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Original Article

Single-Center Results of Choledochal Cysts in Turkish Population

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Abstract

Background: Choledochal cysts are seen commonly in Asian populations, but rarely in Western populations. The pathogenesis of these premalignant lesions is not fully understood yet and the risk of malignant transformation increases with age. The overall malignancy risk is 10%–15% in East Asian countries. In this study, we aimed to present our surgical experience as a hepatobiliary center to the literature.

Methods: We retrospectively analyzed the data from the medical records of 70 patients operated for choledochal cyst between 2008–2019.

Results: Sixty-two of the 70 (89%) patients were female and 8 (11%) were male, the mean age was 45.89 ± 15.32 years. Overall, 44 (63%) patients had type I (a+b+c), 20 (28%) type V (Caroli), 2 (3%) type II, 2 (3%) type III and 2 (3%) type IVb cysts. The most common operation was cyst excision combined with hepaticojejunostomy (n: 26, 37%). The median diameter of the resected cysts was 3 cm (min- max: 1–11 cm). Malignancy was observed only in three (4%) patients with type III, type Ib, and type V cyts, who were 19, 38, and 72 years old, respectively. Mortality was not observed, morbidity was determined totally in 30 (43%) cases during early and late postoperative periods.

Conclusion: Type of surgery in choledochal cysts differs according to the type of the cyst. Malignancy was observed at a rate of 4% in all age groups. Although the frequency of malignancy varies, the main treatment of choice should be surgery because malignancy can be seen at a young age.

Keywords: Caroli's disease, Choledochal cyst, Malignancy, Surgery

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Introduction

Cystic dilatations of the intrahepatic and/or extrahepatic biliary tree are called choledochal cyst (CC). Although the etiology of CC is still unclear, many theories have been suggested for it. The estimated incidence of CC is 1/1000 in Asian populations whereas it is 1/100000–150000 in Western populations. Two-thirds of the cases in the East are observed in Japan for unknown reasons, especially in women.[1] Alonso-Jel et al proposed the first classification in 1959 and divided CCs into three types,[2] but later on this was revised by Todani et al in 1977 who classified CCs into five types, which is currently in use.[3]

In recent years, an isolated cystic duct dilatation was described as type VI in a case report, but this has not been included in the Todani classification yet.[4] CC is known as a disease of childhood, whereas more than 25% of the patients are diagnosed in adulthood.[5]

In this study, we presented such adult patients operated for CC.

Patients and Methods

Classification

Todani et al in 1977 classified CCs into five types[3];

- Type Ia: Diffuse cystic dilatation of the extrahepatic bile ducts, with normal intrahepatic ducts.
- Type Ib: Focal, segmental cystic dilatation of the extrahepatic bile ducts.
- Type Ic: Fusiform dilations, usually extending from the pancreaticobiliary junction to the intrahepatic duct.
- Type II: A thin-stemmed diverticulum of the extrahepatic bile duct.
- Type III: Cystic dilatation of the distal extrahepatic bile duct, extending into the duodenal lumen (choledochocele).
- Type IVa: Cystic or fusiform dilatations of the intrahepatic or extrahepatic bile ducts.
- Type IVb: Multiple cystic dilations of the extrahepatic bile ducts (radiographically appear as a string of beads or bunch of grapes).
- Type V: Multiple, cystic or saccular dilatations of the intrahepatic bile ducts. These CCs refer to Caroli's disease, and occur as connecting cavernous ectasia.

Patients

Seventy patients operated for CC between 2008–2019 were

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included in the study. The data in the electronic medical records of the patients were analyzed retrospectively.

Perioperative Management

Patients were followed up preoperatively by a multidisciplinary team consisting of gastrointestinal surgery, gastroenterology and interventional radiology clinics. The decision for surgery was made by this team. Aspartate aminotransferase, alanine aminotransferase, bilirubin, international normalized ratio, albumin, C-reactive protein, carcinoembryonic antigen, cancer antigen 19-9, and alpha-fetoprotein blood levels were measured and a hemogram was ordered preoperatively. Patients underwent abdominal ultrasonography, triphasic abdominal CT and, if necessary, magnetic resonance cholangiopancreatography (MRCP) to evaluate the biliary tract (Figure 1). Bilirubin levels were reduced by endoscopic retrograde cholangiopancreatography (ERCP) to provide drainage in those patients with biliary stones. In patients with cholangitis, piperacillin + tazobactam sodium (Tazocin EF 4.5 g/vial lyophilized powder, Wyeth Lederle SpA, Catania, Italy) was initiated. Decision for surgery in such patients was made when the levels of infection indicators and bilirubin decreased. Conventional operation techniques were performed in all patients. The patients were called for follow-up every 3 months in the first year, every 6 months in the second year, and once a year in the following years.

Results

Sixty-two of 70 (89%) patients recruited in the study were female, 8 (11%) were male and the median age was 45.8 (range 19–78) years. Of these patients, 44 (63%) were type I (a+b+c), 20 (28%) type V (Caroli), 2 (3%) type II, 2 (3%) type III and 2 (3%) type IVb. Preoperative ERCP was performed in 10 (14%) patients, percutaneous transhepatic cholangiography (PTC) in 1 (1%) and ERCP+PTC in 1 (1%) in order to provide drainage in bile ducts. When stone formation was analyzed, a stone was observed in the cyst of 12 (17%) patients, in the gallbladder of 10 (14%), and in both the cyst and the gallbladder of one patient (1%). There was no mortality whereas a total of 30 (43%) morbidities were found during early and late postoperative periods. Wound site infection was observed in 10 (14%) patients and they were treated with antibiotic therapy. Intraabdominal abscess occurred in 9 (13%) patients and percutaneous drainage was performed. Biliary fistula was identified in 6 (9%) patients and all these regressed without any additional intervention during follow-up. Hepaticojejunostomy (HJ) stricture developed in four (6%) patients in 1–4 years, and three were treated by PTC. In one patient, however, a decision for surgery was made three years later due to stenosis and proteinous content in the remnant bile duct. This patient underwent the Whipple operation in the 3rd postoperative year and the pathology was reported as benign. Malignancy was observed only in three (4%) patients. Pathologies reported in benign cases were: benign biliary diseases (n: 42, 60%), Caroli disease (n: 11, 16%), low-grade dysplasia (n:7, 10%), biliary cystadenoma (n: 3, 4%), mucinous cystadenoma (n: 1, 1%), serous cystadenoma (n: 1, 1%), secondary biliary cirrhosis (n: 1, 1%), and foregut cyst (n: 1, 1%). The median diameter of the excised cysts was 3 cm (min-max: 1–11 cm) (Table 1).

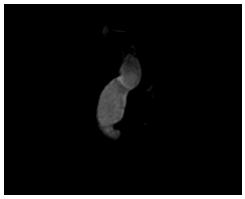

Figure 1. MRCP Image of Type Ia Choledochal Cyst.

Three patients (type 3, type Ib, and type V) with malignancy were 19, 38, and 72 years old, respectively. The overall risk of cancer was 4% (n: 3). On an individual basis, the cancer risk was 2% for type I, 50% for type III, and 5% for type V. The risk of cancer was 6% for patients aged 19-30 years, 4% for those aged 31–50 years and 3% for those aged 51–78 years (Table 2).

Type 1 CC was operated the most. (Figure 2) Cyst excision + hepaticojejunostomy was the most common surgery performed for type I and type II patients (n: 26, 37%). Cyst excision + Roux-en-Y HJ was performed totally in 20 (28%) patients with type I, type II and type IVb Ccs. Two patients had double anastomoses to the right and left hepatic ducts. One of the two patients with type III underwent duodenotomy and the other patient underwent a Whipple procedure due to duodenal hematoma. The pathology was reported as choledochal adenocarcinoma (Table 2, no: 1). Resections were performed at one or multiple liver segments in 14 (20%) patients with Caroli's disease, while five (7%) patients underwent left hepatectomy. A 22-year-old patient with aortic stenosis and mitral stenosis (who underwent recurrent PTC and ERCP for frequent cholangitis attacks due to diffuse Caroli's disease) underwent liver transplantation by the decision of the team (Table 3). As for congenital anomalies in the patients, one patient had mitral stenosis and one patient had congenital atrial septal defect (ASD).

Discussion

The most distinguished theory explaining CC formation is Babbitt's theory. According to Babitt's theory, the pancreatic duct and the common bile duct meet outside the ampulla of Vater, forming an abnormally long common duct (abnormal pancreaticobiliary duct junction). In this common duct, pancreatic fluids and bile join together and activate pancreatic enzymes. Activated pancreatic enzymes eroding the wall of the bile ducts

Table 1. General Characteristics of the Patients

General Features	
Median age	45.8
Range (min-max)	(19–78)
Interquartile range (25–75)	31.50–57
Gender, No. (%)	
Female	62 (89%)
Male	8 (11%)
Type of the cyst, No. (%)	
Type Ia	30 (43%)
Type Ib- upper	2 (3%)
Type Ib- middle	5 (7%)
Type Ib- lower	5 (7%)
Type Ic	2 (3%)
Type II	2 (3%)
Type III	2 (3%)
Type IVa	0
Type IVb	2 (3%)
Type V	20 (28%)
Preoperative intervention, No. (%)	
ERCP	10 (14%)
PTC	1 (1%)
ERCP+PTC	1 (1%)
Stone	
Only in the gallbladder	10 (14%)
Only in the cyst	12 (17%)
Both	1 (1%)
Mortality (30 days), No. (%)	0 (0)
Morbidity/early period, No. (%)	
Wound site infection	10 (14%)
Intraabdominal abscess	9 (13%)
Bile duct fistula	6 (9%)
Hematoma	1 (1%)
Morbidity/late period, No. (%)	
HJ stricture	4 (6%)
Pathology, No. (%)	
Malign	3 (4%)
Benign	42 (60%)
Caroli disease	11 (16%)
Low-grade dysplasia	7 (10%)
Biliary cystadenoma	3 (4%)
Mucinous cystadenoma	1 (1%)
Serous cystadenoma	1 (1%)
Secondary biliary cirrhosis	1 (1%)
Foregut cyst	1 (1%)
Median diameter of the cyst	3 cm
Range (min-max)	1–11 cm
Interquartile range (25–75)	2-5 cm
Median postoperative follow-up time (months)	83
Range(min-max)	(6–135)
Interquartile range (25–75)	52.25–99.25

ERCP, endoscopic retrograde cholangiopancreatography, PTC, percutaneous transhepatic cholangiography.

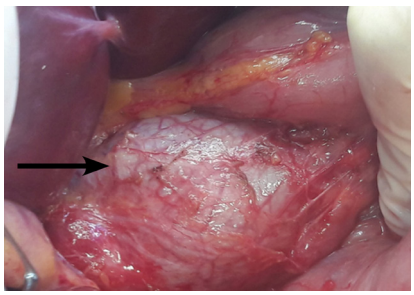

Figure 2. A Type I Choledocal Cyst.

cause inflammation. At the end of this process, the walls get thinner and bile duct dilatation occurs.[6] Furthermore, high-pressure fluids passing through the pancreatic duct lead to further thinning of the already thinned bile duct walls, resulting in cyst formation.[7] Another theory is the congenital theory of Davenport and Basu. Aganglionic structures occurring at the distal common bile duct lead to obstruction and proximal dilation over time, just as occurs in Hirschsprung's disease. Subsequent biliary stasis and inflammation are common in both theories.[8] ventricular septal defect, duodenal atresia, aortic hypoplasia, congenital atresia of portal vein, and familial adenomatous polyposis, accompanying CCs in certain cases, support the congenital theory.[1] In our study, congenital anomaly was observed in two (3%) patients (namely ASD and congenital mitral valve stenosis).

The incidence rates reported in the literature are 50%–80% for type I, 2% for type II, 1.4%–4.5% for type III, 15%–35% for type IV and 20% for type V.[1,9] The incidence rates determined in our study were consistent with the literature, except for type IV – namely, type I: 63%, type II: 3%, type III: 3%, type IV: 3%, type V: 28%. CC is considered a premalignant lesion. Cancer occurs as a result of DNA damage and dysplasia due to biliary stasis, irritation, and inflammation.[10,11] Todani et al observed developing carcinogenic formations at a rate of 68% in type I, 5% in type II, 1.6% in type III, 21% in type IV, and 6% in type V CCs.[12] The overall risk of cancer is 10%–15% and increases with age.[10,13] It is 2.3% between 20–30 years, while it increases to 75% between 70 and 80 years of age. However, all these data originate from the East, and these rates differ in the West compared to the East. Baison et al. published a remarkable article on this topic in 2019.[15] They compared all single-center and multi-center reports from the East and West and

Table 2. Characteristics of Patients with Cancer

No of Patients	Age	Gender	Type of CC	Type of Surgery	Pathology	Rate (Type)	Rate (Age Range)
1	19	F	3	Whipple (hematoma in the duedenum during duedenotomy)	Choledochal adenocarcinoma	2% (n: 44)	6% (19–30 years, n: 17)
2	38	F	1b	Cyst excision+HJ	Choledochal squamous cell carcinoma	50% (n: 2)	4% (31–50 years, n: 22)
3	72	F	5	Left hepatectomy	Ductal adenocarcinoma	5% (n: 20)	3% (51–78 years, n: 31)

CC, choledochal cyst.

determined the malignancy rate at 0–17% in the East and 3%–8% in the West, recurrence rate at 0–10% in the East and 0–3% in the West, and APBJ at 71%–93% in the East and 8%–57.3% in the West. Mortality and morbidity rates, type of CCs, previous operations and complaints were similar. Basion concluded that although there is no evidence, overtreatment is a potential risk for Western patients with bile duct cysts, because they have been treated according to the Asian treatment guidelines, but they carry a lower risk for developing cancer in CCs. In the West, there is a group of CCs patients with a low risk of malignancy, having undergone a gallbladder operation without APBJ, especially type I patients. However, there is no study in the literature following up such patients and reporting the results. In a study by Ulas et al. in the West, malignancy was found in none of their 23 patients.[16] Our study also supports the results obtained by Baison et al. The overall cancer risk was found at 4% (n: 3). Considering them separately, the risk of cancer was 2% for type I, 50% for type III, and 5% for type V. Considering the age range, the risk of cancer was 6% for those aged 19–30 years, 4% for 31–50 years and 3% for 51–78 years of age (Table 2). Contrary to Eastern sources, the risk of cancer decreased with age in our study. The types of cancer associated with CCs are adenocarcinoma 73%–84%, followed by anaplastic carcinoma 10%, undifferentiated carcinoma 5%–7%, squamous carcinoma 5% and other types of carcinoma 1.5%.[14,17,18] In our study, two (66%) patients had adenocarcinoma and one (33%) had squamous cell carcinoma.

CCs are more common in women. Eighty percent of the patients manifest symptoms before they reach 10 years of age. The classic triad of symptoms consist of abdominal pain, jaundice, and an abdominal mass. Two thirds of the patients present with two of these three cardinal symptoms. Ultrasound imaging is used in the diagnosis (except for types III and V), with a sensitivity of 71–79%. Apart from that, technesium-99 HIDA scan (sensitivity: type I 100%, type IVa 67%), abdominal tomography (sensitivity; biliary tree 93%, CC 90%), MRCP (sensitivity: 90–100%) or ERCP can be used.[19] In our study, the ratio of women to men was approximately 8/1. All patients underwent ultrasonography, CT and/or MRI/MRCP examinations.

Surgery is the main treatment strategy. Primarily, bile drainage is used preoperatively in treating the cases with cholangitis and sepsis. Subsequently, complete excision of the cyst + drainage into the enteric system is recommended in hepatobiliary centers, if possible, as well as routine cholecystectomy, in case it is not already implemented.[16,20] As a hepatobiliary center, we performed ERCP in 10 patients (14%), PTC in 1 patient (1%), and both PTC and ERCP in 1 patient (1%) in order to provide preoperative biliary tree drainage and to prevent cholangitis.

The treatment algorithm varies according to the cyst type. Treatment modalities have changed from Todani (1977) to Baison (2019), although the main principles have remained unchanged (Table 4). Cyst excision and hepaticojejunostomy is the treatment of choice for type I CCs. Roux-en-Y hepaticojejunostomy is the gold standard. T-tube applications and sphincteroplasty are not recommended today. Excision of diverticulum (diverticulectomy) is now routinely performed for type II

Table 3. Type of Surgery Performed by Type of Choledochal Cyst

Operation	Type I	Type II	Type III	Type IVb	Type V
Cyst excision + Hepaticojejunostomy	25	1			
Cyst excision + Roux-en-Y Hepaticojejunostomy	17	1		2	
Cyst excision + double Roux-en-Y Hepaticojejunostomy	2				
Cyst excision + Roux-en-Y Hepaticojejunostomy + duodenotomy			1		
Segmental liver resection					14
Left hepatectomy					5
Whipple procedure			1		
Liver transplantation					1

Table 4. Surgical Treatment from Past to Present

1977-Todani	2019-Baison
Type I: Cyst excision+ Roux-en-Y HJ (T-tube for Ib, sphincteroplasty for Ic)	Cyst excision+ Roux-en-Y HJ
Type II: No experience (case: excision of diverticulum)	Excision of diverticulum
Type III: No experience (case: transduodenal excision+sphincteroplasty)	Endoscopic transduodenal excision+sphincteroplasty
Type IVa: Cyst excision (if possible, total + intrahepatic HJ)	Cyst excision+HJ+ unilateral: partial resection, multiple: liver transplantation
Type IVb: Cyst excision+ sphincteroplasty+HJ	Cyst excision+HJ
Type V: Partial resection in localized disease	Partial resection for partial disease, liver transplantation for diffuse disease, PTC as the palliative treatment

PTC, percutaneous transhepatic cholangiography.

CCs, although it used to be described only in case reports in the past. Transduodenal excision and sphincteroplasty were at the experimental stage in the past, but they are endoscopically performed with ERCP today in cases with type III CCs; otherwise surgery is applied as the second choice. In the past, cyst excision+HJ was recommended for type IVa, but today, partial liver resection (even liver transplantation, when necessary) is integrated. The current treatment of choice for type IVb is merely cyst excision + HJ. Pertinence of partial resection for type V was a controversial topic in the past. Today, resection is recommended for partial disease, liver transplantation for diffuse disease and PTC as palliative treatment.

Authors' Contribution

VO, MAU and EP have substantial contributions to conception, writing and design of the study; MKC, OA, TTK and YMO has contribution by acquisition, analysis and interpretation of data; EA, YBO and EBB have contribution by drafting the article or revising it critically for important intellectual content and final approval of the version to be published.

Conflict of Interest Disclosures

No conflict of interest was declared by the authors.

Informed Consent

Informed consent was obtained from patients who participated in this study.

Ethical Statement

This study is a retrospective study.

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