

Clinical Case Seminar

A6(1-9)

Choledochal cyst. An extremely rare malformation with potential severe complications.

**¹Enrica Antonelli, ¹Pietro Impellizzeri, ¹Salvatore Arena, ¹Saveria Parisi
¹Flora Maria Peri, ¹Rosario Caruso, ²Jean De Ville de Goyet, ¹Carmelo Romeo.**

¹Department of Human Pathology of Adult and Childhood “G.Barresi”, Unit of Pediatric Surgery, University of Messina, Messina; ²ISMETTPalermo, Italy

Abstract

Introduction: Choledochal cysts (CC) are rare congenital dilations of the extrahepatic and/or intrahepatic biliary tree with heterogeneous clinical pictures and high risk of malignancy. Case report: We reported a clinical case of 9 years old child with abdominal pain and jaundice. Strumental investigation with ultrasonography and magnetic resonance showed a CC. For this reason the patient underwent CC surgical excision and hepaticojejunostomy. Conclusion: CCs are a rare disease entity in Caucasian, with potential severe complications. A nearly diagnosis and a long term follow-up is recommended.

KeyWords: Choledochal cyst; hepaticojejunostomy; malformation jaundice

Introducing Member: Pietro Impellizzeri

Corresponding Author: Pietro Impellizzeri, - impellizzerip@unime.it -

Introduction

Choledochal cysts (CCs) represent focal outpouching or dilatation of the hepatobiliary system and occur with an overall incidence of approximately 1/100,000–1/150,000 and 1/1000 in Western and Asian populations, respectively¹. It is reported that females are at higher risk for this abnormality with a nearly 4:1 ratio as compared with males^{2,3}.

Approximately 80% of CCs are diagnosed within the first decade of life²⁻⁴, although in utero and adult diagnosis is not a rare event^{5,6}. The classic triad of abdominal pain, right upper quadrant mass and obstructive jaundice is mainly seen in paediatric population^{7,8,9}.

Infants are more likely to present with the jaundice clay coloured stools. Less commonly presentations include duodenal obstruction and perforation. Even if these lesions are considered benign, it is recommended their surgical removal after diagnosis because of complications as cholangitis, pancreatitis, cholelithiasis and malignant degeneration.

Case Report

A 9 years old girl has been evaluated by general practitioner (GP) for chronic abdominal pain for

about one year. Objective examination was unremarkable and GP suggested a parasitological examination of the stool that documented an intestinal infection by *EnterobiusVermicularis*.

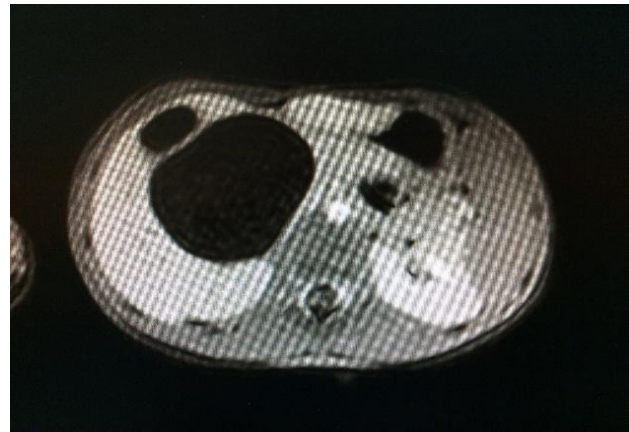
For this reason, an oral therapy with mebendazole was prescribed but the abdominal pain persisted despite successful therapy against the parasitological infection. So, GP suggested an abdominal ultrasonographic (US) evaluation that displayed a 49mm x 44mm anechoic lesion between liver and pancreas (Fig. 1) and a nuclear magnetic resonance (MR) was recommended. The parents refused the suggested examination.

For the persistence of the abdominal symptoms, after three months the child was admitted at emergency department. Blood analysis showed an enhanced of total and direct bilirubin (3.5 mg/dl, n.r. 0.2 to 1.2 mg/dL and 1.3 mg/dL, n.r. 0 to 0.4 mg/dL, respectively), AST 76 U/L (n.r. 10 to 40 U/L) , ALT 103 U/L (n.r. 7 to 56 U/L), GGT 291 U/L (n.r. 9 to 48 U/L) while abdominal ultrasonography documented a significant enlargement of the anechoic lesion (68mm x 78mm).

Fig.1 Abdominal ultrasound showing a 49 mm x 44 mm anechoic lesion (CC) containing iperechoic formations (gallstones).



Fig.2 MR with contrast medium



Then, the child was transferred to our institution, where an hepatobiliary RM with and without gadoxetate disodium-enhanced has been performed that confirmed a T2 weighted lesion of 76x58x89mm without opacification of a suspected choledochal cyst type IA (Fig. 2-6). For this reason, patient underwent surgery including choledochal cyst excision and hepatic-jejunostomy. Macroscopic evaluation confirmed the type of the cyst. Postoperative was uneventful and patients was discharged ten days after operation with normalization of the laboratory tests.

At the immunoistochemical level, epithelial cells lining the cystic lesion were negative for p53(Fig.7). The same cells were diffusely immunoreactive with CA19.9 (Fig.8), whereas Ki-67 labelling index was 1% (Fig 9). Even if there is a positivity, CA19.9 and Ki-67 observed levels exclude an under way malignancy.

Fig. 3: MR with contrast medium



Fig.4 MR without contrast medium



Discussion

CCs are rare congenital dilations of the extrahepatic and/or intrahepatic biliary tree.

Although several theories have been worked out, the etiology of this disease is still unclear. According to Babbitt's theory, the presence of an abnormal pancreatic-biliary duct junction (APBDJ), defined as a longer than 15 mm "common-channel". This condition should allow mixing of the pancreatic and biliary juices, which then activates pancreatic enzymes. These active enzymes should cause inflammation and deterioration of the biliary duct wall with greater pressures in the pancreatic duct, both leading to an abnormal dilation of the choledocus^{10, 11}.

Commonly CCs are classified, as reported by Todani in 1977, into five types depending upon the position of the cyst.

Type I CC are fusiform or spherical dilations of the extrahepatic biliary tree, further subdivided into TypeIA, IB and IC. In particular, type IA CCs have the gallbladder arising directly from the CC with a dilated extrahepatic biliary tree and a non-dilated intrahepatic tree. Type IB CCs contain a mostly normal appearing extrahepatic biliary tree with an isolated dilatation of the most distal aspect of the CBD, with no evidence of ABPU¹². Type IC CC are represented by a fusiform dilatation of the common hepatic duct and common bile duct in the presence of APBDJ^{2, 5, 13}.

Type II CCs consist of a diverticular dilatation of the extrahepatic bile duct system². Type III CCs, or choledochoceles, are located within the duodenal wall at the pancreaticobiliary junction¹⁴.

Fig.5 MR without contrast medium

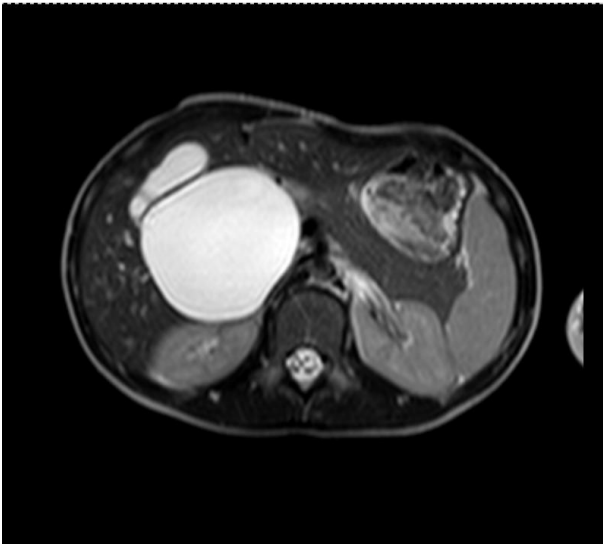
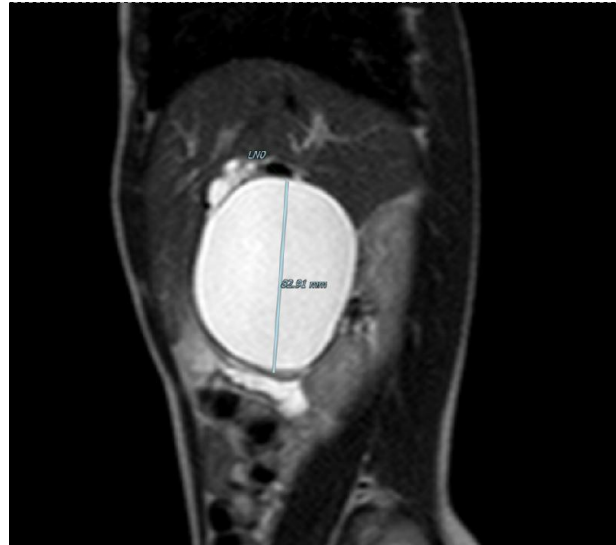


Fig.6 MR without contrast medium



Type IV CCs are multiple cysts which can involve both the intrahepatic and extrahepatic biliary tree. Type IV CCs can be further subdivided into Type IVA and IVB cysts. Type IVA CC refers to extrahepatic biliary dilatation with at least one intrahepatic cystic dilatation. Type IVB refers to multiple extrahepatic biliary cysts without intrahepatic involvement¹⁴.

Type V, or Caroli disease, demonstrates intrahepatic cystic dilatation without evidence of extrahepatic biliary tree involvement¹⁴. CCs may be associated with many different developmental anomalies, including colonic atresia, duodenal atresia, imperforate anus, pancreatic arteriovenous malformation, multiseptate gallbladder, OMENS plus syndrome, ventricular septal defect, aortic hypoplasia, pancreatic division, pancreatic aplasia, focal nodular hyperplasia, congenital absence of the portal vein, heterotopic pancreatic tissue and familial adenomatous polyposis^{15, 16}.

In our case the macroscopic evaluation during surgical excision showed a cystic dilatation of extrahepatic biliary tree which communicate directly with gallbladder. these characteristics confirmed the diagnosis of a type IA CC by Todani. The diagnosis of CCs is typically first accomplished during abdominal ultrasonography which can occasionally show direct communication with the biliary tract, yielding a definitive diagnosis^{17, 18}.

After US examination, MR must be performed, ideally with magnetic resonance cholangiopancreatography (MRCP) with contrast administration that is better able to delineate CCs subtype and associated abnormalities¹⁹ and is the tests of choice for preoperative planning because contrast enhancement can show malignant transformation, necessitating an alternative approach²⁰.

Endoscopic ultrasound and endoscopic retrograde cholangiopancreatography (ERCP) are also

able to detect a long common channel; however, their invasive nature and inherent risks like cholangitis, bleeding, pancreatitis and perforation, make MRCP the preferred diagnostic modality in the pediatric population.

CT may be the initial test in the adult emergency setting for undiagnosed choledochal malformations incidentally detected or presenting later in life whereas in pediatric population is utilized less frequently²⁰. The differential diagnosis among patients presenting with suspected CCs is broad, including biliary atresia, infectious hepatitis, biliary lithiasis, pancreatitis and biliary hamartoma².

In our study case the presence of CC was suspected after abdominal ultrasound that showed an anechoic cystic lesion between liver and pancreas. The diagnosis was confirmed by abdominal MR. Although benign, CCs can be associated with serious complications including cholestasis with stone formation that can cause recurrent cholangitis, pancreatitis, biliary and hepatic fibrosis, and malignant transformation.

Cholestasis is the result of prolonged inefficient bile drainage by the malformed biliary tract or from extrinsic compression in cases in which the extrahepatic cystic formation is large enough to cause regional mass effect³. Recurrent cholangitis and cholecystitis are likely multifactorial, with chronic inflammation from static lithogenic bile salts, refluxed pancreatic enzymes, and refluxed intestinal bacteria being implicated²¹.

Recurrent bouts of cholangitis regardless of the underlying cause lead to cyst wall fibrosis, ductal sclerosis, and increased risk of malignant degeneration².

Moreover patients with CCs have an elevated risk of malignant transformation with increasing age. Histologically, the most common cancer cell type is adenocarcinoma (73-84%), followed by anaplastic carcinoma (10%), undifferentiated (5-7%), carcinoma, and squamous cell carcinoma (5%)²². The origin of cancer progression remains unclear. Researchers hypothesized that chronic inflammation, cell regeneration, and DNA breaks may lead to dysplasia^{1, 23}.

Furthermore, it has been reported that pancreatic reflux may result in local inflammation with subsequent K-ras mutations, cellular atypia, and overexpression of p53, CA19.9 and Ki-67. In the majority of cases, cancer has been localized in the extrahepatic bile ducts (50-62%) and the gallbladder (38-46%)²⁴. However, malignant potential in our case was ruled out based on immunohistochemical findings such as negative immunohistochemistry for p53, very low Ki-67 labelling index as well as intense immunoreactivity for CA19.9, a glycoprotein highly expressed in normal bile duct.

Fig.7 The negative immunoreaction against p53 antibody (original magnification X20, Mayer's Haemalum nuclear counterstain)

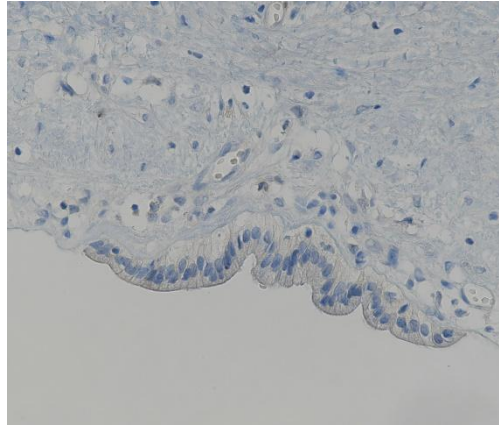


Fig.8 The uniform cytoplasmic CA19-9 positive immunostaining (original magnification X20, Mayer's Haemalum nuclear counterstain)

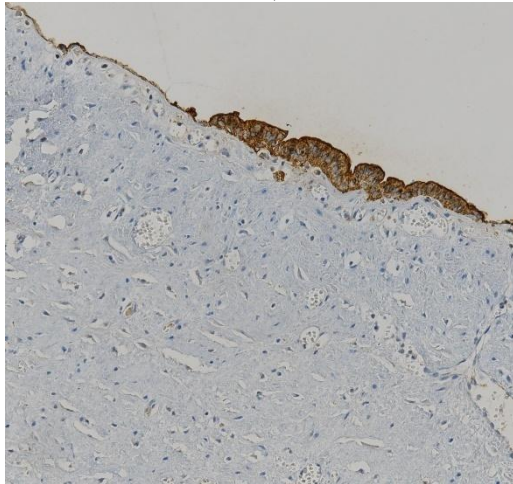
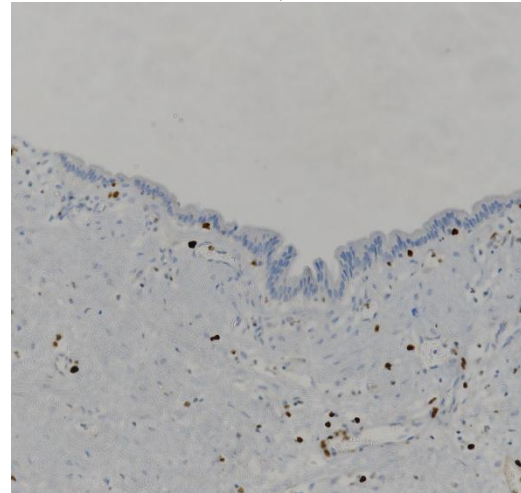


Fig. 9: A heterogenous staining pattern with low Ki-67 expression (1%). (original magnification X20, Mayer's Haemalum nuclear counterstain)



In 1979, Todani et al confirmed an association between cancer and cyst type²⁵. The incidence of malignancy was 68% in type I and 21% in type IV choledochal cysts. Traditionally, CCs management consisted of internal or external drainage procedures along with cholecystectomy²⁶. However, this approach resulted in unacceptably high rates of infection, pancreatitis, cholangitis, cholangiocarcinoma, and recurrent stenosis⁹.

The current management consists of complete cyst excision and reconstruction by hepatic-enterostomy; Hepatic-duodenostomy and Roux-en-Y hepatic-jejunostomy (RYHJ) are the two most commonly utilized techniques of reconstruction. Even if hepatic-duodenostomy has been preferred by some groups²⁷, most series suggest significantly more bile reflux compared with RYHJ, which is currently the most commonly utilized reconstruction.

When RYHJ is employed, an end-to-end anastomosis of the jejunum to the common bile duct is recommended if technically possible to avoid the elongation of a blind pouch as the child

grows²⁸. Recently, numerous authors have promoted laparoscopic surgical treatment of CC.

Although operative times have been longer, benefits of laparoscopic surgery for CCs include reduced postoperative pain, shorter hospitalization stay, reduced blood loss, fewer postoperative adhesions, better cosmesis, and earlier return to activity^{29, 30}.

However, major accordance have been reported about laparoscopic approach. In particular, the bilioenteric anastomosis is frequently performed to the common hepatic duct rather than a wide hilar hepaticoenterostomy^{27, 31, 32}, representing a higher risk for a late bilioenteric stricture.

Moreover, hepatic-duodenostomy has been usually preferred over hepatic-jejunostomy because it is technically easier and quicker to perform laparoscopically^{27, 33, 34}; this procedure predisposes to duodenogastric bile reflux and gastritis, raising doubts about a potential long-term risk of cancer³⁴.

A minimal invasive approach with the use of robotic surgical systems has been reported. Thanks to the magnified 3D imaging, the enhanced control of instruments, tremor filtration, motion scaling, and articulated wrists that allows high degree of freedom of movement, robotic surgery involves substantial technical advantages relative to conventional laparoscopy³⁵ facilitating complex minimal access procedures and allowing a complete intracorporeal cyst's resection and reconstruction of Roux-en-y hepatic-jejunostomy as open surgery technique.

Despite advantages, robotic surgery is still not extensively used because of high costs, the need to improve the tactile feedback, a worse cosmetics than laparoscopy and the current controversy about how old children need to be to undergo robotic surgery³⁶.

Following cyst excision in childhood, patients should be seen yearly due to the risk of short and long term complications as postoperative cholangitis, bile duct stones, anastomosis strictures and carcinogenesis. Abdominal ultrasound examination, as well as a control of laboratory parameters of cholestasis, should be performed³⁴. Unfortunately, the risk of malignant degeneration is only partially mitigated by complete resection.

In this regards, Tocchiet al. reported that chronic inflammatory changes consequent to biliary-enteric anastomosis for benign biliary diseases should be closely monitored for the late development of biliary malignancies, suggesting that the risk of subsequent biliary malignancy may be associated with bilioenteric anastomosis itself.

For this reason, annual CA19–9 controls, are performed after the patients reach adulthood to ensure early diagnosis of malignancy and referral to oncological centers³⁷.

Conclusion

CCs are a rare disease entity, more commonly seen in Asian population; clinical presentation varies and most often consists of non-specific abdominal pain. Generally, diagnosis of CCs in pediatric population can be performed by ultrasound and achieved by MRCP. Management consists of cyst excision and bilioenteric reconstruction. CCs total resection does not exclude the possibility of malignant transformation, so a long-term surveillance is recommended.

Conflicts of Interest: There is no potential conflict of interest, and the authors have nothing to disclose. This work was not supported by any grant

References

1. SinghAm, J., Yoshida, E.M., Scudamore, C.H., (2009). Choledochalcysts. Part 1. Classification and pathogenesis. *Can J Surg*; 52:434–440.
2. Soares, K.C., Arnaoutakis, D.J., Kamel, I., Rastegar, N., Anders, R., Maithel, S., Pawlik, T.M. (2014) Choledochal cysts: presentation, clinical differentiation, and management. *J Am CollSurg* 219(6):1167–1180. doi:10.1016/j.jamcollsurg.2014.04.023
3. Lipsett, P.A., Pitt, H.A. (2003) Surgical treatment of choledochal cysts. *J Hepatobiliary PancreatSurg* 10(5):352–359. doi:10.1007/s00534-002-0797-4.
4. Wiseman, K., Buczkowski, A.K., Chung, S.W., Francoeur, J., Schaeffer, D., Scudamore, C.H. (2005) Epidemiology, presentation, diagnosis, and outcomes of choledochal cysts in adults in an urban environment. *Am J Surg* 189(5):527–531. doi:10.1016/j.amjsurg.2005.01.025
5. Rozel, C., Garel, L., Rypens, F., et al. (2011) Imaging of biliary disorders in children.; *PediatrRadiol* 41:208–220.
6. Gong, L., Qu, Q., Xiang, X., Wang,. (2012) Clinical analysis of 221 cases of adult choledochal cysts.; *J. Am Surg* 78:414–418.
7. Akhan, O., Demirkazik, F.B., Ozmen, M.N., Ariyurek, M. (1994) Choledochal cysts: ultrasonographic findings and correlation with other imaging modalities. *Abdom Imaging*. 19:243–247
8. Stringer, M.D., Dhawan, A., Davenport, M., et al.. (1995)Choledochalcysts: lessons from a 20 year experience.; *Arch Dis Child* 73:528–531.
9. De Vries, J.S., De Vries, S., Aronson, D.C., et al., (2002)Choledochalcysts: age of presentation, symptoms, and late complications related to Todani's classification.; *J PediatrSurg* 37:1568–1573.
10. Babbitt, D.P. (1969) Congenital choledochal cyst: new etiological concept based on anomalous relationships of the common bile duct and pancreatic bulb. *Ann Radiol (Paris)*;12:231–40.
11. Han, S.J., Hwang, E.H., Chung, K.S., et al.. (1997) Acquired choledochal cyst from anomalous pancreatobiliary duct union.; *J PediatrSurg* 32:1735–8.
12. Lee, H.K., Park, S.J., Yi, B.H., et al.. (2009) Imaging features of adult choledochal cysts: a pictorial review. *Korean J Radiol*. *Korean J Radiol*; 10:71–80
13. Todani, T., Watanabe, Y., Toki, A., Morotomi, Y. (2003) Classification of congenital biliary cystic disease: special reference to type Ic and IVA cysts with primary ductal stricture. *J Hepatobiliary PancreatSurg* 10(5):340–344. doi:10.1007/s00534-002-0733-7
14. Martin, R.F., (2014) Biliary cysts: a review and simplified classification scheme. *SurgClin North Am* 94(2):219–232. doi:10.1016/j.suc.2014.01.011
15. Elton, E., Hanson, B.L., Biber, B.P., et al. (1998) Dilated common channel syndrome: endoscopic diagnosis, treatment, and relationship to choledochoceles formation.; *GastrointestEndosc* 47:471–8.
16. Ramnarine, I.R., Mulpur, A.K., McMahan, M.J., et al.. (2001)Pleurobiliary fistula from a ruptured choledochal cyst *Eur J CardiothoracSurg*.;19:216–8.
17. SinghAm, J., Yoshida, E.M., Scudamore, (2010) Choledochal cysts. Part 3. Management.; 53:51–56
18. Soares, K.C., Goldstein, S.D., Ghaseb, M.A., Kamel, I., Hackam, D.J., Pawlik, T.M. *PediatrSurgInt* (2017) Pediatriccholedochal cysts: diagnosis and current management.; .H., *Can J Surg* 33:637–650
19. Sacher, V.Y., Davis, J.S., Sleeman, D., Casillas, J. (2013) Role of magnetic resonance cholangiopancreatography in diagnosing choledochal cysts: case series and review. *World J Radiol* 5(8):304–312.

doi:10.4329/wjr.v5.i8.304

20. Lewis, V.A., Adam, S.Z., Nikolaidis, P., et al. (2015) Imaging of choledochal cysts.; *Abdom Imaging* 40:1567–1580
21. SinghAm, J., Yoshida, E.M., Scudamore, C.H., *Abdom Imaging* (2009) Choledochal cysts. Part 2. Diagnosis.; *Abdom Imaging* 52:506–511
22. Fieber, S.S., Nance, F.C. (1997) Choledochal cyst and neoplasm: a comprehensive review of 106 cases and presentation of two original cases. *Am Surg*; 63:982–7.
23. Todani, T., Tabuchi, K., Watanabe, Y., Kobayashi, T., (1979) Carcinoma arising in the wall of congenital bile duct cysts.; 44(03): *Cancer* 1134–1141
24. Jabłońska, B. (2012) Biliary cysts: etiology, diagnosis and management.; *World J Gastroenterol* 18(35):4801–4810
25. Visser, B.C., Suh, I., Wy, L.W., et al. (2004) Congenital choledochal cysts in adults.; *Arch Surg.* 139:855–62.
26. Todani, T., Watanabe, Y., Narusue, M., et al., (1977) Congenital bile duct cysts: Classification, operative procedures, and review of thirty-seven cases including cancer arising from choledochal cyst.; *Am J Surg* 134:263–269.
27. Yeung, F., Chung, P.H., Wong, K.K., Tam, P.K. (2015) Biliary-enteric reconstruction with hepaticoduodenostomy following laparoscopic excision of choledochal cyst is associated with better postoperative outcomes: a single-centre experience. *Pediatric Surg. Int* 31(2):149–153. doi:10.1007/s00383-014-3648-x
28. Miyano, T., Stringer, M.D., Oldham, K.T., Mouriquand, P.D.E. (eds), (2006) long-term outcomes. *Pediatric surgery and urology*, Cambridge University Press, Cambridge pp 465–479
29. Diao, M., Li, L., Cheng, W. (2011) Laparoscopic versus open Roux en-Y hepatojejunostomy for children with choledochal cysts: intermediate-term follow-up results. *SurgEndosc* 25:1567–1573. doi:10.1007/s00464-010-1435-x
30. Margonis, G.A., Spolverato, G., Kim, Y., et al (2015) Minimally invasive resection of choledochal cyst: a feasible and safe surgical option. *J Gastrointest Surg* 19:858–865. doi:10.1007/s11605-014-2722-y
31. Hong, L., Wu, Y., Yan, Z., Xu, M., Chu, J., Chen, Q.M. (2008) Laparoscopic surgery for choledochal cyst in children: a case review of 31 patients. *Eur J Pediatr Surg* 18:67–71. doi:10.1055/s-2008-1038486
32. Senthilnathan, P., Patel, N.D., Nair, A.S., Nalankilli, V.P., Vijay, A., Palanivelu, C. (2015) Laparoscopic management of choledochal cyst-technical modifications and outcome analysis. *World J Surg* 39:2550–2556. doi:10.1007/s00268-015-3111-8
33. Narayanan, S.K., Chen, Y., Narasimhan, K.L., Cohen, R.C. (2013) Hepaticoduodenostomy versus hepaticojejunostomy after resection of choledochal cyst: a systematic review and meta-analysis. *J Pediatr Surg* 48:2336–2342. doi:10.1016/j.jpedsurg.2013.07.020
34. Omid, M.S., Thomas, C.W., Joachim, F.K., Claus, P., Benno, M.U. (2017) Choledochal Cyst and Malignancy: A Plea for Lifelong Follow-Up. *Eur J Pediatr Surg*. DOI: 10.1055/s-0037-1615275.
35. Wang, S.E., Chen, S.C., Shyr, B.U., Shyr, Y.M. (2017) Robotic assisted excision of type I choledochal cyst with Roux-en-y hepaticojejunostomy reconstruction. *HepatoBiliary Surg. Nutr.* 6(6): 397–400. doi: 10.21037/hbsn.2017.01.15.
36. Wang, X.Q., Xu, S.J., Wang, Z., Xiao, Y.H., Xu, J., Wang, Z.D., Chen, D.X. (2018) Robotic-assisted surgery for pediatric choledochal cyst: Case report and literature review. *World J Clin Cases.* 16;6(7):143-149. doi: 10.12998/wjcc.v6.i7.143.
37. Tocchi, A., Mazzoni, G., Liotta, G., Lepre, L., Cassini, D., Miccini, M. (2001) Late development of bile duct cancer in patients who had biliary-enteric drainage for benign disease: a follow-up study of more than 1000 patients.; *Ann. Surg.* 234: 210–214.



©2018 by the Author(s); licensee Accademia Peloritana dei Pericolanti (Messina, Italy). This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution 4.0 International License (<https://creativecommons.org/licenses/by/4.0/>).

Communicated and received June 26 2018, revised September 21, 2018, published on line December 18, 2018