Management of choledochal cysts

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INTRODUCTION

Choledochal cysts are characterized by single or multiple cystic dilatations of the intrahepatic and/or extrahepatic biliary ducts. Choledochal cysts occur infrequently in Western populations (1 in 100,000 to 1 in 150,000 individuals) compared with the considerably higher incidence in Asian populations (approximately 1 in 13,000 individuals) [1]. Although predominately diagnosed in children, choledochal cysts are found with increasing frequency in adults such that adults comprise the majority of patients in recent series [2,3*,4]. In both adults and children, a female preponderance is characteristic (approximately 4:1 ratio) [3*,5**]. Conventionally, patients with choledochal cysts were treated with cyst decompression (cyst enterostomy) in order to relieve symptoms of pain, obstruction, and jaundice [6]. However, complete cyst excision with biliary-enteric reconstruction is indicated in order to ameliorate long-term sequelae. We herein review choledochal cysts with a focus on patient presentation and diagnostic modalities, as well as the current indications and management strategy for choledochal cyst.

BACKGROUND

The precise etiology of choledochal cysts is not well understood, although anomalous pancreaticobiliary duct union (APBDU) is a generally accepted hypothesis [1]. A long common channel (>10 mm proximal to ampullary sphincter) is thought to predispose to pancreatic enzyme reflux into the biliary tree with consequent biliary duct inflammation and pressure, leading to duct dilation [7–9]. The theory...
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- MRCP is the diagnostic modality of choice for infants or children and has likely surpassed ERCP as the best imaging test for adults given the noninvasive nature and ability to characterize cyst anatomy in relation to the biliary tree and surrounding structure.
- Prior to surgical intervention, control of biliary sepsis or resolution of pancreatitis must occur; additionally, the extent of biliary tree involvement by the choledochal cyst must be established.
- When determining whether to use a MIS versus open approach, factors to consider include patient age, comorbidity, and type of cyst.
- Given the complex nature of choledochal cyst and limited experience of most centers, choledochal cyst patients should be evaluated and treated at high-volume HPB centers familiar with management of choledochal cyst.

is substantiated by the increased occurrence of APBDU among patients with choledochal cyst (approximately 30–96%) compared with 2% in the general population [1,10]. Experimental studies have corroborated the associated between APBDU and choledochal cysts; however, this anomaly cannot be solely responsible given the variable incidence in patients with choledochal cysts [1,8].

The Todani system classifies choledochal cysts based on anatomic findings and extent of biliary involvement (see Fig. 1) [10–12]. Type I cysts are the most commonly encountered in both adults and children (60–80%) and demonstrate either cystic (IA or IB) or fusiform (IC) dilation of the extrahepatic duct. Of note, the intrahepatic biliary tree can be dilated in type I cysts as a consequence of biliary stasis. Type II cysts (1–2%) are supraduodenal diverticulum, whereas type III cysts (choledochocele, 0.5–4%) are intraduodenal. Both malignancy and APBDU are rare in type III choledochal cysts. Moreover, type III choledochal cysts lack the female preponderance characteristic of other choledochal cysts. Type IV cysts are distinguished by multiple extrahepatic (IVB, 1–2%) or both intrahepatic and extrahepatic (IVA, 15–30%) dilation and are the second most common cyst encountered [3,4]. Type V cysts (Caroli’s disease) involve only the intrahepatic ducts [2]. The vast majority (approximately 90%) of choledochal cysts in both adults and children are comprised of type I or type IV cysts, and consequently, many of the results from investigations pertain to these subcategories.

**DIAGNOSIS**

Nearly 80% of choledochal cysts present in childhood [5,6]. Symptomatic patients typically present with nonspecific abdominal pain. However, complaints suggesting biliary or pancreatic origin including right upper quadrant pain, jaundice, pancreatitis, and nausea and vomiting are also common [2]. Children typically experience abdominal pain, jaundice or an abdominal mass; however, the classic triad consisting of these three aforementioned symptoms is rare, particularly in adults. Adults generally present with abdominal pain, infectious complications, or malignancy (Table 1) [13,14]. A recent series evaluating choledochal cysts in pediatric and adult patients identified abdominal pain as the presenting complaint in 61% of patients, which was the most common symptom in both adults (72%) and children (41%). Pancreatitis and jaundice were also common presentations (18.8% and 18.5%, respectively), whereas 16% of patients were asymptomatic at the time of diagnosis [5,6]. Asymptomatic patients are increasingly identified because of frequent use of cross-sectional imaging and currently comprise approximately 10–36% of patients with choledochal cysts [15].

Initial workup for many patients begins with ultrasound or contrast-enhanced computed tomography, and follow-up cholangiography can delineate the cyst type (percutaneous transhepatic cholangiography, endoscopic retrograde cholangiopancreatography (ERCP), or magnetic resonance cholangiopancreatography (MRCP)). MRCP is the diagnostic modality of choice for infants or children. MRCP has likely surpassed ERCP as the best imaging test for adults given the noninvasive nature and ability to characterize cyst anatomy in relation to the biliary tree and surrounding structures [1,11,14,16,17]. However, ERCP and percutaneous transhepatic cholangiography are particularly beneficial when a therapeutic intervention is needed (i.e., in the management of choledochal cyst-associated complications such as cholangitis) [11,18].

**TREATMENT**

**Indications**

Subsequent to diagnosis, treatment of choledochal cysts aims to avoid the numerous hepatic, pancreatic, or biliary sequelae that may occur. Acute inflammatory conditions include recurrent cholangitis, liver
abscess, acute pancreatitis, and sepsis; chronic changes, such as hepatic cirrhosis, portal hypertension, chronic pancreatitis, and cholangiocarcinoma/gallbladder cancer may also develop [8,14]. Prior to surgical intervention, control of biliary sepsis or resolution of pancreatitis must occur; in addition, the extent of biliary tree involvement by the choledochal cyst must be established [16]. Although partial cyst excision with biliary-enteric anastomosis may initially alleviate obstructive symptoms, complete duct excision is indicated to circumvent the high rates of pancreatitis, cholangitis, recurrent stricture, and potential malignancy [1]. In high volume series, approximately 90% of patients with malignancy are associated with type I or IVA choledochal cyst, in contrast to the rare occurrence in type II, III, or V [4]. Therefore, the complexity associated with choledochal cyst treatment includes degree and severity of symptoms, type of choledochal cyst present (and perceived rate of malignancy), operation required for complete cyst excision and patient comorbidities. Given these considerations combined with the rarity of choledochal cyst, operative management should be determined in a multidisciplinary setting.

**Table 1.** Presenting symptoms in patients with choledochal cysts, stratified by age

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<th>Infants (0–1 year)</th>
<th>Children (1–18 years)</th>
<th>Adults (&gt;18 years)</th>
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<tr>
<td>Prenatal diagnosis</td>
<td>Abdominal pain</td>
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<td>Abdominal mass</td>
<td>Jaundice</td>
<td>Biliary lithiasis</td>
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<td>Acholic stool</td>
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**FIGURE 1.** Choledochal cyst classification. Type I cysts are either cystic (IA or IB) or fusiform (IC) dilation of the extrahepatic duct. These are best treated with extrahepatic duct excision and Roux-en-Y hepaticojejunostomy reconstruction. Type II cysts are supraduodenal diverticulum and can be excised via cystectomy or duct excision with restoration of biliary-enteric continuity. Type III cysts (choledochocele) are intraduodenal and should be treated via endoscopic means (smaller cyst) or transduodenal sphincteroplasty. Type IV cysts exist as multiple extrahepatic (IVB) or both intrahepatic and extrahepatic (IVA) dilation. Treatment of these cysts includes extrahepatic duct excision with restoration of biliary-enteric continuity ± hepatic resection. Type V cysts involve only the intrahepatic ducts and generally require hepatic resection or liver transplantation. (Figure used with permission from Park et al. [11]).
Infants and children

Infants (age 0–1 year) may be diagnosed prenatally or may present with symptoms resembling biliary atresia including jaundice, hepateomegaly, and acholic stools. The risk of progression to liver fibrosis warrants early excision. In patients who are clinically symptomatic (jaundice, acholic stool, emesis, and distension), liver damage has been shown to occur early despite excision within the first 6 months of life [19]. Early cyst excision is also appropriate in asymptomatic patients (diagnosed prenatally). In a study examining timing of surgery for neonates diagnosed prenatally, those randomized to cyst excision within 1 month demonstrated significantly less fibrosis and cirrhosis compared to those who were randomized to cyst excision after 1 month, with no perioperative morbidity or mortality in either group [13].

Children (age 1–18 years) often present with symptoms of abdominal pain, jaundice, or abdominal mass, and in contrast to adults, development of malignancy is rare (< 1%) [14]. In a study by Hung et al. [14] evaluating infants and children at a single institution undergoing cyst excision and hepaticojejunostomy (type I or IVA cysts), neonates presented with jaundice (100%) and acholic stools (75%) versus abdominal pain (82.4%), jaundice (29.4%), and abdominal mass (11.8%) in the pediatric population. No patients were identified to have malignancy; instead, pathologic evaluation demonstrated only chronic cyst inflammation. There were no perioperative deaths and late complications such as stricture, cholangitis, or cholangiocarcinoma did not occur at a follow-up of 8 years. These results indicate complete cyst excision with biliary enteric anastomosis is feasible and safe in neonates (both asymptomatic and symptomatic) and the pediatric population [13,14,19].

Adults

Similar to pediatric patients with choledochal cysts, the majority of adult patients present with symptoms related to complications from their choledochal cyst. However, the most feared complication remains malignant transformation. Adenocarcinoma comprises 73–84% of malignancy associated with choledochal cysts, and additional histologic subtypes include anaplastic carcinoma (10%), undifferentiated cancer (5–7%), squamous cell carcinoma (5%), and other (1.5%) [16].

Cholangiocarcinoma in the general population is quite rare (incidence of 0.8/100,000 individuals in the United States versus 50–100/100,000 individuals in Thailand) [7]. In contrast, patients with choledochal cysts are estimated to harbor a 6–30% chance of developing malignancy [2,8]. This risk appears to be low in childhood (< 1%), but increases with age to an estimated 30–40% of those greater than 50 years [8]. The precise risk of cholangiocarcinoma in patients with choledochal cyst is unknown because of the predilection for symptomatic patients to be included in studies.

In a review examining the occurrence of malignancy in 5780 patients with choledochal cyst, the overall incidence of biliary tract cancer was 7.5% [15*]. The incidence in children (age 0–18) was low (0.4%) with increased rates in those older than 18 years (11%). The incidence steadily increased with age up to 38% in those patients older than 60 [15*]. Among patients who develop malignancy, 70% arises as cholangiocarcinoma within the cyst wall and approximately 24% arises as gallbladder cancer [15*]. Furthermore, malignant transformation most commonly occurs in type I or type IV cysts, with decreased frequency in type V cysts. Transformation is exceedingly rare in type II or III cysts [6]. The association with malignancy also appears to be influenced by presence or absence of APBDU. In a recent series by Chang and colleagues [9] of 453 patients with gallbladder cancer, APBDU was identified in 17.2% and all patients with choledochal cysts who developed gallbladder cancer had APBDU.

To better understand the pathogenesis of carcinoma in patients with choledochal cysts, Katabi and colleagues [20] performed a clinicopathologic study of 36 symptomatic patients who had undergone resection (cyst excision ± pancreatic resection ± hepatectomy). The authors noted APBDU in 64% of patients and evidence of chronic inflammation of the cyst wall in 73% of patients. Forty percent had evidence of metaplasia (pyloric, intestinal, or squamous metaplasia), 29% had biliary intraepithelial neoplasia (six with BilIN-1, two with BilIN-2, and two with BilIN-3) and five patients (14%) had carcinoma. Histologically, metaplasia was identified in all specimens containing carcinoma, and three of the five had concomitant biliary neoplasia and carcinoma in the pathologic specimen. Median survival among patients with cholangiocarcinoma was 22 months. Given the pathologic findings, a metaplasia to neoplasia to carcinoma sequence appeared evident for the development of carcinoma in this patient population [20]. Although the exact etiology of malignant change remains unclear, pancreatic reflux, biliary stasis, and mutagenic secondary biliary acids are thought to play a role [21].

A recent series by Soares and colleagues [5**] identified 394 patients in multiple Western institutions who underwent operative management of choledochal cysts. In this series, the majority of
patients were adults (65.7%) and the mean age at diagnosis was 45 years for adults and 5.2 years for children. In this patient population, the majority presented with symptoms attributable to the choledochal cyst (84.5%), whereas 15.5% were asymptomatic. The rate of malignancy at presentation for the entire cohort was low (3.3%); 91% of the choledochal cyst-associated cancers arose in patients with type I or type IV cysts. An additional 13 (3.3%) patients (one child, 12 adults) experienced metachronous malignancy following cyst resection (type I, n = 6; type IV, n = 6; type V, n = 1). Although the overall survival for the entire study population was quite good, patients with cholangiocarcinoma experienced poor survival (see Fig. 2) [5**]. These data emphasize the importance of close follow-up of patients undergoing resection for choledochal cysts.

Among patients who undergo incomplete cyst excision because of an unresected intra pancreatic segment, the remnant cyst can still undergo malignant transformation. In a retrospective study of 808 adult patients with choledochal cysts, Lee and colleagues [4] identified a metachronous extrahepatic cholangiocarcinoma rate of 5.3% in patients undergoing cyst enterostomy versus 0.6% in those undergoing cyst excision (median interval of 52 months). Xia and colleagues [3] evaluated 41 patients with type I or type IVA cysts who underwent incomplete cyst resection at the initial operation. Approximately 14% developed malignancy in the cyst remnant as documented at the time of repeat operation for completion cyst resection. Repeat operation occurred at a median of 11–12 years following the initial resection (performed for symptomatic purposes). Of these patients who were found to have malignancy, the majority (83%) expired as a result of their disease [3*].

### Surgical approach

Historically, the treatment of choledochal cysts entailed cyst enterostomy. However, this suboptimal approach resulted in long-term complications, including stricture, jaundice, cholangitis, cholangiocarcinoma, and often times the need for reoperation [3*,22]. To avoid complications from incomplete cyst excision and to minimize the need for reoperation, current surgical strategy aims to excise the entire cyst (including gallbladder), followed by restoration of biliary-enteric continuity.

Type I cysts should undergo complete cyst excision with Roux-en-Y biliary-enteric reconstruction. The proximal and distal extent should be identified prior to resection to assist with operative strategy. Occasionally, the cyst may extend into the pancreatic head in which case the risk of residual choledochal cyst must be weighed against the risk of pancreaticoduodenectomy [16]. Alternatively, the mucosa of a dilated distal common bile duct may be stripped in order to protect the pancreaticobiliary junction. Infrequently, because of recurrent episodes of cholangitis, the cyst wall is densely adherent to the portal vein, precluding safe resection. When this occurs, resection of the anterior wall with careful fulguration of the mucosa of the posterior wall and Roux-en-Y H-J reconstruction can be performed [23]. Depending on the location of the cyst, type II choledochal cyst may undergo simple cyst excision or diverticulectomy. Reconstruction may be necessary if significant narrowing of the bile duct is noted. Type III choledochal cyst can be managed by endoscopic means (sphincterotomy), by sphincteroplasty alone, sphincteroplasty with
cyst excision, or pancreaticoduodenectomy. However, given the low incidence of malignancy associated with type III cysts, choledochoceles are best managed with unroofing (endoscopic or transduodenal sphincteroplasty) or transduodenal excision (larger cysts) [1,6].

Type IV choledochal cyst is approached differently based on presence or absence and location of intrahepatic disease. The extrahepatic bile duct should be excised and if the intrahepatic disease is limited (i.e., left hemiliver), hepatectomy with Roux-en-Y reconstruction to the remaining hepatic duct can be performed. In a series of 629 patients with choledochal cysts, Xia and colleagues [24] identified 198 patients with type IVA cysts. Of these, 59 were able to undergo extrahepatic cyst excision with partial hepatectomy and hepaticojejunostomy. There was a low rate of perioperative morbidity (15%) and mortality (0%). At a median follow-up of 42 months, disease-specific survival was 98%, with a 4.1% reoperation rate and acceptable biliary function in 85.8% of patients [24]. However, not all patients are appropriate candidates for partial hepatectomy. Those patients with obvious dilatations and stenosis of intrahepatic ducts, intrahepatic duct stones, or parenchymal atrophy may benefit from hepatectomy [4]. These patients appear more susceptible to intrahepatic cholestasis, hepatic abscess, recurrent cholangitis, hepaticolithiasis, and potential carcinogenesis [24]. If hepatectomy is planned concomitantly with extrahepatic duct excision, the distribution should allow removal of all disease (or the vast majority of severe disease) with adequate future liver remnant. Of note, type I choledochal cyst may present with intrahepatic dilatation because of biliary stasis and therefore differentiating between type I and type IVA choledochal cyst is critical because of the therapeutic implications. However, in patients without indications for hepatectomy, type IV choledochal cysts can be treated similarly to type I choledochal cysts. This approach is justified by studies demonstrating that patients who progress to malignancy most commonly develop extrahepatic cholangiocarcinoma or gallbladder cancer (approximately 95% of malignancy), whereas intrahepatic cholangiocarcinoma rarely occurs [4]. This consideration may allow tailoring of surgical resection depending on location and distribution in patients with type IV or V choledochal cysts.

Management of patients with Caroli’s disease can be particularly difficult given the location of cysts and frequent necessity for surgery [considerable potential for cholangitis, liver complications, and biliary cirrhosis; moderate potential for neoplasia (7%)] [1,8,25]. For focal disease, hepatic lobectomy may be performed. However, in diffuse forms, biliary drainage procedures are ineffective at preventing recurrent bouts of cholangitis as well as cholangiocarcinoma. In these patients, liver transplantation provides a durable treatment option [8,25]. Mabrut and colleagues [25] performed a multicenter study, which included 155 patients with type V choledochal cysts from Western surgical centers. Approximately 90% of patients were symptomatic including abdominal pain, jaundice, GI bleed, and cholangitis. Synchronous cancer was identified in 5.2% of patients. Appropriate preoperative evaluation was critical for determining the extent of resection and the authors emphasized the importance of complete resection to optimize long-term results. The majority of patients possessed unilobar involvement (69%) with a predilection for left-sided disease, whereas 31% had bilarb involvement. Patients underwent either hepatic resection (75%) or liver transplantation (19%), with excellent or good results achieved in 86%. Five-year overall survival was 97% after liver resection and 89% after liver transplant [25].

In those with known malignancy, oncologic principles should apply; patients who can undergo safe resection with negative margins are appropriate for operation. Resection may include hepatectomy with regional lymphadenectomy, extirpation of extrahepatic bile ducts with regional lymphadenectomy (and cholecystectomy), or pancreaticoduodenectomy [16]. However, malignancy associated with choledochal cyst (cholangiocarcinoma or gallbladder cancer) is universally associated with poor prognosis [5**,25].

Choledochal cysts can also be addressed via open excision or minimally invasive surgery (MIS). In general, children are more likely to undergo laparoscopic cyst excision compared with adults, and the operative strategy most commonly entails Roux-en-Y hepaticojejunostomy. In a multi-institutional investigation of Western patients with choledochal cysts, Margonis and colleagues [26**] noted 36 of 368 patients underwent an MIS approach, and this cohort was more likely to occur in children (24%) versus adults (2.1%, P < 0.001). Operations utilized were most often cyst excision with hepaticojejunostomy (85.4%), cyst excision with hepaticoduodenostomy (7.3%), cyst excision alone (3.7%), or whipple (2.8%). Complications occurred in 35% of patients, readmission in 27%, and reoperation in 12% with no mortality at 30 days. Five-year overall survival was 98.6%. In a propensity-score-matched analysis, there was no difference in complication rate, readmission, or reoperation between the MIS group and open group, indicating both approaches are safe. When
determining whether to use a MIS versus open approach, factors to consider include patient age, comorbidity and type of cyst (70% of MIS patients had type I cyst) [26*]. In another series by Senthil
nathan et al. [23] 110 patients (55 pediatric and 55 adult) underwent laparoscopic resection and reconstruction of type I or type IVA choledochal cysts. The overall mortality was 1%, operative rate was 2% and morbidity 10%, demonstrating the safety and feasibility of laparoscopic approach in specialized, high-volume centers [23].

CONCLUSION

Patients with choledochal cysts may present as a neonate, child, or adult, and presentation can be quite variable. Once diagnosed, most situations warrant surgical resection of the choledochal cyst. Although the true incidence of malignant transformation is unknown, the propensity for complications associated with partial cyst resection mandates complete resection of the cyst when feasible. Management of the choledochal cyst and the operative conduct will depend upon the patient comorbidities and choledochal cyst subtype. However, given the complex nature of choledochal cysts and limited experience of most centers, these patients should be evaluated and treated at high-volume hepatopancreatobiliary centers familiar with management of choledochal cysts.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

■ of special interest
■■ of outstanding interest

10. Park SW, Koh H, Oh JT, et al. Relationship between anomalous pancreati-
12. Todani T, Watanabe Y, Naruse M, et al. Congenital bile duct cysts: classification, operative procedures, and review of thirty-seven cases includ-
13. Diao M, Li L, Cheng W. Timing of surgery for prenatally diagnosed asympto-
16. This compilation of numerous Eastern and Western studies evaluating choledo-
chal cysts provides insight to the overall rate of malignancy seen (7.5%) in the entire population and the association with increasing age.

This paper demonstrates that the majority of minimally invasive surgery for patients with choledochal cysts is being performed in the pediatric population and in those with type I choledochal cysts. However, the importance derives from the propensity score analysis which demonstrates that compared to open, MIS can be performed in a safer manner with no increase in complication rate and an apparent decrease in length of stay. Additionally, this population was comprised of patients from Western institutions and is the largest comparative study in Western patients to date.