Effectiveness of prognostic nutrition index in predicting outcomes after whipple procedure in pancreactic head cancer

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Abstract

Introduction: Pancreatic cancer is associated with poor outcomes, and surgery is the only curative treatment for pancreatic head cancer, though prognostic factors are limited. This study aims to evaluate the effectiveness of the Prognostic Nutritional Index (PNI) in predicting outcomes in a Vietnamese population undergoing the Whipple procedure.

Patients and Methods: A total of 89 patients who underwent the Whipple procedure for pancreatic head cancer between January 2013 and August 2020 at Viet Duc University Hospital were included. The patients were classified into two groups based on their PNI: <50 and ≥ 50.

Results: Statistically significant differences were observed between the two groups in terms of lymphocyte count (1.6 ± 0.6 vs. 2.2 ± 0.7) and albumin levels (36.8 ± 3.9 vs. 42.4 ± 2.8) (P<0.05). Complications above grade III were more common in the PNI <50 group (12.5%) compared to the PNI ≥ 50 group (3%). Although the 3-year survival rate was higher in the PNI ≥50 group, the difference was not statistically significant.

Conclusion: Larger studies are needed to confirm the prognostic role of this index in Whipple procedure surgery.

Keywords: Prognostic nutrition index, pancreatic head cancer, pancreaticoduodenectomy.

Introduction

Pancreatic cancer is one of the most aggressive malignancies of the gastrointestinal tract. According to GLOBOCAN 2018, nearly 460,000 new cases and over 430,000 deaths are reported annually worldwide. In Vietnam, the annual incidence and mortality are approximately 1,000 cases each. [1]. Radical surgery with lymph node dissection remains the only curative treatment. Nutritional status is crucial for both early and long-term postoperative outcomes. Recent studies have emphasized the importance of inflammation and nutrition in the pathogenesis, progression, and metastasis of pancreatic cancer [2, 3]. Some prognostic indicators have also been proposed to predict the patients outcomes. Among them, the Prognostic Nutrition

Index (PNI) is one of the simple and commonly applied indicators for systemic immune-nutrition by reflecting the albumin level and lymphocyte count[4]. Our aim is to evaluate the role of the PNI index in short and long-term outcomes after Whipple procedure.

Patients and methods

Participants: Eighty-nine patients who underwent the Whipple procedure with lymph node dissection for pancreatic ductal adenocarcinoma were included in the study.

Location and duration: Viet Duc University Hospital from 1/2013 to 8/2020.

Study design: This was a longitudinal study with convenient sampling.

Inclusion criteria: Patients with histopathologically confirmed pancreatic ductal adenocarcinoma who underwent the Whipple procedure with lymph node dissection. Patients with severe comorbidities affecting postoperative prognosis were excluded.

Surgical procedures: Standard pancreaticoduodenectomy with the pancreatojejunostomy or pancreaticogastrostomy by surgeons preference. Standard lymphadenectomy was performed according to the guidelines of ISGPS - including lymph node (LN) 13 and 17 (peripancreatic), LN8 (hepatic artery), LN12 (hepatoduodenal), LN5 and 6 (supra/infra-pyloric), and LN14b and 14c (superior mesenteric artery); portal/superior mesenteric vein (PV/SMV) was resected if was founded invasive.

Study variables: General characteristics (age, gender, performance status - according to ECOG, BMI). Laboratory results (hemoglobin, white blood cell count, lymphocyte count, bilirubin, albumin). Operation time, length of hospital stays, complications (classified based on Clavien-Dindo classification), overall survival. The PNI index is calculated using the formula (10 * albumin (g/dl) + 0.005 * total lymphocyte count), divided into 2 groups: <50 and ≥50 determined by ROC curve analysis for complications over grade III.

Data analysis: Variables were presented as mean ± SD or percentages. The comparison between groups were analysed using the T-test for quantitative variables and chi-square for qualitative variables. Data collection and analysis were performed using SPSS 25.0 software.

Research ethics: The study obtained approval from the Ethics Committee, Hanoi Medical University.

Results

Table 1. Demographics of study population

Variables	Classification	PNI < 50 (n (%))	PNI ≥ 50 (n (%))	p-value
Sex	Male	32 (57.1)	25 (75.8)	0.077
	Female	24 (42.9)	8 (24.2)	
Age	< 60	28 (50)	25 (75.8)	0.017
	≥ 60	28 (50)	8 (24.2)	
Performance status (n=84)	0	2 (3.8)	3 (9.7)	-
	1	49 (92.5)	28 (90.3)	
	2	2 (3.8)	0 (0)	
BMI	< 18,5	7 (12.5)	2 (6.1)	-
	18,5 - 25	46 (82.1)	32 (93.9)	
	≥ 25	3 (5.4)	0 (0)	

Table 2. Laboratory results and operative characteristics

Variables	Classification	PNI < 50 (n (%))	PNI ≥ 50 (n (%))	p-value
Laboratory results (mean ± SD)	Total bilirubin (umol/l)	178.2 ± 115.7	104.1 ± 116.4	0,005
	Albumin (g/L)	36.8 ± 3.9	42.4 ± 2.8	<0,001
	Hemoglobin	122.9 ± 15.7	134.0 ± 10.4	0,001
	White blood cell	8.4 ± 3.8	7.6 ± 2.0	0,255
	Lymphocyte	1.6 ± 0.6	2.2 ± 0.7	<0,001
T staging	T1,2	3 (5.4)	8 (24.2)	0.066
	T3,4	53 (94.6)	25 (75.8)	
N staging	N0	25 (44.6)	10 (30.3)	0.181
	N1	31 (55.4)	23 (69.7)	
PNI (mean ± SD)		43.3 ± 7.2	53.5 ± 2.8	-
Operation time (minutes)		344.6 ± 101.9	379.6 ± 77.6	0.092
Days of hospitalization		13.9 ± 6.2	14.2 ± 5.3	0.846
Complications over grade III		7 (12.5)	2 (3.0)	0.25
3-year survival rate		7 (12.5)	6 (18.2)	0.46

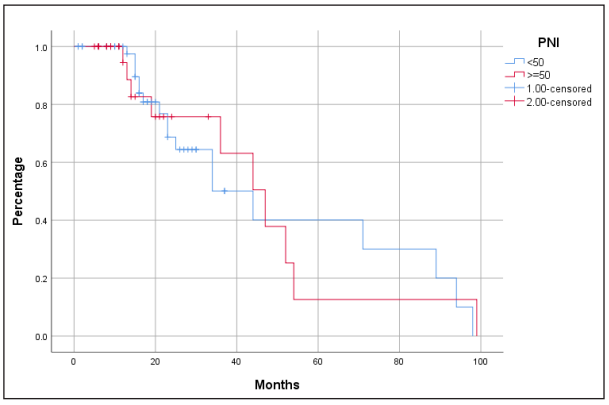

Figure 1. Overall survival and PNI

The proportion of individuals aged 60 and above in the PNI <50 group was higher compared to the other group (50% versus 24.2%), and the difference was statistically significant (p=0.017). Males predominated in both groups (57.1% and 75.8%, respectively), with no significant gender difference. Low BMI was observed in 12.5% and 6.1% of the PNI <50 and PNI ≥50 groups, respectively, while high BMI was 5.4% and 0%, respectively (Table 1).

There were significant differences in the levels of bilirubin (178 vs 104 umol/l), albumin (36.8 ± 3.9 vs 42.4 ± 2.8 g/l), hemoglobin (122.9 ± 15.7 vs 134.0 ± 10.4, and lymphocyte (1.6 ± 0.6 vs 2.2 ± 0.7) between the two groups (p<0.05). The length of hospital stay for the two groups was 13.9 ± 6.2 and 14.2 ± 5.3, respectively, the difference was insignificant. There was a difference in the proportion of complications over grade III between the two groups; however, this difference is not statistically significant (12.5% and 3.0%, p>0.05). Furthermore, there is no statistically significant difference in the proportion of 3-year overall survival (p>0.05) (Table 2, Graph 1).

Discussion

Pancreaticoduodenectomy remains a challenge, even for experienced surgeons because of its aggressiveness, high recurrent and complications rate. More specific, pancreatic head cancer, not other types of periampullary cancer is the most advanced one. Only 10% are eligible for radical resection. Patients were mainly at the advanced stage at the time of surgery, with the rate of obstructive jaundice, low/none tumor differentiation, neural invasion, and nodal metastasis quite high.

The prevalence of malnutrition among gastrointestinal surgery patients in Vietnam ranges from 0-63% [5,6]. In our study, this rate was 10.1%. Our study showed a difference in the age between the two groups, suggesting that older age groups often have poorer nutritional and immune status. The over grade 3 complication rates between the two groups showed no statistically significant differences, although the complication rate in the PNI <50 group in our study was higher. And Whipple procedure surgery remains a complicated operation, so good nutrition support still needs to be prioritized [7].

Previously, individuals over 70 were considered a risk factor for surgery. However, recent evidences showed that patients over 80 undergoing pancreatic surgery have a 30-day mortality rate and overall survival similar to younger patients, although their complication rates are higher [8]. Therefore, advanced age is not an absolute contraindication to surgery and should be thoroughly discussed with patients relatives [8]. Decisions regarding radical surgery for elderly patient groups still need a careful consideration.

The PNI index is based on the values of albumin and lymphocyte count. Albumin is primarily synthesized by liver cells. Low albumin levels indicate poor nutritional status, increasing the risk of postoperative complications and gastrointestinal anastomotic leaks. Some studies suggest that cytokines such as TNF-α are among the pathogenic factors causing malnutrition. Additionally, low albumin reflects poorer immune system responses, suggesting poor prognosis in pancreatic cancer [9]. Furthermore, indicators like lymphocyte count also play a crucial role in the immune system. Low lymphocyte counts reflect a weaker immune response, and are considered a prediction of tumor progression [10].

Some prognostic factors in pancreatic cancer have been demonstrated, including lymph node invasion, neural invasion, chemotherapy... but immunological and nutrition index was recently reported. Our study did not show a significant difference in overall survival between the two groups. This could be due to the retrospective study design, the relatively small sample size, inadequate monitoring of recurrence, postoperative treatment. However, a meta-analysis by Zhao (2023) showed that patients with low PNI had lower overall survival rates (HR=1.664, 95%CI: 1.424–1.944, I2=42.6%, p value=0.046). Although there was a difference in progression-free survival, it was not statistically significant [3]. Additionally, the cutoff value for PNI is not consistent across studies. Other models such as the Glasgow Prognostic Score (GCS), neutrophil-to-lymphocyte ratio... are also being developed to provide appropriate prognosis for patients, showing promising results [11]. Since the annual case is limited, our duration of period was longer. Future studies need to be conducted with larger sample sizes to confirm the role of this index.

PNI, reflecting nutritional index and immune response, was correlated with both short- and long-term outcomes. This underscores the importance of nutritional interventions (oral supplementation (e.g. arginine, omega-3 fatty acid, maltodextrin...), oral feeding with energy-dense formulation or parenteral feeding if enteral feeding provides less than 50% of caloric requirement...) to improve postoperative outcomes [12]. Clinicians should consider incorporating PNI into preoperative assessments to better stratify risk and guide patient management strategies.

Conclusion

The prevalence of malnutrition before Whipple procedure surgery was 10.9%. The rate

of complications from grade III and above was four times higher and the 3-year survival rate was lower in the low PNI group, although the difference was not statistically significant. Larger studies are needed to confirm the prognostic role of this index in Whipple procedure surgery.

References

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. Sep 12 2018;doi:10.3322/caac.21492
2. Dang C, Wang M, Zhu F, Qin T, Qin R. Controlling nutritional status (CONUT) score-based nomogram to predict overall survival of patients with pancreatic cancer undergoing radical surgery. Asian J Surg. Jun 2022;45(6):1237-1245. doi:10.1016/j.asjsur.2021.08.011
3. Zhao P, Wu Z, Wang Z, Wu C, Huang X, Tian B. Prognostic role of the prognostic nutritional index in patients with pancreatic cancer who underwent curative resection without preoperative neoadjuvant treatment: Asystematic review and meta-analysis. Front Surg. 2022;9:992641. doi:10.3389/fsurg.2022.992641
4. Onodera T, Goseki N, Kosaki G. [Prognostic nutritional index in gastrointestinal surgery of malnourished cancer patients]. Nihon Geka Gakkai Zasshi. Sep 1984;85(9):1001-5.
5. Hue PK, Huong LT, Dinh LTK. Nutritional status of patients undergoing peritoneal surgery at the Department of general surgery in Can Tho central general Hospital. Vietnam Medical Journal. 2023;529(1B)
6. Evaluation of patient care results after pancreaticoduodenectomy. Journal of 108 - Clinical medicine and pharmacy. 2020;15
7. Baba H, Sanada T, Goseki N. Preoperative malnutrition is associated with prognosis of pancreatic cancer. HPB. 2011;
8. Melis M, Marcon F, Masi A, et al. The safety of a pancreaticoduodenectomy in patients older than 80 years: risk vs. benefits. HPB. 2012;14(9):583-588. doi:https://doi.org/10.1111/j.1477-2574.2012.00484.x
9. Karayiannakis AJ, Syrigos KN, Polychronidis A, Pitiakoudis M, Bounovas A, Simopoulos K. Serum levels of tumor necrosis factor-alpha and nutritional status in pancreatic cancer patients. Anticancer Res. Mar-Apr 2001;21(2b):1355-8.
10. Grivennikov SI, Greten FR, Karin M. Immunity, inflammation, and cancer. Cell. Mar 19 2010;140(6):883-99. doi:10.1016/j.cell.2010.01.025
11. Li Q, Feng Z, Miao R, Liu X, Liu C, Liu Z. Prognosis and survival analysis of patients with pancreatic cancer: retrospective experience of a single institution. World journal of surgical oncology. Jan 7 2022;20(1):11. doi:10.1186/s12957-021-02478-x
12. Sanchez Leon RM, Rajaraman A, Kubwimana MN. Optimizing Nutritional Status of Patients Prior to Major Surgical Intervention. Methodist Debakey Cardiovasc J. 2023;19(4):85-96. doi:10.14797/mdcvj.1248