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Risk factors for postoperative stone formation in pediatric choledochal cysts: a study of 457 cases

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Postoperative bile duct stones, including intrahepatic bile duct (IHD) stones and remnant distal common bile duct (remnant intrapancreatic common bile duct, RIPD) or common channel duct (CCD) stones, are long-term complications following choledochal cyst (CC) excision. We aimed to retrospectively review occurrence, associated factors, and treatment of postoperative bile duct stones. Records of 457 pediatric patients who underwent CC excision at Asan Medical Center (1992–2021) were retrospectively reviewed. Data on cholelithiasis, operation, and outcomes were analyzed. Overall, 457 pediatric patients underwent CC excision, with 21 developing intrahepatic duct (IHD) stones, primarily associated with Todani type IVa cysts, especially Tsuchida types 2 or 3, which are often linked to IHD dilation and upstream stenosis. Patients with RIPD/CCD stones were all identified with complicated Komi types, and the impact of pancreas divisum itself was unclear. Early surgery even before 6 months of age is associated with improved prognosis regarding the occurrence of IHD stones, but not related with RIPD/CCD stones. This is the largest retrospective study to date, comprising 21 IHD and 18 RIPD/CCD stones from 457 pediatric patients with CCs and their clinical outcomes. We found that the structural characteristics of the bile duct influence stone formation. In addition, our findings indicate the need for more systematic and long-term follow-up of patients with CCs after surgery.

Keywords Bile duct stone, Choledochal cyst, Intrahepatic duct stone, Intrapancreatic common bile duct stone, Pediatric

Abbreviations

APBDU	Anomalous pancreaticobiliary ductal union
CCA	Cholangiocarcinoma
CCD	Common channel duct
CC	Choledochal cyst
CT	Computed tomography
EUS	Endoscopic ultrasound
HJ	Hepaticojejunal
IHD	Intrahepatic duct
JJ	Jejunojejunal
RIPD	Remnant intrapancreatic common bile duct
MIS	Minimally invasive surgery
MRI	Magnetic resonance imaging
MRCP	Magnetic resonance cholangiopancreatography
PTBD	Percutaneous transhepatic biliary drainage
PTCS	Percutaneous transhepatic cholangioscopy
SPSS	Statistical Package for Social Sciences
US	Ultrasonography

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A choledochal cyst (CC) refers to an abnormal dilation of the biliary tract, affecting both intra- and extrahepatic bile ducts. CCs are highly prevalent in Asian populations, with an estimated incidence of approximately 1 in 1000 individuals[1]. The morphology-based Todani classification categorizes CCs into five types, with type I being the most frequent (75–85%)[2,3]. Although the etiology of CC formation is unclear, congenital weakness in the bile duct wall, genetic predisposition, bile duct obstruction, abnormal pressure, structural changes, and chronic inflammation may be involved[1,4]. Treatment involves resection of the dilated bile ducts and hepaticojejunostomy. With the advent of minimally invasive surgery is now performed at high rates.

However, rare, long-term complications, such as cholangitis, pancreatitis, lithiasis, biliary tract malignancy, cholangiocarcinoma (CCA), and pancreatic carcinoma, may occur[3]. Specifically, bile duct stenosis and subsequent cholangitis or pancreatitis are associated with progressive duct stricture and carcinogenesis[5,6]. During the process described above, stones can occur in the IHD, remnant intrapancreatic common bile duct (RIPD), and common channel duct (CCD) and trigger inflammation and carcinogenesis. IHD stones are the most common late complication of CC surgery, occurring in 2.7–11.0% of the patients and attributed to incomplete excision, anastomotic stricture, residual debris, etc.[7] Despite complete surgical excision of CCs, CCA has been reported in several studies, with an incidence of 0.7–5.4%[8]. IHD stones are believed to increase the risk of carcinogenesis, possibly due to chronic inflammation-induced dysplasia occurring concurrently with stone formation. Furthermore, anomalous pancreaticobiliary ductal union (APBDU) and pancreatic divisum are risk factors for RIPD/CCD, pancreatitis, and pancreatic duct stricture[9]. However, other factors contributing to these complications are largely unknown.

The 5-year outcomes of CC surgery are excellent, and until recently, major studies on CC surgery have mainly focused on the effectiveness of minimally invasive surgery (MIS), such as laparoscopic, single-port laparoscopic, and robotic approaches[10–12]. Studies on a small number of patients from single institutions with 10–20 years of follow-up revealed that long-term complications are relatively rare[9]. This finding is attributable to the nature of the disease, which has excellent short-term outcomes, making long-term follow-up difficult. In addition, when long-term complications occur in adulthood, patients are less likely to be assessed at the same center or pediatric hospital where the initial surgery was performed.

As patients age, it becomes crucial to reassess the long-term complications of CC surgery, particularly the formation of stones in the remaining bile ducts, and consider appropriate management strategies. In this context, we investigated the incidence and characteristics of postoperative bile duct stones following conventional surgical procedures.

Materials and methods

Patients

This retrospective study was conducted for 455 pediatric patients who had CC excision and Roux-en-Y hepaticojejunostomy (HJ) procedures at Asan Medical Center between 1995 and 2021 (Fig. 1). The specific characteristics of IHD and RIPD/CCD stones in the imaging studies are presented in Supplementary Tables 1 and 2. Two patients who had surgery at other centers but were transferred for postoperative choledocholithiasis management were included. Thus, 457 patients were included in the study. At our center, CC is currently diagnosed via ultrasonography (US); magnetic resonance imaging (MRI) including magnetic resonance cholangiopancreatography (MRCP); and hepatobiliary scan (HBS) when necessary (Supplemental Fig. 1). Since November 2012, MRI has been included in the evaluation process, whereas earlier, diagnosis was made via US and computed tomography (CT). In cases in which the initial evaluation was conducted in the emergency department because of obstructive symptoms, such as jaundice and pancreatitis, diagnosis was primarily made via CT, and endoscopic retrograde cholangiopancreatography (ERCP) was performed when necessary.

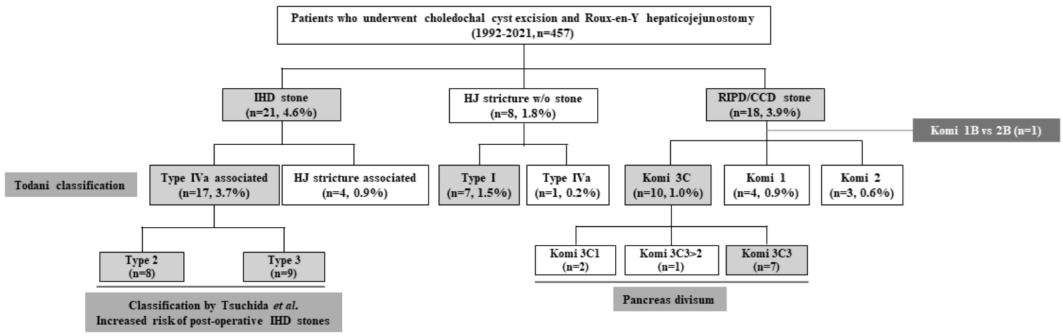

Fig. 1. Characteristics of patients with postoperative choledocholithiasis. Over 30 years, 457 patients had choledochal cyst excision and followed up at our institution. In 21 patients (including two who had surgery at other centers), intrahepatic bile duct stones were identified. Four patients developed stones due to HJ stricture, but in 17 (81%) patients, the stones were associated with Todani type IVa, which involves IHD dilation. One-half of the patients with stones in RIPD/CCD in the intrapancreatic portion had confirmed pancreas divisum, classified as Komi type IIIC. *HJ, hepaticojejunostomy; IHD, intrahepatic bile duct; RIPD, remnant intrapancreatic common bile duct; CCD, common channel duct.

The initial classification of CC was based on the interpretation by a pediatric radiologist with > 5 years of experience in pediatric diagnostic imaging. Patients diagnosed with stones were reevaluated, classifying them according to the Todani and Komi classification[3,13]. Image analysis was performed primarily on MR images, including MRCP[14]. Briefly, MRCP includes the following sequences: precontract axial T1 in- and out-of-phase, axial T2, axial single-shot fat-saturated T2, axial diffusion-weighted imaging, coronal single-shot fat-saturated T2, 3D coronal turbo spin echo with maximal intensity projection image, 2D T2 with thick-slab imaging, and 3D T1-weighted gradient echo sequences in the hepatic arterial/portal venous/delayed phase. The classification proposed by Tsuchiya in 2002 was also incorporated[15]. Comprehensive data, including demographics, surgical procedures, and subsequent follow-ups of each patient, were collected in addition to anatomical classification. The follow-up period was calculated from the date of the most recent outpatient visit. Complications were assessed using the Clavien–Dindo classification system. This study adhered to the principles of the Declaration of Helsinki and was approved by the Institutional Review Board of Asan Medical Center (approval No: 2023-0840). Informed consent was waived due to the retrospective nature of the study.

Surgical procedure

Open or minimally invasive approach was applied based on the surgeon's preference and timing. Ever since our center first adopted the laparoscopic approach in 2008, we have considerably expanded the rate of MIS. Recently, MIS has frequently been performed, except in patients with severe inflammation. The annual number of surgeries performed at this center is presented in Supplemental Fig. 1. Right subcostal incision was used as an open approach, and a three- or four-port system was utilized as minimally invasive approach. Once CC was identified during exploration, both the cystic duct and artery were found and tied off before cyst removal, serving as landmarks for dissection.

In some cases, the cyst was cut horizontally to prevent artery damage to confirm the hepatic artery during dissection. Proximal resection was done at the level of the normal common bile duct to ensure complete cyst removal. Distally, the bile duct was dissected toward the inside of the pancreatic head. Upon confirming the normal duct, it was cut and tied off using a Hem-o-lock clip.

An end-to-side jejunojejunal (JJ) anastomosis was made approximately 40 cm distal to the Treitz ligament, leaving a 40 cm length of jejunum between the JJ and hepaticojejunostomy (HJ) anastomoses. The HJ anastomosis was formed in a retrocolic manner. After ensuring no leaks at the HJ anastomosis site, a drain was placed in the posterior HJ, and the operation ended with skin closure.

Postoperative follow-up

Our routine postoperative follow-up protocol is illustrated in Supplemental Fig. 2. We implemented this system in 2024. Serum liver enzyme levels were monitored during every outpatient visit. Our previous routine follow-up was conducted separately as follows: During outpatient-based follow-up, ultrasonography was performed at intervals of 6–12 months for cases within 3 years postoperatively and every 2 years for those beyond 3 years postoperatively. MRCP was performed as necessary. Ultrasonography was employed to evaluate the state of the anastomosis site and intrahepatic ducts (IHD) (e.g., dilatation, pneumobilia, tortuosity, and stone formation) as well as to assess RIPD/CCD. Serum liver enzyme levels were monitored at the discretion of each practitioner.

Treatment strategies for IHD stone

Percutaneous transhepatic cholangioscopy (PTCS) has been traditionally employed as the initial approach for IHD stone removal, with a high success rate. Even in complex cases, complete stone clearance has been reported to achieve a success rate of almost 100%[16]. Considering the anatomical characteristics of Roux-en-Y HJ anastomosis, PTCS has been employed as the first-line approach owing to its relatively easy access and feasibility for repeated procedures. However, for adolescent patients, maintaining percutaneous transhepatic biliary drainage (PTBD) posed several challenges.

According to a review by Paik and Park, the clinical success rate of endoscopic ultrasound-guided hepaticogastrostomy (EUS-HGS) when performed by experienced practitioners was reported to be approximately 90% (range: 66%–100%)[17]. At our institution, after stone removal under EUS-HGS, the stent was typically maintained for at least 3–6 months. This prolonged stent placement facilitated the clearance of tiny stones and sludge following stone removal and enabled better patient compliance than PTBD.

We adopted a multidisciplinary approach to determine the optimal treatment plan for pediatric patients with stones. Currently, we prioritize the feasibility of EUS-HGS as the first-line approach, and PTCS is considered as an alternative if this method is not viable. Surgical intervention is reserved as the final option when interventional approaches, such as PTCS, are not feasible.

Statistical analysis

All statistical analyses were conducted using SPSS version 27.0 for Windows (IBM Corp., Armonk, NY, USA), and Student's *t*-test was used to compare the means between groups. Regression analysis was employed to test for risk factors. Statistical significance was set at a p-value of < 0.05.

Results

IHD stones were identified in 21 patients (Fig. 1). In four patients, stones developed due to HJ stricture, and 17 (81%) were diagnosed with Todani type IVa-associated IHD stone related to IHD dilatation. Among them, > 50% ($n = 9$) were classified as Tsuchida type 3, suggesting a proximal IHD stenosis at the bifurcation level. Among the eight patients who had surgical treatment for HJ stricture without stone formation, one was confirmed Todani type IVa. The surgical approach did not affect the formation of IHD stones. No difference was observed in IHD stone formation regardless of the surgical method employed—open (n = 14, 5.7%), laparoscopic (n = 3, 2.1%), or

	N = 21
Male:female	5:16
Clinical presentation at diagnosis of IHD stones	
Cholangitis (abdominal pain and fever)	9 (43.0%)
Asymptomatic	8 (38.1%)
Abdominal pain	3 (14.3%)
Liver abscess	1 (4.8%)
Age at choledochal cyst excision (months)	
Neonate (age ≤ 30 days)	2 (9.5%)
Infants (age ≤ 1 year)	0
Children (age ≥ 1 year)	19 (90.5%)
Preoperative intervention	8 (38.1%, ERCP (n = 7), PTBD (n = 1))
Age at choledocholithiasis diagnosis (years, range)	17.4 ± 6.2 (4.5–33.6)
Time from operation to stone occurrence (months, range)	122.2 ± 70.6 (18.6–277.1)
Follow-up duration (months, range)	41.8 ± 47.9 (2.2–155.9)
Outcome	
Symptoms: Persisting/resolved/no symptom	5 (one with mild symptoms)/15/1 (23.8%/71.4%/4.8%)
Residual stone: large stones/small stones/no residual stone	3/9/7
Follow-up loss	1 (4.8%)
Plan	
Observation (small stones > clear)	4 (19.0%)
Regular follow-up (clear > small stones)	8 (38.1%)
Medical treatment	1 (4.8%)
Planning PTCS	4 (19.0%)
Planning endoscopic HJ	2 (9.5%)

Table 1. Characteristics of patients with intrahepatic bile duct (IHD) stones ($n = 21$). *IHD, intrahepatic bile duct; PTCS, percutaneous transhepatic cholangioscopy; HJ, hepaticojejunostomy.

robotic (n = 4, 4.3%). The anastomosis size was larger in the group with IHD stone progression (15.0 [10.0–20.0] mm) than that in the group without (8.0 [5.0–11.0] mm) ($P = 0.03$), with no differences observed in other factors. Notably, there were no reports of postoperative hepatic artery injury, HJ leak, fluid collection, or bleeding in the group with IHD stone formation.

Of the patients with RIPD/CCD stones, 16 could be analyzed with MRI, with nine having concomitant pancreas divisum of Komi type 3C. The next most common type was Komi type 1.

Detailed descriptions of the 21 patients with IHD stones are provided in Table 1. Initial symptoms of stone occurrence were cholangitis in 9 (42.9%) patients and incidental findings on follow-up ultrasound or MR in 8 (38.1%) patients. CC excision was performed after the age of 1 year in 19 (90.5%) patients, and stones were diagnosed at 17.4 ± 6.2 years of age and 122.2 ± 70.6 months after surgery. Figure 2 illustrates the occurrence

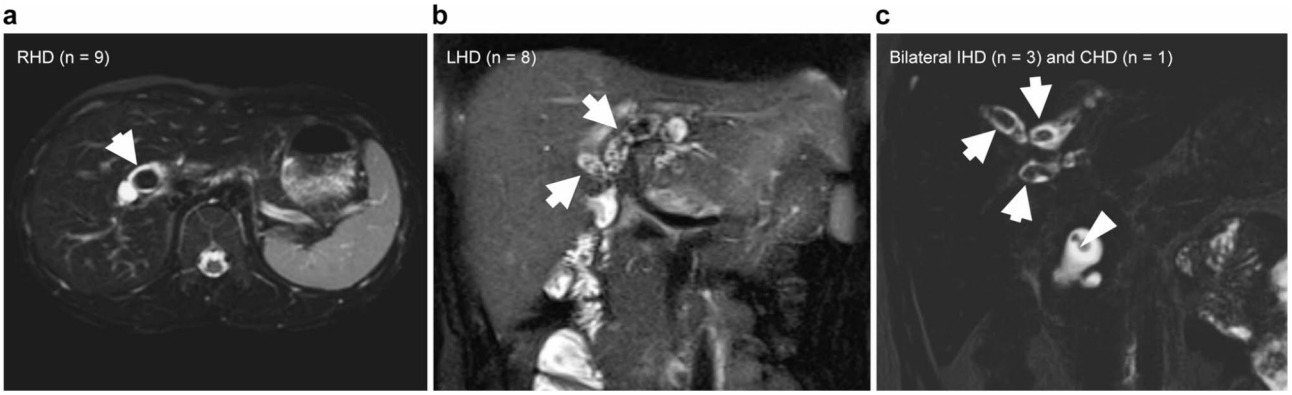

Fig. 2. Characteristics of IHD stones in the patients included in the study. IHD stones occurred in left and right bile ducts with similar frequency. Stones developed in bilateral IHDs in three patients, whereas in one patient, they originated from the CHD. This patient had a residual choledochal cyst remaining on the CHD side, which was surgically resected. *RHD, right hepatic duct; LHD, left hepatic duct; CHD, common hepatic duct.

of IHD stone in the right hepatic duct ($n=9$), left hepatic duct ($n=8$), and bilateral IHD ($n=3$). In one patient with common hepatic duct stones, residual CC was identified, and remnant cyst excision was performed. Treatment for IHD stones primarily involved PTCS ($n=10$, 47.6%) and surgical removal ($n=5$, 23.8%). In three patients, stone removal under endoscopic retrograde cholangiopancreatography (ERCP) (Fig. 3) was attempted. A pediatric colonoscopy was used to directly access the HJ along the R-en-Y-limb in one patient, and endoscopic ultrasound-guided hepaticogastro/jejunostomy was performed in two for stone removal and stent insertion (Fig. 4). All the patients showed favorable outcomes without complications. With a follow-up period of 41.8 ± 47.9 months from stone diagnosis, five patients are preparing for further treatment due to recurrence or recent diagnosis (Table 1). No CCA associated with IHD stones has been diagnosed in our study population.

Majority of the 18 patients with RIPD/CCD stones experienced pancreatitis ($n=13$, 72.2%, Table 2). Stones were observed in 45% of patients showed postoperative dilatation of RIPD/CCD (18/40). CC excision was performed after the age of 1 year in all patients, and stones occurred at the age of 10.5 ± 5.4 years and 65.6 ± 72.3 months after surgery. RIPD/CCD stones were found in various parts of the common channel and residual common bile duct in the pancreas head. In case of pancreas divisum, stones developed in both dorsal and ventral ducts. ERCP was performed in 14 (77.8%) patients, and for three symptom-free (16.7%) patients, observation was performed. Repeated ERCP procedures were required for most patients, and endoscopic retrograde pancreatic drainage insertion was done in four patients (Fig. 5). All patients showed resolution of symptoms during 72.7 ± 56.3 months of follow-up after stone diagnosis, although ERCP was under consideration in case of symptom recurrence for two patients (Table 2). There were differences in the timing and age at the occurrence of RIPD/CCD stones and IHD stones after surgery, with IHD stones occurring relatively later (Table 3). Subgroup analysis was conducted to identify and evaluate factors associated with stone formation (Table 4). IHD and RIPD/CCD stones occurred less frequently in patients operated on during infancy. For IHD stones, the age at occurrence was significantly higher in patients with stones than without stones ($p<0.01$). Linear regression analysis revealed that age at surgery significantly influenced the occurrence of IHD stones ($p<0.001$).

Discussion

Bile duct stones occurring after CC excision serve as indicators of chronic inflammation in the biliary tract and perpetuate conditions such as cholangitis or pancreatitis. Ultimately, they can worsen ductal stricture and elevate cancer risk. Therefore, the need for long-term follow-up was suggested for their diagnosis[18,19]. IHD stones emerge as the most common late complication following CC excision, significantly increasing after > 10 years postoperatively. Takimoto reported that IHD stones developed in 1.7% of patients who underwent CC excision in 2009 but confessed that incidence may increase in their recent report[8]. In our study, stones were diagnosed 122.2 ± 70.6 months after surgery, and the patient age was 17.4 ± 6.2 years (Table 1). This aligns with previous reports. Ono et al. reported cases of a 14-year-old girl and a 26-year-old man succumbing to cholangiocarcinoma 2 and 26 years after CC excision, respectively, in 2009[9,20]. Nishiyama et al. reported a case of cholangiocarcinoma 33 years following complete excision of CC, highlighting the necessity of > 30 years of long-term follow-up[21]. Nonetheless, considering Ono's report of a 96% overall survival rate, early diagnosis and treatment of CC can yield favorable outcomes[9].

In 2022, Takimoto et al. reported that postoperative IHD stone occurred in 10.2% of patients[8]. In our study, IHD stones were identified in 4.6% of patients. Takimoto observed that patients who developed IHD stones were significantly younger at surgery, with type IVa being significantly higher in this group. In our study, type IVa was present in 17 (81.0%) patients. The number of patients with clearly identified types of choledochal cysts (n = 332) was significantly higher than those (n = 34; 10.9%) without IHD stones (p < 0.001). According to Kemmotsu et al. and Tsuchida et al., anatomical features, such as stricture at the hepatic duct bifurcation site, are associated with the formation of IHD stones[15,22,23]. Based on this data, Urushihara et al. and Nakagawa et al. suggested

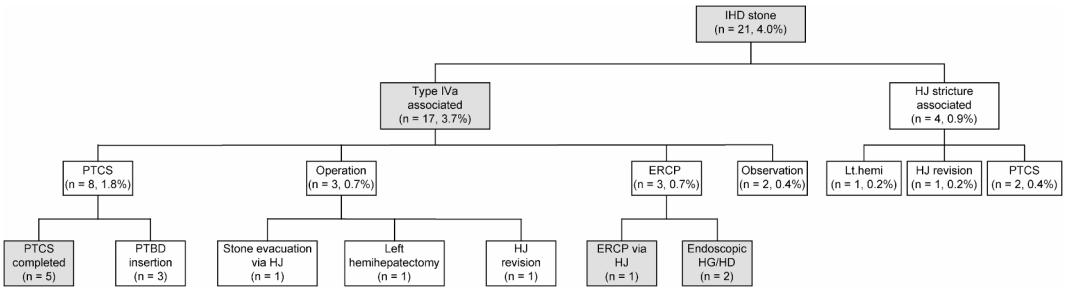

Fig. 3. Treatment for IHD stones. The approach of stone removal through PTCS was attempted frequently ($n=10$). Surgical removal of stones or revision of hepaticojejunostomy was performed through HJ anastomosis in three patients, whereas left hemihepatectomy was performed in two patients, followed by favorable outcomes and regular follow-ups. Recently, stone removal has been initiated using hepaticogastrostomy stent insertion under endoscopic ultrasound (EUS) guidance. This approach offers the advantage of performing the procedure without additional visible scars but faces high technical barriers in terms of entry. *IHD, intrahepatic bile duct; PTCS: percutaneous transhepatic cholangiography; HJ, hepaticojejunostomy; ERCP, endoscopic retrograde cholangiopancreatography; Lt. hemi, left hemihepatectomy; HG, hepaticogastrostomy; HD, hepaticoduodenostomy.

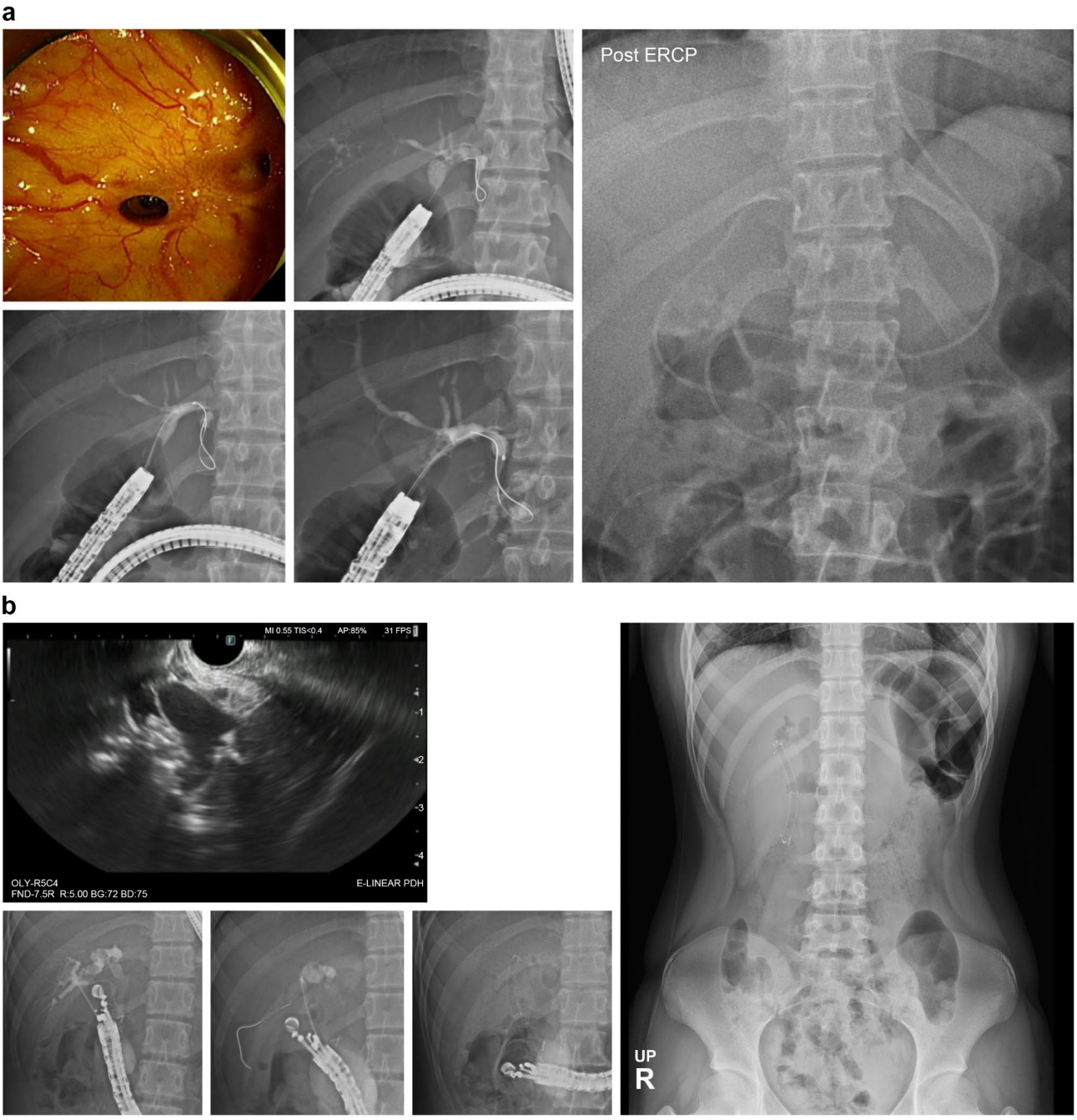

Fig. 4. Endoscopic treatment for IHD stones. (**a**) The images show stone removal through ERCP, utilizing pediatric colonoscopy with a cap. The endoscope was advanced to the site of HJ anastomosis, where the anastomosis was visualized (top left), and a cholangiogram was obtained (top right). Removal was performed in a patient with stricture at Roux-en-Y side-to-side pancreaticojejunostomy with ductal drainage (RSPD), with accompanying stones. (**b**) Using EUS, a window was secured through the duodenal wall to visualize the HJ. The right posterior hepatic duct was punctured to obtain a cholangiogram. Hepaticoduodenostomy was performed, followed by dilation of the stricture site using a cystotome and a 4-mm REN balloon. Finally, an HD stent (Mitech dual 6×8 mm) was inserted through HD. A follow-up X-ray was performed immediately after ERCP, confirming the presence of the inserted HD stent. *ERCP, endoscopic retrograde cholangiopancreatography; HJ, hepaticojejunostomy; HD, hepaticoduodenostomy.

preventive hilar ductoplasty, citing promising results and feasibility[24–26]. After securing the long-term outcomes of plasty and the complications associated with it, such as postoperative leaks and re-stenosis at the plasty site, it may be necessary to introduce this procedure in the future. However, it is known that in patients with type IVa before surgery, IHD dilatation resolves within 1 year after surgery for choledochal cysts. Considering this, it is also necessary to establish evidence regarding which patients should be considered candidates for plasty. Based

	***N* = 18**
Male:female	4: 14
Clinical presentation at diagnosis of RIPD/CCD stones	
Pancreatitis	13 (72.2%)
Asymptomatic	5 (27.8%)
Age at choledochal cyst excision (months)	
Neonate (age ≤ 30 days)	0
Infants (age ≤ 1 year)	0
Children (age ≥ 1 year)	18 (100.0%)
Symptoms at the time of choledochal cyst diagnosis	
Biliary obstruction	4 (22.2%)
Pancreatitis	5 (27.8%)
Both	9 (50.5%)
Preoperative intervention	11 (61.1%)
Age at choledocholithiasis diagnosis (years)	10.5 ± 5.4 (3.4–18.8)
Time from operation to stone occurrence (months)	65.6 ± 72.3 (0.4–210.3)
Follow-up duration (months)	72.7 ± 56.3 (4.4–212.9)
Outcome	
Symptoms: Persisting/no symptom	0/18 (0%/100.0%)
Residual stone: Residual stone/no residual stone/	4/14 (22.2%/77.8%)
Follow-up loss	1 (5.6%)
Plan	
Regular follow-up	16 (88.9%)
Further ERCP	2 (11.1%, ERPD insertion in 1 patient)

Table 2. Characteristics of patients with stone in remnant intrapancreatic common bile duct/common channel duct (RIPD/CCD) ($n = 18$). *RIPD, remnant intrapancreatic common bile duct; CCD, common channel duct; ERCP, Endoscopic retrograde cholangiopancreatography; ERPD, endoscopic retrograde pancreatic drainage.

on this, it is also considered necessary to establish criteria for determining the optimal timing for performing ductoplasty to maximize patient outcomes. In this study, we retrospectively analyzed clinical data from our center where conventional HJ without stricturoplasty was performed to identify factors contributing to the formation of IHD stones. The findings of this study can serve as a basis for future comparative analyses on the long-term benefits of ductoplasty.

Age at surgery was significantly lower in patients who did not develop IHD stones compared with those who did. Subgroup analysis between patients with and without stone formation revealed that IHD stone occurrence was lower in patients who received CC excision ($p < 0.05$). Patients who developed IHD stones were significantly older at surgery ($p < 0.001$), and linear regression analysis confirmed an association between age at surgery and occurrence of IHD stones ($p < 0.001$). Considering the results of our study, we hypothesize that diagnosis and operation at a younger age would be advantageous for prognoses related to IHD stones. Although early diagnosis and surgery have a positive effect on prognosis, waiting until 6 months of age for surgery is suggested considering the technical aspects of surgery, such as HJ stricture. Ryu et al. reported the outcomes of 43 neonates who underwent CC excision via open and laparoscopic approaches and were followed for an average of 37 months[27]. Except for cholangitis and ileus in three patients who underwent open surgery, no known complications occurred in patients. These findings demonstrated the technical feasibility of CC excision in neonates, emphasizing that there is no reason to avoid prompt surgery after diagnosis.

In terms of treatment, oral ursodeoxycholic acid (UDCA) may be beneficial for asymptomatic small-sized stones[8]. Takimoto reported the resolution of IHD stones in two patients included in the study, with unchanging in three patients. Among patients diagnosed with IHD stones, 16 (76.2%) were taking UDCA. At our center, we suggest UDCA supplementation not only for patients with events related to stones or asymptomatic small stones but also for adolescents at high risk of stone formation, as indicated by follow-up imaging showing IHD dilatation or pneumobilia. Şenyüz reported the use of extracorporeal shock wave lithotripsy for stone removal[28]. PTCS has been the most longstanding therapeutic approach. It was performed in 11 patients in our study. EUS-HGS for stone removal has been recently introduced. In addition to Takimoto's approach, which involves accessing the hepaticojejunostomy through the Y-limb, we performed hepaticogastro/jejunostomy by directly puncturing the stomach or duodenal wall under endoscopic ultrasound guidance[8]. Stone removal and balloon dilatation was performed via stomy and a stent was maintained for repetitive procedures[7]. Two patients have exhibited favorable outcomes without complications and were satisfied with the aesthetic aspect of the procedure. Considering that patients developing stones are adolescents in their 10 s to 20 s, endoscopic ultrasound-guided stone removal would be a promising modality. Hepatectomy can be considered in cases of recurrent IHD stones or severe ductal stenosis. Left hepatectomy was performed in two patients with no stone recurrence and favorable outcomes.

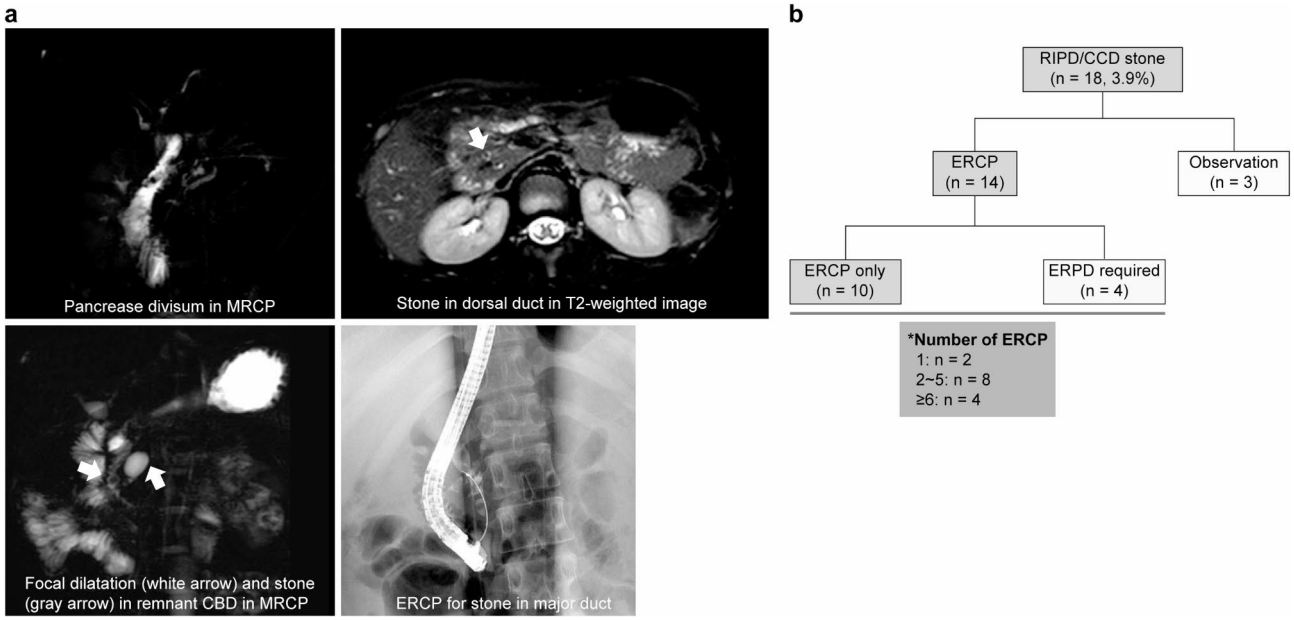

Fig. 5. Choledocholithiasis in RIPD/CCD**.** (a) Each image shows the following: pancreas divisum as seen on the 2D T2 thick-slab turbo spin echo image (top left), stone in the duct of Santorini as seen on the axial fat-saturated T2 weighted image (arrow in top right), stone in the RIPD/CCD (arrow) as seen on the 2D T2 thick-slab turbo spin echo image MR image (bottom left), and removal of a stone from the duct of Wirsung through ERCP (bottom right). (b) In 18 patients, stones were identified in the RIPD/CCD. The observation was conducted in three asymptomatic patients, whereas in patients with larger stones or accompanying pancreatitis, stones were removed through ERCP. Four patients required ERPD due to severe stenosis of the pancreatic duct, and except for two patients, all required ERCP procedures more than twice. *RIPD: remnant intrapancreatic common bile duct; CCD: common channel duct; MR: magnetic resonance; ERCP: endoscopic retrograde cholangiopancreatography: ERPD: endoscopic retrograde pancreatic drainage.

	The time between the operation and diagnosis (months)	Age at diagnosis (years)
IHD stone ($n = 21$)	122.2 ± 70.6	17.45 ± 6.2
RIPD/CCD stone ($n = 18$)	65.6 ± 72.3	10.5 ± 5.4
p-Value	0.018*	0.001*

Table 3. The difference in occurrence patterns between RIPD/CCD stones and IHD stones. *RIPD, remnant intrapancreatic common bile duct; CCD, common channel duct; IHD, intrahepatic bile duct.

	IHD stone			RIPD/CCD stone		
	Yes	No	p-value	Yes	No	p-value
Gender			0.533			0.952
Male	6 (28.6%)	99 (22.7%)		4 (3.8%)	100 (96.2%)	
Female	15 (71.4%)	337 (77.3%)		14 (4.0%)	338 (96.0%)	
Neonate	2 (9.5%)	57 (13.1%)	0.636	0 (0.0%)	59 (13.4%)	0.096
Infant	2 (9.5%)	132 (30.3%)	0.041*	1 (5.6%)	133 (30.3%)	0.024*
OP age (days)	2890.76 ± 1872.23	1315.08 ± 1401.21	0.001*	1866.11 ± 1514.23	1356.89 ± 1457.66	0.157

Table 4. Factors associated with stone formation: subgroup analysis. *RIPD: remnant intrapancreatic common bile duct; CCD: common channel duct; IHD: intrahepatic bile duct. OP: operation.

No CCA case was identified in our study population. Mukai's 2018 report, which conducted a 20-year follow-up, also did not identify any case of biliary carcinoma in pediatric patients[29]. Considering that stone occurrence increases after at least 10 years and CCA is reported to occur after 20 years from the operation, a longer-term follow-up seems necessary for patients who have experienced or are at risk of stone formation.

RIPD/CCD stones are poorly understood, with factors such as APBDU and pancreas divisum being considered influential, however, independent reports from patients with CC are limited[1,13]. Komi asserted that even after radical operation, in patients with complicated types, such as type Ib, IIb, and IIIc3, chronic pancreatitis can progress due to protein plugs or pancreatic calculus in the dilated duct[13]. Except two patients, whose MRCP was not available, we could identify the type of APBDU in the rest of patients. Two patients were included in Komi type 1A and the rest in complicated type. Among them, Komi type IIIC accompanying pancreas divisum was identified in nine patients. Typically, pancreas divisum is believed to be associated with pancreatitis. However, Terui reported that pancreas divisum is found in 1.4% of APBDU cases and does not always lead to pancreatitis[30]. In patients with pancreas divisum, if the minor duct serves as the main drainage pathway, sludge in the common channel may have a lower likelihood of inducing pancreatitis, whereas if the major duct is involved, the risk of pancreatitis may increase. Moreover, given that most cases of pancreas divisum associated with CC are incomplete type, this introduces additional variables to consider[31,32]. Therefore, it seems difficult to establish a direct association between pancreas divisum and increased incidence of pancreatitis. Thus, prospective studies conducting subgroup analysis based on presence of stones is warranted to elucidate the relationship with RIPD/CCD stones. In our study, stones occurred at various sites, including the common channel, major duct, and minor duct. All patients exhibited obstructive symptoms at CC diagnosis, and 11 had preoperative ERCP, suggesting the need to consider the contribution of preoperative obstructive lesions and ERCP to long-term stone formation in RIPD/CCD[33]. Stones occurred at 65.6 ± 72.3 months postoperatively, significantly earlier than IHD stones (Table 3). Subgroup analysis and linear regression results ($p = 0.05$) revealed no association between age at surgery and stone (Table 4). Considering previous reports of biliary epithelial hyperplasia in CC excision specimens, early surgery might reduce inflammation in the biliary system, potentially decreasing IHD stone occurrence, especially in younger patients[34–36]. Treatment primarily involved ERCP in all patients except three asymptomatic patients with favorable outcomes. One patient underwent pylorus-preserving pancreaticoduodenectomy and later required lateral pancreaticojejunostomy due to recurrent stones and resultant severe pancreatic duct stricture. Although many patients had repeated ERCP, none showed dilatation of the main pancreatic duct.

The retrospective nature of this study posed limitations in comparing imaging results between the stone occurrence and non-occurrence groups. Most patients with stones got imaging tests since symptom onset, with subsequent tight follow-up. Conversely, asymptomatic patients were primarily monitored with ultrasonography, leading to an insufficient retrospective comparison of anatomy. Additionally, early MRCP images lacked precision, hindering interpretation and direct comparison of anatomical features, potentially influencing stone formation. A prospective study, including MRCP follow-up, is necessary to determine whether Tsuchida type 2 or 3 persists following surgery and assess the characteristics of patients with pancreas divisum and complicated APBDU types in whom changes in RPID/CCD occur.

In previous studies, postoperative stones were included in postoperative complications, but only few studies have meaningfully reported the importance of anatomical variation. We separately analyzed the effect of anatomical variation on postoperative complications, such as HJ stricture, and confirmed its clinical significance in a large cohort of pediatric patients. For patients exhibiting Todani type IVa or tortuous IHD (e.g., Tsuchida type 2 or 3 findings), it is necessary to consider stricter follow-up regarding stone occurrence and surgical options, such as ductoplasty. The detection of complicated APBDU or pancreas divisum may be crucial for predicting the formation of RIPD/CCD stones and guiding therapeutic approaches.

Conclusion

This study provides insights into one of the long-term complications, i.e., stone formation in the residual bile duct, in a large number of patients. Specific anatomical features of residual bile ducts, such as IHD tortuosity and complicated APBDU, may contribute to the formation of stones regardless of the completeness of the surgery in the long term. In this regard, our findings highlight the importance of early detection in this patient group and the need for a more systematic approach and long-term follow-up plan.

Data availability

The datasets generated and/or analyzed in the current study are available from the corresponding authors with permission from the Institutional Review Board of Asan Medical Center.

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Author contributions

These authors contributed equally: Sujin Gang, MD and Pyeong Hwa Kim, MD, PhD Conceptualization: S.G., J-M.N. Formal Analysis: S.G., PH.K. Investigation: S.G. Methodology: S.G. Project Administration: S.G., J-M.N. Writing—Original Draft: S.G. Writing—Review and Editing: All authors. Material preparation, data collection, and analysis were performed by Sujin Gang, Pyeong Hwa Kim, and Jung-Man Namgoong. The first draft of the manuscript was written by Sujin Gang, and all authors, including Hyunhee Kwon and Hee Mang Yoon, commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Declarations

Competing interests
The authors declare no competing interests.

Ethical approval
This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Asan Medical Center (Date: 17 October, 2023 /No.: 2023-0840).

Informed consent
Informed consent was waived by committee due to the retrospective nature of our study. This study did not involve human intervention.

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