Study of reoperation after Pancreatico-duodenectomy

Abd Elrahman Elmaraghy, Mahmoud Saad Farahat and Mohammed abdo MD
Department of General Surgery, Ain Shams University

ABSTRACT

Background: *reoperation after pancreatico-duodenectomy is a difficult decision but sometimes needed for treatment of complications after failure of other conservative measures.* ***Aim:*** *To identify the incidence, indications and results of surgery for patients undergoing reoperations for treatment of complications after pancreatico-duodenectomy.* ***Methods:*** *retrospective analysis of data records of patients undergoing pancreatico-duodenectomy from June 2011 to August 2016 was performed.* ***Results:*** *46 patients underwent pancreatico-duodenectomy; 30 whipples, 10 underwent pylorus preserving pancreatico-duodenectomy and 6 underwent total pancreatectomy. 11 patients (24 %) were re-operated. All re-operated patients were done once except for 2 patients that had been re-operated twice. Timing for re-operation ranged from 1- 24 days after pancreatico-duodenectomy. Indications for re-operation were post pancreatectomy hemorrhage in 3 patients (27.3 %), persistent pancreatico-jejunal anastomotic leak in 6 (54.5%), hepatico-jejunostomy leak in 3 (27.3%), leakage from gastro-jejunal and duodeno-jejunal anastomosis in 2 (18%) and peritonitis which is not amenable for U/S guided drainage in 6 (54.5%). Mortality was higher in the reoperated group (36.4%) compared to 1 (2.9%) in the other group. Operations done included drainage, refashioning of anastomosis and completion pancreatectomy and all were accompanied with feeding jejunostomy.* ***Conclusion:*** *re-operations following pancreaticoduodenectomy, although difficult decision and carries high risk of morbidity and mortality, it is sometimes mandatory to treat complications refractory to conservative measures. Completion pancreatectomy may have a role as a last surgical option in treatment of post pancreatectomy complications. high pre-operative total bilirubin > 10 mg%, Pancreatico-jejunal anastomotic (PJA) leak, Intraabdominal collections and Septicemia are all independent risk factors (predictors) for reoperation after pancreatectomy.*

Key words: *pancreatico-duodenectomy, early complications, re-operations and completion pancreatectomy.*

INTRODUCTION

Pancreaticoduodenectomy was first described more than 65 years ago by Kausch and Whipple and although operative mortality has been significantly reduced from that time till now [(1, 2)], the rate of complications still remains as high as 60% [(3)]. Important complications include haemorrhage, pancreatic anastomotic leakage and intraabdominal abscesses for which mortality rates range between 8 and 88% [(4, 5)]. Treatment of such complications is difficult. Conservative treatment which includes TPN, U/S or CT guided aspiration and pig tail insertion is usually the 1st choice but it is not always successful and re-laparotomy may be needed [(6, 7)].

In septic patients, the aim for operation is drainage and preservation of a small pancreatic remnant aiming to preserve the endocrine function and revision of anastomosis. Completion pancreatectomy was reported to be the last surgical option [(8, 9, and 10)].

The aim of this study is to determine incidence, indications and outcome of patients undergoing reoperations following pancreaticoduodenectomy at our hospital.

PATIENTS AND METHODS

Starting from June 2011 to August 2016 the data of all patients undergoing pancreaticoduodenectomy at Ain Shams university hospitals, Cairo, Egypt (including preoperative data, follow-up data, any reoperation data and outcome data) were kept at a specific database. Retrospective analysis of the patients" data was done afterwards. All operations were performed by an experienced team of surgeons.

Statistical analysis:

Data were analyzed using Statistical Program for Social Science (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

The following tests were done:

- Independent-samples t-test of significance was used when comparing between two means.
- Chi-square (X2) test of significance was used in order to compare proportions between two qualitative parameters.
- Multivariate analysis was done to determine factors predictive of early reoperation.
- Probability (P-value)
  - P-value <0.05 was considered significant.
  - P-value <0.001 was considered as highly significant.
  - P-value >0.05 was considered insignificant.

RESULTS

Between June 2011 and August 2016, 46 patients underwent pancreaticoduodenectomy all for malignant disease whether pancreatic head or periampullary carcinoma, except for one patient that was diagnosed pre-operatively as malignant by tumor marker and CT but proved by pathology as chronic pancreatitis.

30 had classic Whipple procedure. 10 underwent pylorus preserving pancreaticoduodenectomy and 6 underwent total pancreatectomy from the start. Choice of the procedure was always according to the surgeon's preference but usually total pancreatectomy was preferred in small pancreatic duct especially in diabetic patients.

Pancreatic reconstruction was performed by an end to side duct to mucosa pancreatico-jejunostomy in all patients of classic Whipple's procedure and pylorus preserving pancreaticoduodenectomy except 3 patients for whom pancreaticojejunostomy was done end to end with invagination (telescoping). Stenting of pancreatic duct was used in 2 cases only (not done routinely). This was followed by an end to side hepatico-jejunostomy and lastly duodeno-jejunostomy or gastro-jejunostomy. Abdomen was closed with wide pore tube drains. A nasogastric tube was placed for gastric decompression. All patients were given 3rd generation cephalosporin plus metronidazole post-operatively and oral feeding was started once patients became open bowel. Patients then were followed up for occurrence of any complication.

Post-operative complications included Post pancreatectomy haemorhhage (PPH), Pancreatico-jejunal anastomotic (PJA) leak, Hepatico-jejunostomy anastomotic (HJA) leak, Duodeno-jejunostomy or gastro-jejunostomy (DI/GI) leak, Intraabdominal collection and septicemia. Other complications included wound infection and dehiscence.

Complications following the operation were treated at 1st by non-operative measures and if failed operative treatment was done.

11 patients (24%) needed reoperation during the study period. Operations done included drainage, refashioning of anastomosis and completion pancreatectomy. Reoperations were repeated in two patients and both were treated with completion pancreatectomy (table 1).

Table (1): surgical procedures done during re-operation.

	No	**Operation done**
post pancreatectomy hemorrhage	3	1) Revision of Gastrojujenostomy, Evacuation of clot and higher gastrectomy 2) bleeding pancreatico jujenostomy → suturing of bleeding site and refashioning of anastomosis 3) Evacuation of clot (pseudo aneurysm)and suturing of bleeding site (pancreatico jujenostomy) All patients had feeding jejunostomy.
persistent pancreatico-enteric anastomotic leak	6	3 patient→ refashioning of anastomosis and drainage→ one of them failed and resurgery done and completion pancreatectomy. 3 patients→ completion pancreatectomy (due to friable tissues and small duct)
hepaticojejunostomy leak	3 (after total pancreatctomy)	refashioning of anastomosis over T-tube or tube jejunostomy with drainage
leakage from gastro-jejunal or duodeno-jejunal anastomosis	2 (one after Whipple and the other after pylorus preserving pancreatico duodenectomy)	refashioning of anastomosis with gastro-jejunostomy.
collection not amenable for U/S guided drainage	6 (all except one is accompanying other complications).	1 patient → drainage 5 patients→ completion pancreatectomy (management is directed to treatment of the primary pathology plus drainage)

Re-operations are generally divided into those occurring during the same hospital admission (early) or performed after discharge (late). Timing for re-surgery ranged from 1- 24 days. Number of re-operations was only one for 9 patients and twice for 2 patients. Indications for re-operation were post pancreatectomy hemorrhage in 3 patients (27.3 %), persistent pancreatico-jejunal anastomotic leak in 6 (54.5%), hepatico-jejunostomy leak in 3 (27.3%), leakage from gastro-jejunal and duodeno-jejunal anastomosis in 2 (18%), peritonitis not amenable for U/S guided drainage in 6 (54.5%) (Usually accompanying other complications).

Of the 11 patients undergoing reoperation, 3 had post pancreatectomy haemorrhage (PPH), one intra luminal inside the stomach from gastric erosions and gastro-jejunostomy and this needed higher gastrectomy and revision of gastro-jejunostomy. The second from pancreatic surface which was managed with suture ligation, evacuation of haematoma and wide drain it was also accompanied with minor leak from pancreatico-jejunostomy and the 3rd patient had pseudo aneurysm of the gastroduodenal artery and massive haematoma failed to be controlled by angiographic embolization. Evacuation of haematoma and ligation of bleeding artery was done. In all these patients, feeding jejunostomy was done to avoid complications of TPN.

The 6patients re-operated for pancreatico-jejunal annastomotic (PJA) leak with intra-abdominal collection were done due to failure of percutaneous drainage. During operation 3 had revision of anastomosis but the remaining 3 patients had completion pancreatectomy due to friable tissues for re-anastomosis and or small duct. Of the 3 patients underwent revision of anastomosis one had persistent fistula indicating re-operation and completion pancreatectomy. All of these patients also had feeding jejunostomy for post-operative enteral feeding.

3patients were re-operated for hepatico-jejunal anastomotic (HJA) leak. All of them showed persistent bile leak via sub-hepatic tube drain. Revision of anastomosis was done in all; one over t-tube and the other two over tube jejunostomy.

2 patients with leakage from gastro-jejunal and duodeno-jejunal anastomosis (one after Whipple and one after pylorus preserving pancreatico duodenectomy) were recorded.

Refashioning of anastomosis was done in both with feeding jejunostomy.

Mean postoperative stay was significantly longer in patients undergoing reoperation compared to those without re-operation (19.83 ± 2.1days versus 15.11± 3.16 days; P = 0.015). The in-patient mortality was also significantly more in patients undergoing reoperation and patients usually died from septicemia and organ failure (4 versus 1) (36.4% versus 2.9%; P= 0.011).

In order to identify the risk factors (predictors) for reoperation, patients were divided into two groups; group 1 (those who were re-operated) and group 2 (who did not need re-operation) and both were compared to each other. First, univariate analysis was done identify the significantly different parameters between both groups.

Univariate analysis of demographic characteristics did not show any difference between both groups as shown in (table2).

Table (2): Comparison between group 1(patients needed reoperations) and group 2 (patients not re-operated) according to demographic parameters.

Parameters	**Re-operations (n=11)**	**Not re-operated early (n=35)**	**t*/x2**	**p-value**
Age in years (Mean± SD)	49.21±8.68	50.16±9.91	0.781	0.483
Gender (M/F)	7/4	25/10	0.013	0.909
Comorbid conditions (DM, HTN, ISHD, COPD)	2 (18.2%)	9 (25.7%)	0.017	0.917

Univariate analysis of pre and intra operative data, showed that only high preoperative serum bilirubin level was significantly different between both groups as shown in (table 3 & figure 1).

Table (3): Comparison between group 1(patients needed reoperations) and group 2 (patients not re-operated) according to pre and intra operative data.

Parameters	**Re-operations (n=11)**	**Not re-operated (n=35)**	**t*/x2**	**p-value**
Duration of jaundice >3 months	4 (36.4%)	6 (17.1%)	2.874	0.076
Preoperative hemoglobin (Mean± SD)	11±1.2	11.5±1.8	0.860*	0.394
Preoperative albumin (Mean± SD)	3.4±1.7	3.5±1.25	0.242*	0.810
High total bilirubin (>10 mg %)	5 (45.5%)	4 (11.43%)	4.196	**0.041**
Preoperative biliary drainage	6 (54.55%)	22 (62.86%)	0.019	0.889
Blood transfusion	7 (63.64%)	17 (48.57%)	0.278	0.593

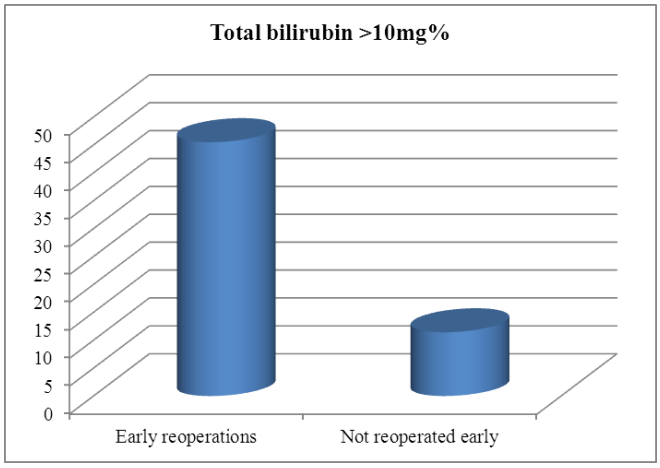

Fig. (1): Comparison between group 1 and group 2 according to pre-operative high bilirubin level.

Univariate analysis of postoperative complications was done to identify which of them is a risk factor for reoperation was done and revealed that Pancreatico-jejunal anastomotic (PJA) leak Intraabdominal collection and Septicemia were significantly different between both groups as shown in (table 4 & figure 2).

Table (4): Comparison between group 1 and 2 regarding postoperative complications.

Causes	reoperations (n=11)	Not re-operated (n=35)	t/x2*	p-value
Post pancreatectomy hge (PPH)	3 (27.3%)	1 (2.9%)	3.565	0.059
Pancreatico-jejunal anastomotic (PJA) leak	6 (54.5%)	2 (5.7%)	10.695	**0.004**
Hepatico-jejunostomy anastomotic (HJA) leak	3 (27.3%)	2 (5.7%)	2.110	0.146
Duodeno-jejunostomy or gastrojejunostomy (DI/GI) leak	2 (18.2%)	1 (2.9%)	1.188	0.275
Intraabdominal collection	6 (54.5%)	2 (5.7%)	10.695	**0.004**
Septicemia	6 (54.5%)	2 (5.7%)	10.695	**0.004**

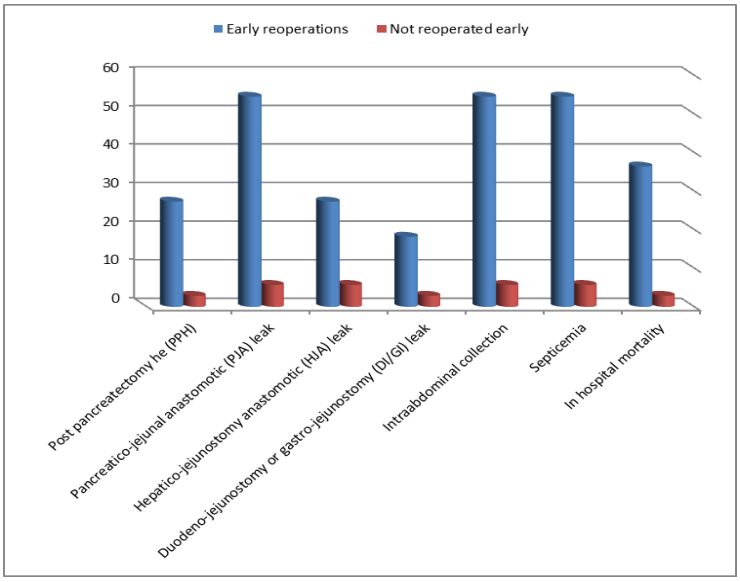

Fig. (2): Comparison between group 1 and 2 regarding postoperative complications.

Factor identified to be significant by univariate analysis were subjected to multivariate analysis using the logistic regression model, to identify which of them is an independent factor for reoperation. The analysis had proved that high pre-operative total bilirubin > 10 mg%, Pancreatico-jejunal anastomotic (PJA) leak, Intraabdominal collections and Septicemia are all independent risk factors (predictors) for reoperation after pancreatectomy as shown in (Table 5).

Table (5): Multivariate analysis of factors predicting the need for early reoperation.

Parameters	p-value	Exp. (B)	95% C.I.	
Duration of Jaundice >3 months	**0.048**	4.123	1.882	15.968
Intraabdominal collection	**0.014**	0.862	0.466	7.681
PJA leak	**0.014**	0.862	0.466	7.681
Septicemia	**0.016**	0.962	0.469	8.081

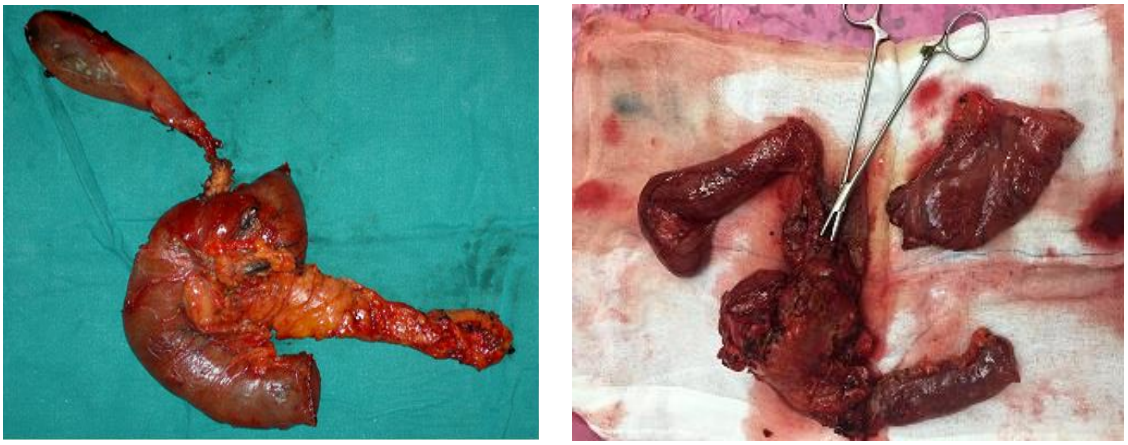

Fig. (3): (a) total pancreatectomy, b) Whipples pancreatectomy.

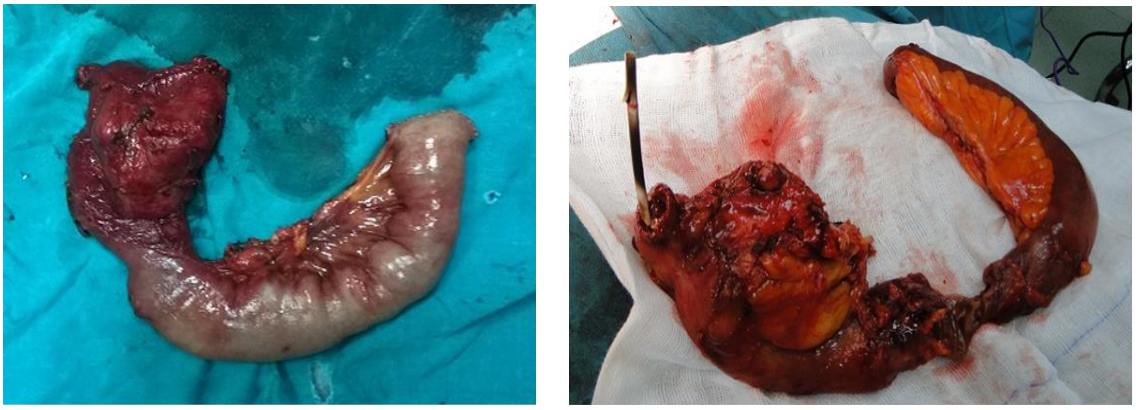

Fig. (4): (a, b) pylorus preserving pancreatectomy.

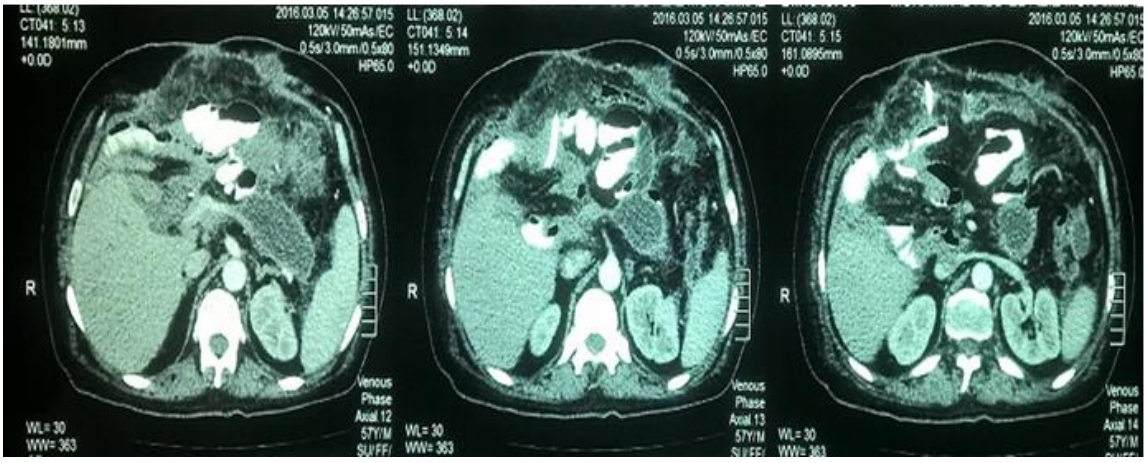

Fig. (5): CT post total pancreatectomy complicated by multi-septated collection.

DISCUSSION

Surgery of the Pancrease has improved dramatically throughout the past years. Although mortality after Whipple's procedure in the 1980s exceeded 20%, nowadays it has been reduced to less than 5% in high volume centers [11].

But morbidity is still high even in highly specialized centers ranging from 30–60% [12, 13]. Post pancreatectomy complications include post pancreatectomy hemorrhage and leakage from different anastomoses whether from pancreatico-jejunal or hepatico-jejunal anastomosis or even anastomosis between stomach or duodenum from one side and jejunum from the other side. Other complications include sepsis, wound dehiscence and intra-abdominal collections.

The 1st line treatment of these complications is mainly conservative. Bleeding can be terminated with the aid of endoscopy and argon laser. Angiographic embolization can be also used. Intra-abdominal collection can be treated by using interventional radiology as u/s guided drainage and pig tail insertion. Bilioenteric anastomotic leak is not common following pancreatico-duodenectomy and the management is usually conservative[14]. Although that, failure of interventional procedures to control the problem is common and also it is not always present as an emergency. In these cases, re-operation is the last option.

The rate of re-operation is variable in different series from 4-11%[15]. Other series reached 18.5% [16]. In our study, re-operation rate was higher (24%), this may be due to the fact that other published series were done in centers with significantly higher case volume with better expertise, resulting better postoperative outcomes.

Post pancreatectomy haemorrage (PPH) occurs in nearly 2-20% following pancreatectomy [17-18]. Others reported incidence of 13-18% [16]. In our study we found that incidence was about 6.5% of patients underwent pancreatico-dodenectomy (which is similar to other reports). Haemorrage was a predictor of need for re-operation in both univariant and multivariant analysis. This was due to failure of other measures to arrest bleeding and hemodynamic instability of patients.

Causes of post pancreatectomy haemorrage included bleeding from the pancreatic stump that may be accompanied or not with disrupted pancreatic anastomosis. Also bleeding may be intraluminal (haematemesis) or intra-abdominal (in drains) [19]. Other causes of bleeding include erosive gastritis and bleeding from gastro-jejunal anastomosis suture line. This can be diagnosed by upper GIT endoscopy. Bleeding can be also generalized oozing from surgical bed due to infection and in these cases control of bleeding is difficult and packing is needed until re-laparotomy.

Pancreatico-enteric anastomotic leakage with intra-abdominal collection is an important complication. It can be managed with good drainage using U/S guided aspiration and pig tail insertion but sometimes it needs re-operation. In our study, its incidence was 13% of all patients and 54.5% of re-operated patients. Other series found it around 34.6% of early re-operated patients and 14.3% of late re-operation patients [16]. Different treatment options are present; the anastomosis can be resutured while others dismantle the anastomosis and close the jejunum and drain the pancreatic duct (controlled fistula)[19, 20].

In our study, 3 patients underwent resuturing and drainage (one of them needed re-operation and completion panceatectomy) and the other 3 had completion pancreatectomy for treatment of fistula and the septic focus as the tissues were friable and it couldn't hold sutures.

In our study, pancreatico-enteric anastomosis leakage and disruption was a predictor for re-operation in both univariate and multivariate analysis.

Biliary enteric anastomosis leakage is not common following pancreaticodudenectomy. It usually responds well to conservative treatment in the form of good drainage [20] except if major disruption occurs early (within the 1st 48hs) following surgery (technical fault). In these cases, early re-operation is indicated for better results.

In our study, it occurred in 3 patients and all were reanastomosed (one over T-tube and the other two over tube jejunostomy). In our study, hepatico-jejunal anastomosis leakage was not a predictor for re-operation in both univariate and multivariate analysis.

Anastomotic leakage from gastro-jejunostomy or duodenojejunostomy is rare. It occurred in 2 patients one of them had solitary duodenojejunal leakage and the other had also pancreatico jejunal anastomosis leakage. All patients underwent re-operation and revision of anastomosis and the

pancreatic anastomosis was re-enforced with wide drain. Feeding jejunostomy was also done.

Our study had shown that independent risk factors for re-operation after pancreatectomy are high preoperative serum bilirubin levels, post pancreatectomy hemorrhage, Intraabdominal collection, duodeno-intestinal/gastro-intestinal leak, pancreatico-enteric anastomotic leak and Septicemia

Reddy et al. in 2012 found longer pre-operative duration of jaundice (>3 months), postoperative occurrence of complications such as PPH, presence of intra-abdominal collections, and leakage of alimentary tract reconstructions, to be risk factors for reoperation [(16)]. Nakano et al. in 2008 found patients with longer duration of preoperative jaundice are more nutritionally depleted due to prolonged poor oral intake which thereby leads to increased postoperative complications [(21)].

The in-patient mortality in our study was significantly higher in re-operated patients than in non-re-operated patients. Standop et al. found mortality in early re-operated patients from different series to be around 13-60% [(22)]. Shukla et al. showed decreased mortality in early re-operated patients to reach 13% [(23)] while Reddy et al. [(16)] found overall mortality following re-operation to be around 33.3%.

CONCLUSION

Re-operation following pancreaticoduodenectomy is sometimes needed to manage complications failed to respond to conservative measures. It carries high rate of morbidity, mortality and prolonged hospital stay. In our study the incidence was 24%. Its main indications were Post pancreatectomy hge (PPH), Pancreatico-jejunal anastomotic (PJA) leak, Hepatico-jejunostomy anastomotic (HJA) leak, Duodeno-jejunostomy or gastro-jejunostomy (DI/GI) leak and Intraabdominal collection. Intra-operative management include drainage, control of bleeding, re-anastomosis but completion pancreatectomy may have a role as a last option in treatment of post pancreatectomy complications especially post pancreatectomy fistula. When re-surgery is decided early interference is better before tissues become more edematous and friable. high pre-operative total bilirubin > 10 mg%, Pancreatico-jejunal anastomotic (PJA) leak, Intraabdominal collections and Septicemia are all independent risk factors (predictors) for reoperation after pancreatectomy.

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