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The Impact of Prognostic Nutritional Index in Patients with Colorectal Cancer Undergoing Colorectoanastomosis

[1]Jaqueline Guillén-Martínez, Departamento de Cirugía General, Unidad Médica de Alta Especialidad Número 25, Centro Médico Nacional del Noreste, Monterrey, Nuevo León, México

[2]José F. Rodríguez-Salinas, Departamento de Cirugía General, Unidad Médica de Alta Especialidad Número 25, Centro Médico Nacional del Noreste, Monterrey, Nuevo León, México

Corresponding Author: Jaqueline Guillén-Martínez, Departamento de Cirugía General, Unidad Médica de Alta Especialidad Número 25, Centro Médico Nacional del Noreste, Monterrey, Nuevo León, México

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Abstract

Objective: To determine the impact of PNI on the development of post-surgical complications in patients with colorectal carcinoma undergoing colorectal anastomosis.

Material and methods: This is an observational, analytical, retrospective, non-experimental cohort study in patients diagnosed with CRC with colorectal anastomosis at from January 1, 2021 to January 31, 2023. They are described in means, standard deviations, medians, and interquartile ranges.

Results: Using the chi-square test, a relationship was found for surgical site infection, with age p=0.660, with gender p=1.000, with days of hospitalization p=0.001, and with IPN p=0.116. enteric fistula and PNI p=0.205, and anastomotic leak p=0.397.

Conclusion: There is a relationship between PNI and the development of post-surgical complications in oncological patients with colorectal anastomoses, with an incidence of 18.9% considering a PNI of at least 45 as a cut-off point.

Keywords: colorectal surgery, surgical anastomosis, colorectal cancer

Introduction

Colorectal carcinoma (CRC) is the second most common cancer in Western countries. It is a genetically heterogeneous disease that is generated from at least 3 main oncogenic pathways: chromosomal instability, microsatellite instability and the methylator phenotype. Each pathway produces different clinical phenotypes that can overlap with each other. Likewise, these pathways can be represented in sporadic CRC and hereditary CRC syndromes.[1-5]

Multiple screening methods have been considered, such as fecal occult blood testing, immunohistochemistry in fecal occult blood testing, computed tomography colonography, capsule endoscopy, flexible sigmoidoscopy, and double-contrast barium enema. Colonoscopy is a primary screening option and the follow-up exam par excellence: it is considered the gold standard in screening programs, although the cost and poor accessibility of these studies limit their screening potential.[3] Currently more than 80% of patients have advanced stages at the time of presentation (stages III and IV), the incidence of mortality in Mexico is less than 5/100,000 inhabitants: late diagnosis contributes to low survival and affects quality of life. The 5-year relative survival rate for all cancers diagnosed in 2004-2010 was 68%, and increases to 90% when detected in early stages.[4-6]

Among tumors of the gastrointestinal system, malnutrition has been found to be more common in CRC due to the direct effects of intestinal occlusion and malabsorption. In addition, it has been associated with higher 30-day postoperative mortality and longer hospital stay.[7-9]

Classically, hypoalbuminemia has been considered one of the markers of patient malnutrition, which is why it has been related to a worse prognosis, both in tumor and non-tumor diseases. Within cancer processes, and specifically in CRC, hypoalbuminemia has been postulated as a predictive factor of postoperative complications such as prolongation of ileus, suture dehiscence or infection of the surgical wound. In recent years, and in addition to its influence on nutritional status, albumin has gained importance as an acute phase protein, included in the patient's systemic response to CRC, and therefore possibly involved in prognosis.[10]

Within tumor development, the growth of malignant cells occurs as a result of interactions between the tumor, host-derived stromal tissues including blood vessels, and immune/inflammatory cells, with chronic inflammation playing an important role in tumor progression. In the last 10 years, systemic inflammatory response markers including C-reactive protein (CRP), hypoalbuminemia, Glasgow prognostic score (GPS, which is combined with CRP and albumin), and white blood cells or their components (neutrophils, neutrophil/lymphocyte ratio and platelet/lymphocyte ratio) have been investigated as prognostic and predictive markers in different cancer populations with the best evidence of their use demonstrated in surgical patients with CRC.[11] In addition to these prognostic markers, the prognostic nutritional index (PNI) that has been widely used, due to its efficiency, simplicity and convenience in the evaluation of preoperative conditions and in the prediction of surgical risk for patients with gastrointestinal malignancy.[12] Some studies have reported that Cancer progression and prognosis are determined not only by tumor characteristics but also by nutritional and immunological conditions.[12-15] PNI, calculated from serum albumin levels and peripheral lymphocyte count, reflects both the nutritional status as well as the immune status of the patient.[16-17] Many recent studies demonstrate that PNI is a significant prognostic indicator for some malignancies[18], including hepatocellular carcinoma[19], pancreatic cancer[20], laryngeal cancer[21], renal cell carcinoma[22] and gastric carcinoma[23]. Although several studies on PNI have evaluated prognosis[24,25], few studies have actually explored the prognostic role of PNI in patients with CRC. PNI was first suggested as a nutritional index and a predictor of surgical risk by Buzby et al. in 1980 and

was corroborated by Onodera et al. in 1984.[16,26-27] It has since been further investigated, with numerous recent studies demonstrating that low PNI is an independent adverse prognostic factor for short-term postsurgical complications and long-term outcomes in many different classes of cancer, for example: gastric, colorectal and esophageal cancer. A low PNI was initially linked as a predictor of high risk of short-term post-surgical complications in the gastrointestinal tract. Recently, it has been shown that a low PNI has also been related to lower survival in several types of malignant tumors.[28] In previous reports, various cut-off values have been used for PNI. Some Japanese authors set the cutoff at 40 for patients with colorectal cancer.[26,29] Ikeya found that the optimal cutoff value was 44.5 according to their analysis curve.[30] However, for other types of malignant tumors, most Studies determine a value of 45, since a PNI <45 was considered malnutrition and was accompanied by a high risk of postoperative complications.[28]

On the other hand, PNI is statistically significantly related to worse pathological staging, that is, to more advanced disease in terms of local invasion, pathological lymphadenopathy or distant metastasis.[28,31] It is a variable that independently and statistically significantly influences the oncological prognosis of various cancers, with worse overall survival and disease-free survival being obtained the lower its value.[19,32,33] Likewise, it is inversely linked proportional with a higher rate of complications after curative surgery for CRC, especially for serious and infectious ones, although there are still very few published articles.[8,24,25] statistically significant with a worse anatomopathological staging, that is, with a more advanced disease in regarding local invasion, pathological lymphadenopathy or distant metastases.[28,31] It is a variable that independently and statistically significantly influences the oncological prognosis of various cancers, with worse overall survival and disease-free survival being obtained the lower its value.[19,32,33] Likewise, it is inversely linked to a higher rate of complications after curative surgery for CRC, especially for serious and infectious complications, although there are still very few published articles.[8,24,25]

Postoperative complications are one of the main points of concern for the surgeon, since they not only influence the patient's quality of life in the short term, but have been observed to affect the long-term oncological prognosis.[34] In patients undergoing surgery, curative surgery for CRC, there is a small number of studies that analyze the effect of prognostic markers on morbidity and mortality. The vast majority of them are retrospective and only use one or two of them, focusing preferably on global and serious complications, such as infectious complications, anastomotic leak and prolonged postoperative stay, among others.[35]

As a prognostic factor, presurgical PNI has the advantage of being easily available, since serum albumin and total lymphocyte count are standard parameters commonly evaluated in the hospital. A low PNI is relevant, since it has been associated with postsurgical complications, prolonged hospital stay, poor oncological outcomes, and aggressive tumor phenotypes.[36]

The PNI can predict the results of colorectal cancer (CRC), in addition, some work has been carried out with the main objective of associating it with TNM staging. Yang et al. retrospectively analyzed a cohort of patients from the Department of Surgical Oncology of the First Hospital of China Medical University (CMU-SO). The Bayesian Information Criterion (BIC) was used to determine the optimal PNI cut-off values for classifying prognosis in CMU-SO patients. The CMU-SO result

confirmed that low PNI was significantly associated with poor prognosis and advanced stages of TNM. Among CMU-SO patients, the optimal cutoff values were "41-45-58" (PNI < 41, 41 ≤ PNI < 45, 45 ≤ PNI < 58, PNI ≥ 58), which divided the patients into 4 stages. The BIC value for TNM staging combined with PNI was lower than that for TNM staging alone (-325.76 vs. -310.80). In conclusion, low PNI was predictive of poor prognosis and was associated with clinicopathological characteristics in patients with CRC and the four-stage division of 41-45-58 may be appropriate to determine prognosis.[37-40]

Material and methods

It is an observational, analytical, retrospective and non-experimental cohort study in patients diagnosed with CRC with colorectal anastomosis from January 1, 2021 to January 31, 2023. Sampling is non-probabilistic, for consecutive cases. The IBM SPSS statistical package, version 20.0, was used.

Inclusion criteria

Patients with a diagnosis of colorectal carcinoma at any stage. Adult patients from 18 to 80 years old. Patients who underwent tumor resection and colorectal anastomosis were performed at our clinical center between January 2021 and January 2023.

Exclusion criteria: Patients with infectious processes prior to intervention. Patients in whom resection and terminal stoma were performed. Patients with intestinal fistulas prior to intervention. Patients with diagnoses other than colorectal carcinoma. Patients with immuno deficiencies.

Elimination criteria

Patients whose file is incomplete. Patients without laboratory test results required for the calculation of the prognostic nutrition index (serum albumin and lymphocytes)

The present research study was carried out in accordance with the internal institutional regulations, with the ethical standards of the Regulation of the General Health Law on Research and with the Declaration of Helsinki in its last modification by the General Assembly in October 2013, as well as such as current international codes and standards of good clinical research practices. Patient confidentiality was preserved, in favor of care, safety and well-being. The principles contained in the Tokyo amendment, Nuremberg Code, the Belmont report, the procedure for the evaluation, registration, monitoring, amendment and cancellation of research protocols presented to the local health research committee and the local committee were respected. of research ethics 2810-003-002 of 2018, and in the United States Code of Federal Regulations and is authorized by the ethics committee.

Results and Discussion

The statistical analysis of the quantitative variables was carried out through measures of central tendency and dispersion. These variables were: age with a mean of 63 years, days of hospitalization with a mean of 4 days and the prognostic nutritional index (PNI) with a mean of 47.8. The study of absolute and relative frequencies was carried out for the independent variables. For the prognostic nutritional index, a distribution by category of 21.6% for malnutrition, 40.5% for mild malnutrition and 37.8% for normal nutritional status was found. Likewise, a relative frequency of 10.8% for the INP value of 52. Regarding the days of hospitalization, a relative frequency of 75.7% for 4 days. And in the age variable, a frequency of 8.1% for ages 66 and 78 each.

Statistical analysis of absolute and relative frequencies was carried out for the qualitative variables. These being variable by gender (43.2% female and 56.8% male) and post-surgical complications for their presence or absence (n=37,18.9% presented complications). Subsequently, a breakdown of frequencies was carried out for the types of post-surgical complications.

The types of complications were found with an absolute frequency of 4 patients for surgical site infection (n=37, 10.8%), and the rest with a frequency of 1 patient (n=37, 2.7%) for each variable.

The association of nominal variables was evaluated by non-parametric tests, in this case, Pearson's chi square except when the assumption that the expected number of troops was greater than 5 in more than 80% of the cells was not met; Then, Fisher's exact test was performed in 2x2 contingency tables, considering a statistical significance of p= <0.05. However, not all cross tables met the characteristics for chi square or the Fisher test; in this case, the value of the likelihood ratio was chosen, which was used when the data set was too small to meet with the assumption of sample size suitable for chi square. A cross-table study was performed for post-surgical complications. The nutritional prognostic index was converted to an ordinal variable when it was defined according to the nutritional status it represented (normal, mild malnutrition, and malnutrition).

Chi square tests were performed in cross tables for each post-surgical complication, it was found for surgical site infection (n=4): with age p=0.660, with gender p=1.000, with days of hospitalization p=0.001 and with the INP p=0.116. Enteric fistula (n=1), reflected for age p=1.000, with gender p=0.432, in days of hospitalization p=0.497 and for INP p=0.205. In anastomotic leak (n=1), it was related to age p=1.000, to gender p=1.000, to days of hospitalization p=0.108 and to INP p= 0.397. Finally, for intra-abdominal abscess (n=1), it was found for age p=1.000, with gender p=1.000, in days of hospitalization p=0.108 and for INP p=0.397.

The bivariate analysis of Independence was carried out, according to the dependent variable (surgical complications) with the independent variables, and the same study was repeated for each type of postsurgical complications. The results are shown in Table 1.

The PNI of the 37 patient patients was identified and the frequency and type of complications could be determined. An average INP of 47.8 was found. Cut-off points were made at <45 (malnutrition) which corresponds to 21.6%, 46 to 50 (mild malnutrition) which covers 40.5% and more than 50 (normal) which was 37.8%. The average of the population was found in the category of mild malnutrition in terms of age, an average of 63 years (26-89). With an average hospitalization of 4.97 days (3-11). 56.8% were male patients and 43.2% were female patients. It can be stated that there is a relatively equal distribution between both genders. According to the presence of complications, 18.9% of the population had post-surgical complications and 81.1% had no complications. Compared to other groups studied, the group of Tokunaga et al. obtained an incidence of 34.2% of complications from 556 patients studied, of which 15.3% presented severe complications. Patients with severe complications presented a lower PNI than those who did not present complications (p=<0.001). Compared to this study, the sample presented a lower incidence of complications (18.9% vs 34.2%) but in this work it was not The differentiation of severe complications was emphasized and the sample available was smaller.

The correlation between the NPI and the presence of postsurgical complications was performed using the likelihood ratio test with a result of p=0.020. Which indicated the direct relationship between nutritional status and the presence of complications. With a total of 7 patients with complications, 5 presented mild malnutrition (71.4%), 2 patients with malnutrition (28.6%). Thus, patients with mild malnutrition and malnutrition are more likely (18.9%) to present postsurgical complications in the first 30 postoperative days compared to patients with normal nutritional status. According to Ikeya's studies, their cut-off point for NPI was 44.5, on the other hand, Nozoe et al. us6 a cut-off point of 40 in this study, the value is similar if only patients with malnutrition are taken into account, but the cut-off point used is higher and is subdivided into malnutrition and mild malnutrition (where more complications were found). Therefore, it is concluded that the NPI related to the presence of complications is due to a higher rate than the two studies that are compared. Thus, in the classification used in this study, where the group with normal nutritional status did not present complications, it is more appropriately related to other authors, such as Liang et al. that found that NPI was predictive of poor prognosis was with a four-stage division with NPI of 41-45-58. In this work, 78.3% of the patients correspond to an NPI >45, covering a significant proportion of those patients who presented complications in this range. Therefore, cut-off points less than 45 cannot be considered as a standard for nutritional status, but rather a higher value. It is concluded that larger studies would be required to determine the best INP value corresponding to a significantly low nutritional status.

In the study of postsurgical complications in relation to age and gender, it was not significant. According to the experience of Tokunaga et al. expressed a relationship with the male sex and the presence of severe postsurgical complications, presenting an incidence in this gender of 20.6% and 7.5% in females. It is possible that this discrepancy is related to the size of the sample of this work. In the analysis of the relationship between complications and days of hospitalization, the likelihood ratio test was performed with p= <0.001. By which, the fewer days of hospitalization (<4), the lower the probability of presenting surgical complications in the first 30 postoperative days.

4 complications were identified within 30 days of post-surgery: 4 patients with surgical site infection (10.8%, n=37), 1 patient with enteric fistula (2.7%, n=37), 1 patient with anastomotic leak (2.7%, n=37), and 1 patient with intra-abdominal abscess (2.7%, n=37). Surgical site infection was the most frequent complication, it was related to age, gender, days of hospitalization and PNI, a significant result was only found with days of hospitalization. Enteric fistula, anastomotic leak and abscesses did not demonstrate significant relationships with the independent variables.

Certain limitations were found, the data were obtained retrospectively from a single institution; Only preoperative INP was considered, not postoperative INP, which could be relevant to assess the real nutritional status at the time of development of complications and whether surgery modifies the determining values of INP.

Conclusion

An PNI less than 50 is associated with postsurgical complications and reflects a nutritional state of malnutrition, and finally, performing curative surgery for CRC only in patients who have an adequate PNI is a

protective factor for the presence of postsurgical complications.

In this study, surgical complications were found in patients with INP >45 and <50, so it can be assumed that an INP of at least 45 could be considered as a cut-off point.

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Legend Tables

Table 1: Clinical characteristics and postsurgical complications in 37 patients undergoing colorectal anastomosis surgery for colorectal cancer

Post-surgical complications				
Study variables	Total (n=37)	Si (n=7)	No (n=30)	p
Age (years)	63 (26-89)	65(38-89)	63(26-87)	0.449
Gender				1.000
Female	16 (43.2%)	3 (42.9%)	13(43.3%)	
Male	21 (56.8%)	4 (57.1%)	17 (56.7%)	
Hospitalization days	4 (3-11)	8.8 (5-11)	4 (3-7)	< 0.001
Prognostic nutritional index				0.020
Malnutrition	8 (21.6%)	2 (28.6%)	6 (20%)	
Mild malnutrition	15 (40.5 %)	5 (71.4%)	10 (33.3%)	
Normal	14 (37.8%)	0 (0.0%)	14 (46.7%)	
Post-surgical complications				
Surgical site infection	4 (10.8 %)			
Enteric fistula	1 (2.7%)			
Anastomosis leak	1 (2.7%)			
intra-abdominal abscess	1 (2.7%)			

The range (quantitative variables) and the percentage (qualitative variables) are shown in parentheses. Gender and prognostic nutritional index are represented in number of patients. The distribution of each postsurgical complication is described.