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The Usefulness of Nutritional Index CONUT for Risk Assessment and Prognosis after Pancreaticoduodenectomy

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Abstract

Purpose: Pancreaticoduodenectomy (PD) is a highly invasive surgery. Therefore, assessment of pre-operative nutritional status may contribute to the postoperative course.

Methods: Patients (n = 116) who had undergone PD were included in this study. We evaluated the usefulness of the body mass index (BMI), prognostic nutrition index (PNI), and controlling nutritional status score (CONUT) for evaluating post-operative complication risk by examining the relationship between pre-operative nutritional status and the occurrence of post-operative complications such as surgical site infection (SSI) and remote infection (RI).

Results: Eighty-nine of 116 patients (76.7%) developed post-operative complications. Of the 89 patients, who developed complications, SSI and RI occurred in 38 (32.8%) and 23 (19.8%) patients, respectively. Logistic regression revealed the association between the CONUT score and survival in univariate analysis (p = 0.012). BMI was also associated with survival in univariate analysis (p = 0.020). Patients in the high CONUT sore and BMI < 18.5 group, had poorer prognosis compared with Low CONUT score group.

Conclusions: CONUT is a simple and useful marker for identifying patients at increased risk for predicting long-term survival after highly invasive surgery such as PD. Based on our results; we suggest that CONUT should be included in the routine assessment of patients undergoing highly invasive surgery.

Keywords

Pancreaticoduodenectomy, Body mass index (BMI), Prognostic Nutrition Index (PNI)

Introduction

Pancreaticoduodenectomy (PD) is a highly invasive surgery. Evaluation of low nutritional status of pre-operative patients and appropriate nutrition therapy contribute to the improvement of compromised immune function and the reduction of post-operative complications. Although post-operative mortality rates after PD have decreased, morbidity rates remain high, at 30%-88% [1-8]. The pre-operative nutritional and immunological status are not only limited by post-operative complications, but has also been implicated in the long-term prognosis of patients with malignant tumors [9-13].

Table 1: CONUT: a tool for controlling nutritional status.

	Parameter's values			
	Without deficit	With deficit		
		Light	Moderate	Severe
Serum albumin	≥ 3.50	3.00-3.49	2.50-2.99	< 2.50
(Score)	(0)	(2)	(4)	(6)
Total lymphocyte count	≥ 1,600	1,200-1,599	800-1,199	< 800
(Score)	(0)	(1)	(2)	(3)
Total cholesterol	≥ 180	140-179	100-139	< 100
(Score)	(0)	(1)	(2)	(3)
Interpretation				
Total score	0-1	2-4	5-8	9-12
Undernutrition Alert	Nomal	Mild	Moderate	High

The prognostic nutritional index (PNI) was calculated using the following formula: 10 × serum albumin (Alb) + 0.005 × total lymphocyte count (TLC) in peripheral blood. It has been shown to be associated with poor outcomes in various types of malignancies [14-18].

Controlling nutritional status score (CONUT) is one of the suitable nutritional assessment indexes [19-25] for screening malnourished patients. It is a convenient method for evaluating the three elements [proteins (Alb), immunity (TLC), and lipids (T-chol)] and is useful for the pre-operative nutritional assessment of surgical patients (Table 1). In this study, we evaluated the impact of pre-operative nutritional assessments from their correlations with post-operative complications in PD scheduled patients. Next, we investigated the long-term prognosis in patients with malignant tumors of the biliary tract and pancreas.

Materials and Methods

Patients (n = 116) who underwent PD from 2000 to 2014 at the Toyama University Hospital were identified. In this study, we examined the utility of body mass index (BMI), PNI, and CONUT

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for determining the risk for post-operative complications. Factors such as gender, age, cause of disease, operative time, blood loss, and the presence of diabetes were also included. In malignant cases, the final stages of cancer were identified according to the seventh edition of the TNM classification system of malignant tumors as published by UICC.

Complications that occurred within 60 days of surgery were recorded and graded according to the Clavier-Dindo classification [26].

Table 2: Number of patients undergoing pancreatoduodenectomy with complications

Total patients undergoing pancreatoduodenectomy		**116**
Diagnosis		
	Bile duct Cancer	37 (31.9%)
	Ampullary Cancer	19 (16.4%)
	Pancreatic Cancer	60 (51.7%)
Patients with complications		89 (76.7%)
	Post operative pancreatic fistula	37 (31.0%)
	GradeA	11 (8.6%)
	GradeB	26 (22.4%)
	GradeC	0 (0%)
	Delayed gastric emptying	29 (25.0%)
	Anastomic leakage/ulcer	16 (13.8%)
	Atrial fibrillation/Tachyarrhythmia	2 (1.7%)
Infectious complications		66 (56.9%)
	Surgical site infection (SSI)	38 (32.8%)
	Superficial incisional	17 (14.7%)
	Deep incisional	4 (3.4%)
	Organ or Space	17 (14.7%)
	Remote infection(RI)	23 (19.8%)
	Colitis/Ileus	6 (5.2%)
	Pneumonia/ARDS	6 (5.2%)
	Catheter-related bloodstream infection (CRBSI)	7 (6.0%)
	Intraabdominal abscess	5 (4.3%)
	Urinary tract infection	2 (1.7%)
	Sepsis	2 (1.7%)
	Mortality within 30days	0 (0%)

Surgical site infection (SSI)

As defined by the CDC guidelines, SSI was identified when purulent discharges were observed within 30 days from any incision or intraoperatively manipulated space, with or without microbiological evidence of infection [24].

Remote infection (RI)

Presence of pneumonia, cholangitis, urinary tract infection (UTI), enterocolitis, and catheter- related bloodstream infection (CRBSI) within 4 four days or more after surgery.

Pancreatic fistula and delayed gastric emptying

Pancreatic fistula and delayed gastric emptying was defined according to the International Study Group of Pancreatic Surgery (ISGPF) criteria [27-30]. Statistical analyses were performed with using JMP software for Windows (SAS Institute Inc., Cary, NC, USA). To evaluate the relationship between each independent factor and presence of SSI and RI, univariate analysis was conducted using the χ^2 test. Prognostic factors were examined by both univariate and multivariate analyses. Evaluations were performed using the Kaplan–Meier method, and differences between survival curves were analyzed using the log-rank test. A p-value of < 0.05 was considered statistically significant.

Results

The analysis sample consisted of 116 consecutive cases that underwent PD. The average age was 69.7 years (range, 48–87

Table 3: Patient characteristics.

		Overall (n = 116)	Complications (n = 89)	No complications (n = 27)	p value
Patient characteristics					
Age		69.7 (48-87)	71.0 (48-87)	65.4 (48-81)	0.003**
Gender					
	Female	53 (45.7%)	42	11	
	Male	63 (54.3%)	47	16	0.555
Diagnosis					
	Biliary tract	56 (48.3%)	52	4	
	Pancreas	60 (51.7%)	37	23	< 0.001**
BMI					
	BMI < 18.5	14 (12.1%)	11	3	
	18.5 ≦ BMI<25	85 (73.3%)	65	20	
	25 ≦ BMI	17 (14.7%)	13	4	0.985
Preoperative					
PNI		43.8 (25.3-55.1)	43.1	45.6	0.032*
[PNI = (10 × Alb) + (0.005 × TLC)]			(25.3-55.1)	(37.4-53.7)	
CONUT Score					
	Nomal	27 (23.3%)	20	7	
	Mild	62 (53.4%)	47	15	
	Moderate	24 (20.7%)	19	5	
	High	3 (2.6%)	3	0	0.614
Serum albumin		3.62 (1.8-4.5)	3.59 (1.8-4.5)	3.72 (3.0-4.3)	0.157
Total lymphocyte count		1554.2 (360-4670)	1494.2 (360-4670)	1752.0 (410-2720)	0.052
Total cholesterol		157.1 (80-379)	158.5 (80-321)	152.6 (118-379)	0.581
Obstructive jaundice					
	Present	69 (59.5%)	53	16	
	Absent	47 (40.5%)	36	11	0.911
Diabetes					
	Present	37 (31.9%)	26	11	
	Absent	79 (68.1%)	63	16	0.267
Operative					
Length of operation	(min)	534.4 (313-1333)	533.3 (313-1333)	531.6 (344-945)	0.911
Blood loss	(ml)	1000.2 (180-4020)	1003.0 (215-3700)	990.7 (180-4020)	0.931

Table 4: Relationship between the clinical characteristics and infectious complications.

			Infectious Complications			SSI			RI		
			(+)	(-)	P	(+)	(-)	P	(+)	(-)	P
			(n = 66)	(n = 50)		(n = 38)	(n = 78)		(n = 23)	(n = 93)	
Pre operative											
	Age										
		≤ 70	31	31		18	44		11	51	
		>70	35	19	0.107	20	34	0.36	12	42	0.547
	T										
		1/2	20	18		12	26		8	30	
		3/4	46	32	0.518	26	52	0.85	15	63	0.818
	N										
		Absent	30	28		17	41		12	46	
		Present	36	22	0.26	21	37	0.428	11	47	0.816
	CONUT score										
		Nomal	13	15		6	22		3	25	
		Mild/Moderate/High	53	35	0.201	32	56	0.132	20	68	0.144
	PNI										
		< 43.8	29	16		18	27		12	33	
		43.8 ≤	37	34	0.189	20	51	0.188	11	60	0.146
	BMI										
		BMI < 18.5	9	6		5	10		5	10	
		18.5 ≤ BMI	57	44	0.794	33	68	0.96	18	83	0.184
	Obstructive jaundice										
		Present	40	29		25	44		16	53	
		Absent	26	21	0.777	13	37	0.332	7	40	0.265
	Diabetes										
		(+)	19	18		11	26		8	29	
		(-)	47	32	0.410	27	52	0.633	15	64	0.742
	Blood loss										
		< 1000	39	33		22	50		15	57	
		1000 ≤	27	17	0.447	16	28	0.519	8	36	0.727
	Length of operation										
		< 530	36	36		20	52		12	60	
		530 ≤	30	14	0.053	18	26	0.146	11	33	0.279

Table 5: Association between PNI and the prognosis.

Patient characteristics	p value		RR	95%CI	p value
Age (≥ 70 years)	0.63		1.234	(0.710-2.127)	0.447
Sex (Female)	0.687		1.047	(0.620-1.762)	0.863
Diagnosis (Pancreas)	0.054				
Depth of tumor invasion (T1-2)	< 0.001	* *	0.598	(0.270-1.258)	0.598
Lymph node metastasis (Absent)	< 0.001	* *	0.357	(0.186-0.654)	< 0.001
Obstractive jaundice (Absent)	0.036	*	0.771	(0.407-1.425)	0.409
PNI (< 43.8)	0.205				
BMI (< 18.5)	0.018	*	0.523	(0.275-1.081)	0.077
CONUT (Low)	0.013	*	0.677	(0.315-1.350)	0.276
Blood loss (< 1000 ml)	0.138				
Length of operation (< 530 min)	0.058				
Infectious Complications (Absent)	0.038	*	0.656	(0.377-1.109)	0.117

years). In the classification of, the patients diagnosis, there were 60, 37, and 19 cases of pancreatic, bile duct, and Ampulla of Vater cancers, respectively. Table 2 shows the number of patients with complications. Of these, 89 (76.7%) patients had a complication, and mortality rate within 30 days of surgery was 0%. The most frequent complications were pancreatic fistulas (31.0%) and delayed gastric emptying (25.0%). Thirty-five and 27 patients developed SSI (32.8%) and RI (19.8%), respectively (Table 2). Among the 116 patients, 89 patients comprised the complication group (CP) and 27 patients were included in the no complication group (NCP). Pre- and post-operative clinical data including age, sex, BMI, PNI, CONUT score, length of operation, blood loss, and diabetes are reported in table 3. The pre-operative values of the PNI ranged from 25.3 to 55.1 with a mean value of 43.8. Twenty-seven (23.3%), 62 (53.4%), 24 (20.7%), and 3 (2.6%) patients had normal (0–1), mild (2–4), moderate (5–8), and high (9–12), CONUT scores, respectively. In this study, 76.7% of patients were at risk of malnutrition.

Table 4 shows the relationship between the clinical characteristics and infectious complications. No significant differences in the operative characteristics were observed between patients with SSI and RI. Kaplan–Meier analysis revealed significantly less favorable overall survival rate rates in patients in low CONUT group than in the other groups (Log-rank test, p = 0.013). BMI was also associated with survival in univariate analysis (p = 0.018). There was no association between PNI and the prognosis (Table 5). Patients in the high CONUT sore and BMI < 18.5 group, had poorer prognosis compared with Low-CONUT score group (Figure 1).

Discussion

Evaluation of nutritional status may provide additional prognostic information for patients who are undergoing highly invasive surgery such as PD/PpPD. Post-operative infection is the most frequent complication following surgery. Post-operative surgical and medical complications are negative predictors for long-term malignancy outcomes. In this study, postoperative infection was one of the prognostic factors in univariate analysis.

Albumin level is a better predictor of some types of morbidity, particularly sepsis and major infections [31,32]. However, because the albumin level is strongly affected by the body fluid volume and medical condition, it has poor reliability for nutritional status screening. The shorter half-life of albumin is a sensitive reflection of the nutritional status in real time. Nevertheless, the evaluation of the retinol binding protein (RBP), transferrin (Tf), and pre-albumin (PA). levels is often costly. As shown by Onodera et al. PNI is useful for the prediction and prognosis of post-operative complications. In table 2, PNI low value cases were significantly higher in the complication group. The average age of the complication group is also significantly high. For this reason, the elderly are considered to be due to included many complications group.

Compared with biochemical indicators, it has the advantage

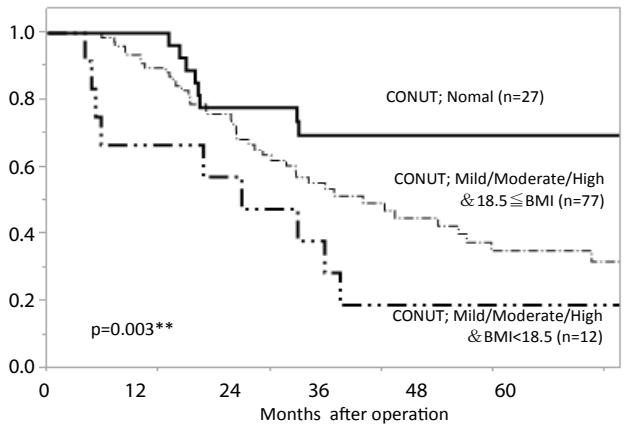

Figure 1: Survival rates according to CONUT score and BMI.

of determining the patient's malnutrition risk. On the other hand, because PNI decreases concomitantly with age, it may not be an accurate measure of malnutrition in the elderly. When it comes to the elderly, due to a decrease in blood albumin value also decreased PNI. It is also one of the factors that elderly patients are included in the significant complications group. In originally reported risk assessment criteria, older patients were evaluated as those at a risk or contraindicated for surgery. CONUT score is calculated in a general three blood sampling results, which are performed in most patients at the time of hospitalization. In this score, it is possible to extract a mild malnourished patients before severe the albumin value decreases. It is capable of selecting the high-risk patients who will require strict clinical management in the immediate post-operative period. BMI, by combining the most easily obtained parameters, it is useful as a prognostic factor as figure 1.

Although various tools for pre-operative nutritional assessment have been studied, only few have shown an association with long-term prognosis in patients after PD. The CONUT scoring method could be a useful and objective screening tool for nutritional condition, and it has also been used for cancer cases. By using a combination of parameters, such as the CONUT score and the subjective comprehensive evaluation (SGA), to understand the nutritional status, it is possible to achieve a more precise nutritional management plan.

Conclusions

There is a high incidence of infection after post-operative PD. It is difficult to use nutritional therapy in the presence of compromised immune function such as organ failure and sepsis. Before complications arise, it is important to detect malnutrition early in order to improve and maintain the nutritional status with the appropriate nutritional management. In addition, the CONUT and BMI scores may be able to predict the long-term prognosis of PD.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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