

Key words: Surgical Oncology; Nutritional Status; Sarcopenia; Postoperative Complications; Mortality.

RESUMO

Introdução: Pacientes cirúrgicos, que apresentam risco nutricional ou de sarcopenia, podem evoluir com piores desfechos no pós-operatório.

Objetivo: Investigar se existe associação entre o risco nutricional e a sarcopenia com complicações e mortalidade no pós-operatório de pacientes oncológicos submetidos a cirurgias de grande porte. **Método:** Estudo bicêntrico de coorte, prospectivo, realizado com 220 pacientes oncológicos adultos, submetidos a operações de grande porte no Hospital de Câncer e na Santa Casa de Misericórdia em Cuiabá, Mato Grosso. Os pacientes foram classificados com ou sem risco nutricional pela *Nutritional Risk Screening 2002* e de sarcopenia segundo o questionário *Strength, Assistance with walking, Rise from a chair, Climb stairs - and Falls*, no pré-operatório.

As variáveis de desfecho foram complicações infecciosas e óbito no pós-operatório. **Resultados:** Os pacientes com risco nutricional mostraram maior risco de complicações infecciosas (24,6 vs. 5,1%; RR=4,8 IC95% 1,94-12; p<0,001) e de óbito (11,5 vs. 1,0%; RR=11,2 IC95% 1,5-84,0; p=0,002) no pós-operatório, quando comparados aos sem risco nutricional. Não houve associação do risco de sarcopenia com a presença de complicações infecciosas e óbito ao longo do período pós-operatório (p>0,05). **Conclusão:** Os pacientes oncológicos em risco nutricional foram aqueles que apresentaram maior risco de complicações infecciosas e de óbito no pós-operatório, quando comparados aos sem risco nutricional ou em risco de sarcopenia.

Palavras-chave: Oncologia Cirúrgica; Estado Nutricional; Sarcopenia; Complicações Pós-Operatórias; Mortalidade.

RESUMEN

Introducción: Los pacientes de cáncer quirúrgico con riesgo nutricional o de sarcopenia pueden evolucionar con peores resultados en el postoperatorio.

Objetivo: Investigar si existe una asociación entre el riesgo nutricional y la sarcopenia con complicaciones y mortalidad en el postoperatorio de pacientes con cáncer sometidos a operaciones mayores. **Método:** Estudio prospectivo de cohorte bicéntrico realizado con 220 pacientes adultos con cáncer que se sometieron a operaciones importantes en el Hospital de Câncer y Santa Casa de Misericórdia en Cuiabá, Mato Grosso. La muestra estudiada se clasificó con o sin riesgo nutricional por *Nutritional Risk Screening 2002* y sarcopenia de acuerdo con el cuestionario *Strength, Assistance with walking, Rise from a chair, Climb stairs - and Falls*, en el pre operatorio. Las variables de resultado fueron complicaciones infecciosas y muerte en la postoperatorio.

Resultados: Los pacientes con riesgo nutricional mostraron un mayor riesgo de complicaciones infecciosas (24,6 vs. 5,1%; RR=4,8 IC95% 1,94-12; p<0,001) y muerte (11,5 vs. 1,0%; RR=11,2 IC95% 1,5-84,0; p=0,002) en la postoperatorio en comparación con aquellos sin riesgo nutricional. Sin embargo, no hubo asociación entre el riesgo de sarcopenia y la presencia de complicaciones infecciosas y muerte durante el período postoperatorio (p>0,05). **Conclusión:** Los pacientes con cáncer en riesgo nutricional según *NRS-2002*, fueron aquellos que tenían un mayor riesgo de complicaciones infecciosas y muerte en la postoperatorio, en comparación con aquellos sin riesgo nutricional o con riesgo de sarcopenia.

Palabras clave: Oncología Quirúrgica; Estado Nutricional; Sarcopenia; Complicaciones Postoperatorias; Mortalidad.

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INTRODUCTION

Nearly four decades ago, Studley¹ documented that weight loss was associated with increase of mortality in surgical patients. Currently in Brazil, nearly 42% of oncologic patients hospitalized have weight loss and 45% are admitted mal-nourished or in risk of malnourishment². However, among the patients with oral cavity, esophagus and stomach tumors, malnourishment is around 62% and 84%².

In this context, the damages of the nutritional condition have been constantly associated with worst clinical outcomes which reflect in the response to the oncologic treatment, increase of complications, death rates and hospital costs³⁻⁵. Specifically, in relation to nutritional risk, 30% to 70% of the patients are hospitalized with this diagnosis^{4,5} which is significantly associated with the increase of postoperative complications⁵⁻⁸. In this sense, a study showed that patients submitted to radical gastrectomy by cancer who were in nutritional risk had increased postoperative complications and death rates⁶.

Sarcopenia mainly in the last decade started to be associated with postoperative damages in the evolution of patients⁹⁻¹¹. Sarcopenic syndrome is characterized by progressive and generalized loss of the skeletal function and muscle mass leading to the reduction of the functional condition and performance⁹⁻¹¹. Particularly among oncologic patients, sarcopenia is a recent predictor of increase of hospitalization time, readmissions, infectious complications, and mortality⁹⁻¹³.

Therefore, within peri-operative care, it is important to widen the monitoring with nutritional risk and sarcopenia screening¹¹⁻¹⁵. However, regardless of nutritional risk and sarcopenia screening being widely accepted and known, so far, no study investigated at the same time in the same population of oncologic patients which of these risks have better or higher association with postoperative worse prognosis. Therefore, the team should intervene quickly through multi-modal care to accelerate the recovery of the surgical patient¹⁶.

Based in the aforementioned, a prospective study was conducted to determine the association between nutritional risk and sarcopenia with postoperative complications and mortality of oncologic patients submitted to major surgeries.

METHOD

Bicentric prospective cohort study carried out from July 2018 to April 2019 with adult oncologic patients (age ≥ 18 years), admitted at Cancer Hospital and Hospital of “*Santa Casa de Misericórdia*” (Holy House of Mercy)

of Cuiabá-MT. The patients who accepted to join the study signed the Informed Consent Form (ICF). The Institutional Review Board of the Federal University of Mato Grosso (UFMT) approved the study, number 2.666.168/2018.

Adult patients with cancer eligible for major oncologic surgeries were included. Major surgeries are defined as those with more odds of blood and fluid loss according to report number 006/2015 of the Federal Council of Medicine¹⁷. Patients diagnosed with non-melanoma skin cancer, advanced disease and who refused to sign the ICF or did not want to participate in any study phase were excluded. The patients whose data were lost, or their surgeries were suspended by any reason or were transferred to another hospital post-operation were excluded too.

The patients were classified with or without postoperative nutritional risk and sarcopenia pursuant to the following definition. The main variables were the occurrence of postoperative infectious complications and death. As co-variables, age (older patients were ≥ 60 years), gender, body mass index (Kg/m²), score of the American Society of Anesthesiologists (ASA), type of operation according to the tumor site, time of operation (minutes) and hospitalization (days until hospital discharge or death). The data were collected in the immediate pre-operation, that is, nearly one to two hours before the operation and in post-operation until hospital discharge or death in the hospital.

To determine the nutritional risk, the tool Nutritional Risk Screening 2002 (NRS-2002) was utilized. The patients with score ≥ 3 were classified as being in nutritional risk^{5,18}. To evaluate the risk of sarcopenia, the questionnaire Strength, Assistance with walking, Rise from a chair, Climb stairs - and Falls (SARC-F)^{11,19} was utilized. This questionnaire consists of five questions that evaluate the strength, walk, rise from a chair, climb stairs and history of falls. The scores range from 0 to 10 points, being 0-2 points for each item¹¹. The patients with score ≥ 4 points were classified in sarcopenia risk (SARC-F ≥ 4)^{11,19}.

Infectious complications include the presence of pneumonia, infection at the surgical site, dehiscence of anastomose or wall, urinary tract infection and sepsis. All the definitions of infectious diseases were cited in other articles published by the same group^{20,21}. The complications were also classified per the criteria of Clavien-Dindo²².

Initially the Kolmogorov-Smirnov test was applied to determine the normality of the continuous data. Data normally distributed were presented as means and standard deviation and those with non-normal distribution were presented as median and interquartile range (M;IQR).

The chi-square test (relative risk and confidence interval of 95%) was utilized to determine the association of nutritional risk and sarcopenia with the presence of infectious complications and death. The Mann-Whitney test was utilized to compare the time of hospitalization in days (non-normal distribution) among patients with and without nutritional risk or sarcopenia. A statistical significance limit of 5% ($p < 0.05$) was established. For the statistical analysis, the software Statistical Package for the Social Sciences 20.0 (SPSS Statistics; IBM, Armonk, NY, USA) was utilized.

RESULTS

338 patients were eligible of which 12 were excluded because they did present non-melanoma skin cancer, 14 by advanced disease, 13 for loss of data and 79 for suspension of the surgery. 220 patients submitted to major surgeries with mean age of 58.7 ± 14.0 years joined the study. Table 1 shows other clinical and demographic data.

Figure 1 presents the results of pre-operative nutritional risk and risk of sarcopenia.

37.7% ($n=83$) of the patients presented at least one postoperative complication, being 15.9% ($n=35$) infectious. Most of the complications was mild, being 61 (27.7%) classified as Clavien-Dindo I or II. Fifteen patients (6.8%) died in post-operation.

Table 1. Clinical and demographical characteristics of the patients investigated ($n=220$)

Variables	Values
Older adults (n; %)	111 (50.5)
Gender (n; %)	
Female	109 (49.5)
Male	111 (50.5)
BMI (kg/m^2) (M; IQR)	26.1 (23.0-30.1)
Score ASA I and II (n; %)	202 (91.8)
Type of operation according to the tumor site	
• Urologic	86 (39.1)
• Digestive tract	69 (31.4)
• Breast	29 (13.2)
• Head and neck	17 (7.7)
• Others	19 (8.6)
Time of surgery (minutes) (M; IQR)	125 (90-205)
Time of hospitalization (days) (M; IQR)	3 (2-7)

Captions: BMI: Body Mass Index (Kg/m^2); ASA: American Society of Anesthesiologists.

Note: Values expressed in mean and standard deviation ($M \pm SD$); number and percent (n; %); median and interquartile range (M; IQR) according to the distribution of the data.

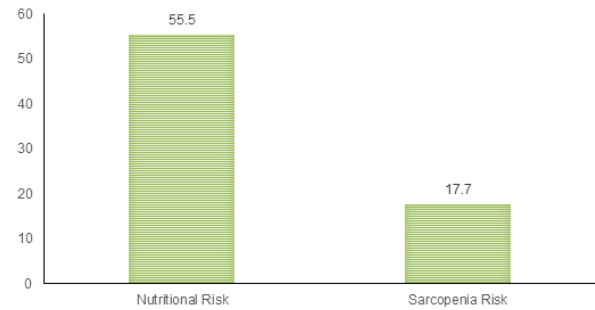


Figure 1. Distribution of the nutritional and sarcopenia risk of the patients investigated

Patients in nutritional risk were those who remained hospitalized for more time than the patients without nutritional risk [5.0 (3-9) *vs.* 2(1-3); $p < 0.001$]. There was no difference of days of hospitalization among patients with and without sarcopenia risk [4 (1-8) *vs.* 3 (2-7); $p = 0.781$].

According to Table 2, the patients in postoperative nutritional risk had more odds of infectious complications (24.6 *vs.* 5.1%; $RR = 4.8$ $CI_{95\%} 1.94-12$; $p < 0.001$) and death (11.5 *vs.* 1.0%; $RR = 11.2$ $CI_{95\%} 1.5-84.0$; $p = 0.002$) when compared to those without nutritional risk. There was no association of postoperative risk of sarcopenia with the presence of infectious complications (23.1 *vs.* 14.4%; $RR = 1.61$ $CI_{95\%} 0.82-3.15$; $p = 0.177$) or death (10.3 *vs.* 6.1%; $RR = 1.69$ $CI_{95\%} 0.58-5.02$; $p = 0.348$) (Table 2).

DISCUSSION

Nutritional risk diagnosed by NRS-2002 showed a significant association with postoperative risk of infectious complication and mortality. The risk of infectious complications among patients with nutritional risk increased nearly five-fold and risk of death, more than 11-fold when compared to patients without nutritional risk. The patients in postoperative nutritional risk too were those who remained hospitalized for three more days when compared to those without nutritional risk.

The same outcomes were not found in the study of patients in sarcopenia risk. In this line, the last European Consensus EWGSOP2 (European Working Group on Sarcopenia in Older People)¹¹ recommends the use of the questionnaire SARC-F to screen sarcopenia in patients with clinical suspicion. This questionnaire is useful, simple, low cost and easily applicable^{11,19}, however, no association of the sarcopenia risk diagnosed with the questionnaire SARC-F was found with postoperative occurrence of infectious complications and death when compared with patients in nutritional risk. This may have been impacted by the percentage of patients who were in nutritional and sarcopenia risk.

Table 2. Association of nutritional risk and sarcopenia with infectious complications and death

Event	Nutritional Risk		Sarcopenia Risk	
	RR (CI95%)	p	RR (CI95%)	p
Infectious Complications	4.8 (1.94-12)	<0.001	1.61 (0.82-3.15)	0.177
Death	11.2 (1.5-84.0)	0.002	1.69 (0.58-5.02)	0.348

Captions: Chis-square test; RR: relative risk; CI95%: confidence interval of 95%.

The European Consensus¹¹ itself mentions that SARC-F is a tool which diagnoses severer cases of alteration in muscle strength²³. Further it adds that this questionnaire has moderate to low sensitiveness and high specificity¹¹. In this sense, a recent article of this group showed that patients in sarcopenia risk according to SARC-F who also presented postoperative low palmar handgrip strength were those who had more odds of infectious complications²⁴. In 2016, Barbosa-Silva et al.²⁵, likewise, showed that the evaluation of SARC-F combined with calf circumference (SARC-CalF) was more sensitive to detect patients in sarcopenia risk when compared to SARC-F alone (p=0.027).

According to the tool NRS-2002 there was three-fold more patients in nutritional risk than in sarcopenia risk in immediate pre-operation. It is noticed that the two screening tools investigated revealed quite different values of the risk each one expresses; that is, 55.5% and 17.7%. Pursuant to a meta-analysis conducted with 12,800 patients, the questionnaire SARC-F presented low sensitiveness to sarcopenia screening, although with high specificity²⁶.

Therefore, SARC-F appears to be an effective tool to select patients who need to be submitted to more tests to confirm the diagnosis of sarcopenia²⁶. In the current study, the result was surprising since SARC-F evaluates the functioning ability and muscle performance related conditions^{11,19,26,27} that modify rapidly prior to the anthropometric alterations²⁸⁻³¹, which allows to diagnose the damages of the patient conditions earlier^{11,12} and still the association with worse outcomes. On the other hand, NRS-2002 is an instrument the European Society for Clinical Nutrition and Metabolism (ESPEN) recommends for nutritional screening and has been used frequently to associate the nutritional risk and postoperative complications^{9,10}.

Former studies showed that NRS-2002 is an excellent screening tool to diagnose nutritional risk, which corroborates the data encountered in this investigation⁴⁻⁸. Unlike the questionnaire SARC-F, NRS-2002 was developed to identify patients who can benefit from a nutritional intervention, that is, those with weight loss, low body mass index, reduction of food intake, advanced age and/or increase of metabolic stress related to the clinical or surgical condition¹⁸.

All the NRS-2002 data may have contributed jointly to reach the results found in this study. In this sense, a study published in 2018 showed that patients with rectal cancer in nutritional risk were those who were at a more advanced stage of the disease, higher ASA score (OR=2.4), more time of operation (OR=1.97) and higher NRS-2002 score (OR=2.04) when compared with patients without nutritional risk⁸. The authors concluded that the presence of nutritional risk according to NRS-2002 is an independent risk factor for surgical patients with cancer⁸. Another issue deserving notice is that when compared to other screening tools, NRS-2002 allows to score the disease effect (score 1 to 3) and this prompts the analyzer to score the patients with nutritional risk because of the disease severity⁸.

As an example, the condition of being a patient scheduled for a major surgery reveals a very important level of severity and stress for malnourishment risk^{8,18} and this has certainly collaborated for higher percentage of patients who were in risk of malnourishment. Additionally, another question that needs to be addressed is about data collection to define the diagnosis of the presence or not of the risk.

SARC-F scores were reached through five questions¹¹. Scores were concluded subjectively and the final score shows the patient's interpretation^{11,19}. This is quite different from NRS-2002 since the score comprehends objective and technical criteria according to the condition the skilled professional evaluated and not the patient's judgment^{7,8}. Pursuant to these results, a meta-analysis conducted with 3,527 patients submitted to abdominal surgeries showed that the rate of complications, mortality and time of hospitalization increased for those in nutritional risk according to NRS-2002⁸.

The authors stressed that it is widely assumed that preoperative nutritional status is determinant for postoperative outcomes in patients submitted to major surgeries. And still that several aspects of nutritional deficiencies can lead to malnourishment⁸. Although many studies have demonstrated that patients in nutritional or sarcopenia risk are in severer conditions and evolve with worst outcomes, no study has compared these two screening scores so far in the same population of patients⁵⁻¹⁰. Therefore, these results can contribute for other questioning about which screening should be used in postoperative clinical practice.

Both screening tools are simple and fast and can be conducted with the patient lying or seated, it is important to emphasize, which optimizes the screening, allowing early interventions to reduce complications and costs. However, the data of this study showed that nutritional risk alone according to NRS-2002 was able to predict postoperative unfavorable outcomes. For these patients, early nutritional intervention to prepare the patient in advance for the elective surgery should be incorporated into perioperative care.

The evidence reinforces that patients in risk of malnourishment according to NRS 2002 and who receive nutritional therapy prior to the operation present fast postoperative recovery with low occurrence of adverse events¹⁶. In 2003, Kondrup et al.¹⁸ showed that surgical patients who presented nutritional risk equal to three points have more benefit with nutritional therapy unlike those with score lower than three points.

Consequently, it is worth mentioning that multi-mode projects of perioperative care as the Postoperative Accelerated Recovery Protocols (ACERTO) recommend within proactive actions the screening of nutritional risk and the beginning of nutritional pre-habilitation for the patients in nutritional risk¹⁶. Although the results found in this study raise more discussions about the oncologic surgical patient's screening, they should be analyzed cautiously. The sample was heterogeneous according to the tumor type and location.

The sample size can also have influenced the results found in the percentage of patients who were in sarcopenia risk mainly. Still, half of the patients were older adults. However, because of the expressive quantity of major surgeries occurring with oncologic patients, nutritional screening is determinant to reduce the operatory morbidity and costs with the surgical patient^{16,21}.

CONCLUSION

In summary, it was possible to conclude that oncologic patients in nutritional risk diagnosed through NRS-2002 were those who had higher risk of infectious complications and death when compared to those without nutritional risk. The diagnosis of sarcopenia risk based in the questionnaire SARC-F was unable to show these associations in oncologic patients submitted to major surgeries.

CONTRIBUTIONS

All the authors contributed for the conception and/or design of the study, collection, analysis and interpretation of the data, wording, and critical review. The authors approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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