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Bile Leak after Pancreaticoduodenectomy - Our Experience

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Abstract: ***Background*: Mortality of pancreaticoduodenectomy (PD) has come down but morbidity of PD remains high. pancreaticojejunostomy (PJ) leak is common complication and is well studied but there are very few studies regarding post PD bile leak. *Methods*: Review of our experience with bile leak after PD over a period of three years. Bile leak was defined as hepaticojejunostomy leak (HJ) if drain fluid amylase was normal. *Results*: Bile leaks were identified in five out of 46 patients who underwent PD. Two patients had HJ leak only and three had combined HJ/PJ leak. All 3 patients with postoperative pancreatic fistula had main pancreatic duct diameter ≤3 mm. All 5 patients had bile duct diameter >15 mm and all HJ were done in continuous manner. No patient required reoperation for complications and all were managed conservatively. One patient required angioembolization for pseudo aneurysmal bleeding. There was no mortality during hospital stay but two patients died, one of UGI bleeding and another secondary to sepsis after discharge from hospital on day 14 and day 30. None of the patient developed biliary stricture during follow - up of 21 (18 - 25) months. *Conclusion*: HJ leak is an uncommon complication of PD. Most patients can be managed with conservative treatment.***

Keywords: Pancreaticoduodenectomy, bile leak, hepaticojejunostomy, pancreaticojejunostomy

1. Introduction

Pancreaticoduodenectomy (PD) is the preferred first - line treatment for resectable periampullary and pancreatic neoplasms. With the advancement in the operative techniques and perioperative care, mortality of PD was reduced from 20% to 1 - 2% [1]. However, the morbidity after PD remains high, between 40 and 60% [2, 3].

The operation can be divided into two principal components: resection and reconstruction. Three anastomoses are typically performed: pancreaticojejunostomy (PJ), hepaticojejunostomy (HJ), and gastrojejunostomy (GJ) or duodenojejunostomy (DJ) depending upon whether or not the pylorus is preserved.

Post PD anastomotic leaks account for 8–29% of the complications [4, 5]. Majority of the anastomotic failures after PD are because of PJ leaks, comprising of 8–28% of patients, and, as such, the focus of the surgical literature has largely been on defining and characterizing PJ leaks after PD. HJ leaks occur much less frequently than PJ leaks after PD, with rates ranging from 3 to 8% [6 - 8].

HJ leaks appear to be underreported in the surgical literature, especially when compared to leaks at the PJ anastomosis. Over 600 studies have been published on pancreatic leaks after PD, in contrast to a single study from Japan on HJ leaks [8]. There are conflicting conclusions regarding management and outcomes of post PD biliary complications [9 - 11].

There are fewer reports in the literature reporting the incidence, diagnosis, management, and outcomes of HJ leaks following PD [8 - 11]. In this study, we present our experience of HJ leaks after PD.

2. Patients and Methods

2.1 Patients

Between April 2018 and July 2021, total 46 patients underwent PD for different etiologies and 5 patients developed bile leak. Retrospectively reviewed the medical records of these patients regarding demography, clinical characteristics, preoperative laboratory profile, intraoperative findings, type of reconstructions, postoperative outcomes and follow - up.

For the purpose of the study, an HJ leak (also referred to as a bile leak) was defined simply as bilious abdominal drainage observed after PD. In most cases (not in our study), leakage from the HJ anastomosis was confirmed by imaging with a contrast study through an abdominal drain or a cholangiogram. The diagnosis can be made without imaging confirmation by observing bile - rich, amylase - poor drainage. High - output drains were defined as those producing greater than 250 ml/day of fluid; drainage less

than this amount was characterized as low - output. In order to capture additional patients, records were reviewed if the length of hospital stay was more than 9 days, the patient was readmitted, or an interventional radiology procedure was performed in the postoperative period.

2.2 Surgical techniques

Staging laparoscopy was done in all patients to look for metastasis followed by laparotomy with modified Makuuchi incision. Pancreatoduodenectomy with standard lymph node dissection was done. Reconstructionwas done using single loop of jejunum; PJ with modified Blumgart technique followed by hepaticojejunostomy was made either in continuous or interrupted manner with PDS sutures depending on the size of the duct and lastly GJ/DJwas done in end to side manner. Two abdominal drains were placed one behind the HJ and another anterior to PJ. Postoperative drain fluid amylase was estimated on 3rd postoperative day.

Postoperative pancreatic fistula (POPF), delayed gastric emptying (DGE) and post pancreatoduodenectomy hemorrhage (PPH) were defined as per the International Study Group on Pancreatic Surgery (ISGPS) [12].

Surgical mortality was defined as a postoperative death within 30 or 90 days from the index operation. All statistical test were done by statistical package of Microsoft Excel 2019.

3. Results

During the study period, 46 patients underwent PD. Of these 46 patients, 5 patients developed bile leak; 3 of these had pancreatic leak also, so we can say that only 2 patients had true HJ leak and 3 had a combined HJ/PJ leak. Characteristics of these patients are summarized in Table 1.

There was no relation of POPF with bile leak but all three patients with POPF had main pancreatic duct (MPD) diameter <3mm. The 5 patients who developed bile leak had continuous type of HJ anastomosis. None of the patients required percutaneous transhepatic biliary drainage (PTBD) or reoperation for the complications. One patient developed bleeding secondary to pseudoaneurysm of pancreatic artery and underwent angioembolization. There was no mortality during the hospital stay but two patients died on follow - up; one developed UGI bleed with sepsis and other died at home, developed sepsis with multiorgan dysfunction syndrome, 14 and 30 days after discharge. Rest of three patients were managed conservatively and bile leak stopped spontaneously. None of the patients developed biliary stricture on follow - up of 21 (18 - 25) months.

Table 1: Summary of patients with bile leak

Particulars	Case 1	Case 2	Case 3	Case 4	Case 5
Age (years)	49	55	38	36	51
Sex	M	M	M	F	M
Preop Bilirubin (mg/dl)	5	22	16	1	10
Preop ERCP	Yes	No	No	Yes	Yes
Pancreas texture	Firm	Soft	Soft	Soft	Hard
MPD (mm)	7	1	2	5	3
CBD (mm)	15	15	15	15	12
HJ technique	Continuous	Continuous	Continuous	Continuous	Continuous
Bile leak	Yes	Yes	Yes	Yes	Yes
POPF grade	**No**	C	BL	**No**	BL
DGE	No	Yes	Yes	No	No
Bleeding	No	**Yes**	No	No	No
SSI	Yes	Yes	Yes	Yes	No
Reoperation	No	No	No	No	No
Clavien - Dindo grading of complications	I	IIIa	I	I	-
Hospital stays (days)	14	25	10	6	7
30 - day mortality	No	No	No	No	No
Readmission	Yes (UGI bleed)	No	No	No	No

BL - Biochemical leak, CBD - Common bile duct, DGE - Delayed gastric emptying, ERCP - Endoscopic retrograde cholangiopancreatography, HJ - Hepaticojejunostomy, MPD - Main pancreatic duct, Preop - Preoperative, POPF - Postoperative pancreatic fistula, SSI - Surgical site infection, UGI - Upper gastrointestinal.

4. Discussion

Today extensive literature exists regarding the specific complications that occur after PD, particularly addressing POPF, DGE, and postoperative hemorrhage [1, 2, 4, 13]. Over the past 20 years, as the number of PD being performed at high - volume pancreatic centers has increased; rare complications are being observed with increasing frequency.

International study groups have met and composed white papers discussing each of these complications and established standardized complication grading systems [14 - 16]. Despite improvements in postoperative mortality, morbidity remains in the 40–60% range [2].

Biliary complications following PD are poorly described in the literature, mainly as biliary leak, and very few papers were specifically dedicated to these complications. Little has been written on HJ leaks after PD. HJ leaks occur at one sixth the rate of PJ leaks after PD (~12 vs.2 %) [9], but the impact of the complication can be similarly severe, and the management is nearly as complex.

One might expect the ratio of studies in the literature to reflect the observed difference in occurrence rates, but surprisingly, HJ leaks have received disproportionately less attention. A PubMed search for "pancreaticoduodenectomy" and "pancreatic fistula" yielded over 600 articles. However, in a similar search, only a few studies and one of from Japan (Suzuki et al.) focused on HJ leaks after PD. They reported an 8 % HJ leak rate (nine patients) in a series of 107 PDs. Intraoperative HJ leak testing was performed in a large number of patients (n=28), and utilized indwelling transhepatic biliary drainage catheters for leak testing when available. There was no bile leak after a normal intraoperative anastomotic leak test and suggested that this step may be preventive, but did not further characterize the impact of this complication [8].

As an increasing number of PDs are being performed, emerging data regarding biliary fistulae after PD have been published. Burkhart et al. published their experience with the incidence of HJ leaks after PD by describing the clinical presentation and management of such leaks and proposing a grading system similar to the clinical grading scale for postoperative pancreatic fistulae. They observed an HJ leak rate of 2.2% (16 patients) in a series of 715 patients and demonstrated that this resulted in a significant increase in wound infection, delayed gastric emptying, sepsis, length of stay, and total hospital cost when compared to those without HJ leak. However, no mortality was observed in patients suffering a HJ leak. Eight of the 16 patients (50%) also experienced a concomitant PJ leak, and these were included in the HJ leak group for analysis. A low preoperative albumin and male gender were found to predispose patients to HJ leak. All patients were managed non - operatively with the operatively placed drain (grade A), percutaneous drain (grade B), or percutaneous transhepatic biliary drainage (grade C) [9].

After this, two additional studies have further examined biliary complications after PD with varying results. Duconseil et al. observed a biliary complication in 30 (7.9%) of 397 patients who underwent PD, and these were characterized as either an HJ leak in 13 (3.3%) patients or a biliary stricture in 17 (4.3%) patients; no mortality was observed in HJ leak group [10].
Malgras et al. published their experience with early biliary complications after PD and observed an HJ leak in nine (3%) of the 352 patients who underwent PD [11]. Also demonstrated a need for reoperation with revision of the HJ anastomosis and placement of a T - tube in four (44%) of the nine HJ leaks. Of note, patients with a high drain amylase suggesting a concomitant PJ leak were excluded from the analysis.

In this study we examined the HJ leak and combination of HJ and PJ leak. We observed the HJ leak in two patients out of 46 patients, resulting in HJ leak rate of 4%. This is similar to recently been reported in literature [9, 10, 17]. Combined HJ/PJ leak observed in 3 patients out of 46, resulting in leak rate of 6%, which slightly higher than Jester et al. [17] where it was 3%. Patients with a combined HJ/PJ leak are a novel subset of patients that have not been specifically examined as these patients have previously either been included in the analysis of HJ leaks overall or have been excluded from analysis completely.

HJ leaks generally can be attributed to either a result of poor technique or compromised blood supply at the level of the bile duct where the anastomosis was performed. Preoperative biliary stenting is another variable with potential to negatively affect biliary leak rates, yet in this series only had an association with pancreatic and not biliary fistulae. Any of these reasons could be considered as major contributing factors, although none have been proven. HJ/PJ leaks are likely a completely different process in which a severe pancreatic fistula leads to a complete dehiscence of the entire most proximal portion of the afferent limb affecting both the pancreatic and biliary anastomoses. The PJ likely breaks down first and is so severe that the hepaticojejunostomy likely follows suit. In the future, maybe this category should be classified as the most severe of pancreatic fistulae and possibly classified as the worst subset of the grade C pancreatic fistula [17].

In our study none of bile leak patient required reoperation and all managed conservatively, in contrast to the experience reported by Burkhart et al. in which all patients with an HJ failure were able to be managed non - operatively, [9] we found that 6 of the 24 identified HJ leaks (25%) and 7 of the 31 (23%) combined HJ/PJ leaks required operative management to control biliary sepsis [17]. The reason for this disparity in management is not clear. In our series, patients that required reoperation did so for uncontrolled biliary sepsis, thereby mandating operation exploration. The mantra of prompt and effective control of an HJ leak reported by Burkhart et al [9] is paramount regardless of approach. However, the need for operative intervention has also been reported by Duconseil et al. and Malgras et al. in which operative management in 5 of 13 patients (33%) and 4 of 9 patients (44%) was necessary for HJ leaks [10, 11].

In our series of five patients, two patients died on follow - up but in the majority of literature, there has been no mortality associated with HJ leaks after PD [9, 10]. However, in series of Jester et al., four deaths (17%) were observed in the HJ leak group at 90 days. This surgical mortality was significantly greater than that observed in patients with PJ leaks (5%, $p = 0.001$) and in patients with no leak (2%, $p = 0.001$). The combined HJ/PJ leak group demonstrated significantly greater 90 - day mortality than any other group with ten observed deaths (32%, $p = 0.0001$). These results suggest that a failure of the HJ anastomosis with or without a concomitant PJ leak is a devastating complication that can have lethal consequences [17].
Several limitations to this study are first the retrospective study and the small sample size of HJ leaks and combined HJ/PJ leaks.

The normal rate of biliary stricture following PD is 2.6 %, with an increased risk in patients requiring percutaneous biliary drainage [18]. We were not able to detect any biliary strictures in patients experiencing an HJ leak.

In our study we have not done any comparative study between HJ leak and no leak group but some studies demonstrated a statistical association between poor

nutritional status (as indicated by preoperative albumin) and an increased rate of HJ leak, the mechanisms behind this complication remain somewhat elusive [9].

5. Conclusion

Bile leak is rare but may be a serious complication of PD. Our experience suggest continuous anastomosis technique may be associated with increased risk of leak in spite of well dilated bile duct. Biliary obstruction (based on the use of a preoperative stent, bile duct diameter, or preoperative bilirubin) does not appear to be associated with the risk of a leak, while poor nutrition (using albumin as a surrogate) is a negative risk factor.

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