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Pancreatic fistula and bleeding following choledochal cyst excision: Experience of two decades

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ABSTRACT

Objective: Choledochal cyst excision (CDCE) with hepaticojejunostomy is standard of care in choledochal cysts. Complications related to inadequate healing of distal stump like post-operative pancreatic fistula (POPF) and bleeds have not been addressed in literature. We report two decade experience with these complications following CDCE.

Material and Methods: Retrospective analysis of demographics, operative details and post-operative course of patients who developed POPF (according to International Study group of Pancreas surgery classification) and bleeds following CDCE were compared with those who did not develop these complications.

Results: POPF was seen in in 34 out of 377 operated patients (incidence of 9%). In those with POPF, 24/34 (70%) had biochemical leak and 10/34 (30%) had clinically relevant POPF (B and C). All grade B POPF 6/34, required additional percutaneous drains while all grade C 4/34 required operative intervention to control sepsis. There was no mortality in the POPF group while two patients in control died from non-surgical causes. A difficult distal stump precluding closure was the only factor found associated with subsequent development of POPF (5.9% in POPF group vs. 0.5% in control group, p= 0.03). Post-operative bleeding was seen in 2 (6%) patients with POPF and in 5/343 (1.4%) in control group.

Conclusion: It is possible to anticipate development of POPF intraoperatively, during CDCE. Most of these POPFs can be managed conservatively with adequate drainage. Surgery is required only in grade C fistula and bleeds. Since these are isolated pancreatic fistulas, unlike those seen after pancreaticoduodenectomy, they are associated with more favourable outcomes.

Keywords: Choledochal cyst, choledochal cyst excision, biliary cyst, Roux-en-Y hepaticojejunostomy, post-operative pancreatic fistula, pancreatic fistula

INTRODUCTION

Choledochal cyst (CDC) is a congenital abnormal dilatation of the biliary tract in the absence of any acute obstruction constituting about 1% of benign biliary diseases (1,2). The high likelihood of complications like cholangitis, pancreatitis and a substantial lifetime risk of cholangiocarcinoma mandate a complete cyst excision once the diagnosis has been made (3). There is considerable literature regarding strategies for difficult to excise CDC and post-operative complications related to transacted proximal end, like bile leak and hepaticojejunostomy stricture (4). However, there is scant literature on the consequences of blowout of distal stump following choledochal cyst excision (CDCE), like post-operative pancreatic fistula (POPF) and secondary haemorrhage. POPF and bleeds following biliopancreatic surgery are recognised as important complications resulting in considerable morbidity prolonging hospital stay and even mortality. Although there are several management guidelines and strategies for the prevention of these complications following pancreaticoduodenectomy (PD) and distal pancreatectomy (DP), there is little published experience on these complications following CDCE. In this study, from a tertiary care teaching hospital, it was aimed to report our experience of natural course and management of POPF and bleeds following CDCE (5).

MATERIAL and METHODS

Institutional ethics committee clearance was obtained for the study. Data pertaining to demography, clinical features, operative findings, surgical procedure details and post-operative course were extracted from hospital records of all patients who underwent CDCE in the department of surgical gastroenterology, a tertiary care teaching hospital, from January 2000 to December 2020. Clinical presentation, prior history of acute pancreatitis, episodes of cholangitis and management

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strategies and upper abdomen surgery were noted (6-8). The CDC were classified on basis of cholangiographic findings (MRCP or ERCP) as suggested by Alonso Lej (9).

Surgical Technique

All type I and IV CDCs underwent open complete excision of the extrahepatic biliary tree with restoration of bilio-enteric continuity via a Roux-en-Y hepaticojejunostomy (RYHJ) at hilum (10,11). While proximal mobilization of the CDC till the biliary confluence is straightforward unless the surgical dissection is made difficult by adhesion of the cyst to hepatic artery and portal vein secondary to inflammation, excision of the distal segment of CDC necessitates dissection from the pancreatic tissue in addition to the hepatic artery and portal vein (12,13). This might be particularly challenging, especially if the surrounding planes are inflamed and friable and/or the main pancreatic duct is intimately related. We maintain the plane of dissection right on the cyst wall, controlling the vessels from epicholedochal plexus with bipolar coagulation, taking care to not deviate into the pancreatic parenchyma and injure the pancreatic duct during this step. The CDC is opened in order to identify the opening of the ventral pancreatic duct from within (when possible), before transecting the CDC just below the start of waisting. We ensure vascularity at this end by flush, sharp division. The distal end is flushed with saline through a feeding tube to remove any calculi or protein plugs in the common segment. The end is then secured with continuous delayed absorbable monofilament polydioxanone suture. The suture size depends on local factors, 5-0 for thin, friable duct and 3-0 for non-inflamed duct wall holding sutures well. We do not use staplers for distal transection since we ensure it is in the narrowed distal end. RYHJ restores biliary drainage. Single wide bore (24Fr) soft latex drain is placed in the Morrison's pouch.

The drain fluid is assessed daily for volume and character (serous/haemorrhagic) and amylase values are obtained on days three and five. The drain is removed when output is clear, output less than 50 cc and amylase value less than three times if serum amylase values of the day.

Those who develop POPF are monitored for clinical signs of peritonitis or sepsis. Any unexplained tachycardia, fever, leucocytosis is evaluated with a contrast enhanced CT scan (CECT). If any undrained collection is identified, image guided percutaneous drains are placed. The patient is rigorously monitored. If sepsis persists or signs of generalised peritonitis develop, exploratory laparotomy with lavage and drainage is done. Any patient with haemorrhagic drain output is investigated with triple phase CT angiogram (TPCTA). If the potential bleeding source is identified, it is further evaluated for suitability for endovascular intervention. If no source is identified and there is increased haemorrhagic output with drop in haemoglobin or change in patient hemodynamics, the patient is taken for surgical exploration.

Inclusion criteria: All patients undergoing open CDCE in a single unit, whose drain fluid amylase (DFA) on post-operative day three was more than three times of upper limit normal amylase level.

Exclusion criteria: Patients who underwent CDCE along with any additional pancreatic surgery and patients who were referred after CDC excision done elsewhere, were excluded.

Operational definitions: POPF following choledochal cyst was defined as elevation of drain fluid amylase (DFA) to more than three times upper normal serum amylase levels (90 mg/dL) on or after post-operative day three (14). These were further subdivided into the following:

- Type A POPF or Biochemical leak included patients with documented POPF without any features of sepsis and who did not require any intervention.
- Type B POPF included patients with documented POPF, with signs of infection/without organ failure, requiring percutaneous or endoscopic drainage, angiographic procedures for bleeding.
- Type C POPF included patients with documented POPF, with organ failure and/or requiring surgical intervention.

Difficult distal stump: For the purpose of this study the term is used for denoting difficulty in dissecting and or suturing the distal part of intrapancreatic portion of choledochal cyst due to inflammation (15).

Statistical Analysis

Quantitative data was presented as mean ± standard deviation and range. Qualitative data were described as frequencies given in percentage values, based on the distribution of data. Comparisons between two groups were performed using Mann-Whitney U test (continuous variables) and Chi-square test (categorical variables). All statistical tests were two-sided, and $p< 0.05$ were considered statistically significant. Statistical analyses were performed using SPSS software, version 23, IBM Corp., Armonk, NY, United States of America).

RESULTS

During the period spanning two decades, we identified 38 cases of POPF from a total of 381 operated cases of choledochal cysts. After review, four cases were excluded as they underwent an additional procedure (pancreatoduodenectomy= 1, Duodenal preserving pancreatic head resection= 1, lateral pancreatojejunostomy= 2). For the purpose of this study, 34 patients with POPF (cases) were compared to 343 patients without POPF (controls) (Figure 1). All cases were performed by open either midline or subcostal incision.

In the entire cohort, the most common symptom at presentation was abdominal pain in 341/377 (90%) followed by jaundice in 105/377 (28%), and fever in 73/377 (19%). Lump, as a presenting

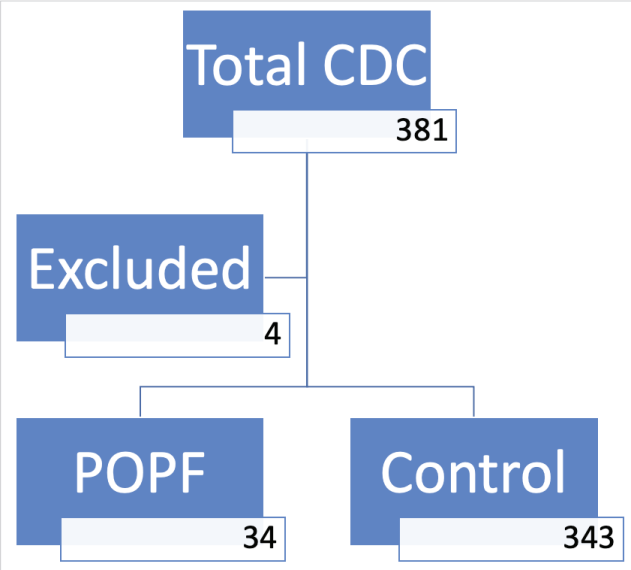

Figure 1. Consort diagram.
CDC: Choledochal cyst, POPF: Post-operative pancreatic fistula.

symptom, was seen in only 6/377 (1%) while 46/377 (12%) presented with all three features of cholangitis.

Table 1 compares the two groups with regard to demographics, clinical characteristics, type of choledochal cyst [Alonso Lej classification (9)], cystolithiasis, previous history of pancreatitis or cholangitis before surgery, need for prior biliary interventions, prior history of abdominal surgery, intra-operative findings like pericholedochal inflammation, difficult distal stump, average duration of intraoperatively placed drain retained, and hospital stay.

One hundred twenty two/377 (32%) patients had some feature to suggest cholangitis; however, most responded to antibiotics and biliary intervention was required in only 90/377 (24%) of them. Table 2 gives the details of biliary intervention. More patients were managed with internal biliary drainage, and percutaneous transhepatic biliary drainage (PTBD) was used only if the patient was deemed unfit due to organ failure or technical difficulties. The nature of biliary intervention before surgery did not impact development of POPF (p= -0.352).

Table 1. Demographics, intraoperative findings, and post-operative course following CDCE

Factors	POPF (n= 34)	Control (n= 343)	p	OR
Age	32 years (7-49 years)	32.5 years (<1-76 years)	0.9	0.3
Sex Males Females	 6 (18%) 28 (82%)	 83 (24%) 260 (76%)	0.39	0.8
Choledochal cyst type	Type 1-22 (64.7%) Type 4-12 (35.3%)	Type 1-264 (76.9%) Type 4-79 (23.1%)	0.16	0.8
History of pancreatitis	1 (2.9%)	23 (6.7%)	0.856	0.4
Prior cholangitis episodes	11 (32.3%)	111 (32%)	0.9	0.3
Cystolithiasis	11 (32.4%)	93 (27.1%)	0.389	1.3
Prior upper abdomen surgery	9 (26.5%)	69 (20.1%)	0.379	1.4
Prior biliary interventions	10 (29.4%)	80 (23.3%)	0.427	1.3
Pericholedochal inflammation	19 (55.9%)	165 (48.1%)	0.657	0.8
Difficult distal stump	2 (5.9%)	2 (0.5%)	0.032	0.7
Post-operative bleed	2 (5.9%)	5 (1.5%)	0.75	1.3
Average duration of drain	15 days (5-95 days)	5 days (1-15 days)	0.001	1.5
Average hospital stay	19 days (5-96 days)	7 days (3-38 days)	0.001	1.2

Table 2. Details of biliary intervention in unresolved cholangitis

Prior Intervention to Biliary system	POPF[a]	Control group	p
Endoscopic drainage	8 (80%)	71 (89%)	0.352
PTBD[b]	2 (20%)	9 (11%)	

[a]POPF: Post-operative pancreatic fistula.
[b]PTBD: Percutaneous transhepatic biliary drainage.

Four patients had a difficult distal stump, two each in either group. Although we did manage to place sutures in three of these patients, one patient in the control group had avulsion of inferior end of CDC and the distal stump could not be secured. Surprisingly, he did not develop POPF. Out of 34 cases of POPF, only two patients had a difficult distal stump intraoperatively. Average duration of drain stay was 15 days (5-95 days) with output of 90 mL (70-120 mL) in POPF group and in control group average drain stay was five days (1-15 days) with output of 50 mL (30-70 mL)

Incidence of POPF in our study was 34/377 (9%). Majority, 24 (70.5%), had grade a biochemical leak. Clinically relevant POPF (B and C) was present in 10 (29.5%). Those who had grade B leak were managed with additional percutaneous drains. Four (11.7%) had grade C POPF with uncontrolled sepsis and required re-exploration, lavage and drainage. There was no mortality in this group.

Seven out of 377 (1.85%) patients following CDCE had bleeding in the post-operative period. Five bleeds happened in those who did not have POPF, and two bleeds in the POPF group. All of these patients required operative intervention due to failure to identify the bleed site on CT angiography. In the POPF group, one had bleeding from hepaticojejunostomy site and was managed with reinforcement of HJ, another had bleeding from a small arterial twig which was managed by ligation. In the control group, one patient had bleeding from the gastroduodenal artery (GDA) pseudoaneurysm which was managed by suturing of GDA, and one patient had bleeding from the small unnamed arterial twig, managed by suture ligation of bleeding vessel. In three patients, no source could be identified after evacuation of clots and thorough exploration.

All cases were followed up for a mean duration of four years, with a range of 1 to 22 years. Table 3 lists all the other complications not related to distal stump in this series.

There was no mortality in the POPF group while two patients in the control group died from non-surgical causes (myocardial infarction in one and arrythmias in the other).

Table 3. List of complications other than those related to the distal stump

Complications	Incidence
Early complications	
Bile leak	18 (4.7%)
Chylous ascites	2 (0.5%)
Intra-abdominal collection	8 (2.1%)
SSI[c]	16 (4.2%)
Pulmonary complications	10 (2.6%)
Late complications	
Anastomotic stricture[d]	12 (3.1%)
Redo stricture	1 (0.2%)
Hepatolithiasis	6 (1.5%)
Cholangitis	2 (0.5%)
Liver abscess	2 (0.5%)
Acute pancreatitis	5 (1.3%)
Adhesive obstruction	5 (1.3%)

[c]SSI: Surgical site infection.
[d]Anastomotic stricture: HJ stricture.

DISCUSSION

In this review of POPF and bleeds following CDCE over two decades, we found a low incidence of POPF (9%) (34/377) and post-operative bleeds (5.9%), and all could be salvaged with timely intervention. While the study by Liu et al. have reported similar incidence of 9.2% (5/54) (15), Okada et al. have reported a higher incidence of 31.6% (6/19) (2014), probably reflecting surgical experience and nature of cases undergoing the surgery (16).

There was no difference in demography, clinical features or CDC related pre-operative complications like pancreatitis, cystolithiasis or prior abdominal surgery between the group which developed these complication and that which did not. Similarly, the incidence of cholangitis was similar in both groups. Internal biliary drainage by endoscopic retrograde cholangiopancreatography (ERCP) was the preferred modality to treat cholangitis. Previous studies suggest that multiple episodes of cholangitis would increase the risk of POPF; however, in our series, prior cholangitis episodes did not contribute to the development of POPF (p= -0.9) (17). Adequate treatment of cholangitis preoperatively by antibiotics with or without adequate drainage and excision surgery only after a cooling off period of eight weeks probably contributed to this. Previous studies suggest pre-operative PTBD to be associated with lower post operative complications than ERCP in patients undergoing PD (18,19). However, recent data suggest internal biliary drainage to be more physiological and equivalent to PTBD (20). Hence, we preferred internal drainage and it did not increase distal stump related complication rates.

Presence of peri choledochal inflammation, resulting in intraoperative difficulty in dissecting the CDC off adjacent structures in hepatoduodenal ligament did not affect the development of POPF (p= -0.65). In an attempt to predict intraoperatively itself the patients who were likely to develop POPF, we defined the entity of a difficult distal stump i.e., difficulty in dissecting and or suturing the distal part of the intrapancreatic portion of choledochal cyst due to inflammation. Intuitively, difficult distal stump should increase chances of POPF, but in our study, not all difficult distal stump resulted in POPF. In the control group, two had difficult distal stump but none developed POPF (21). In

fact, one of the patients in the control group had avulsion of the distal end and could not be secured, but he did not develop POPF. It is our routine practice to flush the distal stump to clear protein plugs and debris in the common channel prior to closure. We believe that if vascularised distal stump is sutured, it does not leak in the absence of distal obstruction.

POPF following CDCE is a kind of isolated pancreatic duct leak as opposed to POPF following PD, in which there is leak of bile mixed with pancreatic secretions. Isolated pancreatic leaks following distal pancreatectomy if drained adequately are known to be associated with fewer septic complications and morbidity and mortality as compared to POPFs following PD (14).

The incidence of POPF in our cohort was 9%. Among those with POPF, clinically significant POPF was seen in 10/34 (30%), and the rest were biochemical leaks 24/34 (70%). Grade B POPF was observed in 6/34 (18%) patients, all of whom required additional drain placement for control of leak. Grade C POPF patients was seen in 4/34 (12%) patients, and they all developed severe sepsis with peritoneal signs, necessitating laparotomy, lavage and additional drainage.

There is evidence on the use of octreotide or long acting somatostatin analogue to prevent POPF after pancreatectomy and in ameliorating the adverse consequences once POPF develops following PD and DP (22,23). All patients who developed POPF in this series had a low output pancreatic fistula. Average volume of drain output was 90 cc in POPF group and 50 cc in the control group. We did not use strategies like dietary modification or pharmacotherapy to decrease these already low output fistula.

The average duration for drains in the group which developed POPF was 15 days, ranging from as short as five days in case of biochemical leak to maximum of 95 days in those with grade C POPF. Even in high grade POPF, the fistula healed in two weeks following laparotomy, lavage and additional drainage once sepsis was controlled. The clinically significant POPF group patients, however, did have a prolonged hospital stay.

While the incidence of post-operative bleed was higher in the POPF group with 2/34 (5.9%) vs the control group with 5/343 (1.5%), it was not statistically significant (p= -0.37). There are several potential sites of bleeding in a patient following CDCE like segmental arteries arising from right hepatic artery or branches from anterior and posterior pancreatoduodenal arteries and veins (24). The bleeds can arise from suture lines as well (hepaticojejunostomy and jejunojejunostomy). One of our patients had a bleeding from HJ site which needed dismantling of anterior layer of HJ and refashioning of anastomosis. Presence of POPF is known to contribute to secondary haemorrhage following PD or DP (25). A leak from the distal stump following CDCE is a leak of pancreatic juice with all its proteolytic enzymes which can contribute to secondary haemorrhage. In our study, two patients with post-operative bleeding had associated POPF. These patients required control of the bleeding site and adequate drainage of collection to eliminate sepsis. If the source of bleeding is identified and properly managed and there is adequate drainage of pancreatic secretions and absence of sepsis, bleeds following CDCE by themselves do not result in mortality. We were able to salvage all secondary bleeds following CDCE in our series.

Despite these two complications, prolonged hospital stay and increased duration of use of drains, they do not increase mortality. CDCE, if done by surgeons, should be associated with low perioperative mortality. The two mortalities in the control group were also due to non-surgical causes. Even grade C POPF or bleeds requiring surgery can be successfully salvaged.

Other post-operative complications in this series have been detailed in Table 3. The incidence of bile leak (4.7%) and RYHJ stricture (3%) are comparable to a large series of CDC excision reported by the Dutch group (6% and 4 %) (26).

Merits, Demerits and Clinical Implications of This Study

Our study is a large, single centre experience of CDCE spanning over two decades which has looked at complications specific to blowout of distal stump (POPF and bleeds), an issue hitherto infrequently addressed in the literature. Since this is a retrospective study, dependent on documented findings, there are limitations like observer bias, documentation bias and interpretation bias. However, the results clearly illustrate that POPF and bleeds following CDCE are not as ominous as those following PD or DP, which can be very reassuring for treating surgeon. POPFs following distal stump blow out following CDCE can be well managed with adequate drainage alone. Secondary bleeds following CDCE are from small segmental arteries in vicinity of the cyst, which may not be evident on CT angiogram. Most stop spontaneously or can be controlled at surgery by suture ligation. This awareness is extremely reassuring to the treating team. Meticulous surgical technique, sticking to the pericholedochal plane, avoiding straying into pancreatic parenchyma, using bipolar diathermy forceps as opposed to hot shears for dissection helps control the pericholedochal plexus even in presence of inflammation and avoid damage to pancreas.

CONCLUSION

POPF and bleeds are rare complications following CDCE as opposed to POPFs following PD or distal pancreatectomy. POPFs following CDCE respond to conservative measures while few require additional drains either percutaneous or surgical. Most POPFs are self-limiting or heal with drainage alone if the surgeon ensures absence of obstruction in common channel. Bleeds following CDCE can arise from HJ site or segmental vessels in the hepatoduodenal ligament. Isolated bleeds do not adversely affect outcomes if appropriately controlled by endovascular or operative techniques and there is adequate

control of sepsis. These POPFs and bleeds following CDCE are a distinct group as opposed to those following PD or DP in terms of management strategies and outcomes.

Ethics Committee Approval: This study was approved by the Sanjay Gandhi Postgraduate Institute of Medical Sciences Ethics Committee (Decision no: 2023-20-MCh-EXP-5, Date: 05.04.2023).

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ORİJİNAL ÇALIŞMA-ÖZET
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Koledok kisti eksizyonu sonrası pankreatik fistül ve kanama: Yirmi yıllık deneyim

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ÖZET

Giriş ve Amaç: Koledok kistlerinde hepatikojejunostomi ile birlikte koledok kisti eksizyonu (KKKE) standart tedavi yöntemidir. Postoperatif pankreatik fistül (POPF) ve kanama gibi distal güdüğün yetersiz iyileşmesine bağlı komplikasyonlar literatürde ele alınmamıştır. KKKE sonrası bu komplikasyonlarla ilgili yirmi yıllık deneyimimizi sunuyoruz.

Gereç ve Yöntem: Koledok kisti eksizyonu sonrası POPF (Uluslararası Pankreas Cerrahisi Çalışma Grubu sınıflamasına göre) ve kanama gelişen hastaların demografik özellikleri, ameliyat detayları ve ameliyat sonrası seyirlerinin retrospektif analizi, bu komplikasyonların gelişmediği hastalarla karşılaştırıldı.

Bulgular: Ameliyat edilen 377 hastanın 34'ünde POPF görüldü (ensidans %9). POPF gelişenlerin 24/34 (%70)'ünde biyokimyasal kaçak ve 10/34 (%30)'ünde klinik olarak anlamlı POPF (B ve C) vardı. Tüm B sınıfı POPF 6/34, ek perkütan dren gerektirirken, tüm C sınıfı 4/34 sepsis kontrolü için operatif müdahale gerektirmiştir. POPF grubunda mortalite görülmezken, kontrol grubundaki iki hasta cerrahi dışı nedenlerle ölmüştür. Kapatmayı engelleyen zor bir distal güdük daha sonra POPF gelişimi ile ilişkili bulunan tek faktördü (POPF grubunda %5,9'a karşılık kontrol grubunda %0,5, p= 0,03). Ameliyat sonrası kanama POPF'li iki (%6) hastada ve kontrol grubunda 5/343 (%1,4) hastada görüldü.

Sonuç: Koledok kisti eksizyonu sırasında intraoperatif olarak POPF gelişimini öngörmek mümkündür. Bu POPF'lerin çoğu yeterli drenaj ile konservatif olarak yönetilebilir. Cerrahi sadece grade C fistül ve kanamalarda gereklidir. Bunlar pankreatikoduodenektomi sonrası görülenlerden farklı olarak izole pankreatik fistüller olduğundan, daha olumlu sonuçlarla ilişkilidir.

Anahtar Kelimeler: Koledok kisti, koledok kisti eksizyonu, biliyer kist, Roux-en-Y hepatikojejunostomi, postoperatif pankreatik fistül, pankreatik fistül

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