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Management of distal benign biliary stricture

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***Abstract*---**Endoscopic treatment consists of passing the stricture and placement of at least one large bore plastic stent, followed by further sessions of stenting with multiple plastic stents. Temporary placement of multiple plastic stents is the recommended approach in patients with benign biliary strictures. Self-expandable metal stents have a larger diameter compared to plastic stents and can be covered and uncovered. Placement of uncovered metal stents in patients with benign biliary strictures is strongly discouraged. However, covered self-expandable metal stents can be safely placed in selected patients.

***Keywords*---**distal benign biliary stricture, endoscopy, surgery.

Introduction

Distal benign biliary stricture (DBBS) carries a significant challenge for gastroenterologists and general surgeons due to the characteristic nature of the disease and difficulty in sustaining long-term solutions. DBBS has a multifactorial etiology including choledocholithiasis, chronic pancreatitis (CP), IgG4 autoimmune pancreatitis, human immune deficiency virus (HIV) cholangiopathy, portal biliopathy, papillary stenosis, choledochal cyst and opium intake. [(1)] In this review article we are going to discuss the etiology, diagnosis, and treatment of distal benign biliary stricture.

Pathogenesis and Etiology of Benign Distal Biliary Stricture

Chronic Pancreatitis (CP)

Chronic pancreatitis is a benign inflammatory disease, characterized by an irreversible loss of pancreatic parenchyma, leading to exocrine insufficiency with maldigestion and in advanced stages endocrine insufficiency. Consumption of alcohol and nicotine abuse are the leading causes in the progress of the disease. Extra-hepatic benign biliary obstruction occurring concomitantly with CP can be due to choledocholithiasis, pancreatic pseudocyst, or fibrosis. The incidence of biliary stricture (BS) in CP ranges from 3 to 46%. [2]

Sphincter of Oddi Dysfunction (SOD)

Sphincter of Oddi was first described by Ruggerro Oddi in 1887 as the sphincter of hepato-pancreatic ampulla. [3] It exhibits a baseline zone of elevated pressure, with superimposed phasic contractions. It demonstrates a cyclical change in motor activity that is closely associated with the migrating motor complex. Patients with SOD diagnosed clinically by typical pancreatobiliary-type pain, this pain (as defined by the Rome IV criteria) characterized by being episodic upper abdominal pain, typically postprandial in nature and combined with nausea. [4]

Post-endoscopic Sphincterotomy Stricture

Various studies have described complications associated with ES, both in the short and long term. Well documented early complications of ES include pancreatitis, bleeding, and cholangitis. While recurrent CBD stones, cholecystitis, cholangitis, hepatic abscess, papillary stenosis, and biliary stricture are the long-term complications of ES. [5] In 1 - 3.9 % of ESs performed for choledocholithiasis and in 16.8 % performed for sphincter of Oddi's stenosis, papillary stenosis develops. The risk factors for papillary stenosis to develop are SOD and ischemia of the ampulla resulted from past complicated endoscopic procedures, such as injection and heater probe for the management of bleeding. Stricture stretches over the intra-duodenal portion of the CBD to the distal part of extra-duodenal CBD in ES related biliary stricture. It occurs in 1 % of patients. [6] Papillary stenosis and biliary stricture related to ES can be treated by extension of the previous sphincterotomy. It also may require sequential stenting. [5]

Diagnosis of Distal Benign Biliary Stricture

The diagnosis of DBBS is often missed or delayed because of its indolent course. Clinically, DBBS can present with a wide array of manifestations, ranging from being completely asymptomatic to complete biliary obstruction with jaundice, pain, pruritus, fever, anorexia, and biliary stones. [7] Charcot's triad is classically used to describe three common symptoms and signs related to ascending cholangitis, namely, right upper quadrant pain, jaundice, and fever. In neglected cases, recurrent attacks of ascending cholangitis will progress to secondary biliary cirrhosis and end stage liver failure. Reynold and Everett later combined Charcot's triad with the features of shock and altered mental status, describing a

pentad of signs and symptoms suggestive of the diagnosis of obstructive ascending cholangitis. This pentad is now termed Reynold's pentad. [8, 9]

DBBS with clinically apparent jaundice showed elevation in serum transaminases and both total and direct bilirubin levels. ALP levels raise up more than three times the normal level. Also, elevations in gamma-glutamyl transpeptidase and 5′ nucleotidase levels occur. Prolongation in prothrombin time and INR indicate manifest hepatic function impairment. *(10)* Malignancy should be expected when there is a more significant elevation in ALP and SGOT levels, together with a bilirubin level of more than 84 micromol/L. Tumor markers such as carbohydrate antigen 19-9 (CA 19-9) and carcinoembryonic antigen may also raise diagnostic yield. It is proved that CA 19-9 has a sensitivity of up to 53% in diagnosing cholangiocarcinoma, with a true negative rate of 92% in DBBS groups. *(11)* Abdominal ultrasound (U/S), Magnetic Resonance Cholangiopancreatography (MRCP) and CT are usually used in the diagnostic work up of CBD strictures, although their value is not high in some cases. *(12)*

The U/S stimulation tests (transabdominal, endoscopic) were used to determine the diameter of the biliary or pancreatic duct after giving CCK and secretin. Relative obstruction caused by SOD is suggested when there is persistent ductal dilatation from baseline. *(3)* Magnetic Resonance Cholangiopancreatography (MRCP) has greatly evolved, providing high resolution images of both the benign and malignant biliary lesions. It is the modality of choice for optimal characterization of the causative lesions in most of the cases of OJ. It is superior to U/S and CT scan. *(13, 14)* Computed tomography (CT) scan is expensive and involves exposure to radiation, both of which lessen the routine use. Spiral (helical) CT scan improves biliary tract imaging by providing several overlapping images in a shorter time than traditional CT scan and improving resolution by reducing the presence of respiratory artefacts. *(15)*

Endoscopic (Minimally invasive)

Endoscopic techniques play a key role in diagnosing and managing BS and preventing complications such as cholangitis. *(16)*

Endoscopic Retrograde Cholangiopancreatography (ERCP)

ERCP depends on successful cannulation of Vater's ampulla as well as biliary-enteric continuity; therefore, it may not be feasible in patients who have undergone previous surgical reconstruction. ERCP with endoscopic sphincter of Oddi manometry (ESOM) is the most standard test used for evaluation of SOD. ESOM enables the direct assessment of ductal pressures to measure the sphincteric hypertension. For pressure measurement a small caliber typically "5 French" (Fr) multi-lumen perfusion catheter with an aspiration port is used. Persistent ductal pressures more than 35 to 40 mm Hg above baseline are significant for SOD. Abnormal pressures may be present in both pancreatic duct and the bile duct (either separately or combined). ERCP used to be the gold standard for the diagnosis of biliary diseases but is being gradually replaced by endoscopic ultrasound (EUS), which has a similar diagnostic yield but without its well-known risks. *(17, 18)*

Endoscopic Ultrasound (EUS)

EUS-fine needle aspiration (FNA) has been shown to be effective in diagnosing malignancy in patients with BS and should be considered as the initial endoscopic modality in all patients with suspected BS without OJ. Therefore, the usefulness of EUS for the diagnosis of unexplained BS warrants urgent debate, because EUS is now the first option for small pancreatic tumor screening that cannot be identified by other imaging modalities and is not associated with complications associated with ERCP. *(19)*

Other Endoscopic Technologies

Intra-ductal ultrasound (IDUS), confocal laser endomicroscopy (CLEM) and direct cholangioscopy have shown promising results in diagnosing biliary stricture. *(20)*

Treatment

DBBS should be managed by a multidisciplinary team comprising hepatobiliary surgeons, interventional radiologists and endoscopists. *(21)* Ultimately, the aim of treatment should be to enhance and preserve the patentability of the bile duct and to avoid stricture recurrence in the most ideal possible technique. Lines of treatment consists of:

1. Endoscopic management
   I- Endoscopic procedures performed by a side view duodenoscope (after performing ERCP): -
      a- Endoscopic sphincterotomy (ES)
      b- Endoscopic balloon dilatation
      c- Endoscopic stent placement
   II- EUS Biliary drainage (EUS-BD)
2. Percutaneous transhepatic (PTC) management
3. Surgical management *(9)*

Endoscopic Management

Endoscopic procedures performed by a side view duodenoscope (after performing ERCP)

Since 1970s, ERCP has increasingly progressed. A large variety of catheters, guidewires, papillotomes, balloons, stents, and other accessories are available to improve diagnostic and therapeutic maneuvers in the management of DBBS. *(22, 23)*

Endoscopic Sphincterotomy (ES)

ES is performed to facilitate various therapeutic procedures such as removal of CBD stone, placement of stents and management of short DBBS. Most ES is performed successfully by standard sphincterotome. The success rate increases markedly in difficult cannulation of the bile duct after the introduction of precut techniques. Also, wire-guided method can avoid injection of contrast media into

the pancreatic duct and is expected to decrease the incidence of post- ERCP pancreatitis (PEP) [24] Endoscopic treatment of ampullary stenosis achieved a long-term success rate of 83% in lesions limited to the intra-duodenal portion of the sphincter complex (type I) and 65% in all other types, including those with extension of the stenosis into the CBD (the latter is considered type II which required in addition balloon dilatation). [25] (Figure 1 and 2)

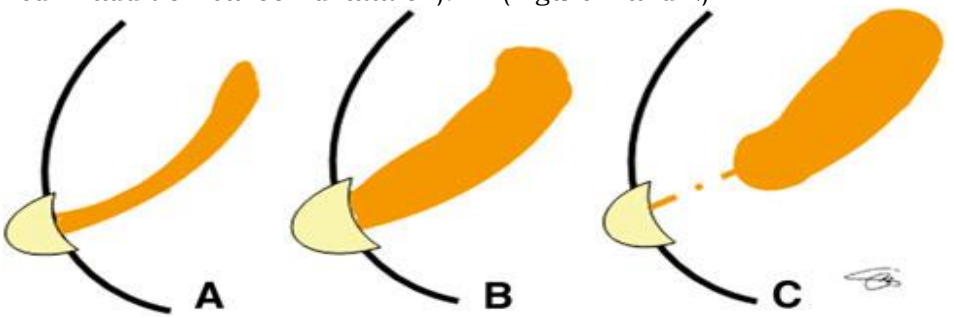

Figure 1: Schematic illustration of CBD and ampulla of Vater
A- Normal distal bile duct and ampulla
B- Ampullary stenosis without BS
C- Distal BS [26]

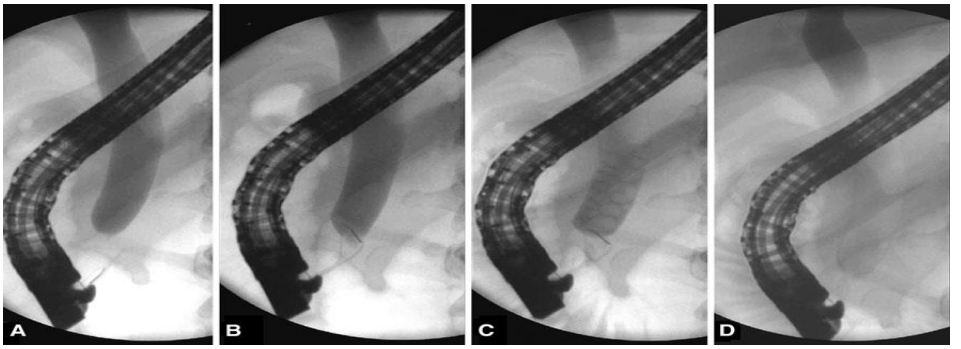

Figure 2: Fluoroscopic images showing short distal BS and its treatment using sphincterotome stricturoplasty.
A= Contrast drainage is poor due to the presence of stricture.
B and C = After sphincterotome stricturoplasty.
D = Contrast drained spontaneously [26]

Endoscopic Balloon Dilatation

Though immediately successful, balloon dilation alone is associated with a high rate of stricture recurrence (up to 47 %) depending on the underlying pathology of the DBBS. [27]

Endoscopic Stent Placement

Single plastic stents used for bridging biliary obstruction are easy to apply and inexpensive, but have insufficient diameter and therefore short stent patency, which is requiring replacement every 2 to 3 months. In general, multiple plastic biliary stents are regularly exchanged for at least one year every 3-4 months, with

or without balloon stricture dilatation. This technique showed better long-term outcomes than leaving a plastic stent in situ for the same time. [28] Covered self-expandable metal stent can achieve larger diameter, providing longer stent patency with less endoscopic interventions, but is reported to have 80% to 90% long-term success rate after stent removal, which is still unacceptably high in a benign disease with long life expectance. [29]

Also, self-expandable metal stent has several early and late complications, such as biliary infection, pancreatitis, bleeding, perforation, and particularly early stent migration. Considering the benefits and disadvantages, the best choice currently for DBBS is the usage of multiple plastic stents, however covered self-expendable metal stents show a promising future as well. [27]

EUS Biliary Drainage (EUS-BD)

EUS-BD is a relatively new therapeutic modality in the arsenal of endoscopists for attaining satisfactory BD when traditional endoscopic methods fail. The first EUS-guided biliodigestive anastomosis was innovated by *Giovannini et al 2001* [30] for a case of pancreatic head carcinoma. Since that time, its use was expanded and conducted for different indications worldwide with recorded combined success rates and post-procedure adverse events of 90% and 17%, respectively.
EUS-BD can be performed by two major approaches:

1. Extra-hepatic (EH)
2. Intra-hepatic (IH)

In the EH approach, the CBD is accessed mainly through the duodenum or through the gastric antrum. BD can be achieved by either trans-luminal stent placement (through the duodenum) or trans-papillary stent placement via the rendezvous technique. On the other hand, when the IH approach is used the Lt lobe of the liver is accessed from the gastric wall and rarely from the distal esophagus or jejunum. Using this approach, BD can be attained by either trans-luminal stent placement (Figure 3) or trans-papillary stent placement via rendezvous technique or antegrade technique. [31] HG has been proposed in cases of hilar strictures, in the presence of altered anatomy, or in cases of inaccessibility of the papilla. [32]Using EUS/FNA needle to create a fistula tract. After obtaining a cholangiography a guidewire is placed into the bile duct and the tract was dilated followed by insertion of stent to accomplish drainage of biliary system into the stomach or the duodenum. [33]

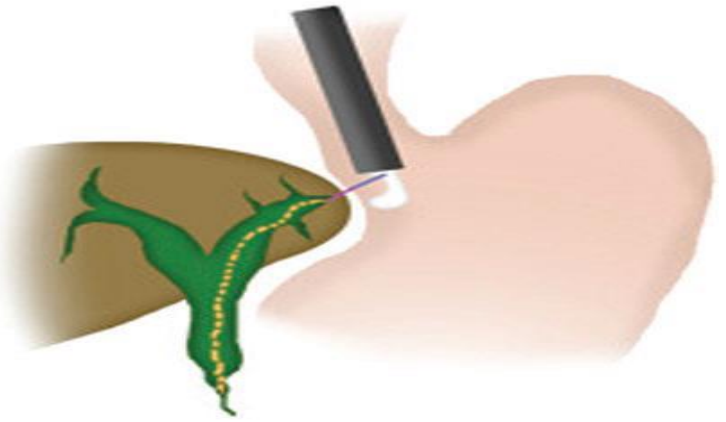

Figure 3: Diagram illustrating IH approach of EUS-BD (HG) [31]

Percutaneous Transhepatic Management (PTC)

Main indications for treatment with PTC are: (1) Presence of comorbid conditions making the patient not candidate for surgery, (2) Difficult or impossible endoscopic cannulation of the ampulla of Vater and (3) A Septic status that requires early or immediate biliary tree decompression. Percutaneous balloon dilation of BBS has been the most widely used alternative to endoscopic treatment; however, the rate of recurrence has varied from 15 to 44 %. Several investigators have reported that percutaneous transhepatic placement of retrievable covered stents is feasible for the treatment of DBBS. However, these studies had only a small number of patients and had short follow-up periods. [34]

Surgical Management

Surgery is mainly reserved for instances when endoscopic or percutaneous approaches are not available or not viable options. Simple removal of stones after choledochotomy followed by primary repair which was the commonest situation earlier is considered as inadequate without associated drainage in the majority, as the spectrum of patients includes those with complicated CBD stones, history of multiple ERCP attempts and related anatomical abnormality like stricture, or diverticulum. When biliary bypass is indicated, three options are available: CDD with side-to-side biliary enteric anastomosis, CDD with end-to-side biliary-enteric anastomosis, and biliary-jejunal anastomosis either as a hepaticojejunostomy or a roux-en-y CJ (RYCJ). All these can be accomplished via open, laparoscopic, and robotic-assisted approaches; however, there is no consensus to which is best due to a paucity of data comparing the techniques. Choice of operation is largely left up to the individual surgeon. [35]

Side to Side Choledochoduodenostomy (CDD)

Open CDD

CDD was first performed by Bernhard Riedel (a German surgeon) in 1888, but the patient died because of leakage into the peritoneal cavity. Oskar Sprengel

(another German surgeon) in 1891 reported the first recovery following CDD. William J. Mayo, in 1905, reported the successful treatment of a CBD stricture following cholecystectomy and choledochotomy by suturing the end of the dilated portion of the duct to the duodenum. [36]

Technique

Both Rt subcostal and midline incisions give sufficient visibility, then the retractors are placed, and the hepatic flexure is inferiorly reflected. Then, generous kocherization of the duodenum is carried out to facilitate duodenal mobility to assure tension-free anastomosis. [37] (Figure 4).

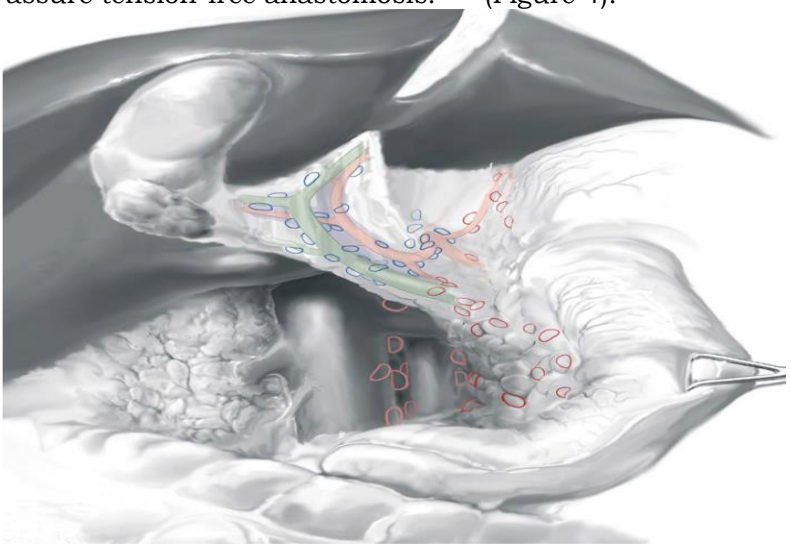

Figure 4: Kocherization of the duodenum [38]

Incise the peritoneal covering of the HDL to expose the anterior surface of the CBD. [39] The site of the CBD can be checked by the aspiration of bile whether the anatomy is uncertain, or the procedure is re-operative. Then, two stay sutures are taken on the lateral sides of the anterior part of the CBD. (Figure 5) [40]

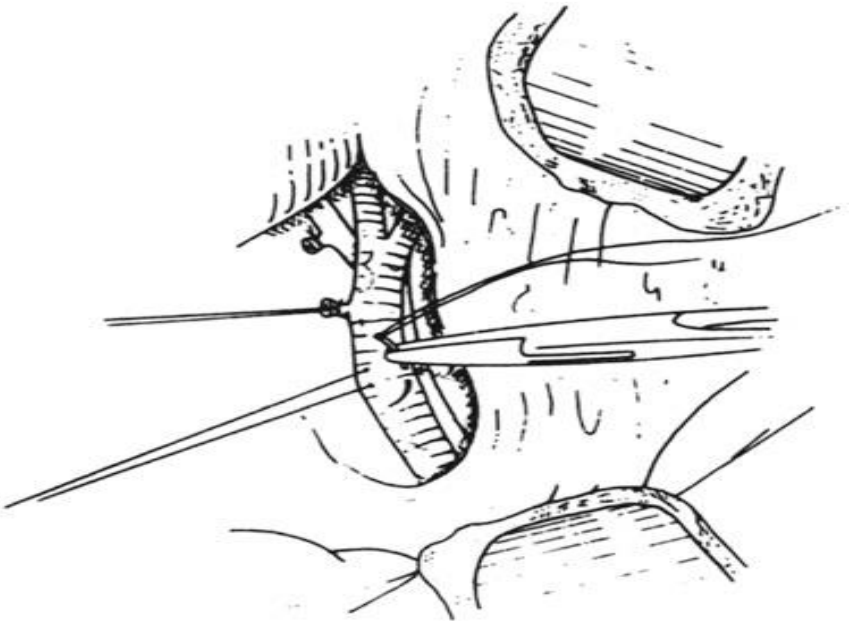

Figure 5: Two stay suture at the lateral sides of the anterior part of the CBD. [40]

A 2 cm longitudinal choledochotomy is done distal to the CD / CHD junction with its distal part close to the upper border of the mobilized duodenum. [41]
A duodenotomy is done on the antimesenteric border of the duodenum. The length of the duodenotomy should be around 70% of the length of the choledochotomy, as it will expand to become the same size (Figure 24). [38]

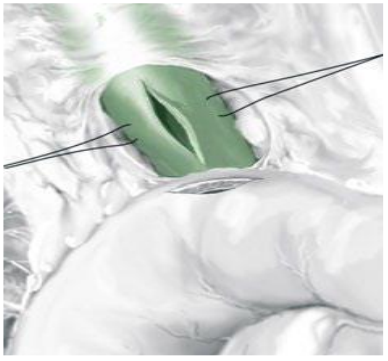

Figure 6: Choledochotomy and duodenotomy [38]

The anastomosis is seen as a clock face, using interrupted 4-0 absorbable sutures, the first suture is placed at the 6 o'clock site going inside-to-outside on the duodenum and outside-to-inside the lumen on the CBD (the knots within the posterior wall lumen). The suture is left none ligated and hold with a clamp. Gentle traction on this suture helps in exposing and placement of the next posterior wall sutures. Between the 6 o'clock and 3 o'clock positions, three additional sutures are taken at regular intervals. Similarly, between the 6 o-clock and 9 o'clock positions, three sutures are taken. Prior to ligation, all the posterior row sutures should be taken. Now, cut and remove the stay sutures. All the

posterior row sutures are ligated, and all except the 3 o'clock and 9 o'clock sutures are removed (Figure 7) [39]

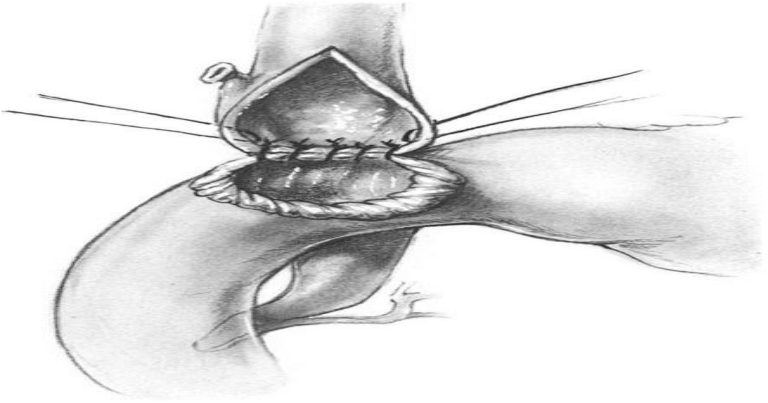

Figure 7: - Posterior wall anastomosis of CDD [42]

Traction on the sutures of the corner guarantees that the corner is inverted. All the anterior row sutures are positioned on the duodenum from outside-to-inside and then on the CBD from inside-to-outside, so that the knots are on the outside of the lumen (Figure 8-a). Before ligating them, all the sutures are arranged (Figure 8-b). Stenting is not needed for anastomosis (Figure 8 a, b, c) [38]

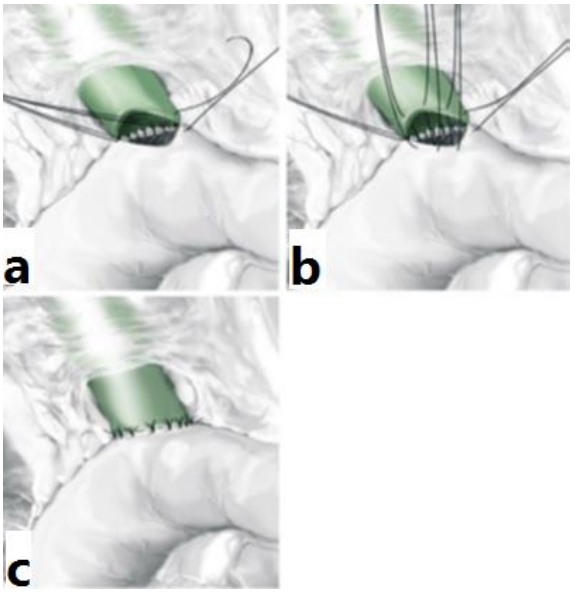

Figure 8: - Anterior wall anastomosis of CDD [43]

Advantages over CJ

- Relatively quick and simple, with fewer anastomotic sites.
- Ease of access for future endoscopic interventions. [44]

Contraindications

- Narrow CBD (< 8 mm)
- Active ulceration of the duodenum
- Malignancy, restricting easy reach of duodenum to the dilated CBD
- Obstruction of the 3rd or 4th part of the duodenum. [38]

Complications of CDD

Post CDD complications can be classified into short term and long term. Short term includes wound infection, bile leakage, intrabdominal abscess, and ileus. The incidence of wound infection is increased in patients who have had preoperative biliary stenting, while bile leakage is uncommon and generally indicates a technical issue with the anastomosis. The priority in management is to establish a controlled fistula and to determine whether there is obstruction in biliary-enteric anastomosis or not. A CT scan and fistulogram via drain are the initial investigations. Most biliary fistulas will heal spontaneously if there is no downstream obstruction and rarely requires revision of the anastomosis. While the long term includes recurrent cholangitis either due to sump syndrome, anastomotic stricture, recurrent CBD stones, or other proximal CBD diseases. [38]

Anastomotic stricture typically presents with cholangitis as described above, but in some patients, it can present with progressive jaundice without other signs of cholangitis. The incidence of stricture may increase if the choledochotomy at the time of surgery was less than 2 cm. Some patients may respond to endoscopic dilation and stenting, but patients who fail endoscopic management require conversion to roux-en-y hepaticojejunostomy. The incidence of recurrent CBD stones after bilio-enteric anastomosis is not truly mentioned in many studies. [45]

Laparoscopic CDD

The first LCDD was performed by Franklin and Balli in 1991[46]since then, few groups around the world have adopted the technique and reported their results. Wide acceptance of the procedure has been slow because of the rarity with which these problems could not be managed endoscopically, and it requires significant advanced laparoscopic skills.

Robotic CDD

The advent of robotic technology has allowed for further refinement of minimally invasive techniques with the advantage of better three-dimensional visualization, stable platform, increased skill, tremor filtering, ease of suturing, and improved access to the critical portal structures in comparison to conventional laparoscopy. [47]

End to Side CDD

End-to-side CDD was established by *Walter and Kelly 1953* [48], as a procedure for biliary reconstruction after traumatic or iatrogenic injury or benign stricture of the bile duct. In this approach dissection of the CBD all around is a must, with

transection of the CBD, ligation of the distal stump, and performing the anastomosis between the proximal part of the CBD and the side of the duodenum (end to side fashion). (Figure 9) This technique can be performed laparoscopically however it is technically more difficult than side to side LCDD (Figure 10). [35]

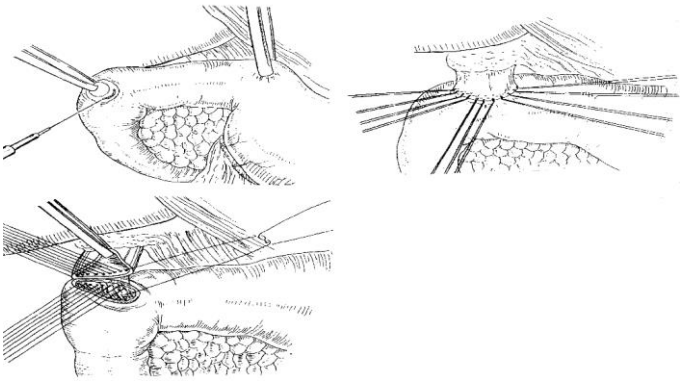

Figure 9: End to side open CDD [49]

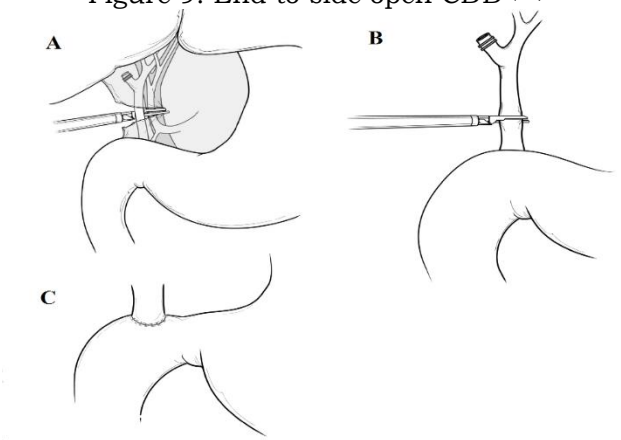

Figure 10: Steps of end-to-side LCDD [35]

A = Dissection and encircling of the CBD
B = Transection of the CBD
C = End to side CDD

Choledochojejunostomy (CJ)

RYCJ is considered to have a lower incidence of post-operative cholangitis and recurrent stones than the other techniques of bilio-enteric anastomosis. The main steps of this technique (either open or laparoscopic) are to dissect, encircle the CBD, performing CBD exploration with removal of stones, transection of the CBD and ligation of the distal part of the CBD (Figure 11 A). A roux-en-y reconstruction of the jejunum (Figure 11 B), in which the roux limb (biliary limb) will be anastomosed with the bile duct with end to side fashion (Figure 11 C) either ante- (Figure 12) or retro-colic. The y limb (alimentary limb) is anastomosed with the roux limb in a side-to-side fashion using staplers and the common enterotomy is closed hand sewn (Figure 11 D). With the development of laparoscopy, laparoscopic RYCJ has become a new choice for the treatment of

biliary tract diseases. However, due to its technical difficulty few have reported about this procedure. [50]

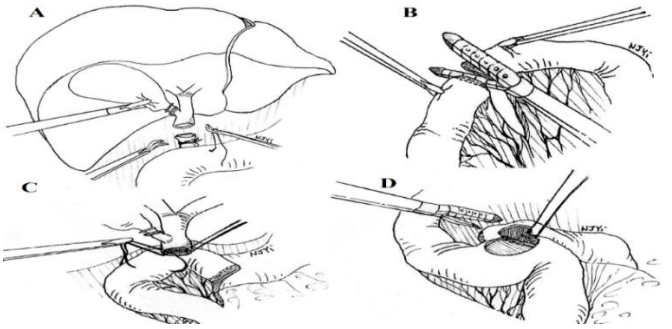

Figure 11: - Steps laparoscopic RYCJ [50]

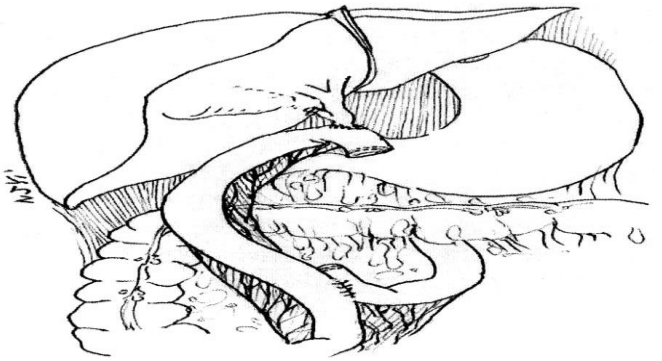

Figure 12: - Antecolic RYCJ [50]

Conclusion

Benign biliary strictures (BBSs) may form from chronic inflammatory pancreaticobiliary pathologies, postoperative bile-duct injury, or at biliary anastomoses following liver transplantation. Treatment aims to relieve symptoms of biliary obstruction, maintain long-term drainage, and preserve liver function. Endoscopic therapy, including stricture dilatation and stenting, is effective in most cases and the first-line treatment of BBS. Radiological and surgical therapies are reserved for patients whose strictures are refractory to endoscopic interventions. Response to treatment is dependent upon the technique and accessories used, as well as stricture etiology.

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