# Management of Biliary Atresia: Experience in a Single Institute

Mao-Meng Tiao, MD; Jiin-Haur Chuang[1], MD; Li-Tung Huang, MD; Chih-Sung Hsieh[1], MD; Shin-Yi Lee[1], MD; Chi-Di Liang, MD; Chao-Long Chen[2], MD

**Background:** The management of biliary atresia (BA) has evolved with time. The outcome of BA treatment in the Chang Gung Memorial Hospital-Kaohsiung Medical Center had not been recorded and we addressed this issue in this study.

**Methods:** Medical records of the 93 patients with BA who underwent Kasai portoenterostomy (KP) in the Chang Gung Memorial Hospital-Kaohsiung Medical Center from 1986 to 2005 were reviewed retrospectively. There were 46 male and 47 female patients included in this study. Sixty patients received KP before 60 days of age and 33 patients received KP after 60 days of age.

**Results:** Jaundice-free survival with native liver was accomplished in 29 of 60 patients who received KP before 60 days of age but in only 9 of 33 after that age ($p$ = 0.048). Cholangitis developed in 56 patients (60.2%). Incidence of cholangitis was not significantly different between the patients free of jaundice (22/38) and those with persistent jaundice (34/55) ($p$ = 0.704). Seven patients had single cysts and 1 had multiple cysts, with 4 being jaundice-free. Five out of 9 were free of jaundice after re-do KP. Among the 62 patients followed for more than 5 years, 32 (51.6%) survived with native liver.

**Conclusion:** This study revealed that half of the patients with BA survived with their native liver for more than 5 years. Age at operation, not post-KP cholangitis or liver cysts, was the most determinant factor of BA outcome.

*(Chang Gung Med J 2007;30:122-7)*

**Key words: biliary atresia, Kasai portoenterostomy, cholangitis**

Biliary atresia (BA) is an intractable surgical disease of infancy.[1-4] It is a sclerosing lesion of the bile ducts that presents in the neonatal period with obstructive jaundice.[1-6] The etiological factors of this condition are unknown.[2,3,5-9] Recently, the established animal models of BA induced by infection of newborn mice with rhesus rotavirus indicate involvement of viral infection and type 1 interferon signaling in the pathogenesis of BA.[8,10,11] Early diagnosis of BA is difficult,[1,3,12-15] and untreated cholestasis will result in cirrhosis, hepatic failure and death.[13,16,17] Kasai portoenterostomy (KP) is used commonly as the first line of treatment but its long-term efficacy still remains controversial.[4,13,16,18-24] About half of these children remain jaundiced and suffer from repeated attacks of cholangitis or variceal hemorrhage after KP.[1,3,13,17,25-27] Liver transplantation (LT) offers hope for these chil-

From the Department of Pediatrics, [1]Department of Pediatric Surgery, [2]Department of Surgery, Chang Gung Memorial Hospital - Kaohsiung Medical Center, Chang Gung University College of Medicine, Kaohsiung, Taiwan.
Received: Feb. 14, 2006; Accepted: Oct. 24, 2006
Correspondence to: Dr. Chih-Sung Hsieh, Department of Pediatric Surgery, Chang Gung Memorial Hospital. 123, Dapi Rd., Niaosong Township, Kaohsiung County 833, Taiwan (R.O.C.) Tel.: 886-7-7317123 ext. 8715; Fax: 886-7-7338009; E-mail: pc006581@yahoo.com.tw, tmm@cgmh.org.tw

dren.[1,3,12,13,17,22,25-29] Combined programs of KP and LT have resulted in higher success rates in the treatment of BA.[1,12,13,17,22,25-28] In this study, we reviewed our experience of treating BA in a medical center known for LT and analyzed determinant factors for outcome.

## METHODS

Ninety-three children with BA were treated from 1986 to 2005 and were reviewed retrospectively. Forty-six males and 47 females were included. BA was confirmed with serum bilirubin level and complete liver function profile, and by using sonography, hepatobiliary scan, liver histology and intraoperative findings. Patients were born in spring (n = 28, 30.1%), autumn (n = 26, 27.9%), winter (n = 21, 22.6%) and summer (n = 18, 19.4%). Blood type was O in 33 (34.9%), B in 30 (32.5%), A in 26 (27.7%) and AB in 4 (4.8%).

Cholescintigraphy was performed when the patients received an intravenous injection of 37 MBq (1 mCi) Tc-99m DISIDA (diisopropyl-phenylcarbamoylmethyl-iminodiacetic acid, Disofenin). The images were taken with the patient in a supine position with a large-field-of-view gamma camera (Starcam 4000XR, General Electric Medical Systems, Milwaukee, WI, USA) equipped with a low-energy high-resolution collimator. Abdominal ultrasonography (US) was obtained by using a mechanical-sector real-time unit with 5.0-7.5 MHz sector transducers and was performed by a pediatric gastroenterologist or a radiologist. All studies were performed after an adequate period of fasting of at least 4 hours.

All cases were divided into the following three types according to their anatomical findings, as proposed by Kasai et al. and the Japanese Association of Pediatric Surgeons.[4] Type I, the atresia affects the common bile duct and a patent proximal duct. Type II, the atresia affects the common hepatic duct. Type III, the atresia and obliteration affect the entire extrahepatic biliary tree (Fig. 1).

Exploratory laparotomy was indicated when a jaundiced patient had direct hyperbilirubinemia, and positive findings from abdominal US and cholescintigraphy that were highly suspicious of BA. KP was performed when intraoperative findings revealed any of the above three types of BA. The age of the 93 patients receiving KP ranged from 20-127 days (60.3 ± 20.3 days).

type I
11 (11.8%)

type II
4 (4.3%)

type III
78 (83.9%)

**Fig. 1** Macroscopic types of biliary atresia. Type I and type II involve the segmental obliteration of the common bile duct and the common hepatic duct, and type III involves the whole biliary tree to the level of the porta hepatis.

Jaundice-free survival was defined as a patient who had serum total bilirubin of less than 2 mg/dL at any time after KP. LT was indicated in the cases with worsening cholestasis, portal hypertension and variceal bleeding, recurrent cholangitis and intractable ascites.

Data were presented as mean ± standard deviation, and were compared using Student *t*-test for continuous variables and chi-square tests for categorical variables. Patient survival was assessed using Kaplan-Meier method and log rank test. Survival with native liver was analyzed starting at birth and ending at death or LT. The analysis of overall survival also started at birth and ended at death. The statistical analyses were performed using the Statistical Package for Social Science (SPSS, version 13) software package. A $p$ value less than 0.05 was considered statistically significant.

## RESULTS

Scintigraphic scans had 100% sensitivity, 81.5% specificity and 87.6% accuracy for the diagnosis of BA (odds ratio 5.40, 95% CI: 4.00-7.28) (Table 1). Gallbladder lengths of less than 15 mm on abdominal US were present in 72 of 93 cases, with 77.4% sensitivity, 69.8% specificity and 72.3% accuracy for the diagnosis of BA (odds ratio 7.94, 95% CI: 4.46-14.14) (Table 1).

Cholangitis developed in 56 patients (60.2%). Incidence of cholangitis was not significantly different between the patients free of jaundice (22/38) and those with persistent jaundice (34/55) ($p$ = 0.704). Seven patients had single cysts, 4 being jaundice-free; 2 received LT and 1 died. The patient with mul-

**Table 1.** Results of Hepatobiliary Scintigraphy and Abdominal Ultrasonography in Infants with Neonatal Cholestasis

| Final diagnosis | Hepatobiliary scintigraphy | | Abdominal ultrasonography | |
|---|---|---|---|---|
| | Non-visualization | Visualization of bowel radioactivity | Size gallbladder < 15 mm | Size gallbladder ≥ 15 mm |
| Biliary atresia (n = 93) | 93 | 0 | 72 | 21 |
| Neonatal hepatitis (n = 189) | 35 | 154 | 57 | 132 |

tiple cysts died at 2 years 7 months of age. Five out of 9 were free of jaundice after re-do KP, while 2 died of bacteremia and 2 received LT.

Among the sixty patients who received KP before 60 days of age, 29 survived with native liver and were jaundice-free, which was significantly higher than the 9 of 33 patients who received KP after 60 days of age ($p = 0.048$) (Fig. 2). Among the 62 patients treated between 1986 and 2000, the survival rate with native liver at 3 and 5 years postoperatively was 70.9% and 51.6%, respectively (Fig. 3). The 5 year survival rate was significantly higher in those free of jaundice compared with those with persistent jaundice (86.9 ± 6.1% vs. 31.4 ± 6.8%, $p < 0.001$). The 5 year survival rate was not significantly different between patients with or without cholangitis (50.1 ± 7.2% vs. 59.2 ± 8.9%, $p = 0.208$). The 5 year survival rate of patients suffering more than 3 episodes of cholangitis was lower than that for those suffering less frequent episodes (44.3 ± 8.9% vs. 58.4 ± 7.3%, $p = 0.054$). The age of the patients receiving LT was from 9 months to 10 years (3.4 ± 2.4 years) and the survival rate after LT was 95% (19/20) in the follow-up period from 4 years to 17 years (8.7 ± 4.1 years).

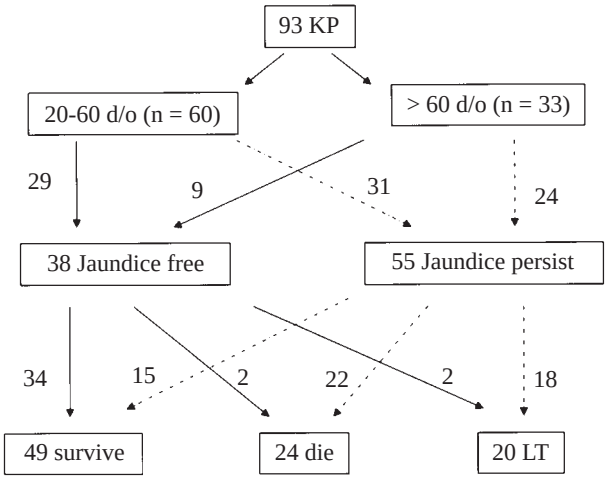


**Fig. 2** Outcome and survival data for patients with biliary atresia. KP: Kasai portoenterostomy; d/o: days old; LT: liver transplantation.

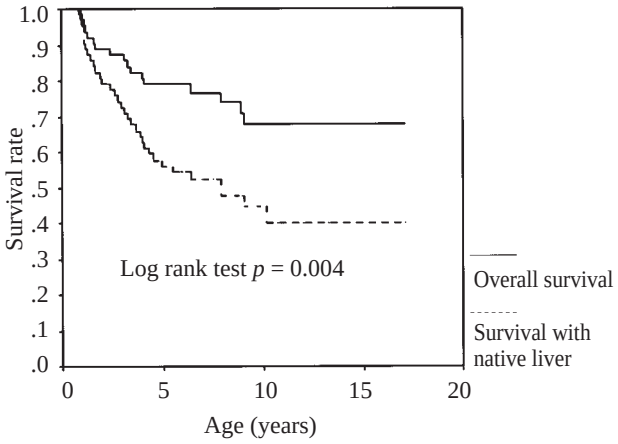


**Fig. 3** The survival rate (1986-2000, n = 62) after Kasai portoenterostomy with native liver and overall survival rate (including the survival period after transplantation).

## DISCUSSION

No test is unequivocally reliable in the diagnosing BA.[30,31] In this study, scintigraphy seems to have had better diagnostic accuracy than US, probably because US is an operator-dependent tool. Although Lee reported that the triangular cord (TC) sign with 4-mm thickness on US had a sensitivity of 80% and specificity of 98% for the diagnosis of BA,[32] we did not use that criterion for the diagnosis of BA. The difficulty in identifying the TC sign was that there are different patterns and sizes of fibrous ductal remnant in the porta hepatis in BA.[32] Instead, we used a more common criterion of gallbladder length for the diagnosis of BA, which provided diagnostic sensitivity and specificity comparable to Lee's report. It is well known that better preparation with a longer period of fasting or performing serial US provides better diagnostic accuracy.[5,15]

Abdominal computed tomography is not useful in the diagnosis of BA but it can provide important anatomical data before LT.[33] Miyazaki et al. reported that the diagnostic accuracy of magnetic resonance cholangiopancreatography (MRCP) was 100% in congenital BA.[34] They used MRCP with a half-Fourier acquisition single-shot turbo spin-echo (HASTE) sequence as a noninvasive imaging technique, which obtained an image in 1.4 sec without breath-hold.[34] However, this is not available in every hospital. Generally, MRCP fails to demonstrate the absence of bile ducts because they are barely visible in normal subjects.[35] In one report, the use of three-dimensional MRCP with a fast spin-echo T2-weighted pulse sequence for evaluation of two BA patients was unsuccessful in identifying BA in one.[36]

Cholangitis developed in 60.2% of our patients after KP, which was comparable to 70%-90% of patients with at least one episode before the age of 2 years in previous reports.[18,37,38] Although most reports stated that cholangitis affected outcome of the patients receiving KP,[37] we did not find a difference in the incidence of cholangitis between the patients who survived without jaundice and those with persistent jaundice. The difference in the results may be due to different ways of calculation used to address the same issue. Bu et al. reported a 25.3% incidence of intrahepatic cysts in BA patients post-KP.[17] Among them, 10.4% had multiple intrahepatic cysts. Both are higher than our results. The difference might lie in different scanning time, follow-up periods or in cyst size reduction after antibiotic treatment.[17]

Re-do KP has sometimes been considered useless, especially in advanced liver fibrosis.[25] However, jaundice may be cleared in one-third to one-quarter of cases after re-do KP.[25] Our results were surprisingly good with 5 of 9 (55.6%) free of jaundice after re-do KP. Although some claim that the procedure may result in more severe bowel adhesions that make further LT more difficult,[25,26] it did not worsen the results of two patients receiving LT after failed re-do KP. The results indicate that re-do KP can still offer hope for selected patients who develop cholangitis and suffer abrupt cessation of bile flow after KP. Consistent with the results reported previously, our results also showed a significant difference in jaundice-free survival rate of patients who received KP before 60 days and after 60 days of age.[24]

In conclusion, the results of this study showed that about half of the patients with BA survived for more than 5 years with their native liver. Age at operation, not post-KP cholangitis and liver cysts, was the most determinant factor of outcome in BA.

**Acknowledgements**

This study was supported in part by a grant (CMRPG850281) from the Chang Gung Memorial Hospital.

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# 膽道閉鎖的預後：高雄長庚醫院二十年經驗

刁茂盟 莊錦豪[1] 黃立同 謝志松[1] 李信儀[1] 梁啓迪 陳肇隆[2]

**背 景**： 膽道閉鎖的處理隨著時代而進步，但在高雄長庚醫學中心的處理經驗仍未被報告。

**方 法**： 回顧及分析於 1986 到 2005 年間，在高雄長庚醫學中心診斷爲膽道閉鎖，且在本院接受葛西手術的病人，共有 93 位，包括 46 位男性及 47 位女性。接受葛西手術早於 60 天有 60 位，晚於 60 天有 33 位。

**結 果**： 接受葛西手術早於 60 天，黃膽緩解爲 29/60 (48.3%)；晚於 60 天爲 9/33 (27.3%) ($p$ = 0.048)。膽道炎病例總共 56 人 (60.2%)，膽道炎在黃膽緩解病人中佔 22/38 (57.9%)，在黃膽病人中佔 34/55 (61.8%) ($p$ = 0.704)；1 人有 3 個肝臟囊腫並於後來死亡，其他 7 人爲單一肝臟囊腫 (4 人黃膽緩解，2 人接受肝臟移植，1 人死亡)；第二次做葛西手術病人中，黃膽緩解總共 5/9 (55.6%)；從 1986 到 2000 年中病例，手術後 5 年存活率爲 32/62 (51.6%)。

**結 論**： 本研究指出，5年存活率超過一半；接受葛西手術時的年齡，比術後發生膽道炎或肝臟囊腫，更具有預後決定性。

(長庚醫誌 2007;30:122-7)

**關鍵詞**：膽道閉鎖，葛西手術，膽道炎

長庚紀念醫院 高雄院區 兒童內科，[1]兒童外科，[2]外科部；長庚大學 醫學院

受文日期：民國95年2月14日；接受刊載：民國95年10月24日

通訊作者：謝志松醫師，長庚紀念醫院 兒童外科。高雄縣833鳥松鄉大埤路123號。Tel.: (07)7317123轉8715; Fax: (07)7338009; E-mail: pc006581@yahoo.com.tw, tmm@cgmh.org.tw