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Risk factors of short-term complications after pancreaticoduodenectomy treated periampullary carcinomas

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Abstract: ***Introduction:*** Pancreaticoduodenectomy has been a radical treatment for periampullary carcinoma, which is a collection of malignant neoplasia of the periampullary region. Although the mortality has declined dramatically, the complications are still high. This study aims to determine the occurring rate of short-term complications after pancreaticoduodenectomy and to identify the risk factors related to those complications. Comprehension of these problems help increase the outcome. ***Materials and Method:*** It is a cross-sectional study of the patients with periampullary cancer, who undergo pancreaticoduodenectomy at Cho Ray Hospital from January 2012 to October 2016. ***Results:*** Overall complication rate was 25.65% from 230 patients. In which, pancreatic fistula and surgical site infection were the two most frequent complication (10.43% and 4.38% respectively). Pancreatic fistula was highly significantly associated with Wirsung's duct diameter less than 3 mm (p = 0.015) and soften pancreatic parenchyma (p = 0.004). The soften pancreatic parenchyma also increased the risk of surgical site infection (OR 4.588), but it was not statistically significant (p = 0.056). Soften pancreatic parenchyma increased the haemorrhage complication significantly (p = 0.04) (OR: 10,668, 95% confidence). ***Discussions:*** Pancreatic main duct's diameter, pancreatic density and Hemoglobin may relate to the early postoperative complications following pancreaticoduodenectomy. Detailedly, in particular for pancreatic fistula, 2 risk factors recognized are Wirsung's diameter less than 3mm and soft pancreatic density. Meanwhile low concentration of hemoglobin in blood may increase the risk of incisional infection. Pancreatic density related to the complication of haemorrhage. ***Conclusions:*** Short-term complications' rate following pancreatoduodenectomy remains high. Understanding the risk factors help us choose which case should be operated and do pre-operative preparation better.

Keywords: Pancreatoduodenectomy, Periampullary cancer.

1. INTRODUCTION

Periampullary cancers are a collection of malignant neoplasia of the periampullary region [6]. The 5-year survival rate of periampullary cancers is less than 15% for pancreatic cancer and quite low in ampullary cancer (39%), distal common bile duct's cancers (27%), and duodenum cancer (59%) [1].

Pancreaticoduodenectomy is still the most radical treatment for periampullary cancer nowadays [2]. The mortality rate after surgery has been reduced by less than 2%, but the complications remain high, accounting for 30-50% [5]. Consequently, there are more than 3% of patients had to undergo re-operation or even dead.

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In a study conducted by JP Lerut [10] on 103 patients with pancreaticoduodenectomy in treatment periampullary cancers, the rate of postoperative complication is about 19.4%, of which the pancreatic fistula complication is the most importantly, accounting for 14.5%. Factors related to postoperative complications were age (> 65 years), preoperative total bilirubin> 6 mg / dl, pancreatic parenchyma and the emergency degree of surgery. The complications of postoperative haemorrhage were also analyzed in the study by Sanjay P. et al. [15], suggesting that the related factors were the status of biliary obstruction, pancreatic parenchyma and pancreatic fistula.

In Viet Nam, post operation complications have never been monitored in patients underwent pancreaticoduodenectomy. Most of Vietnamese studies were only focus on the result of pancreatoduodenectomy [9], [13]. From that, we performed this study in order to discover some factors related to complications after pancreatoduodenectomy, especially short – term complications are necessary, to determine the ratio of short-term complications following pancreaticoduodenectomy and identification of the risk factors related to those complications.

2. MATERIALS AND METHOD

This is a retrospective cross-sectional study. Data has been retrospectively collected from medical records of all patients with periampullary cancer, who performed pancreaticoduodenectomy at Cho Ray Hospital from January 2012 to October 2016. Data analysis has been performed using SPSS 22.0. Qualitative variable is expressed in terms of numbers, frequency and analysed by Chi squared test. For descriptive analysis, continuous variables are expressed as mean and standard deviation (SD) and compared between groups using Student's independent samples t test. The impact of complication risk-factors has been evaluated by Odds-ratio derived from a multivariate logistic regression analysis. The difference statistically significant when $p < 0.05$.

3. RESULTS AND DISCUSSION

There were 230 cases that suitable with the selected criteria in the sample. The survey included 109 males and 121 females, average age was 54 ± 11.5 years. Indication of pancreaticoduodenectomy included ampullary carcinoma in 113 cases (49.1%), pancreatic carcinoma in 82 cases (35.7%), distal CBD carcinoma in 31 cases (13.5%), and duodenum carcinoma in four cases (1.74%). Average postoperative hospitalization was 19,7 ± 11.2 days.

Table 1: Complications after pancreaticoduodenectomy

Clinical events / types of complication	Frequency (%) n = 230
Pancreatic fistula	24(10.43%)
Biliary leak	2(0.87%)
Abdominal abscess	2(0.87%)
Haemorrhage	6(2.61%)
Wound Infections	10(4.35%)
Cardiopulmonary complications	1(0.43%)
Re-operation	14(6.09%)
Mortality	5(2.17)
Total	59 (25.65)

The overall complication rate was 25.65% and the mortality rate was 2.17%. As presented in Table 1, the most frequent complications include pancreatic fistula (10.43%) and followed by wound infection (4.38%).

Table 2: Association of clinical factors and pancreatic fistula complication

	Frequency (n=230)	Pancreatic fistula (%)	p
Age			
< 65	191	8.37	0.024
≥65	39	20.51	
Location of the tumor			
Head of pancreas	82	8.54	0.061
Beyond the pancreas	148	11.48	
Pre-operation realbumin			0.034
<20 g/dl	48	18.75	
≥20g /dl	182	8.2	
Hemoglobin			
≥10 g/dl	217	9.67	0.125
<10 g/dl	13	23.07	
Pre-operation biliary drainage (ERBD/PTBD)			0.027
Yes	78	16.67	
No	152	7.23	
Tumor differentiation			
Well	18	22.22	0.094
Normal or Bad	209	9.56	
Pre-operation CA 19-9			
<100	178	7.86	0.018
≥100	52	19.23	
Pre-operation Bilirubin Total (mg/dl)			0.898
<5	156	10.25	
≥5	74	10.81	
Pre-operation Serum Albumin (g/dl)			0.462
<3,5	52	7.69	
≥3,5	178	11.23	

As showed in Table 2, the aging over 65 years old was significantly associated with pancreatic fistula ($p = 0.024$). Monovarietal analysis showed that preoperative prealbumin that less than 20 g / dL had a statistically significant effect on pancreatic fistula rate ($p = 0.034$). The preoperative CA 19-9 greater than or equal to 100 U / mL had effect on pancreatic fistula ($p = 0.018$ by Chi squared test).

Table 3: Multivariate analysis of pancreatic fistula

Prognostic factor	Odds ratio	p-value
Diameter of Wirsung's duct < 3mm	5.356	0.015
Pancreatic parenchyma	6.57	0.004
Pre-operation biliary drainage	0.818	0.708
Age	0.425	0.137
Prealbumin <20g/dl	0.455	0.169

Table 4: Multivariate analysis for risk factors related to surgical site infection complication

	Regression coefficient	OR	p	Confidence interval 95%
Age				
<65	-0.709	0.492	0.350	0.111-2.176
≥ 65				
Hemoglobin				
<10 g/dl	2.293	0.101	**0.014**	0.016-0.628
≥ 10 g/dl				
Pancreatic parenchyma				
Soften	1.523	4.588	0.056	0.963-21.868
Harden				
Biliary drainage				
Yes	-1.182	0.307	0.111	0.072-1.313
No				

Table 5: Multivariate analysis for risk factors related to haemorrhage complication

	Regression coefficient	OR	p	Confidence interval 95%
Bilirubin				
<5	-2.026	0.132	0.860	0.748-76.966
≥ 5				
CA 19-9				
<100g/dl	-1.413	0.243	0.149	0.036-1.658
≥ 100g/dl				
Pancreatic parenchyma				
Soften	2.367	10.668	0.040	1.118-101.791
Harden				
Differentiation				
Well	-1.316	0.268	0.201	0.036-2.014
Moderately and poorly				

Two risk factors related to pancreatic fistula were pancreatic diameter of Wirsung's duct and pancreatic tissue density.

The patients who have the soften pancreatic parenchyma would have the risk of surgical site infection by 4.588 times. but it was not statistically significant (p = 0.056). The risk of Hemoglobin less than 10 g / dl increased by 10 times in presence the risk of surgical site infection and was statistically significant (OR: 0.101. p = 0.014).

Pancreatic parenchyma increased the haemorrhage complication significantly (p = 0.04) (OR: 10.668. 95% confidence).

4. DISCUSSION

Short-term complication after pancreaticoduodenectomy was high 25.65%. including pancreatic fistula of 10.43%. followed by surgical site infection. abdominal abscess. haemorrhage and biliary leakage. Risk factors including age. preoperative tests. characteristics of surgery and postoperative pathology are considered with those short-term complications. Author Christopher L W. refer that age above 70, operation time and type of anastomosis are related to pancreatic fistula [4]. Diabetes is also one of the risk factor for complication [3].

Pancreatic fistula rate is 10.43%. This result is quite similar to J.P.Lerut [10]. We found a correlation between Wirsung duct's diameter and pancreatic parenchyma with pancreatic fistula (p <0.05). This conclusion is also the same as DiMagno [7].

Table 6: The previous study about pancreatic fistula after pancreatoduodenectomy

Author	Year	Sample size	Pancreatic fistula rate	Risk factors	p
J.P.Lerut [10]	1968-1981	103	14.50%	Age ≥65	<0.01
				Preoperative Bilirubin ≥ 6 mg/dl	<0.02
Ying-Mo-Yang [17]	2000-2003	66	10%	Diameter of Wirsung duct	0.007

				Pancreatic parenchyma	0.017
Schmidt C. [16]	1980-2002	510	9%	Preoperative biliary dranage	0.07
				Internal pancreato-jejono-anastomosis dranage	0.001
Nguyen Cao Cuong [12]	2000-2007	73	8.2%	Diameter of Wirsung duct	
				Pancreatic parenchyma	
Our study	2011-2016	230	10.43%	Diameter of Wirsung duct	0.015
				Pancreatic parenchyma	0.004

Treatment for pancreatic fistula mainly is preservation diet fasting parenteral nutrition and may be prescribed octreotide [14]. Five cases underwent reoperation to reconstruct pancreato-jejuno-anastomosis and drainage. There is a severe case resulted to death.

Infection of the incision: the rate is 4.38%. usually happened on the day of 9th after surgery and no case detected later than 23th postoperative day the patient was given antibiotics according to the antibiogramme cleansing the surgical site twice a day. The patient recovered within a week. Preoperative hemoglobin concentrations were associated with this complication ($p = 0.014$)

Haemorrhage after surgery accounted for 2.61%. According to Osamu Nakahara [11] in 2012 457 patients undergoing pancreaticoduodenectomy were noted that postoperative hemorrhage accounting for 2%. The pancreatic parenchyma was associated with this complication ($p = 0.04$). this result was also similar to Sanjay [15]. There might be mild haemorrhage was only detected through upper digestive endoscopy usually haemorrhage from the gastric-jejuno-anastomosis or there might be severe haemorrhage resulting to shock. Conservative treatment included hemostasis through endoscopy or intravascular intervention. Four cases had to undergo reoperation. Intra operation we detected haemorrhage from the left gastric artery or common hepatic artery. Two situations had severe haemorrhage after that.

Postoperative biliary leakage was rare. Only a few of studies had been reported this complication before. According to Courtney M. [5]. the postoperative biliary leakage rate was 2%. our study was 0.8%. It might be because patients in our study were well drained by placing a feeding tube through this anastomosis and draining outside the skin. Only two cases of postoperative biliary leaked during the follow-up period. None of the above risk factors were associated with biliary leakage complication.

Chyle leakage accounted for about 3.48%. It is slightly different from what discovered by author Kim (2013) in which Chyle leakage accounted for about 10.8% [8]. There are no risk factors associated with this complication.

5. CONCUSION

In particularly. there are two risk factors related to pancreatic fistula complication: Wirsung duct's diameter less than 3mm and soften pancreatic parenchyma. Meanwhile. preoperative Hemoglobin concentrations were associated with surgical site infection. Pancreatic parenchyma is associated with haemorrhage complications. Understanding the risk factors associated with short-term complications after pancreaticoduodenectomy helps us in preparing preoperation and selecting the patient to perform surgery better.

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