Congenital Intrahepatic Bile Duct Dilatation is a Potentially Curable Disease

Long-Term Results of a Multi-institutional Study

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Objective: To report clinical presentation, perioperative outcome, and long-term results of surgical management of congenital intrahepatic bile duct (IHBD) dilatations (including Caroli disease) in a multi-institutional setting.

Summary Background Data: Congenital IHBD dilatations are a rare congenital disorder predisposing to intrahepatic stones, cholangitis, and cholangiocarcinoma. The management remains difficult and controversial for bilobar forms of the disease or when concurrent congenital hepatic fibrosis is associated.

Methods: From 1976 to 2004, 33 patients (range 11 to 79 years) were retrospectively enrolled. Disease extent into the liver was unilobar in 26 patients and bilobar in 7 patients (21%). Cholangiocarcinoma, congenital hepatic fibrosis, and intrahepatic stones were present in 2, 10, and 20 patients, respectively. Transplantations or liver resections were performed in 5 and 27 patients, respectively, whereas 1 asymptomatic patient was managed conservatively.

Results: Postoperative mortality was nil. Postoperative complications occurred in 16 of 32 operated patients (50%) and additional procedures for residual stones were required in 5 patients. During a median follow-up of 80 months (1 patient being lost for follow-up) no patient developed metachronous carcinoma. Six patients (30%) developed recurrent intrahepatic stones but satisfactory late outcome was achieved in 27 patients (87%).

Conclusions: Partial or total liver resection achieves satisfactory late outcome in congenital IHBD dilatations, when the affection is treated at an early stage and when the extent of liver resection is tailored to intrahepatic disease extent and takes into consideration the presence and severity of underlying chronic liver and renal diseases.

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Congenital intrahepatic bile duct (IHBD) dilatations are a rare disorder resulting from abnormal development of the ductal plate responsive to dilatations of the biliary tree limited to the IHBD,[1] belonging thus to the spectrum of congenital bile duct cysts (BDC). Congenital IHBD dilatations correspond to type V BDC according to the Todani et al classification.[2] This entity was first defined by Caroli et al[3] in 1958, distinguishing between a simple and a fibrous type of the disease, the last one being associated with congenital hepatic fibrosis (CHF) as previously described by Grumbach et al.[4] The initial description by Caroli et al concerned communicating IHBD dilatations of peripheral bile ducts.[3] However, Guntz et al[5] reported later as Caroli disease similar fusiform or saccular IHBD dilatations of large IHBD, the initial disease form described by Caroli et al corresponding to type I in their classification (Fig. 1).

Intrahepatic BDC predispose to biliary stasis and intrahepatic stones (IHS) formation leading to cholangitis, liver abscesses, septicemia, and ultimately to secondary biliary cirrhosis. Moreover, the tendency to cholangiocarcinoma development on these abnormal bile ducts is well documented.[6–8] Congenital IHBD dilatations may present itself from a localized form limited to 1 hepatic lobe or segment to a bilobar and diffuse form involving the entire intrahepatic biliary tree. When the disease is associated with coexistent CHF, possibly responsible for portal hypertension, and sometimes to inconstant associated renal disease (from tubular ectasia to polycystic kidney disease), the entity is then called Caroli syndrome.[9,10] The management of this rare disease is particularly difficult. The degree of disease extension into the liver and the presence of concurrent underlying chronic liver or kidney disease and
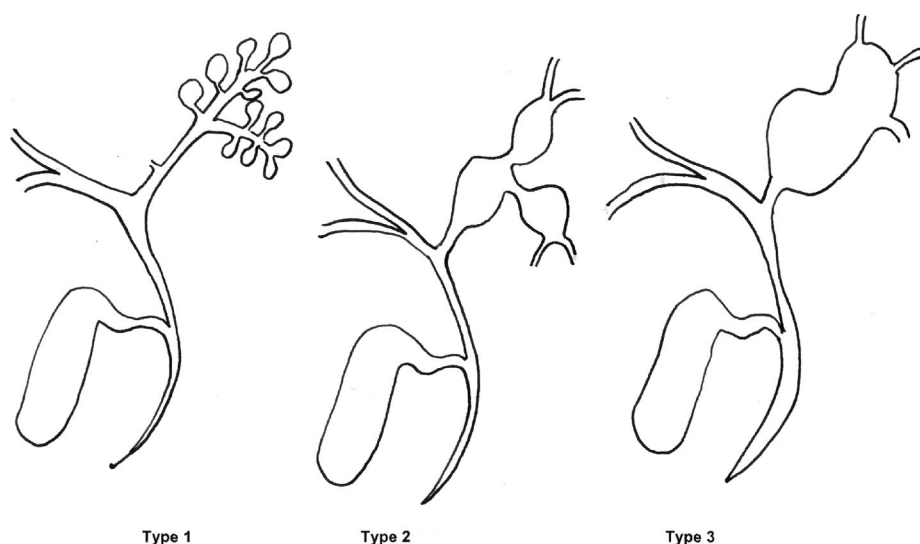
FIGURE 1. Schematic representation of Guntz et al subclassification of congenital IHBD dilatations, according to the aspect and extent of intrahepatic bile ducts dilatations. Type 1: grape-bunch-like saccular communicating dilatations of peripheral IHBD; type 2: fusiform dilatations of large IHBD; type 3: saccular dilatations of large IHBD.

cancer are decision-making factors influencing the surgical management. Liver resection is reputed to be the treatment of choice for localized unilobar forms of the disease but the management of diffuse bilobar forms remains controversial.[11] Moreover, few data concerning long-term postoperative results are reported in the literature.

The purpose of the present series is to report clinical presentation, perioperative outcome, and to focus on long-term results of the surgical management of congenital IHBD dilatations in a multi-institutional setting according to the disease extent into the liver and the presence and severity of concurrent underlying chronic liver or kidney disease.

PATIENTS AND METHODS

During a 28-year period of time (1976–2004), 142 consecutive patients with BDC were retrospectively enrolled from 5 European academic surgical centers. Liver transplant and pediatric surgery were available in 4 and 2 of these centers, respectively. The type of BDC was classified according to the Todani et al classification,[2] based on pre- and intraoperative imaging studies. From this group, 33 patients (23%) issued from 4 of these centers had IHBD dilatations. Four of these patients have already been reported.[12,13] IHBD dilatations were defined as the presence of congenital segmental communicating biliary dilatations limited to IHBD.[1] The intrahepatic disease extent was defined as being unilobar or bilobar from careful review of imaging studies. The Guntz et al[5] subclassification concerning the aspect and location of congenital IHBD dilatations was used, including fusiform or saccular dilatations of large IHBD and "grape-bunch-like" saccular communicating dilatations of peripheral IHBD alternating with normal IHBD (Figs. 1–4). However, when congenital IHBD dilatations were associated with extrahepatic bile duct dilatation, as encountered in 22 of the 142 patients, the disease was not considered as type V BDC but was classified as type IV-A BDC, according to the Todani et al classification. Acquired dilatations of IHBD because of proximal biliary obstruction, such as benign or malignant stricture

or obstructive primary IHS, were excluded. Pediatric patients were defined as younger than 15 years. Demographic features, disease, and operative data were collected using standardized questionnaires. Patient operative risk was evaluated according to the American Society of Anesthesiologists (ASA) physical status score.[14] The presence of concurrent CHF was confirmed by histologic examination or liver biopsies from both sides of the liver. Radiographic studies included percutaneous ultrasound in 33 patients (100%), computed tomography in 27 patients (82%), magnetic resonance cholangio-pancreatography in 15 patients (45%), and T-tube cholangiography in 2 patients (6%). Invasive imaging studies of the biliary tract, such as endoscopic retrograde cholangio-pancreatography or percutaneous transhepatic cholangiography were used in 9 patients (27%) and 4 patients (12%), respectively. However, the purpose of endoscopic retrograde cholangio-pancreatography and percutaneous transhepatic cholangiography was therapeutic in 8 and 1 patients, respec-
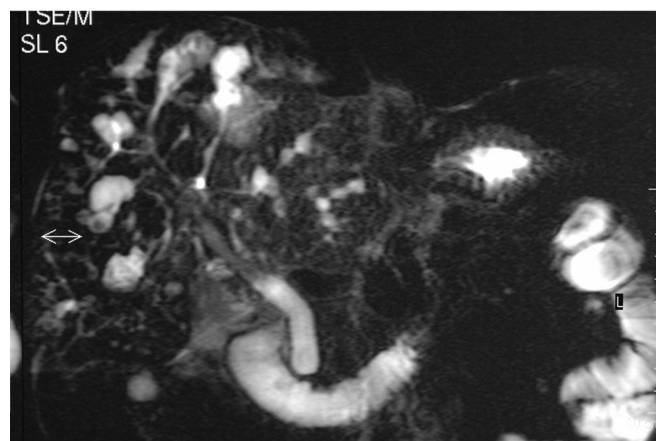

FIGURE 2. Magnetic resonance cholangiography. Communicating IHBD dilatations of peripheral bile ducts corresponding to type I in the Guntz et al classification (Caroli disease).
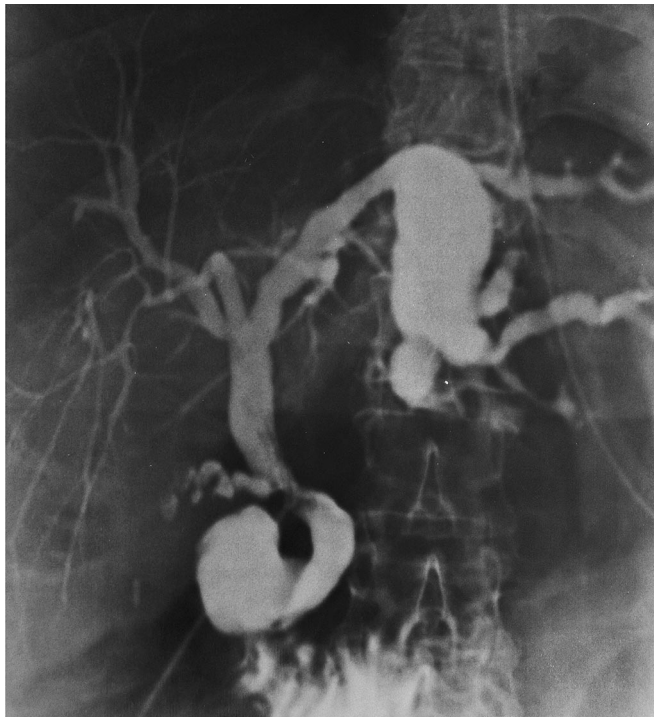
FIGURE 3. Intraoperative cholangiography. Fusiform IHBD dilatations of large IHBD corresponding to type II in the Guntz et al classification.

FIGURE 4. Endoscopic retrograde cholangiography: saccular IHBD dilatations of large IHBD corresponding to type III in the Guntz et al classification.

tively. The type of hepatic resection was classified according to the International Hepato-Pancreato-Biliary Association classification reported by Strasberg et al.[15] At postoperative follow-up, all patients were assessed by clinical and radiologic examination.

Definition of Endpoints

Evaluation criteria included type and details of operative procedures, early postoperative course, including complications and reoperation rate, postoperative hospital stay, and late patient outcome. Postoperative mortality and morbidity were defined at 2 months or during hospital stay. The severity of postoperative complications was categorized according to the Clavien et al classification.[16] Late clinical results were evaluated according to a modification of the Mayo Clinic score of results evaluation previously reported for congenital BDC[17]: *excellent* if the patient remained free of symptoms without further reintervention; *good* if the patient presented occasional and mild attacks of cholangitis or pancreatitis not impairing the quality of life; *fair* if the patients had repeated episodes of cholangitis or pancreatitis, or had portal hypertension without further reintervention; and *poor*, if the patient required later biliary or liver-related reoperative procedures, developed biliary cirrhosis or complications because of portal hypertension (such as variceal bleeding, for example), or died of cyst-related malignancy or liver and biliary-related complications.

Statistical Analysis

Statistical analysis was performed using Fisher exact test or χ^2 tests for categorical variables and Mann-Whitney nonparametric rank sum tests for continuous variables, when appropriate. A *P* value <0.05 was considered statistically significant.

RESULTS

Prevalence

The annual incidence per center of congenital IHBD dilatations over a 28-year period was 0.234 (range 0–0.6) in the present series, indicating an obvious referral bias. Indeed, at the 2 centers where experience in HBP, pediatric, and liver transplant surgery was concentrated, the total number of patients varies from 5 to 18, respectively, totaling 70% of the whole study population.

Demographic Features

Thirty-two adults and 1 child (an 11-year-old girl) with congenital IHBD dilatations were included in the present study. The median age of adults (11 women and 21 men) was 55 years (mean age: 53 years, range: 24–79 years). Six patients (18%) were at high risk, being classified ASA III or IV.

Clinical Presentation

The median delay between first symptoms and surgical treatment was 14 months (mean 54 months, range 1–500

months). This delay was <1 year in 13 patients (39%) but >5 years in only 8 patients (24%). Details of clinical patient presentation are reported in Table 1. Complicated clinical presentation was not correlated with unilobar or bilobar intrahepatic disease extent or to duration of symptoms.

Coexistent HBP and Renal Diseases

Details of HBP and renal coexistent diseases are given in Table 1. Both hepatobiliary and renal coexistent diseases were associated in 6 patients (18%). Synchronous cholangiocarcinoma was encountered in 2 patients (6%), one of which was located within the left hepatic duct, presenting a 3-cm papillary tumor preoperatively diagnosed on imaging studies and corresponding at final pathology to high-grade dysplasia and focal microinvasive cancer. In the second patient, having undergone a left hemihepatectomy, final pathology discovered large focal areas of high-grade dysplasia within the IHBDs. Duration of symptoms in these patients was 1 and 22 months, respectively. Associated renal disease was significantly more frequent in patients with coexistent CHF (with-

out CHF: 2 of 23 patients vs. with CHF: 5 of 10 patients; *P* = 0.016).

Biliary Disease

Bilobar and unilobar (left hemiliver: 20 patients, right hemiliver: 6 patients) disease extent was observed in 7 patients (21%) and 26 patients (79%), respectively. There was no difference in terms of patient age, sex ratio, ASA score, severity of clinical presentation, coexistent HBP or renal coexistent disease, and previous treatment modalities between patients with unilobar or bilobar disease extent, and between patients with or without CHF, except for coexistent renal disease and portal hypertension, which were more frequent in CHF patients.

According to the Guntz et al[5] classification, type I, II, and III were encountered in 9, 22, and 2 patients, respectively. There was no significant difference among the 3 groups in term of patient age, sex ratio, ASA score, severity of clinical presentation, coexistent HBP (including CHF) or renal coexistent disease, and previous treatment modalities.

Previous Disease-Related Treatments

Details of previous biliary-related treatments are reported in Table 1. One patient with CHF associated with portal hypertension had also undergone a surgical portosystemic shunt. Two of the 5 patients who had undergone common bile duct (CBD) exploration at another institution, allowing adequate disease diagnosis, were referred to the secondary referral treatment center where they underwent liver resection within 1 month after referral.

Type of Surgical Procedures

Except for 1 asymptomatic patient with a right unilobar form of congenital IHBD dilatations associated with CHF and with prior kidney transplantation, 32 patients underwent liver resection (27 patients; 84%) or transplantation (5 patients; 16%). The 4 remaining asymptomatic patients who had undergone liver resection had elevated liver function tests related to unilobar or bilobar IHS. No patient underwent emergency operation for control of sepsis. Details of treatment according to unilobar or bilobar disease extension and according to the presence of CHF with or without portal hypertension are reported in Table 2. Transplanted patients with the bilobar form of the disease had associated CHF with portal hypertension, except 2 patients without portal hypertension who were transplanted for repeated attacks of cholangitis from diffuse IHS. Two patients with Caroli disease associated with CHF and chronic renal insufficiency from polycystic kidney disease underwent combined liver and kidney transplantations. In resected patients with unilobar disease extent, a liver resection smaller than formal hemihepatectomy was performed in 10 patients (40%) (Table 2).

Associated procedures were performed in 22 of 32 operated patients (69%), including contralateral IHS extraction (2 patients), CBD exploration (8 patients), cholecystectomy (11 patients), main biliary convergence excision followed by biliodigestive reconstruction with mucosa-to-mucosa hepaticojejunostomy using a 60 cm in length Roux-Y jejunal loop (5 patients) and kidney trans-

TABLE 1. Clinical Presentation and Coexistent Hepatobiliary and Kidney Diseases in Patients Suffering From Congenital IHBD Dilatations

Clinical presentation	
Asymptomatic	5 Patients (15.2%)
Symptomatic	13 (39.4%)
Isolated RUQ pain	11
Jaundice	2
Complicated	15 (45.4%)
Repeated attacks of cholangitis	15
Cholangitis with oesophageal variceal bleeding	2
Coexistent diseases	
Hepatobiliary diseases	26 (79%)
Congenital hepatic fibrosis (with portal hypertension: 3 patients)	10 (30%)
Biliary stones	21 (64%)
Intrahepatic stones (HIS)	20
Common bile duct stones	9
Gallstones	4
Associated intrahepatic stricture	2 (6%)
Unilobar liver atrophy	3 (9%)
Synchronous biliary cancer	2 (6%)
Renal diseases	7 (21%)
Chronic renal failure	4 (12%)
Polycystic kidney disease	2
Tubular ectasia	2
Previous kidney transplant	3
Stones kidney formation	3 (1 Requiring nephrectomy)
Previous biliary-related treatment	24 (73%)
Cholecystectomy	17
Common bile duct exploration	5
Endoscopic sphincterotomy (for CBD stone extraction: 8)	9
Bilio-digestive anastomosis for IHS	2
Extracorporeal shock-wave lithotripsy	1

Liver Disease Extension	Type of Hepatic Resection Performed
Bilobar (n = 7)	With CHF and portal hypertension: 2 patients
	Liver transplantation: n = 2
	With CHF but without portal hypertension: 2 patients
	Liver transplantation: n = 2
	Without CHF or portal hypertension: 3 patients
	Left hemihepatectomy extended to segment I: n = 1
	Left trisectionectomy n = 1
	Trisegmentectomy 4–5–6: n = 1
Left unilobar (n = 20)	With CHF but without portal hypertension: 4 patients
	Left lateral sectionectomy: n = 1
	Left hemihepatectomy: n = 3
	Without CHF or portal hypertension: 16 patients
	Left lateral sectionectomy: n = 8
	Left hemihepatectomy: n = 6
	Left hemihepatectomy extended to segment 1: n = 2
Right unilobar (n = 6)	With CHF and portal hypertension: 1 patient
	Liver transplantation: n = 1
	With CHF but without portal hypertension: 1 patient
	No treatment (asymptomatic) n = 1
	Without CHF or portal hypertension: 4 patients
	Right hemihepatectomy: n = 3
	Bisegmentectomy 5–6: n = 1

plantation or retransplantation (1 patient each). The reason
for main biliary convergence excision was not the presence
of proximal stricture but of cystic disease involving the
liver hilum. The 2 patients with synchronous cholangio-
carcinoma were radically treated by left hemihepatectomy
and left hemihepatectomy extended to segment 1 associ-
ated with extrahepatic bile duct excision and hepaticoje-
junostomy, respectively.

Postoperative Outcome

Postoperative mortality was nil in the present series.
Twenty-two postoperative complications occurred in 16 of the
32 operated patients (50%). The type and severity of postoper-
ative complications according to the extent of liver resection are
detailed in Table 3. According to the Clavien et al[16] classifica-
tion, major postoperative complications (namely type 3 and 4)
occurred in 7 patients (22%), requiring in all these patients some
sort of reoperative procedures. Overall and major postoperative
complications occurred in 12 (44%) and 5 patients (19%) after
liver resection and in 4 (80%) and 2 patients (40%) after liver
transplantation (not significant). Planned postoperative addi-
tional therapeutic procedure for residual IHS or CBD stones was

required in 5 patients (16%), including endoscopic or radiologic
stones extraction in 4 and 1 patient, respectively. Finally, the
median postoperative hospital stay was 13 days (mean 18 days;
range 8-53 days) in the series.

Late Outcome

The not operated patient is alive and free of symptoms
and complications after 61 months of follow-up. One patient
with left unilobar disease into the liver and without associated
CHF having been treated by left lateral sectionectomy was
lost to follow-up after an uneventful postoperative course at
2 months. The median follow-up for the 31 remaining pa-
tients was 80 months (mean 91 months; range 7–231
months). Twenty-one (67%) and 7 patients (23%) had fol-
low-up longer than 5 and 10 years, respectively. Twenty-
eight patients were alive whereas 3 died of nondisease-related
events (including the patient presenting with high-grade dys-
plasia at a follow-up of 144 months). The remaining patient
presenting with microinvasive cholangiocarcinoma is alive
and disease-free 89 months after surgery.

Patient status during long-term follow-up according
to intrahepatic disease extent is reported in Table 4,
including symptom-free and disease-free status, details of
complications, and reoperative procedures. According to
the modified Mayo Clinic evaluation score, excellent,
good, fair and poor late results were achieved in 26, 1, 0,
and 4 patients, respectively.

During the follow-up period, 6 of 20 patients (30%)
with initial IHS (one of them harboring postoperative residual
IHS) developed recurrent IHS, which led to reoperative
procedures in 3 patients. The type of reoperative procedures
included segmentectomy 4 after prior left lateral sectionec-
tomy (1 patient), extracorporeal shock-wave lithotripsy of
segment 4 stones after prior left lateral sectionectomy (1
patient) and endoscopic extraction procedure in a bilobar
form of the disease (1 patient). The 3 remaining patients with
recurrent IHS were not surgically treated because of associ-
ated secondary biliary cirrhosis with decompensated portal
hypertension in 1 patient, the absence of symptoms in 1
patient, and the refusal of surgery by an elderly patient. No
patient developed late metachronous carcinoma.

Fair and poor late outcome was observed in 4 patients
(13%) in the whole series, which was not significantly dif-
ferent according to intrahepatic disease extent (unilobar: 8%;
bilobar: 29%, not significant), the presence of associated CHF
(with CHF: 0%; without CHF: 18%, not significant), the type
of the disease according to Guntz et al classification (type I:
11%; type II: 14%; type III: 0% (not significant), or the type
of surgical resection (liver transplantation: 0%; partial liver
resection: 15%, not significant). Fair and poor results were
observed in 29% of bilobar disease, 0% of right unilobar
disease, and 11% of left unilobar disease (not significant)
(Table 4). In unilobar disease extent, fair and poor results
were observed in 0% of patients having undergone a hemi-
hepatectomy and in 22% of patients having undergone a liver
resection smaller than a hemihepatectomy (not significant)
(Table 4).

TABLE 3. Postoperative Complications According to the Extent of Liver Resection

No. Resected Liver Segments	No. Patients	No. Patients With Complications	Type of Complications	Reoperative Procedures	Additional Stones Extraction Procedures
2	10 (1*)	5 (50%)	Acute renal insufficiency: n = 1	2 Patients (20%)	Endoscopic: n = 3
			Cholangitis: n = 1	—	
			Segment 4 necrosis: n = 1	Segmentectomy 4: n = 1	
			Biloma: n = 1		
			Bile leak: n = 1	Percutaneous drainage: n = 1	
			Wound infection: n = 1*		
			Symptomatic residual intrahepatic stone: n = 1		
3	10 (3*)	4 (40%)	Pulmonary embolism: n = 1	2 Patients (20%)	Radiological n = 1
			Biloma: n = 2		
			Cholangitis: n = 1*	Percutaneous drainage: n = 2	
4	6	2 (33%)	Pleural effusion: n = 2	0	0
6	1	1	Bile leak: n = 1	1 Patient	Endoscopic: n = 1
			Symptomatic residual common bile duct stone n = 1	Endoscopic stenting: n = 1	
8 OLT	5*	4 (80%)	Acute rejection: n = 2	2 Patients (40%)	0
			Renal insufficiency: n = 1		
			Infectious colitis: n = 1	Retransplantation	
			Epilepsy: n = 1	Femoral artery angioplasty: n = 1	
			Limb ischemia: n = 1		
			Cholangitis: n = 1		
			Wound infection: n = 1		

*Number of patients suffering from congenital hepatic fibrosis.
OLT indicates orthotopic liver transplantation.

TABLE 4. Late Outcome of the 31 Operated Patients According to Intrahepatic Disease Extent and Type of Liver Resection

Disease Extent	Patients	Fair and Poor Results	Symptom-Free During FU	Disease-Free During FU	Details of Late Complications During FU	Reoperative Procedures During FU
Bilobar	7	2 (29%)	6/7 (86%)	5/7 (71%)		Endoscopic extraction: n = 1
Liver resection	3	2	2/3	1/3	Asymptomatic IHS: n = 1	
Liver transplantation	4	0	4/4	4/4	Asymptomatic IHS with secondary biliary cirrhosis with variceal bleeding: n = 1	
Right unilobar	5	0	5/5 (100%)	4/5 (80%)		No treatment
Liver resection	4	0	4/4	3/4	Asymptomatic IHS: n = 1	
Liver transplantation	1	0	1/1	1/1		
Left unilobar	19	2 (11%)	17/19 (89%)	16/19 (84%)		
Left lateral sectionectomy	8	2	7*/8	6*/†/8	Symptomatic segment 4 IHS n = 1	Segmentectomy 4 for symptomatic IHS: n = 1
Left hemihepatectomy	11	0	10‡/11	10‡/11	Asymptomatic segment 4 IHS: n = 1	ESWL for asymptomatic segment 4 IHS: n = 1†
					Mild symptomatic IHS: n = 1‡	

Duplicate symbols correspond to the same patient.
FU indicates follow-up.

DISCUSSION

The present study shows that satisfactory long-term results can be achieved in patients with congenital IHBD dilatations when the disease is treated at an early stage and when extent of liver resection is tailored to intrahepatic disease extent and takes into consideration the presence and severity of underlying chronic liver and kidney diseases.

Congenital IHBD dilatations, including Caroli disease, are a rare congenital disorder with an estimated incidence of 1 in 1,000,000 in the whole population.[9] Because the original description by Caroli et al[3] in 1958, an increasing number of case reports have been reported in the literature. However, very few series exceeding 4 patients treated by liver resection or transplantation are reported[11,18–29] (Table 5). In the

TABLE 5. Reported Series Exceeding 4 Patients Suffering From Congenital IHBD Dilatations Treated by Liver Resection or Liver Transplantation

Authors	Patients Male/Female	Unilobar Right/Left	Bilobar	CHF	Synchronous Carcinoma	Liver Resection (Death)	OLT (Indications [Death])	Duration of Follow-Up (Mo)	Status at Follow-Up
Nagasue et al, 1984[18]	6 (3M/3F)	6 (100%) (2R/4L)	0	NA	0	6 (0)	0	Mean: 54	Well
Mercadier et al, 1984[19]	10 (3M/7F)	6 (67%)	3 (33%)	1 (10%)	0	6 (0)	0	6–12	Well for localized forms
Knoop et al, 1994[20]	8	8 (100%)	0	NA	0	8 (0)	0	Median: 40	Well
Dagli et al, 1998[21]	21 (13M/8F)	9 (43%)	12 (57%)	2 (10%)	0	7 (NA)	NA	NA	NA
Gillet et al, 1999[22]	12 (6M/6F)	12 (100%) (3R/9L)	0	2 (17%)	0	12 (0)	0	NA	Well
Shi et al, 2001[23]	6	NA	NA	NA	0	4	2 (Biliary cirrhosis [0])	24 mo for OLT	Well
Ammori et al, 2002[24]	8 (2M/6F)	3 (37%) (1R/2L)	5 (63%)	NA	1 (13%)	4 (0)	4 (Cirrhosis = 4 [0])	Median: 20	Alive = 4 Secondary OLT for recurrence after prior hepatectomy: n = 2 Metachronous cholangiocarcinoma n = 1
Levy et al, 2002[25]	17* (7M/10F)	14 (82%) (8R/6L)	3 (18%)	5 (29%)	4 (24%)	7 (NA)	5 [NA]	NA	NA
Ullrich et al, 2002[26]	38 (20M/18F)	NA	NA	NA	NA	32 (NA)	4 (1 Biliary cirrhosis 3 refractory cholangitis [0])	OLT: mean: 43	OLT: well
Espinoza et al, 2003[27]	6	6 (100%) (3R/3L)	0	NA	NA	6 (0)	0	Mean: 28	Well
Kassahum et al, 2005[11]	33 (15M/18F)	25 (81%) (13R/12L)	6 (19%)	NA	3 (9%)	27 (2)	2 [0]	Median: 44	Well = 93%
Habib et al, 2006[28]	30 (16M/14F)	NA	NA	9 (30%)	1 (3%)	1 (before OLT)	30 (NA = 8, hepatic decompensation = 20, recurrent cholangitis = 1, diffuse extent = 1)	Median: 93	Patient survival rates 1 yr = 76% 5 yr = 65% 10 yr = 56%
Bockhorn et al, 2006[29]	12 (7M/5F)	8 (67%) (0R/8L)	4 (33%)	2 (17%)	3 (25%)	9 (0)	2 [0]	Median: 31	Alive and well = 92%
Current series, 2006	33 (21M/12F)	26 (79%) (6R/20L)	7 (21%)	10 (30%)	2 (6%)	27 (0)	5 [0]	Mean: 91 median: 80	Well = 87%
Total	240*	123/163 (36R/64L)	40/163 (25%)	31/135 (23%)	14/196 (7%)	156	54		

*Associated to fusiform dilatation (10–30 mm in diameter) of the common bile duct (n = 9).
†After previous hepatectomy (n = 2).
CHF indicates chronic hepatic fibrosis; NA, data not available.

present series, the mean annual experience per center in treating such patients was less than 0.5. Although the prevalence of congenital IHBD dilatations was estimated by Nagorney[30] to be less than 1% of BDC patients, congenital IHBD dilatations represent 23% of all BDC patients in the present series over a 28-year study period. The prevalence observed in our patient population is thus clearly higher than expected and may be the result of referral bias to tertiary referral centers, concentrating experience in pediatric, HBP and liver transplant surgery.

We sticked to the definition of congenital communicating intrahepatic BDC whatever the level of affected IHBD, adopting the Guntz et al classification,[5] even if only type I is corresponding to the initial description of Caroli et al. Indeed, the spectrum of shape and location of IHBD dilatations that has been categorized by Guntz et al[5] may be explained by the time and the degree of embryological malformation of the ductal plate.[1]

A striking particularity of the present series is that 15% of the patients were completely asymptomatic, thus undergoing prophylactic surgery, and that 39% of the patients had a clinical presentation not yet complicated by biliary infection. This feature is in contradiction with other reported series in which most patients with severe septic complications.[11,29]

Patients with congenital IHBD dilatations have a predisposition for synchronous cholangiocarcinoma with an estimated risk of 100 times greater than that of the general population.[31] The prevalence is reported to be 7% by Dayton et al[31] in a large literature review of 142 patients, but possibly reaching 24 and 25%[25,29] (Table 5). In the present series, the prevalence was relatively low (6%), but both patients had early-stage cholangiocarcinoma leading to long-term cure at 89 and 144 months after liver resection, respectively. The early disease diagnosis, illustrated by the relatively short delay between first symptoms and surgical treatment and the aggressive surgical treatment, even in asymptomatic patients, may concur to the relatively low incidence of synchronous cholangiocarcinoma encountered in the present series. The same features may explain why metachronous cholangiocarcinoma was not encountered in the present series during a mean follow-up of 91 months.

Congenital IHBD dilatations may involve the entire intrahepatic biliary tree diffusely or be confined to 1 lobe or segment. Unilobar extension of the disease is more frequent, especially on the left side of the liver (Table 5).[5] Our results are consistent with these findings with 79% of our patients with unilobar extent and 61% from left unilobar disease extent. However, as for the rest of the literature, this feature is clearly the result in the present surgical series of referral bias in patient's selection to surgical centers, with a false overrepresentation of unilobar disease forms. The prevalence of bilobar disease forms is also underestimated because of the lack of referral by physicians for potential surgical treatment.

The treatment of congenital IHBD dilatations is particularly difficult and remains a challenge because of the rareness and the various presentations of the disease, leading to a lack of experience for most of the centers. Various endo-scopic or surgical drainage procedures have been reported, such as biliodigestive anastomoses with or without permanent access stoma using a Roux-Y jejunal loop brought to the skin, to allow retrograde access to the intrahepatic biliary tree for further treatments.[32,33] Furthermore, in case of proximal intrahepatic ductal strictures, intrahepatic bilioenteric anastomosis was also reported to provide proximal biliary drainage.[19,34,35] However, all these drainage procedures are palliative treatment options, which are ineffective in the long term and associated with recurrent septic complications.[19,36] They should thus clearly be abandoned.

Indeed, the only potential surgical treatment remains resection of the diseased liver and aggressive endoscopic biliary drainage procedures should be currently strictly limited to inoperable patients.[37] The disease extent within IHBD, the presence and severity of concurrent underlying chronic liver and renal diseases and the presence of cholangiocarcinoma are key factors for decision making when curative surgical treatment is considered.

In case of unilobar form of the disease without any concurrent liver fibrosis or cirrhosis, partial hepatectomy achieves satisfactory results by providing a radical solution to the recurrent problems of cholangitis, stone formation, and intrahepatic cholangiocarcinoma.[11,18–20,27,29,38–41] In the present series satisfactory long-term results were achieved in 21 of 23 patients (91%) with right or left unilobar forms of the disease after partial liver resection. These findings are in accordance with the recent report by Kassahun et al[11] and Bockhorn et al.[29] However, attention should be paid to the clearance of contralateral IHS, requiring additional postoperative radiologic or endoscopic procedures in nearly 20% of the patients in the present series. A percutaneous transhepatic approach for flexible choledochoscopic stone clearance with or without intracorporeal lithotripsy could be useful for treating residual IHS.[42,43] Additionally, the rate of late complications and reoperation after left lateral sectionectomy in left unilobar congenital IHBD dilatation in the present series emphasized the probable need for performing initially at least hemihepatectomy to remove the whole biliary tree of the affected hemiliver. Moreover, extrahepatic bile duct resection followed by biliodigestive reconstruction may be indicated in up to 25% of the patients,[11] when the disease is involving the main biliary convergence.

In case of unilobar form of the disease with concurrent liver fibrosis or cirrhosis, treatment of the coexistent chronic liver disease by liver transplantation has emerged as a valuable option of curative treatment. Indeed, liver transplantation allows radical treatment of both IHBD dilatations (responsible for infectious and malignant complications) and underlying chronic liver disease (responsible for portal hypertension and/or hepatic insufficiency).[11,24,26] In the present series, only one such patient with Caroli syndrome with right unilobar disease extent (associated with renal insufficiency and concurrent CHF with variceal bleeding because of the portal hypertension) has benefited from combined kidney-liver transplantation, with excellent long-term results during a postoperative follow-up of 18 years.

In case of bilobar congenital IHBD dilatations without liver fibrosis or cirrhosis, the radical surgical options included extended liver resection or liver transplantation, according to intrahepatic disease extent. When the contralateral disease extent was limited or localized and extirpable, extended liver resection was performed in 3 selected patients, achieving long-term symptom-free and disease-free status in 2 and 1 patient, respectively, during a median follow-up period of 74 months (range: 28–80 months). The limited literature experience with such difficult subgroup of patients confirmed that unsatisfactory long-term outcome is usually achieved after such major hepatectomies.[19,24,26,42,44] On the contrary, in case of diffuse bilobar forms of the disease being complicated by cholangitis from diffuse IHS, the sole curative option in our opinion is complete removal of IHBD dilatations by liver transplantation, achieving, good results in the literature[45–47] (Table 5). Two patients in the present series underwent a liver transplant in this setting with good late outcome, despite the need for retransplantation for acute humoral rejection in 1 patient. However, Habib et al[28] have recently reported a significant poor impact on a 1-year-old patient's survival in the presence of preoperative cholangitis before transplantation for Caroli disease.

In case of bilobar congenital IHBD dilatations complicated by liver fibrosis or cirrhosis, liver transplantation seems to be the treatment of choice.[11,23,24,26,28] Two such patients have benefited from this therapeutic option in the present series with excellent long-term results.

Although the surgical management of bilobar forms of congenital IHBD dilatations remains a difficult challenge and controversial, and despite the operative risk in septic patients and consequences of immunosuppressive therapy, we believe that liver transplantation represents the ultimate successful treatment option for complicated forms of the disease (septic complications from diffuse extent of the disease into the liver and fibrosis or cirrhosis responsive to portal hypertension). De Kerckhove et al[13] have recently reviewed the reported literature experience concerning 19 patients and the European Liver Transplant Registry (ELTR) experiences concerning 110 patients who had undergone liver transplant for Caroli disease or syndrome, representing 0.2% of the whole number of liver transplants in the ELTR. In the ELTR experience, the median follow-up was 27 months and the 5- and 10-year actuarial survival rates were 86% and 76%, respectively. In case of chronic renal insufficiency because of the coexistent polycystic kidney disease, combined liver-kidney transplantation should be favored, as illustrated in 2 patients in the present series and 14.5% in the ELTR experience. In the recent Habib et al series of 30 transplanted patients for Caroli disease,[28] the patient survival rates at 1, 5, and 10 years were 76%, 65%, and 56%, respectively, comparable to survival after liver transplantation for other aetiologies of chronic liver disease. However, the 1-year survival rate was worse in patients with Caroli syndrome whereas there was no difference in long-term survival between Caroli disease and Caroli syndrome patients. However, the appropriate timing for transplantation remains difficult to appreciate in this instance. It should also be emphasized that early disease diagnosis and avoidance of multiple ineffective endoscopic or surgical drainage procedures will undoubtedly reduce the technical and septic risk of liver transplantation.[9,28] Finally, the management of invasive cholangiocarcinoma developed on congenital IHBD dilatations is also controversial. Despite the theoretical advantage of liver transplantation to allow radical resection of the carcinoma and of the whole intrahepatic biliary tree at risk for metachronous malignancy,[6,8] a high rate of postoperative recurrence has been reported, favored by immunosuppressive therapy. The introduction of new medication combining immunosuppressive and anticancerous effects might resolve this problem. In localized carcinoma on unilobar disease extent, radical liver resection seems to be an appropriate option, when oncologically possible.

Finally, aggressive surgical management of congenital IHBD dilatations was safe in the present series, which was associated with no mortality but with major postoperative complication and reoperation rates of 19% and 6%, respectively. Kassahun et al[11] reported a mortality rate of 6% after partial liver resections and 1 patient with aborted right hemihepatectomy for intraoperative septic shock after liver mobilization. Early disease diagnosis, treatment at an early disease stage (including 5 patients at a preclinical stage), strict avoidance of endoscopic diagnostic approach and treatment and avoidance of emergency operation on uncontrollable septic patients without adequate percutaneous transhepatic biliary drainage are concurrent factors to explain the low morbidity rate achieved in the present series. In contradiction with Kassahun et al,[11] we promote noninvasive imaging studies, such as magnetic resonance cholangio-pancreatography, to achieve accurate disease diagnosis and staging with no risk of superinfection. Additionally, intraoperative anterior approach using the hanging maneuver[48] may be suggested in right-sided congenital IHBD dilatations when septic presentation was initially severe or when superinfection is not completely controlled by percutaneous transhepatic biliary drainage and wide spectrum antibiotic treatment.

In conclusion, the present series suggests that unilobar forms of congenital IHBD dilatations can be successfully treated by liver resection, whereas bilobar diseases with CHF and portal hypertension or diffuse IHS are only curable by liver transplantation. Treatment at an early stage of the disease, and avoidance of an endoscopic approach and of an emergency operation on septic patients are key factors to reduce the operative risk for the patients. Patients with congenital IHBD dilatations should be referred early for surgical management.

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