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ORIGINAL ARTICLE

Prognostic Nutritional Index Predicts Perioperative Adverse Events in Patients Undergoing Noncardiac Surgery

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Abstract
Although the relation of preoperative prognostic nutritional index (PNI) with perioperative adverse events has been investigated in patients undergoing cardiac surgery and various solid organ cancer surgeries, it has never been investigated in patients undergoing noncardiac surgery as a distinct group. A retrospective analysis of 811 consecutive patients, older than 18 years old and undergoing an elective, noncardiac, and nonvascular surgery between November 2015 and February 2019 was performed. Patients' information, including demographic data, routine preoperative laboratory tests, and PNI were collected to assess the association between these factors and the perioperative complications. PNI was calculated from the following formula: $10 \times$ serum albumin (g/dL) $+ 0.005 \times$ total lymphocyte count (per mm^3). The outcomes of interest were perioperative complications during hospitalization. The perioperative adverse event rate was 9.0% (73 patients). Older patients and those with more comorbid conditions such as atrial fibrillation, history of malignancy, and diabetes mellitus tended to have a higher rate of perioperative complications. Patients with complicated hospital course had lower albumin (3.1 ± 0.41 vs. 3.7 ± 0.62 g/dL; $p < 0.001$) and PNI levels (45.1 ± 4.4 vs. 51.8 ± 5.8; $p < 0.001$) at admission compared to patients without complications. Multivariate analysis showed that age (OR, 2.13; 95% CI, 1.14–4.45; $p < 0.01$), PNI < 47.5 (OR, 2.51; 95% CI, 1.19–5.46; $p = 0.005$), and history of malignancy (OR, 3.11; 95% CI, 1.14–5.33; $p < 0.01$) were significant and independent predictors of perioperative complications. This study demonstrated that the lower preoperative PNI is associated with increased rate of perioperative complications in patients undergoing noncardiac surgery.

Keywords Prognostic nutritional index · Noncardiac surgery · Prognosis

Introduction

Preoperative assessment of patients before noncardiac surgery is common in the clinical practice of the anesthesiologists, cardiologists, and surgeons. Nowadays, the elective surgical population has grown older and more informed over time, and this trend is likely to continue as the surgical population ages [1]. Although noncardiac surgery has made substantial advances in treating diseases and improving the patient's quality of life, such surgery is associated with significant morbidity and mortality [2]. Therefore, risk stratification has an important role in the preoperative evaluation of patients prior to noncardiac surgery [2]. Patient-specific factors and the risk of the surgery itself are the major determinants of perioperative complications, but numerous studies also examined the prognostic value of several risk scores, comorbidities, and clinical or laboratory variables for the risk prediction of patients undergoing noncardiac surgery [3, 4]. These studies revealed that the preoperative health condition is an important consideration when deciding whether or not it is safe to proceed with noncardiac surgery especially in elderly patients.

Nutritional condition, which reflects patients' health status, has emerged as an important preoperative risk factor in the last decades since nutritional status can be corrected prior to surgery [5, 6]. Thus, it has been assessed widely in the literature with regard to the outcomes of various surgical procedures [5,

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6]. While several tools for assessing nutritional status have been evaluated, most of these tools are difficult to use in daily clinical practice due to their complexity. On the other hand, the prognostic nutritional index (PNI) can be easily calculated with parameters that are routinely evaluated in laboratory tests during preoperative diagnostic workup [7].

The PNI is based on serum albumin concentration and total peripheral lymphocyte count, and it was originally proposed to assess the perioperative risk in patients undergoing gastrointestinal surgery [8]. The utility of the PNI in predicting postoperative complications has been reported only in specific types of surgeries and only in a variety of specific surgical populations such as elderly patients undergoing cardiac surgery [9], patients undergoing hepatectomy for hepatocellular carcinoma [10], and elderly patients undergoing gastrectomy for gastric cancer [11]. To the best of our knowledge, there has been no study evaluating the significance of PNI in predicting outcomes in patients undergoing any type of non-cardiac surgery. We, therefore, aimed to assess the value of preoperative PNI as a predictor of perioperative complications in a large cohort of unselected patients undergoing elective noncardiac surgery.

Methods

Study Design and Patients

This was a retrospective, observational, and single-center study. The second (and following) surgeries on the same patient were not included in the present study. A total of 3620 consecutive patients aged 18 years or older underwent elective noncardiac surgery between November 2015 and February 2019. Cardiac, vascular, and intrathoracic surgeries were not performed in our institution. Of the 3620 patients, 1170 were excluded because of incomplete data, 754 were excluded due to emergent surgery, 385 were excluded because they were younger than 18 years of age, 301 were excluded due to day-case surgical procedures which were considered to be very low risk, and 99 were excluded due to having an American Society of Anesthesiologist Physical Status Score (ASA-PS) of 5 (moribund, not expected to live 24 h irrespective of operation). One hundred patients were also excluded due to chronic or infectious disease or due to taking immunosuppressive drugs for disease control that may influence the status of albumin and lymphocyte counts (Fig. 1). Therefore, 811 patients were finally analyzed in this study. Patients undergoing major gastrointestinal surgery (i.e., laparotomy, advanced bowel surgery, gastric surgery), major gynecological surgery (i.e., abdominal hysterectomy, oophorectomy), major open or transurethral urological surgery (i.e., cystectomy, radical nephrectomy, total prostatectomy), major plastic surgery, neurosurgery, major ear/nose/throat surgery, head and neck surgery, and hip or knee surgery were included. The study protocol was approved by the regional ethics committee, and all procedures performed in the study were in accordance with the ethical standards of the institution, and the study required no any formal consent. Definition of demographic variables is presented in the supplementary Table**.**

Measurements

Clinic characteristics, demographic data, comorbidities, and medical history were obtained retrospectively from the medical records. We also collected data from the blood tests performed immediately before surgery, including the level of serum albumin, C-reactive peptide, and total peripheral lymphocyte count. PNI was calculated using the following formula: $10 \times$ serum albumin value (g/dl) + $0.005 \times$ total lymphocyte count in the peripheral blood (per mm^3).

Study Endpoints

The outcome of the study was perioperative adverse events during hospitalization which included death; deep wound infection involving deep tissues, such as facial and muscle layers; major bleeding requiring transfusion; cardiopulmonary complications; thromboembolic events; pulmonary embolism; acute renal injury; pneumonia; cerebrovascular accidents; sepsis; and return to operating room.

The perioperative cardiovascular events were defined as the occurrence of severe arrhythmias requiring treatment, acute heart failure, acute coronary syndrome (non-fatal acute myocardial infarction or unstable angina), pulmonary thromboembolism, non-fatal cardiac arrest, and arterial thromboembolism. Perioperative myocardial infarction was defined when there is an acute myocardial injury with clinical evidence of acute myocardial ischemia and with detection of the rise and/or fall of cardiac troponin values with at least one value above the 99th percentile upper reference limit and presence of symptoms of myocardial ischemia or new ischemic ECG changes. Arterial thromboembolic events were defined as any symptomatic systemic embolism except cardioembolic stroke confirmed by arteriography, magnetic resonance angiography, spiral computed tomography imaging, or Doppler studies.

The perioperative acute renal injury was defined by the RIFLE (risk, injury, failure, loss of function, and end-stage kidney disease) criteria using the maximal change in serum creatinine and estimated glomerular filtration rate during the first 7 postoperative days compared with the baseline values before surgery. The glomerular filtration rate was estimated by using the Chronic Kidney Disease Epidemiology Collaboration formula.

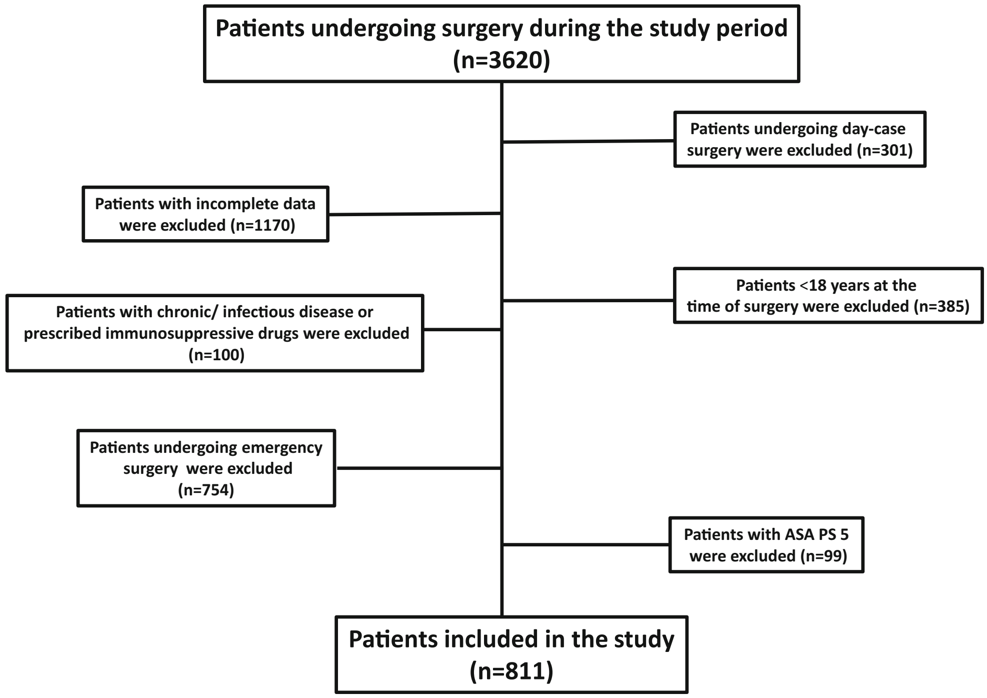

Fig. 1 Flow chart of patients including exclusion criteria. American Society of Anesthesiologist Physical Status Score (ASA-PS)

Statistical Analysis

Data were analyzed using SPSS for Windows (version 15; SPSS Inc., Chicago, IL). The continuous variables were expressed as mean ± standard deviation and were compared between groups by 2-tailed Student *t*-test. Nonparametric tests were also used when necessary (Mann-Whitney *U* test). Fisher exact ($\chi 2$) test was used in comparison of categorical variables. Comparing the patients' characteristics from two groups (patients with and without perioperative complications) was done by using the Chi-square test. Statistical differences among groups were tested by one-way analysis of variance and Kruskal-Wallis tests for parametric and nonparametric variables, respectively. Univariate and multivariate logistic regression analyses were applied to determine the crude and adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for the relationship between preoperative variables and perioperative adverse events. The PNI cutoff value was determined according to the receiver operating characteristic (ROC) curve analysis. The Youden index, calculated as sensitivity (1 – specificity), was estimated to determine the optimal cutoff value for PNI. For all analyses, $p < 0.05$ was considered statistically significant.

Results

A total of 811 patients who had undergone elective noncardiac surgery (mean age 71.2 ± 9.5 years, and 52% male) were enrolled. The perioperative adverse event rate was 9.0% (73 patients). The demographic, clinical characteristics, and laboratory parameters, including PNI levels in patients with and without perioperative complications, are listed in Table 1. There were no statistically significant differences between groups in terms of gender, the prevalence of hypertension, coronary artery disease, or heart failure. However, older patients and those with more comorbid conditions such as atrial fibrillation, history of malignancy and diabetes mellitus tended to have a higher rate of perioperative complications. Patients with complicated hospital course had lower albumin (3.1 ± 0.41 vs. 3.7 ± 0.62 g/dL; $p < 0.001$) and PNI levels (45.1 ± 4.4 vs. 51.8 ± 5.8; $p < 0.001$) at admission compared to patients without complications. Multivariate analysis showed that age (OR, 2.13; 95% CI, 1.14–4.45; $p < 0.01$), PNI < 47.5 (OR, 2.51; 95% CI, 1.19–5.46; $p = 0.005$), and history of malignancy (OR, 3.11; 95% CI, 1.14–5.33; $p < 0.01$) were significant and independent predictors of perioperative complications.

Predictors of Perioperative Adverse Events

In univariate analysis, older age, presence of diabetes mellitus, atrial fibrillation, chronic renal disease, history of malignancy, preoperative albumin, and PNI levels were associated with perioperative complications. However, multivariate analysis showed that only age (OR, 2.13; 95% CI, 1.14–4.45; $p < 0.01$), lower PNI levels (OR, 2.51; 95% CI, 1.19–5.46; $p = 0.005$), and history of malignancy (OR, 3.11; 95% CI, 1.14–5.33; $p < 0.01$) were significant and independent predictors of perioperative

Table 1 Baseline characteristics of patients with and without perioperative complications

	No Complication ($n = 738$)	Complication ($n = 73$)	p value
Male	385 (52.2)	37 (50.7)	0.141
Age	67.4 ± 7.5	73.7 ± 7.9	0.004
Medical History			
Hypertension	352 (47.7)	35 (47.9)	0.62
Hyperlipidemia	286 (38.7)	25 (34.2)	0.67
Diabetes mellitus	201 (27.2)	24 (32.8)	0.09
Atrial fibrillation	103 (13.9)	18 (24.6)	0.02
Chronic obstructive pulmonary disease	105 (14.2)	14 (19.2)	0.13
Malignancy	86 (11.6)	15 (20.5)	< 0.001
Coronary artery disease	189 (25.6)	18 (24.6)	0.72
Heart failure	105 (14.2)	11 (15.1)	0.48
Laboratory results			
Hemoglobin (g/dL)	12.1 ± 1.54	12.4 ± 1.62	0.42
Albumin (g/dL)	3.7 ± 0.62	3.1 ± 0.41	< 0.001
Creatinine (mg/dL)	1.1 ± 0.38	1.1 ± 0.41	0.54
C-reactive protein (mg/dL)	2.1 ± 2.8	1.9 ± 2.7	0.08
Prognostic nutritional index	51.8 ± 5.8	45.1 ± 4.4	< 0.001

Values are given as mean ± SD or number (percentage)

complications (Table 2**).** The optimal PNI cutoff value was 47.5, corresponding to the maximal Youden index, with a sensitivity of 70.1% and a specificity of 67.7%.

Discussion

In this single-center and observational study of 811 consecutive adult patients undergoing noncardiac surgery, the incidence of perioperative adverse events was 9%. The current study demonstrated an association between preoperative PNI level and perioperative adverse events in noncardiac surgery patients.

Patients undergoing noncardiac surgery are at risk of perioperative medical and surgical complications. The major determinants of these complications are the nature of surgery and patients' risk scores [12]. Recent data have revealed that malnutrition has been also associated with increased risk of perioperative complications such as perioperative infection, longer hospital stays, and worse outcome in a variety of patient populations undergoing cardiac or noncardiac surgery [13–15]. Many assessment tools are used to evaluate patients' nutritional status in the previous studies, but those tools are rarely used in daily practice due to their complexity.

Preoperative serum albumin levels have been established markers for nutrition, and hypoalbuminemia, measured by an albumin level less than 3.5 g/dL, has been widely used to determine patients' nutritional status in previous studies [16, 17]. However, the evidence from previous studies is controversial, as some studies have suggested that lower serum albumin as the sole parameter for malnutrition would have low specificity for identifying nutritional status and malnutrition would be underdiagnosed when using hypoalbuminemia as the sole criterion [18]. The PNI is a simple marker of malnutrition which is calculated by using two parameters: the total lymphocyte count in peripheral blood and the serum albumin concentration [19]. Moreover, PNI is not only a marker of nutritional status but also reflective of immunologic status as it contains lymphocyte and albumin levels in the same formula. The previous studies have shown that PNI is a useful marker not only to identify patients at increased risk for postoperative complications but also to predict long-term survival after several surgical procedures [20, 21]. Lee et al. retrospectively reviewed data from a prospectively maintained database of 7781 gastric cancer patients who underwent gastrectomy and found that only low PNI and medical comorbidity were independent predictors of postoperative mortality [20]. Zhou et al. investigated the clinical significance of PNI in glioblastoma

Table 2 Multivariate analysis for the prediction of perioperative complications

	OR	95% CI	P
Age (per 1 y)	2.13	1.14–4.45	< 0.01
Atrial fibrillation (presence vs absent)	1.02	0.44–3.21	0.58
Malignancy (presence vs absent)	3.11	1.14–5.33	< 0.01
Prognostic nutritional index < 47.5	2.51	1.19–5.46	0.005

multiforme and found that a PNI > 44.4 was an independent prognostic parameter of overall survival [21]. However, the prognostic impact of PNI in patients undergoing surgery has been evaluated mostly in cancer patients, and the value of preoperative PNI in an unselected cohort of patients undergoing noncardiac surgery remained unexplored [20–23]. In the present study, we explored the prognostic accuracies of PNI and each of its components—albumin levels and total lymphocyte counts. Although, albumin and total lymphocyte counts did not independently predict perioperative complications, PNI was a significant and independent predictor of perioperative complications according to multivariate analysis. Our result suggest that the preoperative impaired immunonutritional status, determined by low PNI, may result in more perioperative complications and poorer prognosis in adult patients undergoing elective noncardiac surgery. Theoretically, noncardiac surgery patients with malnutrition can benefit from the correction of preoperative immunonutritional disorders.

Limitations

This study has several limitations. First, the retrospective cohort did not include information on the detailed biochemical measures. Second, this study included only patients aged ≥ 18 years undergoing nonemergent noncardiac surgery. Therefore, caution should be taken in extrapolating these results to other surgical populations.

Conclusions

The relation of preoperative PNI with perioperative adverse events has never been described in unselected patients undergoing noncardiac surgery. Our study revealed the prognostic significance of PNI in patients undergoing noncardiac surgery including major gastrointestinal, gynecological, urological, head/neck, plastic, and orthopedic surgery. These results suggest that impaired nutritional status of the patients has affected the surgical outcome after noncardiac surgeries and preoperative measurement of PNI can help identify patients at high risk for of perioperative adverse events after noncardiac surgery. The estimation of the PNI is inexpensive and easily available from the laboratory data in daily clinical practice, and we suggest that the PNI should be calculated routinely before surgery, and it could be a useful indicator for pretreatment nutritional management in adult patients undergoing elective surgery. Assessing the preoperative nutritional status by PNI may help to adopt early nutritional interventions to patients at high risk of developing postoperative complications.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no competing interests

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