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Assessment of risk factors for complications after pancreatic surgery

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Abstract
Introduction: Mortality rates after pancreaticoduodenectomy have decreased dramatically during the last two decades in high volume centers. However, despite a low mortality rate and improvements in perioperative care, morbidity rate is still high after pancreaticoduodenectomy. Studies defining the role of potential risk factors for the development of postoperative complications are few, and sometimes with conflicting results. There is need to identify potential risk factors for predicting complications after pancreatic resections.
Aim: The aim of the present study was to assess the risk factors for morbidity after pancreatic resections, by utilizing a simple grading system and identify the factors affecting them.
Material and Methods: This was a prospective study done in the Department of Surgical Gastroenterology between Feb 2007 to Jun 2009. All patients who underwent elective pancreatic surgeries were included in this study.
Major Morbidity was defined as patients having grade III and above complications. The risk factors assessed were patient factors, disease factors, operative factors and postoperative factors. Risk factors were analyzed for morbidity and major morbidity separately.
Results: One Hundred and Seven patients underwent elective pancreatic surgeries between Feb 2007 to Jun 2009. Pancreaticoduodenectomy was the commonest procedure. Three patients died after pancreatic surgeries. Mortality rate after pancreatic surgery was 2.8% (3/107) and that after Whipple's procedure was 4.68% (3/64).In our study a total of 58 of 107 (54.2%) patients developed complications after pancreatic surgery. Major morbidity defined as Grade III or more complication was seen in 24.2% (26/107). Complications after Whipple's procedure was seen in 49 of 64 (76%) patients. Major morbidity (Grade III and more) was seen in 22 of 64 patients (34.3%). All complications following pancreatic surgeries were graded. The mean postoperative duration was 12.4 days (6 – 47 days).The significant risk factors for morbidity after pancreatic surgery were soft pancreas (OR 5.988; p=.007), SGPT > 73 U/L (OR 3.623; p = .054), age > 50yrs (OR 3.254; p = .053), and absence of chronic pancreatitis (OR 4.363, p = .016).The significant factors for major morbidity were soft pancreas (OR 6.557, p = .005), hypertension (OR 5.803, p = .037) and BMI >25(OR 4.052, p = .05).
Conclusions
1. Independent factors predicting morbidity after pancreatic surgery were soft pancreas, age > 50yrs, SGPT > 73 U/L and absence of chronic pancreatitis.
2. Independent factors predicting major morbidity after pancreatic surgery were soft pancreas, hypertension and BMI > 25.

Keywords: Pancreatic surgery, morbidity, risk factors

Introduction
Mortality rates after pancreaticoduodenectomy have decreased dramatically during the last two decades in high volume centers. However, despite a low mortality rate and improvements in perioperative care, morbidity rate is still high after pancreaticoduodenectomy. While mortality is an objective and easily quantifiable outcome parameter, morbidity is only poorly defined, and this shortcoming has severely hampered conclusive comparisons among centers andwithin the same institution over time. Similarly, the identification of risk factors related to specific complications has been difficult.
Complications are classified in various ways in the literature: medical and surgical, major and minor and early and late. There is wide range of variability in reported morbidity after pancreatic surgeries. This is mainly due to lack of standardized definitions and grading of complications.

A group of experts in pancreas surgery developed a grading system for Pancreatic fistula [1], Delayed gastric emptying [2] and Haemorrhage [3]. Complications following surgery have been graded accordingly by some authors depending on the severity and the required intervention [4]. This grading system can be used for grading pancreatic complications so that the morbidity is more defined and can be compared with other centers. Studies defining the role of potential risk factors for the development of postoperative complications are few, and sometimes with conflicting results. There is need to identify potential risk factors for predicting complications after pancreatic resections.

Aim

The aim of the present study was to assess the risk factors for morbidity after pancreatic resections, by utilizing a simple grading system and identify the factors affecting them.

Material and Methods

This was a prospective study done in the Department of Surgical Gastroenterology between Feb 2007 to Jun 2009.

Inclusion criteria

1. All patients who underwent elective pancreatic surgeries were included in this study.
2. Both benign and malignant conditions of pancreas for which pancreatic surgeries were done were included in the study.

Exclusion criteria

1. Extra pancreaticpseudocysts were excluded from this study.
2. Emergency pancreatic surgeries were also excluded.

A standardized preoperative operative workup was done in all cases. Preoperatively, all patients underwent an abdominal ultrasonography and computerized tomography with intravenous contrast. ERCP, Magnetic resonance imaging and Endoscopic US were only used in select cases. Details of these patients were entered into a prospective database.

Risk factors

Patient risk factors that were studied are age, sex, comorbid factors, Alcoholism, ASA physical status score, BMI, hemoglobin, blood urea, serum creatinine and serum Albumin. Disease factors studied are liver function tests, cholangitis, preoperative pancreatitis, site of tumor, histopathology and positive resection margin. Operative factors studied were Preoperative biliary drainage, type of procedure, total operative time, blood loss, intraoperative blood transfusions, intraoperative hemodynamic status, prophylactic administration of octreotide, pancreatic texture (soft vs hard), pancreatic duct size, bile duct size. Technical factors studied were Pylorus preserving or classical, Pancreaticogastrostomy (PG) vs Pancreaticojejunostomy (PJ), Duct to mucosa vs Dunking method, Antecolic vs retrocolic gastrojejunostomy, pancreatic duct stenting – internal or external, any additional procedures performed. Postoperative factors studied were serum AST and ALT

Mortality and morbidity after all pancreatic surgeries were calculated. Morbidity following pancreatic surgery was further classified based on a therapy-oriented severity grading system (Clavien dindo classification).Classification of Surgical Complication Adopted for Pancreatic Surgery[5] was used. Perioperative mortality was defined as death within 30 days of surgery or during the hospitalization following surgery.

Complications following pancreatic surgeries were classified based on a therapy-oriented severity grading system mentioned above. Pancreatic fistula, Delayed Gastric Emptying and Hemorrhage were also graded according to International Study Group for Pancreatic Surgery definition. Major Morbidity was defined as patients having grade III and above complications. Risk factors were analyzed for morbidity and major morbidity separately.

Statistical analysis

Statistical analysis was performed using SPSS 17 software. Categorical variables were compared by Fisher exact test or Chi-square test when applicable. Continuous variables were analysed by student t test or Mann Whitney U test when applicable. Continuous data was divided into 2 groups based on upper or lower limit of that laboratory value. Each laboratory test was again divided based on the 75th percentile value for the study population to distinguish patients with “high” laboratory values from the remainder of the cohort. The 25th percentile value was used as the cut-off value for 2 laboratory tests (preoperative albumin and Hb), because “low” values for these tests are more likely to be associated with adverse events, rather than “high” values. Analyzing the data consistently using this unbiased strategy permitted comparisons to be made between the different biochemical markers and allowed their relative importance as prognostic markers to be estimated. We performed a univariate analysis examining the relationship between each preoperative and intraoperative variable in the database and the outcomes of major complication or death. Variables with $p< 0.20$ were selected for inclusion as independent factors in the sequential binary logistic regression analysis[6]. Factors with a level of significance of ≤ 0.05 were considered to be significant risk factors.

Results

One Hundred and Seven patients underwent elective pancreatic surgeries between Feb 2007 to Jun 2009. Pancreaticoduodenectomy was the commonest procedure. The procedures are summarized in Table 1.

Table 1: Type of procedure

Type of procedure	Frequency (n)	%
Pancreaticoduodenectomy	64	59.8
LPJ/Freys	31	29.0
Distal pancreatectomy	4	3.7
Median pancreatectomy	2	1.9
Enucleation	3	2.8
DPPHR	1	.9
Subtotal pancreatectomy	1	.9
DP,enucleation	1	.9
Total	107	

Mortality

Three patients died after pancreatic surgeries. All were after Whipple’s procedure. Mortality rate after pancreatic surgery was 2.8%(3/107) and that after Whipple’s procedure was 4.68% (3/64).One patient died of ventricular tachycardia on POD2. He developed ventricular ectopics intraoperatively and was on antiarrhythmic drugs. The second patient died of postoperative liver failure due to ischemic hepatitis. Third patient had Child A cirrhosis preoperatively and postoperatively he developed liver failure.

Morbidity

In our study a total of 58 of 107(54.2%) patients developed

complications after pancreatic surgery. Major morbidity defined as Grade III or more complication was seen in 24.2% (26/107). Complications after Whipple' procedure was seen in 49 of 64 (76%) patients. Major morbidity (Grade III and more) was seen in 22 of 64 patients (34.3%).All complications following pancreatic surgeries were graded. The mean postoperative duration was 12.4 days (6 – 47 days).

Complications after Pancreatic surgeries

Complications after pancreatic surgery and that after Whipple's procedure are shown in Table 2.Pancreatic fistula was seen in 18 of 107(16.8%) patients (Grade A 8; Grade B 6; Grade C 4).Hemorrhage was seen in 9(8.4%) patients (Grade A 2; Grade B 2; Grade C 5).Delayed Gastric Emptying was seen in 31 (29%) patients(Grade A 23; Grade B 8; Grade C 9). Intrabdominal abscess was seen in 11(10.3%) patients (Grade III A 6; Grade IVA 4; Grade IVB 1).Surgical site infections occurred in 33(30.8%) patients. Post-operative pancreatitis was seen in 2 patients (Grade II 1; Grade IVA 1). Sepsis was seen in 15(14%) patients (Grade II 6; Grade IIIa 2; Grade IV A 3; Grade IV B 2; Grade V 2).

Table 2: Complications after pancreatic surgery and that after Whipple's procedure.

Complications	All procedures n(%)	Whipplesn (%)
Pancreatic fistula	18(16.8)	13(20.4)
I	4(22.2)	3(23.1)
II	5(27.7)	4(30.3)
IIIA	5(27.7)	3(23.1)
IVA	2(11.1)	2(15.3)
IVB	2(11.1)	1(7.6)
Hemorrhage	9(8.4)	7(10.9)
II	2(22.2)	1(14.3)
IIIB	2(22.2)	2(28.6)
IVA	5(55.6)	4(57.1)
Delayed Gastric Emptying	31(29)	29(45.3)
II	23(74.2)	23(79.3)
IIIA	6(19.4)	4(13.7)
IVA	2(6.5)	2(16.9)
Intra abdominal abscess	11(10.3)	7(10.9)
Grade IIIA	6(54.5)	4(57.1)
Grade IVA	4(36.4)	2(28.6)
Grade IVB	1(9.1)	1(14.3)
Bowel fistula IIIA	2(1.9)	1(1.5)
Biliary fistula	3(2.8)	3(4.6)
Grade I	2(1.9)	2
Grade II	1	1
Surgical Site Infections	33(30.8)	29(45.3)
Grade I	22(66.6)	20(68.9)
Grade II	2(6.1)	
Grade IIIA	9(27.2)	9(31.1)
Pancreatitis	2(1.9)	1(1.5)
Grade II	1	1
Grade IVA	1	
Wound dehiscence	4(3.7)	3(4.6)
Grade II	1	
Grade IIIA	3	3
Liver failure		
Grade V	2(1.9)	2(3.1)
Sepsis	15(14)	10(15.6)
Grade II	6(40)	4(40)
Grade IIIa	2(14.3)	1(10)
Grade IVa	3(21.4)	2(20)
Grade IVb	2(14.3)	1(10)
Grade V	2(14.3)	2(20)
Cardiac	2(1.9)	2(3.1)
Grade IVa	1	1
Grade V	1	1
Pulmonary	15(14)	12(18.7)
Grade II	7	7
Grade IIIa	2	1
Grade IVa	3	1
Grade IVb	1	1
Grade V	2	2
Renal	5(4.7)	4(4.7)
Grade II	3	1
Grade IVb	1	1
Grade V	1	1

CNS Grade II	1	
Thrombophlebitis Grade II	12(11.3)	7(14.1)
Numbers in parenthesis are percentages		

Complications after Whipple's procedure

Complications after Whipple's procedure are shown in Table 2, Pancreatic fistula occurred in 13(20.4%) patients (Grade A 6; Grade B 4; Grade C 3). The incidence of Grade B & C fistula was 10.9%. Grade C pancreatic fistula occurred in 3 patients. Re-exploration was done in 2 patients. Percutaneous drainage methods were used in 2Grade B and 1 Grade C fistula. Two patients were readmitted with intrabdominal abscess which required percutaneous drainage. There were no deaths. Hemorrhage occurred in 7 patients after Whipples procedure. Early hemorrhage (< 24 hrs) was seen in 3 patients and latehemorrhage (> 24 hrs) in 4 patients. Early secondary hemorrhage (in 1st week) occurred in 2 and late secondary hemorrhage (after 1st week) occurred in 2 patients. Six patients required surgery. Associated conditions were pancreatic fistula 1 and hepatic artery thrombosis and ischemic hepatitis in1.Delayed Gastric emptying occurred in 29 patients (45.3%) according to ISGPS criteria (Grade A 14; Grade B 8; Grade C 7). DGE without intrabdominal complication was seen in 12 patients (18.7%). Other complications after Whipples are summarized in Table 2.

Complications after Lateral pancreaticojejunostomy and Frey's procedure

Complications are summarized in Table 3.Complications developed in 2 of 18 patients after lateral pancreaticojejunostomy and in 1 of 13 patients after Frey's procedure. Major morbidity was seen in only one patient after Frey's procedure who developed delayed bleed from the pancreatic duodenal arcade. He underwent surgery after failed embolisation. After initial surgery and ligation of gastroduodenal artery he had recurrent bleeding for which he underwent emergency Whipples procedure.

Table 3: Complications after LPJ or Frey's

Complication	LPJ (n=18)	Freys(n=13)
Pancreatic fistula	Grade A 1	0
Hemorrhage	Grade II 1	Grade IV A 1
Surgical Site Infections	Grade I 1	Grade I 1
Sepsis	Grade II 1	
CNS	Grade II 1	
Thrombophlebitis	Grade I 1	

Complications after other surgeries

One(1/4) patient developed Grade A pancreatic fistula after distal pancreatectomy. One patient after median pancreatectomy developed splenic infarct (Grade II) postoperatively. After an enucleation for serous cystadenoma one patient (1/4) developed severe necrotizing pancreatitis (Grade IVA) which required necrosectomy. Two patients after enucleation developed pancreatic fistula (Grade B) which required drain placement.

Risk factors for complications after pancreatic surgery

Univariate analysis was done to assess the risk factors for complications after pancreatic surgery. Risk factors were analyzed for both morbidity and major morbidity (Grade 3 or more).

Risk factors for morbidity after pancreatic surgery

Significant Risk factors for morbidity after pancreatic surgery on Univariate analysis

Significant risk factors for morbidity after pancreatic resections were Age > 50yrs (p=0.003), hypertension(p = 0.06), total bilirubin > 2mg/dl (p=0.002), preoperative SGOT > 67U/L (p=0.001), preoperative SGPT > 73U/L (p=0.003), cholangitis (p=0.01), operative time > 360 min (p=0.12), soft pancreas (p = 0.0001), absence of chronic pancreatitis (p = 0.001) and pancreatic duct < 3mm (p =0.007). SGOT and SGPT were found to be significantly raised on POD3 in patients having morbidity. The factors analyzed are shown in Table 4.

Table 4: Risk factors for morbidity and major morbidity after pancreatic surgery

		Morbidity			Major Morbidity		
		Absent	Present	p value	Absent	Present	p value
Age	upto 50 yrs	42(55.3)	34(44.7)	0.003	63(82.9)	13(17.1)	0.01
	>50 yrs	7(22.6)	24(77.4)		18(58.1)	13(41.9)	
Sex	Male	27(42.2)	37(57.8)	0.4	47(73.4)	17(26.6)	0.64
	Female	22(51.2)	21(48.8)		34(79.1)	9(20.9)	
Pulmonary	absent	45(47.9)	49(52.1)	0.3	71(75.5)	23(24.5)	1
	present	4(30.8)	9(69.2)		10(76.9)	3(23.1)	
Cardiac	absent	47(46.1)	55(53.9)	1	79(77.5)	23(22.5)	0.09
	present	2(40)	3(60)		2(40)	3(60)	
Hypertension	absent	47(49)	49(51)	0.06	77(80.2)	19(19.8)	0.004
	present	2(18.2)	9(81.8)		4(36.4)	7(63.6)	
Diabetes	absent	41(47.1)	46(52.9)	0.62	68(78.2)	19(21.8)	0.25
	present	8(40)	12(60)		13(65)	7(35)	
Liver disease	Absent	49(47.1)	55(52.9)	0.24	80(76.9)	24(23.1)	0.14
	Child A	0	3(100)		1(33.3)	2(66.7)	
Smoking	absent	40(45.5)	48(54.5)	1	66(75)	22(25)	1
	present	9(47.4)	10(52.6)		15(78.9)	4(21.1)	
BMI	Underweight	11(55)	9(45)	0.2†	18(90)	2(10)	0.01†
	Normal	33(47)	15(21.7)		54(78.3)	15(21.7)	
	Overweight	9(50)	9(50)		9(50)	9(50)	
	present	19(50)	19(50)		28(73.7)	10(26.3)	
Raised sr creatinine	absent	49(46.7)	56(53.3)	0.4	80(76.2)	25(23.8)	0.4
	present	0	2(100)		1(50)	1(50)	
	present	8(38.1)	13(61.9)		15(71.4)	6(28.6)	
Hypoalbuminemia	absent	32(51.6)	30(48.4)	0.17	46(74.2)	16(25.8)	0.8

(<3.5 gm/dl)	present	17(37.8)	28(62.2)		35(77.8)	10(22.2)	
Total bilirubin > 2 mg/dl	absent	41(56.2)	32(43.8)	0.002	59(80.8)	14(19.2)	0.09
	present	8(23.5)	26(76.5)		22(64.7)	12(35.3)	
Preoperative SGOT	Up to 67U/L	44(53.7)	38(46.3)	0.005	69(84.1)	13(15.9)	0.001
	> 67U/L	5(20)	20(80)		12(48)	13(52)	
Preoperative SGPT	Up to 73U/L	44(54.3)	37(45.7)	0.003	67(82.7)	14(17.3)	0.007
	> 73U/L	5(19.2)	21(80.8)		14(53.8)	12(46.2)	
Preoperative ALP	up to 500	40(49.4)	41(50.6)	0.25	62(76.5)	19(23.5)	0.7
Preop pancreatitis	absent	47(45.6)	56(54.4)	1	78(75.7)	25(24.3)	1
	present	2(50)	2(50)		3(75)	1(25)	
Cholangitis	no	41	35	0.01	59	17	0.46
	yes	8	23		22	9	
Preopbiliary drainage	absent	40(51.9)	37(48.1)	1	58(75.3)	19(24.7)	0.5
	present	9(30)	21(70)		23(76.7)	7(23.3)	
Operative time(min)	Up to 360 min	44(49.4)	45(50.6)	0.12	69(77.5)	20(22.5)	0.37
	> 360 min	5(27.8)	13(72.2)		12(66.7)	6(33.3)	
Intraop Blood loss(ml)		602±123	586±64	0.14	590±76	604±131	0.6
Intraop hypotension	absent	46(47.4)	51(52.6)	0.33	74(76.3)	23(23.7)	0.02
	present	3(30)	7(70)		7(70)	3(30)	
soft pancreas	absent	45(57.7)	33(42.3)	0.0001	64(82.1)	14(17.9)	0.003
	present	4(13.8)	25(86.2)		17(58.6)	12(41.4)	
HPE	benign	4(30.8)	9(69.2)	0.001	9(69.2)	4(30.8)	0.38
	ch pancreatitis	29(80.6)	7(19.4)		34(94.4)	2(5.6)	
	malignant	16(27.6)	42(72.4)		38(65.5)	20(34.5)	
Pancreatic duct < 3mm	absent	15(31.9)	32(68.1)	0.007	30(63.8)	17(36.2)	0.1
	present	0	17(100)		13(76.5)	4(23.5)	
Postop ventilatory support	absent	38(55.1)	31(44.9)	0.01	56(81.2)	13(18.8)	0.1
	present	11(28.9)	27(71.1)		25(65.8)	13(34.2)	
	>200U/L	1(14.3)	6(85.7)		4(57.1)	3(42.9)	
POD3ALT	upto 72 U/L	45(56.3)	35(43.8)	0.001	69(86.3)	11(13.8)	0.001
	> 72 U/L	4(15.4)	22(84.6)		12(46.2)	14(53.8)	
POD3 AST	upto 70 U/L	45(54.9)	37(45.1)	0.001	70(85.4)	12(14.6)	0.001
	> 70 U/L	4(16)	21(84)		11(44)	14(56)	
	> 14	9(34.6)	17(65.4)		18(69.2)	8(30.8)	

Numbers in parenthesis are row percentages; All continuous variables are expreseed as Mean ± S.E.M; * indicate student t test; † indicate Pearson Chisquare test; ‡ indicate Mann Whitney U test; rest all p values are by Fischer Exact Test

Multivariate analysis using logistic regression for risk factors for morbidity after pancreatic surgery

Significant factors were soft pancreas (OR 5.988; p=.007), SGPT > 73 U/L (OR 3.623; p = .054), age > 50yrs (OR 3.254; p = .053), and absence of chronic pancreatitis (OR 4.363, p = .016). Table 5

Table 5: Logistic regression for morbidity after pancreatic surgery

Variable	Odds ratio	95% confidence interval	p value
Soft pancreas	5.988	1.622-22.105	0.007
TSB > 2 mg/dl	0.930	0.276-3.133	0.907
Cholangitis	1.508	0.456-4.9	0.500
SGPT > 73 U/L	3.623	0.98-13.4	0.054
Absence of Chronic pancreatitis	4.363	1.32-14.39	0.016
Age > 50yrs	3.254	0.98-10.75	0.053
Postopventilatory support	0.626	0.21-1.83	0.393

Risk factors for major morbidity after pancreatic surgery

Significant Risk factors for major morbidity after pancreatic surgery on Univariate analysis

Significant risk factors for major morbidity after pancreatic resections were age >50 yrs(p= 0.01), cardiac (p = 0.09), hypertension (p = 0.004), BMI (p = 0.01), total bilirubin > 2 mg/dl (p = 0.09), preoperative SGOT > 67U/L (p = 0.001), preoperative SGPT > 73U/L (p = 0.007), intraoperative hypotension (p = 0.02) and soft pancreas (p = 0.003).SGOT and SGPT was found to be significantly raised on POD3 in patients having morbidity. The factors analyzed are shown in Table 19.

Multivariate analysis using logistic regression for major morbidity after pancreatic surgery

In a multivariate model adjusting for each of the univariate risk factors for postoperative major morbidity, significant factors were soft pancreas (OR 6.557, p = .005), hypertension (OR 5.803, p = .037) and BMI >25(OR 4.052, p = .05). (Table 6)

Table 6: Logistic regression for major morbidity after pancreatic surgery

	Odds ratio	95% confidence interval	p value
Soft pancreas	6.557	1.779 - 24.16	0.005
Preoperative SGOT > 67 U/L	4.023	0.738 - 21.92	0.108
Preoperative SGPT > 73U/L	2.426	0.517 - 11.393	0.261

Intraophypotension	0.567	0.082 - 3.93	0.566
Hypertension	5.803	1.116 - 30.17	0.037
Cardiac	4.603	0.287 - 73.814	0.281
TSB > 2	0.567	0.114 - 2.82	0.488
Overweight & obese	4.052	0.992 - 16.55	0.051
Age > 50	0.476	0.136 - 1.671	0.247
Liver disease	12.16	0.492 - 201.2	0.127

Discussion

Mortality after pancreatic surgery

Elective pancreatic resections have developed into safe surgical procedures in specialized centers with mortality rates less than 5%. Mortality rate after pancreatic surgery in our series was 2.8% (3/107) and that after Whipples procedure was 4.68% (3/64). There was no mortality related to pancreatic fistula or reoperations. Previously mortality was primarily attributed to complications from pancreatic anastomosis [7, 8]. Presently mortality due to surgical complications have decreased. DeOliveira *et al.* [5] in his series of 633 patients had a mortality of 2% of which half are related to systemic complications (myocardial infarction and ventricular arrhythmia in 3, thromboembolism in 2, and mesenteric ischemia in 1 patient).In our series there was 1 mortality related to ventricular arrhythmia. One patient developed hepatic artery thrombosis and developed fatal hepatic ischemia. Se´bastien Gaujoux *et al.* [9] in a recent series reported 4 cases of hepatic artery thromobosis postoperatively. However, in their series, treatment of hepatic artery thrombosis was disappointing because all 4 patients ultimately lost artery patency despite various surgical or radiologic attempts of revascularization, including one immediate prosthetic replacement.

Morbidity following pancreatic surgery

There has been a lot of discrepancy in reported literature about the morbidity following pancreatic surgery. There are numerous definitions for various complications in the reported literature and complications are variedly classified as major or minor. We used the classification proposed by Clavien-Dindo *et al.* [4] to classify postoperative complications. By this classification first each recorded complication was easily converted into a complication grade. Second the grading system provided an effective format to analyze the incidence and severity of different complications, and their impact on overall morbidity. The risk factors for morbidity, as well as for specific complications, could be identified. We also used the standard definitions by International study group for pancreatic surgery to define and grade pancreatic fistula, DGE, and hemorrhage.

In our study, 58 of 107(54.2%) patients developed complications after pancreatic surgery. Major morbidity defined as Grade III or more complication was seen in 24.2% (26/107). Complications after Whipples procedure was seen in 49 of 64 (76%) patients. Major morbidity (Grade III and more) was seen in 22 of 64 patients (34.3%). The mean postoperative duration was 12.4 days (6–47 days). Complications after pancreaticoduodenectomy occurs in up to 60% of patients in various reports [10-15]. More than 50% of our complications were Grade I and II. DeOliveira *et al.* [5] in his series of 663 patients classified all complications after pancreatic surgery according to Clavien-Dindo system and found a complication rate of 58.5% (Grade I complications occurred in10.0%, Grade II in 30.0%, Grade IIIa in 10.5%, and Grade IIIb in 3.0%, Grade IVa in 2.5%, IVb in 0.5%,Grade V complication rate in 2.0%). Grobmyer *et al.* [11] by using a similar grading System reported a morbidity of 47%.

Risk factors for morbidity after pancreatic surgery

Table 7: Risk factors for morbidity after pancreatic surgery.

Authors	No	Surgery type	Risk factors by multivariate analysis
JM Winter *et al.* [16] JACS 2007	2894	Whipples	Blood urea nitrogen > 18, albumin < 3.5 gm/dl, postop amylase > 292 u/l
DeOliveira *et al.* [5] Ann Surg 2006	663	Whipples	Cardiovascular disease
Muscari F *et al.* [17] Surgery 2006	300	Whipples	extended resection, main pancreatic duct diameter of 3 mm or less
Topal B *et al.* [18] Eur J Surg Oncol 2007	351	Whipples	Surgeon, male gender, and pre-operative hyperbilirubinaemia
Gouma,D.J *et al.* [14] Ann Surg 2000	300	Whipples	Serum creatinine levels, need for blood transfusion, and period of resection
Present study	107	Pancreatic surgery	**Risk factors for major morbidity**: soft pancreas (OR 6.557, p = .005), hypertension (OR 5.803, p = .037) and BMI >25(OR 4.052, p = .05)

Effect of age on morbidity after pancreatic surgery

Age more than 50yrs was an independent risk factor for morbidity after pancreatic surgery on logistic regression (OR 3.254, p = .053). But when only major morbidity was considered age was significant only in univariate analysis. In our series we had 8(12.5%) patients above 60 yrs of age. In study from John Hopkins group 207 patients >80 years old underwent a PD. Though advanced age group had higher complication rates, it was not an independent risk factor for perioperative mortality and morbidity following PD after adjusting for preoperative co morbidities. There was no increased incidence of surgical complications.

Obesity

The incidence of patients having BMI > 25 was 16%(18/107) after all pancreatic surgeries and 17%(11/64) after Whipples procedure. Multivariate analysis using logistic regression for major morbidity after pancreatic surgery showed BMI > 25(OR 4.052, p = .05) as a significant risk factor. Williams, T.K. *et al.* [19] in recent study showed that Obese patients undergoing PD have a substantially increased blood loss and longer operative time but do not have a substantially increased length of postoperative hospital stay or rate of serious complications. Wound infections occurred in 21% of the patients with body mass index greater than or equal to 30 kg/m2 compared to 12% of the non obese patients, p=0.03. These findings should be considered when assessing patients for operation and when counseling patients about operative risk, but they do not preclude obese individuals from undergoing definitive pancreatic operations.

Other comorbidities

Hypertension was a significant risk factor on Univariate analysis for morbidity after pancreatic resections (p = 0.06) and Major morbidity after pancreatic resections (p = 0.004) Hypertension was a significant risk factor on multivariate analysis for major morbidity after pancreatic surgery. (OR 5.803, p = .037). Cardiac comorbidity was a significant risk factor on Univariate analysis for Major morbidity after pancreatic resections (p = 0.09)

Liver function tests

1. Significant risk factors for morbidity after pancreatic resections on univariate analysis were total bilirubin > 2mg/dl (p=0.002), preoperative SGOT > 67U/L (p=0.001) and preoperative SGPT > 73U/L (p=0.003)
2. Significant risk factors for major morbidity on univariate analysis after pancreatic resections were total bilirubin > 2 mg/dl (p = 0.09), preoperative SGOT > 67U/L (p = 0.001), preoperative SGPT > 73U/L (p = 0.007).

Though jaundiced patients had significantly more complications after pancreatic surgery on univariate analysis after adjusting for other factors jaundice was an independent risk factor for SSI only. Preoperative SGOT and SGPT were not independent risk factors for any complication though significant on Univariate analysis. In a study from John Hopkins Hospital [16] routine perioperative laboratory data were analyzed for 2,894 patients who underwent a pancreaticoduodenectomy over a 25-year period. Significant multivariate predictors of a postoperative complication included preoperative blood urea nitrogen > 18 mg/dL, preoperative albumin < 3.5 g/dL, and postoperative amylase> 292 U/L. Significant multivariate predictors of a postoperative death included preoperative albumin < 3.5 g/dL and postoperative aminotransferase <187 U/L. Though raised bilirubin was found to be significant factor in univariate analysis in this study it did not attained statistical significance in multivariate analysis similar to our study. We also estimated Serum SGOT and SGPT on POD3 and we found that the mean POD 3 SGOT (56±4 vs 331±162, p = 0.005) and SGPT (62±5 vs 408±278 p = 0.009) were significantly elevated in patients with major morbidity after Whipples procedure. However, we did not consider it as risk factor for complication as it would rather reflect the outcome following a complication. Our results show that raised SGOT and SGPT in the postoperative period would indicate a potential complication apart from predicting postoperative liver ischemia.

Preoperative biliary drainage

Preoperative biliary drainage was done in 39.1% (25/64) of patients with pancreaticoduodenectomy. Cholangitis was present in 72% (18/25) of patients who had preoperative biliary drainage. Preoperative biliary drainage was not associated with statistically significant morbidity after pancreatic surgery. The therapeutic effect of PBD, either by means of ERCP or PTC, has been extensively debated throughout the past few decades. One of the largest prospective randomized trials performed in the USA by Pitt *et al*. [20] concluded that PBD does not reduce operative risk; however, it increases hospital cost and, therefore, should not be performed routinely. A systematic review by Sewnath ME, *et al*. [21] summarized all retrospective and prospective studies, published between 1966 and 2001, with the aim to evaluate the efficacy of drainage in jaundiced patients, compared to patients that underwent direct surgical treatment. Meta-analysis for both level I and level II studies showed no difference in mortality between patients who had PBD and those who had surgery without PBD. If PBD had been without complications, the complication rate would be in favor of PBD based on level I studies, and without difference based on level II studies. Further, overall hospital stay was prolonged after PBD. In a recent review by Gouma DJ *et al*. [22] it was concluded that the potential benefit of PBD, in terms of postoperative rates of death and complications, does not outweigh the disadvantage of the drainage procedure and therefore should not be performed routinely, unless further improved PBD techniques would become available. In previous studies various (outdated) forms of internal and external drainage procedures for both proximal and distal obstruction were included, different durations of drainage were used, and different surgical procedures were followed. The highest level of evidence for PBD to be performed in proximal obstruction, as well as over the preferred mode, is lacking but, nevertheless, assimilated in the treatment algorithm for many centers[22].In our study 7/25(28%) of patients were stented without cholangitis and were referred to our center.

Hypoalbuminemia

Hypoalbuminemia (< 3.5gms%) was seen in 46.9% (30/64) of our patients undergoing PD. Further serum albumin < 3 gms% was seen in 26% (17/64) of our patients undergoing PD. No statistically significant increase in morbidity or mortality was seen in patients with hypoalbuminemia. Serum albumin is a well-established marker of protein calorie malnutrition and continues to be used for that purpose in clinical practice and surgical research. Because the half-life of albumin is approximately 3 weeks, it carries more importance during the preoperative evaluation of surgical patients than during the postoperative period. A low preoperative albumin (among other markers of nutrition status) has been shown in previous studies to be associated with increased morbidity after major abdominal and vascular surgery [23, 24]. Earlier studies of patients who underwent pancreatic surgery have established albumin as an independent risk factor for postoperative mortality [25, 26]. Winter *et al*. [16] has demonstrated that Sr albumin < 3.5 gm/dl was an independent risk factor for mortality and morbidity after PD. No such association was found in our study though majority of them had hypoalbuminemia. We don't have a policy of preoperative TPN administration in patients with hypoalbuminemia. Multiple studies have demonstrated that preoperative parenteral support can have a positive impact on surgical outcomes in malnourished patients. The Veteran Affairs Cooperative Study [27] deserves special mention, because it remains the largest prospective, randomized study on preoperative total parenteral nutrition. Although the study is often used to argue against preoperative parenteral support, a subgroup analysis revealed fewer noninfectious complications in severely malnourished patients who received preoperative total parenteral nutrition, as compared with severely malnourished patients in the control group. In 2002, the American Society for Parenteral and Enteral Nutrition (ASPEN) issued the following recommendation based on available data: moderately or severely malnourished patients undergoing major gastrointestinal operations should receive a 7- to 14-day course of preoperative nutritional support if the operation can safely be postponed. With our policy we did not observed increased morbidity in patients with hypoalbuminemia.

Blood loss

Eleven patients (11/64, 17.2%) did not required blood transfusions. Most of the patients required 2 or less transfusions (56/64, 87.5%). More than 1000 ml blood loss was seen in 11

patients (11/64, 17.2%). More than 1000 ml blood loss was not associated with significant morbidity after pancreatic surgery in our study. In a study from MSKCC [28] on the effect of blood transfusion on outcome after Pancreaticoduodenectomy it was found that patients who received a transfusion had a significantly increased complication rate on univariate analysis. It was also found that median survival was 18 months compared with 24 months for those who did not have a transfusion. In our study short term morbidity was no different in patients with or without transfusions. We are yet to determine the long-term outcome.

Postopventilatory support

Postoperative ventilator support was required in 50% of patients. Postoperative ventilator support was not associated with increased morbidity after pancreatic surgery in our study.

Conclusions

1. Independent factors predicting morbidity after pancreatic surgery were soft pancreas, age > 50yrs, SGPT > 73 U/L and absence of chronic pancreatitis.
2. Independent factors predicting major morbidity after pancreatic surgery were soft pancreas, hypertension and BMI > 25.

Conflicts of interest: None

Ethical committee clearance: taken

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