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Preoperative Hypoalbuminemia as a Predictor of Severe Postoperative Complications in Patients Undergoing Whipple Pancreatoduodenectomy

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ABSTRACT

Background: Pancreaticoduodenectomy (PD) known as Whipple procedure is still one of the most complex abdominal surgeries used for treatment of periampullary tumors. PD is often followed with postoperative complications (pancreatic, biliar or intestinal fistula, haemorrhage, intraabdominal abscess, delayed gastric emptying. Severe postoperative complications (SPC) can be reason for reoperation and reason of bad outcome of treatment and life treathening condition. **Objective:** To investigate predicitive value of preoperative hypoalbuminemia for severe postoperative complications (SPC) in patients who have undergone Whipple pancreaticoduodenetomy (PD). However, no similiar study has been ever reported from our country until now. **Methods:** In this retrospective-prospective study, 100 patients who have had Whipple pancreaticoduodenectomy for malignant periampullary tumors at the Department for Surgery of University Clinic Center Tuzla, Bosnia and Herzegovina were enrolled, from january of 2009 to decembre of 2021. All patients were preoperatively analysed according to serum albumine levels and presensce of hypolabuminemia (serum albumine levels <32g/l). Serum albumine biochemical test were done 1-2 days preoperatively. Clavien Dindo classification was used for determination patients with SPC. Patients who did not have SPC belonged to (I-II) Clavien Dindo group of patients while those who had SPC belonged to(III-V) Clavien Dindo group of patients. **Results:** Out of 100 patients who have undergone pancreaticoduodenetomy, in 55 (55%) patients postoperative complications were noticed. Mortality rate was 18 (18%) and reoperation has been done in 20 cases (20%). SPC were noticed in 19 patients and most often were: delayed gastric emptying (20%), pancreatic fistula (13%) and intraabdominal collections (9%). Hypoalbuminemic patients had a significantly higher rate of severe postoperative complications ($p < 0.05$). Using hypoalbuminemia-SPC correlation analaysis, there is confirmed statistically significant correlation between hypoalbuminemia and SPC ($\rho = 0.236$; $p < 0.05$). **Conclusion:** Preoperative hypoalbuminemia can be used as predictor and prognostic factor for severe postoperative complications after Whipple pancreaticoduodenectomy. Identification and optimization of serum albumin level prior to Whipple pancreatoduodenectomy may improve surgical outcomes.

Keywords: Hypoalbuminemia, Whipple pancreaticoduodenectomy, severe postoperative complications.

1. BACKGROUND

Pancreaticoduodenectomy (PD) known as Whipple procedure is still one of the most complex abdominal surgeries used for treatment of periampullary tumors (1). PD is often followed with postoperative complications (pancreatic, biliar or intestinal fistula, haemorrhage, intraabdominal abscess, delayed gastric emptying (2, 3). Severe postoperative complications (SPC) can be reason for reoperation and reason of bad outcome of treatment and life treathening condition. Postoperative complication rate in high volume surgical centers is less than 15% while in others can reach even 60% (4). Good preoperative preparation and choosing adequate surgery time could be one of the keys for decreasing risk of SPC after PD. Finding excelent preoperative predictors of SPC could help decreasing their number and mortality rate.

Hypoalbuminemia represents decreased level of blood albumine and can be caused with insufficient liver production, increased loss by kidneys and

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gastrointestinal system or irregular body distribution. Decreased albumine level can affect quality of created anastomosis during any surgery (5).

The aim of this study is to determine prognostic value of preoperative hypoalbuminemia for appearance of severe postoperative complications in patients who underwent Whipple pancreaticoduodenectomy.

2. PATIENTS AND METHODS

In this retrospective prospective study, 100 patients who underwent Whipple pancreaticoduodenectomy (open method) for malignant periampullary tumors at the Department for Surgery of University Clinical Center Tuzla, Bosnia and Herzegovina, were enrolled, from January of 2009 to December of 2021. All patients were preoperatively analysed according to serum albumine levels and presence of hypoalbuminemia (serum albumine levels <32g/l). Serum albumine biochemical test were done 1-2 days preoperatively. Clavien Dindo classification was used for determination patients with SPC (6). Patients who did not have SPC belong to (I-II) Clavien Dindo group of patients while those who had SPC belong to (III-V) Clavien Dindo group of patients.

Analysis was performed comparing two groups of patients: a) Patients without SPC b) Patients with SPC, according to presence of preoperative hypoalbuminemia. Including criteria for enrollment of the patients in the study were as follows: a) presence of periampullary malignant tumors who had histopathologic analysis b) malignant periampullary tumors without metastasis c) patients treated only by pancreaticoduodenectomy (Whipple resection) by experienced surgeons. Excluding criteria for this study were as follows a) malignant periampullary tumors with metastasis b) benign tumors of pancreas c) patients treated by some kind of chemoradiologic oncologic palliative procedure. The patients underwent a follow up for 1 month after PD surgery.

Statistical analysis

Statistical analysis was performed using SPSS version 17.0 (Chicago, IL, USA). Continuous data are presented as the means SD and were compared with an unpaired Student test and linear regression analysis. Categorical variables were reported as frequencies (%) and were compared with the Chi-square test or Fisher exact test. Relative risk with 95% confidence intervals (CIs) are presented. Univariate Cox proportional hazard regression models were used to determine prognostic value of variables. The sensitivity and specificity of albumine levels were determined by ROC analysis. Correlation among variables were determined by Pearson's correlation test $p < 0.05$ was considered significant.

Ethical committee approval

The study was approved by the Ethical Committee of University Clinic center Tuzla No: 02-09/ 2-42/21.

Clinical data	Patients with SPC*	Patients without SPC	pa
No. of patients	19	81	
Sex ratio(male/female)	11/8	44/37	n.s.
Age (years)			
Mean (SD)	65.16 ± 8.61**	60.81 ± 9.03	n.s.
Range	49-77	30-78	
Etiology			
Malignant	18/19	72/81	n.s.
Benign	1/19	9/81	n.s.
ASA score			
ASA 1	0/19	1/81	n.s.
ASA 2	4/19	40/81	n.s.
ASA 3	12/19	39/81	n.s.
ASA 4	3/19	1/81	<0.05

Table 1. Characteristics of the patients undergoing pancreaticoduodenectomy. *SPC= severe postoperative complications (Clavien Dindo classification).

** Values are mean ± SD; a unpaired Student's t-test; n.s. = not significant;

Type of complications (after 100 patients with PD)	n (%)	Clavien-Dindo classification	
		Grade I-II n (%)	Grade III-V n (%)
Postoperative pancreatic fistula	13 (13.0)	1 (1.0)	12 (12.0)
Intraabdominal haemorrhage	3 (3.0)	0	3 (3.0)
Biliar fistula	2 (2.0)	1 (1.0)	1 (1.0)
Intestinal fistula	2 (2.0)	0	2 (2.0)
Delayed gastric emptying	20 (20.0)	20 (20.0)	0
Intraabdominal collections	9 (9.0)	8 (8.0)	1 (1.0)
Surgical site infection	6 (6.0)	6 (6.0)	0
Total complications	55 (55.0)	36 (36.0)	19 (19.0)
Reoperation	20 (20.0)		
Mortality	18 (18.0)		

Table 2. Types of postoperative complications after 100 Whipple's pancreaticoduodenectomies.

Variable	Complications		Total n (%)	x ²	df	p
	yes n (%)	no n (%)				
Hypoalbuminemia*	yes 9(9%)	17(17%)	26(26%)	5.567	1	.018*
	no 10(10%)	64(64%)	74(74%)			
Total	19(19%)	81(81%)	100(100%)			

Table 3. Patients with and without hypoalbuminemia distribution according to severe postoperative complications.

3. RESULTS

Out of 100 patients who have undergone Whipple pancreaticoduodenectomy, in 55 (55%) patients postoperative complications were noticed. Mortality rate was 18 (18%) and reoperation has been done in 20 cases (20%). In Table 1 there are demographic and clinical patients data.

Types of postoperative complications and their Clavien Dindo classification after 100 Whipple pancreaticoduodenectomies (Whipple resections) shows Table 2.

Distributions of patients with and without hypoalbuminemia who had SPC are shown in Table 3. Statistical

Variable	Compliacation	
Hypoalbuminemia	Spearman (ρ)	.236
	p	.018*
	n	100

Table 4. Correlation analysis between hypoalbuminemia and severe postoperative complications.

Variable	Value	95% reliability interval	
		Lower border	Upper border
Complication chance ratio (yes / no)	3.38	1.18	9.65
For cohort Hypoalbuminemia = Yes	2.25	1.19	4.25
For cohort Hypoalbuminemia = No	.66	.42	1.03
N	100		

Table 5. Chance ratio for SPC in patients with and without preoperative hypoalbuminemia

analysis (χ^2 test) indicated statistically significant distinctions between these groups ($p < 0.05$).

Using hypoalbuminemia–severe postoperative complications correlation analysis (Table 4), there is confirmed statistically significant correlation between hypoalbuminemia and SPC ($\rho = 0.236$; $p < 0.05$). Realised correlation on the level with 0.05 (95%), shows positive direction and low intensity. Therefore with 95% precision we conclude that preoperative hypoalbuminemia is significant risk factors for outburn of SPC.

Chance ratio results are shown in table 5. Achived results shows that SPC are 3.38 times more often in patients with preoperative hypoalbuminemia (OR=3.38; 95% IP: 1.18- 9.65). It confirms that patients with preoperative hypoalbuminemia have statistically higher risk for SPC than patients without preoperative hypoalbuminemia.

4. DISCUSSION

Whipple pancreaticoduodenectomy still remains only surgical choice for periampullary tumors and despite advances in surgical techniques, postoperative morbidity and mortality are high even today (7,8). Mortality rate after PD has decreased drastically especially in high volume surgical centers over the years (<1,5%) but morbidity remains still high and in some low volume surgical centers range to 50-60 % (9,10). In our study morbidity rate was 55% and mortality rate was 18% which is still high and it correlates with our small annual number of PD surgeries.

The most severe complication after PD is postoperative pancreatic fistula (11-16%) and is the main reason for reoperation and increased mortality rate (11,12,13). In experienced high volume pancreatic surgical centers incidence of postoperative pancreatic fistula (grade C) is under 5% (14,15). In our study 13% of patients had postoperative pancreatic fistula and 12 of them have been reoperated with bad postoperative outcome and high mortality rate. In the study of Lee et al. with 228 patients who underwent PD for pancreatic head cancer,

33 % of patients had preoperative hypoalbuminemia and it is shown that preoperative hypoalbuminemia and prolonged malnutrition impact bad long term outcome and increased morbidity and mortality. SPC are significantly more often in patients with hypoalbuminemia (16). Study of Izumo et al. indicate that except for male gender, high BMI main preoperative risk factors for SPC after Whipple PD is hypoalbuminemia (17). Wellner et al. study for over 1000 patients with pancreatic resections has shown significant impact of preoperative hypoalbuminemia and postoperative haemorrhage and other SPC after PD (18, 19). Our study has proven hypoalbuminemia to be significant independent risk factor for SPC after Whipple PD.

5. CONCLUSION

Preoperative hypoalbuminemia can be used as predictor and prognostic factor for severe postoperative complications after Whipple pancreaticoduodenectomy. This can be used for selection of risk patient groups for severe postoperative complications (SPC) after Whipple pancreaticoduodenectomy, better preoperative preparation and hypoalbuminemia correction and choosing ideal surgery time. Identification and optimization of nutritional status prior to surgery may improve surgical outcomes.

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