

ORIGINAL ARTICLE

Prognostic Nutritional Index as a Predictor of Postoperative Outcome in Patients with Gastrointestinal Malignancies

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ABSTRACT

Background: Nutritional status of patients plays an important role in post-operative recovery. A preoperative index can help predict the post-operative morbidity and in optimizing the patient's status. This study was done to evaluate the usefulness of prognostic nutritional index (PNI) in identifying patients who are at high risk for developing postoperative morbidity.

Methods: In a retrospective study, data were collected from databases during January 2019 and December 2022 by including all patients who underwent surgery for gastrointestinal malignancies with a curative intent. Univariate and multiple logistic analyses were performed to evaluate the factors which affect the postoperative morbidity.

Results: Data of 182 patients was retrieved from the database. Stomach carcinoma was the most common gastrointestinal cancer of our study. Surgical site infection was the most common complication noted among 33.5% (n=61) of patients. On univariate analysis of the factors which contributed to post-operative morbidity, PNI and American Society of Anaesthesiologists score was found to be significant in assessments. On multiple regression analysis, only PNI was found to be helpful in predicting postoperative morbidity. The area under curve for predicting the postoperative complications in our study was 0.608 (95%CI, 0.525-0.690, $p=0.012$). The cut-off value of PNI was 72.9 with a sensitivity and specificity of 62% and 53.3%.

Conclusion: Encouraging the routine use of PNI in preoperative assessments for patients undergoing gastrointestinal cancer surgery can potentially lead to a better risk stratification, more targeted perioperative management, and ultimately improved surgical outcome.

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Introduction

Gastrointestinal (GI) malignancies (carcinomas of the esophagus, stomach, small bowel, and large bowel) account for 26% of the global cancer burden, and 35% of all cancer deaths worldwide. Despite advances in diagnosis and management, GI malignancies remain one of the leading causes of cancer-related morbidity and mortality and remain a major global health problem (1-3). Resection of the tumor-bearing segment and the draining lymph nodes remains the predominant method of treatment; chemotherapy and radiotherapy are additives in improving the resectable rate and survival rate in advanced GI carcinomas (4-7).

Pre-operative nutrition is one of the crucial determinants of surgical morbidity and mortality. Patients with GI malignancies are usually undernourished at the time of presentation due to poor oral intake, impaired digestion, loss of blood from the ulcerative lesion, protein-losing gastropathy, and paraneoplastic effect on metabolism (8-10). Impaired nutrition causes alteration in the inflammatory response, immunological dysregulation, and delay in healing. Thus, it affects the patient's perioperative outcomes resulting in prolonged hospital stay, high postoperative morbidity, and mortality (11-13). The pre-operative nutritional status is the critical indicator and the important prognostic factor in determining the postoperative outcome of patients with GI malignancies who undergo surgery. Therefore, pre-operative nutritional assessment with proper optimization helps decrease postoperative morbidity and improve long-term survival (14-16).

Several studies have explored the individual nutritional factors that can predict postoperative morbidity and mortality. There are very few indices that use the combination of nutritional factors to assess the pre-operative nutritional status in GI malignancy patients. Prognostic nutritional index (PNI) is one of them studied in the literature (17). PNI estimates the risk of postoperative complications in individual malignancies and is based on patients' serum albumin and total leucocyte counts (TLC). Very few studies have used PNI as a predictor of outcomes in GI malignancies. Our study aimed to assess the effect of pre-operative nutritional status assessed by PNI on the postoperative short-term outcome of patients with GI malignancies.

Materials and Methods

In a retrospective observational study, the validity of PNI in predicting postoperative morbidity in patients of GI cancers who underwent surgery with therapeutic intent was evaluated. Also, the correlation between pre-operative nutritional status

and postoperative complications in patients with GI malignancies who have undergone resections with therapeutic intent were assessed. The inclusion criteria were all patients with GI malignancies who underwent surgical resection with curative intent during the study period; and patients who were older than 18 years. The exclusion criteria were patients whose records could not be traced and those with inadequate record details. Therefore, all patients with GI malignancies who underwent surgery with curative intent from January 2019 to December 2022 in department of surgery at our institute were included.

After ethical committee approval, a list of patients who underwent surgery for GI malignancies with curative intent in the department of surgery was made from operation theatre registers. After that, those patients' medical records were retrieved from the medical record department. Pre-operative variables like height, weight, basal metabolic index, hemoglobin, serum albumin, total leucocyte count, serum urea, and serum creatinine were assessed. Physical variables and laboratory values from the blood test that were conducted within seven days before the surgical procedure were collected. Postoperatively, the collected variables were surgical site infection, anastomotic leak, post-operative intra-abdominal collection, hospital-acquired pneumonia, and urinary tract infection based on Clavien-Dindo classification (18). The PNI was calculated using the formula of

$PNI = 10 \times \text{albumin (g/dL)} + 0.005 \times \text{TLC/cu.mm}$ (17).

Continuous variables were represented as median and range. Differences between groups were assessed using Student's t-test. Categorical variables were represented as proportions and analysed using the chi-square test. The cut-off value of PNI was calculated using receiver operating characteristic (ROC) curve. Statistical analysis was performed using SPSS software (Version 19, Chicago, IL, USA) and $p < 0.05$ was judged to be a statistically significant difference. The ROC curve was used to determine the optimal cut-off values, and the goodness of fit was assessed by calculating the area under the curve (AUC). Univariate and multiple logistic regression analyses were undertaken to identify other factors affecting the patients' short-term outcomes.

Results

In this retrospective study, we retrieved the records of 182 patients who underwent surgery for GI malignancies with therapeutic intent. Study flow as in Figure 1. Among them, gastrectomy was the most common procedure performed in 36.3% (n=66).

The median [Inter quartile range (IQR)] age of the patient was 55 (64, 45) years and 68% (n=124) were male patients. The median (IQR) body mass index (BMI) of the patient was 19.2 (25, 17.5) kg/m², and the mean±standard deviation (SD) of PNI value in our population was 72.69±14.97. Other preoperative variables were shown in Table 1. In our study group, 50.2% (n=90) of patients had at least one complication postoperatively and 2.2% (n=4) expired in the hospital before their discharge.

Surgical site infection was the most common complication noted in 33.5% (n=61) of patients, followed by intra-abdominal abscess in 8.8% (n=16) of subjects (Table 2). On univariate analysis of the factors which contributed to postoperative morbidity PNI and American Society of Anaesthesiologist (ASA) score were found to be significant (Table 3). On multiple regression analysis, only PNI was found to be helpful in predicting the morbidity of the patients (Table 4).

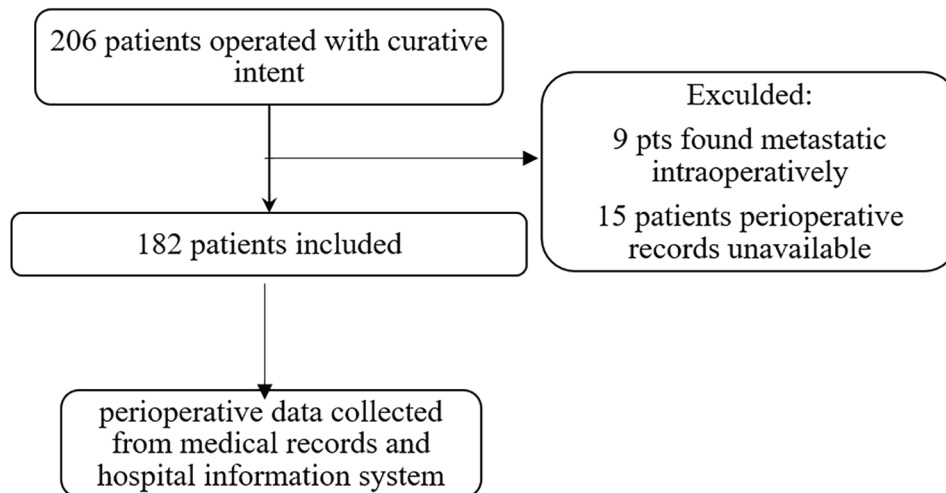


Figure 1: Study flow diagram

Table 1: Demographic and preoperative clinical characters of the patients.		
No.	Variable	N=182 (%)
1.	Age median (IQR: Q3, Q1) years	55 (64, 46)
2.	Sex, male/female	124/58
3.	Smoking	11 (6.0%)
4.	Alcohol	18 (9.9%)
5.	ASA physical status classification	
	Class 1	126 (69.2%)
	Class 2	42 (23.1%)
	Class 3	14 (7.7%)
6.	Diabetes	22 (12.1%)
7.	Hypertension	19 (10.4%)
8.	Cardiac diseases	6 (3.3%)
9.	Pulmonary diseases	7 (3.8%)
12.	Site of malignancy	
	Carcinoma of esophagus	20 (10.9%)
	Carcinoma of stomach	66 (36.2%)
	Carcinoma of colon	35 (19.2%)
	Carcinoma of rectum	35 (19.2%)
	Periampullary carcinoma	24 (13.8%)
	Miscellaneous	2 (1.1%)
13.	Hemoglobin (g/dL), Mean (±SD)	10.1 (2.3)
15.	Platelet count, (Lakhs/μL), Mean (±SD)	3.01 (1.2)
16.	Total leucocyte count, median (IQR: Q3, Q1) (Thousand/μL)	7.580 (9.560, 6.135)
18.	Albumin (g/dl), median (IQR: Q3, Q1)	3.3 (3.9, 2.9)
19.	Urea (g/dl), median (IQR: Q3, Q1)	21 (27, 17)
20.	Creatinine median (IQR: Q3, Q1)	0.7 (0.9, 0.5)

ASA Score: American Society of Anaesthesiology score, IQR:Interquartile range, Q:Quartile, PNI:Prognostic nutrition index, SD:Standard deviation.

Table 2: Postoperative complications following surgery for gastrointestinal malignancies.

No.	Postoperative complications	N=182 (%)
1.	Surgical site infections	61 (33.51%)
2.	Intraabdominal abscess	16 (8.79%)
3.	Pneumonia	14 (7.69%)
4.	Anastomotic site leak	10(5.49%)
5.	Urinary tract infections	8 (4.39%)
6.	Cardiac complications	4 (2.19%)
7.	Septicemia	3 (1.64%)
8.	Deep vein thrombosis	2 (1.09%)
9.	Others ^a	7 (3.84)

A: Upper GI bleeding, Electrolyte abnormalities, Gastroesophageal reflux disease (GERD).

Table 3: Univariate analysis of risk factors for postoperative complications.

Variable	Without postoperative morbidity (n=90)	With postoperative morbidity (n=92)	Odds ratio	95%CI	P value
Age ^a (years)	52.47±12.79	55.88±11.36	-	-	0.058 ^e
Sex	-	-	0.79	0.42-1.47	0.461 ^d
BMI ^b (kg/m ²)	20.7 (22.65, 17.5)	19.5 (21.8, 17.5)	-	-	0.219 ^e
Smoking	-	-	0.53	0.15-1.91	0.332 ^d
Alcohol consumption	-	-	0.98	0.37-2.58	0.961 ^d
Diabetes	-	-	1.2	0.49-2.9	0.689 ^d
Hypertension	-	-	0.53	0.2-1.42	0.207 ^d
Cardiac diseases	-	-	2.0	0.35-11.2	0.682 ^d
Pulmonary diseases	-	-	2.5	0.48-13.3	0.444 ^d
ASA score (≥2)	-	-	0.48	0.23-6.7	0.039 ^d
Haemoglobin ^a (g/dL)	10.08±2.63	10.19±1.98	-	-	0.755 ^e
Total leucocyte count ^b (Thousand/μL)	8.2 (9.6, 6.3)	7.2 (9, 5.6)	-	-	0.25 ^e
Platelet count ^a (Lakhs/μL)	3.0±1.2	2.9±1.2	-	-	0.884 ^e
Albumin ^b (g/dL)	3.3 (4, 2.9)	3.3 (3.7, 2.8)	-	-	0.441 ^e
Urea ^b (mg/dL)	20.5 (27, 16)	21 (26.7, 17)	-	-	0.481 ^e
Creatinine ^b	0.72 (0.9, 0.54)	0.7 (0.8, 0.5)	-	-	0.879 ^e
PNI ^a	75.11±14.4	70.32±15.15	-	-	0.030 ^e

ASA Score: American Society of Anaesthesiology score, PNI: Prognostic nutritional index, CI: Confidence interval, a: Mean±standard deviation, b: Median (Interquartile range, third quartile, first quartile), c: Independent student t-test, d: Pearson Chi-Square test, e: Mann Whitney U test.

Table 4: Multiple logistic regression analysis of risk factors for postoperative complications.

Variable	Odds ratio	95%CI		P value
		Lower limit	Upper limit	
ASA (category≥2)	1.48	0.233	6.7	0.057
PNI (>72.9)	0.979	0.85	0.99	0.044

ASA Score: American Society of Anaesthesiology score, PNI: Prognostic nutritional index, CI:Confidence interval.

The PNI cutoff value in predicting the postoperative complications in our study was 72.9, with AUC for predicting the in-hospital mortality rate that was 0.608 (95%CI, 0.525, 0.690, $p=0.012$), with the sensitivity and specificity of 62% and 53.3%, respectively (Figure 2).

Discussion

Treatment of GI malignancies requires major visceral resection to improve the survival and

has a high risk of postoperative complications. Identifying the patients who are at a high-risk for developing postoperative complications, preoperatively would help in personalising the care and improve the outcomes of the patient (19). In our study, PNI was the only preoperative factor which helped in predicting the patients with high risk of complications. Also in our study, stomach carcinoma was the most common malignancy, followed by carcinoma colon and rectum for

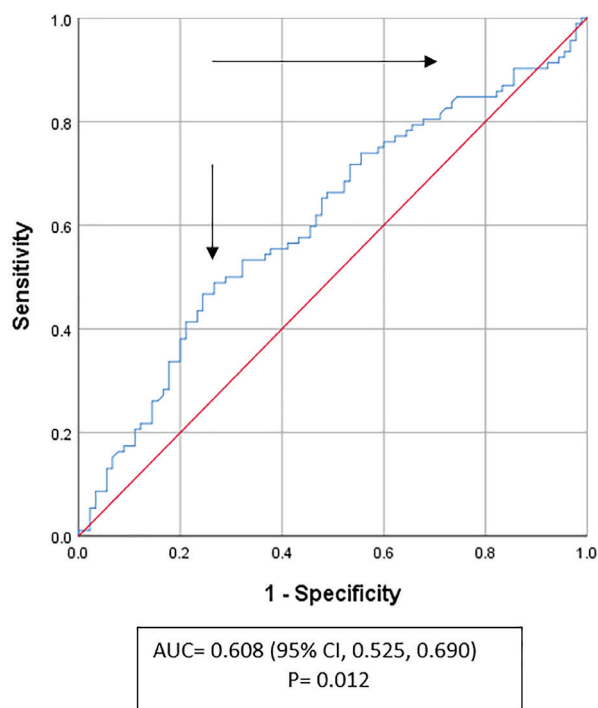


Figure 2: Receiver operating characteristic curve of prognostic nutritional index and in-hospital mortality in patients with gastrointestinal malignancy undergoing surgery.

which curative intent surgery was performed. Carcinoma of colon and stomach are the fifth and sixth most common cancers worldwide, but are the most common GI cancers too (20-22). According to Indian National Cancer Registry Programme, cancer statistic 2020, esophageal carcinoma was the most common GI cancer, followed by carcinoma of stomach, colon and rectum, respectively (23, 24). But, gastric cancer is the most common cancer surgery performed in our center and this may be due to esophageal cancers usually seen in older age, advanced stage, poor nutritional status that lead to lesser number of patients to fit for surgery for curative intent of esophagectomy (25).

Postoperative morbidity following surgery varies widely from 7.2% to 65.5%, depending on the severity of complications, radicality of surgery, surgeon experience and patient factors (26, 27). Cereda *et al.*, in his study revealed complication rate of 65.4%, while 26.9% were severe complications (26). In our study, we observed a complication rate of 50.5%. This high rate of complications is mainly due to consideration of all postoperative derangements and not missing any preoperative factor in predicting the postoperative morbidity. In the literature, several factors have been evaluated as risk factors. In a systematic review by Van Kooten *et al.*, older age, ASA score, male gender, comorbidities, intoxications, nutritional-related risk factors, disease-related factors, and preoperative laboratory test were

reported as main risk factors (28).

In our study, PNI was the preoperative factor found to affect the postoperative morbidity. In patients with GI cancers, some researchers have reported a weight loss among about 79-83% of patients with advanced cancers; while the loss of muscle mass was mainly attributed to anorexia-cachexia syndrome due to these cancers (29). Malnutrition leads to a decrease in healing, an impaired immune response, and a reduction in cardiac and respiratory functions which results in an increase in postoperative morbidity and mortality (30). Hence, nutritional factors are useful in predicting the risk of postoperative complications. In our study, PNI as an index calculated from preoperative albumin level and total leucocyte count represented the nutritional status of the patients and was found to be as a risk factor to influence the postoperative morbidity. PNI is a simple index which can be calculated preoperatively, and helps as a prognostic indicator. This has been evaluated in various cancers like gastric cancer (31), breast cancer (32), lymphoma (33), periampullary carcinoma (34), etc. Our study showed that PNI can be used as a common, independent prognostic factor for postoperative morbidity for all the GI cancers too. There were some imitations in our study including retrospective nature of the study design, evaluating only short-term outcomes without looking onto long-term survival, inclusion of all complications even they do not require intervention, and finally other nutritional factors like sarcopenia, visceral fat area, etc. that were not evaluated.

Conclusion

Nutritional status of patients plays an important role in postoperative recovery of the patients following a complex surgery because of GI cancers. PNI would help identifying these patients who are at higher risk to develop complications. These high-risk patients can be optimised before surgery or personalised for care of these patients to improve the postoperative outcomes.

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Authors' Contribution

UN contributed to the study design, data collection, and manuscript preparation. AS was involved in data collection, data analysis, and manuscript drafting. RA conceptualized and designed the study, supervised data collection, and oversaw the

preparation and submission of the manuscript. RM contributed to the study design and data analysis. CS, USK, AJ, and SG participated in study design, data collection, and manuscript preparation.

Conflict of Interest

The authors declare no conflict of interest.

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