Surg Today
Jpn J Surg (1998) 28:1229–1232

SURGERY TODAY

Editorial

Surgical Treatment of Biliary Atresia in the Liver Transplantation Era

RYOJI OHI

Department of Pediatric Surgery, Tohoku University School of Medicine, 1-1 Seiryomachi, Aoba–ku, Sendai 980-8574, Japan

Abstract: Biliary atresia (BA) still remains one of the most intractable gastrointestinal diseases in infancy despite the concerted efforts of pediatric surgeons all over the world. The introduction of liver transplantation has revolutionized the protocols for the treatment of this condition. In this editorial, the role of hepatic portoenterostomy (the Kasai procedure) in the surgical treatment of BA in the "transplantation era" will be discussed.

Results of Surgical Treatment of Biliary Atresia

The Japanese Biliary Atresia Society, founded in 1975 to investigate all aspects of biliary atresia (BA), established a nationwide registry of BA patients in 1989. The Japanese Biliary Atresia Registry is helpful in determining the present status of the surgical results of BA. Judging from the population and the incidence of this disease (1/10000–12000 live births), approximately 90% of the patients are registered every year. Up to 1996, a total of 852 cases had so far been entered into the registry. An average number of 107 cases from 47 institutions have registered per year, that is, an average of only 2.3 cases per institution per year.

The diagnosis of BA should be made as rapidly as possible, because an early operation is essential for the success of surgical therapy for this disease.[1] Based on the Japanese BA Registry (JBAR), the patients' ages at the time of corrective operation are shown in Fig. 1. Although the number of cases operated on between 30 to 60 days after birth has increased gradually, more than 40% of cases still undergo surgical treatment more than 60 days after birth. Moreover, 15% of all cases had surgery after 91 days. To our regret, the goals of early diagnosis and operation have thus not yet been fulfilled regarding the treatment of this disease.

Seven hundred seventy patients (91%) underwent a hepatic portoenterostomy (the Kasai procedure) and 49, hepaticoenterostomy. A liver transplantation was employed as the primary therapeutic modality in one case in 1996. Thirteen patients (1.5%) died within 1 month after corrective surgery. The age at operation had a definite impact on bile drainage. At less than 70 days of age, we obtained reasonable results while after 70 days the results worsened (Table 1). There was no bile flow after operation in 81 cases, while 735 (90%) obtained a bile flow. Jaundice cleared in 473 patients (58%) and decreased in 179, while it persisted in 75. Figure 2 shows the operative results. In 1996, jaundice cleared once after a corrective operation in 57%. Of course these results are not satisfactory, and these patients should be followed up carefully for a long time, because the postoperative course of jaundice-free BA patients is not always uneventful.[2]

A reoperation of the Kasai procedure was performed in 242 patients (30%). Although the indications for a reoperation were an "unsuccessful initial Kasai procedure" in more than half of these patients, a favorable outcome of such a reoperation is expected only in cases with an active bile flow after the initial operation. Several reports which analyzed the impact of the previous Kasai procedure on liver transplantation have been published in the literature.[3,4] Compared with the single Kasai procedure, multiple Kasai procedures exert an unfavorable influence on liver transplantation. Therefore, we think that a reoperation with the Kasai procedure in the transplantation era should be performed only in patients with a sudden cessation of a good bile flow after the initial procedure.

Liver transplantation has been established as one modality for the treatment of BA. Japanese children with end-stage liver disease have undergone cadaveric liver transplantation outside Japan, but such operations

Reprint requests to: R. Ohi
(Received for publication on Apr. 16, 1998; accepted on July 7, 1998)

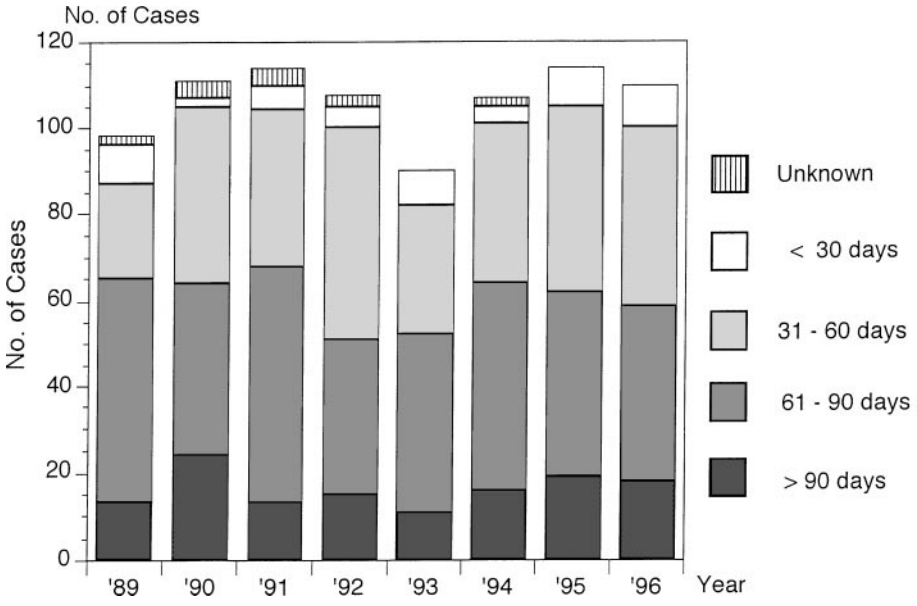

Fig. 1. Patients' age at the time of a corrective operation (Japanese Biliary Atresia Registry, 1989–1996)

Table 1. Age at corrective operation and the short-term results (Japanese Biliary Atresia Registry, 1989–1996)

Age at operation (days)	Number of cases	Jaundice disappearance (%)
≤30	42	25 (60%)
31–45	95	57 (60%)
46–60	164	100 (61%)
61–70	149	92 (62%)
71–80	108	56 (52%)
81–90	59	33 (56%)
>90	112	48 (43%)

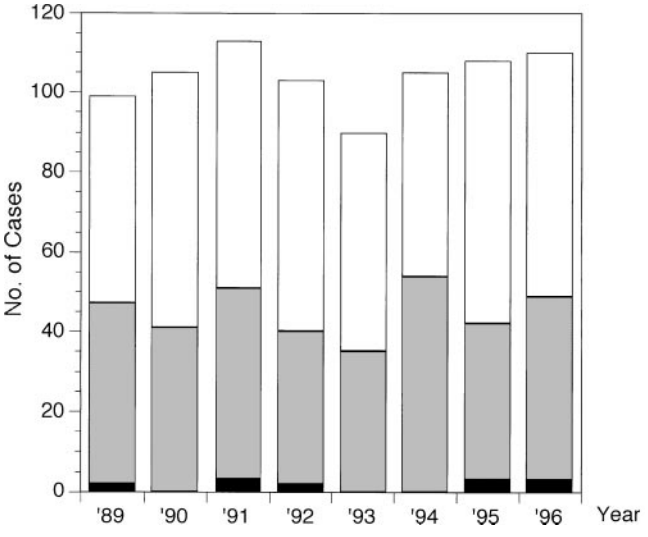

Fig. 2. Short-term operative results (Japanese Biliary Atresia Registry, 1989–1996). *White*, jaundice cleared; *gray*, jaundice persisted; *black*, died

are not yet generally possible, and thus the first living related liver transplantation was carried out in Japan in 1989. In 1996, when the registry had begun to elucidate the role of transplantation in recent years in Japan, the JBAR traced liver transplantation cases back to 1989. Seventeen percent to 25% of patients have undergone transplantation in the last several years even in Japan (Fig. 3). Moreover, the age at transplantation has tended to decrease in recent years. Several studies have reported liver transplantation in small infants not to carry any excessive risk due to improvements in the techniques and overall management of such transplantations.[5,6]

Prediction of the Outcome of the Kasai Procedure

A number of features, including the age at the time of operation, associated anomalies, extrahepatic bile duct histology,[7,8] liver histology including bile canalicular membrane associated filament,[9] labeling index for proliferating cell nuclear antigen-positive hepatocytes,[10] HLA-DR antigen and CD68 antigen,[11] postoperative cholangitis, etc., have been suggested to be useful predictors of the efficacy of the Kasai procedure in the treatment of BA. With the improved survival results of liver transplantation, it is highly desirable that we obtain much more useful and/or accurate factors to suc-

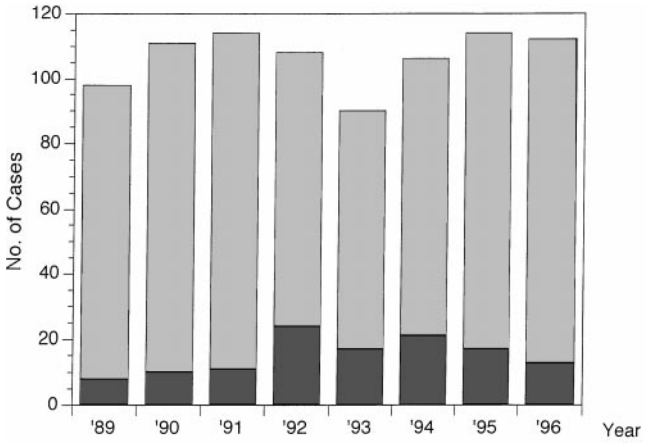

Fig. 3. Number of cases who underwent a liver transplantation (Japanese Biliary Atresia Registry, 1989–1996). *Light gray*, non-transplant patients; *dark gray*, transplant patients

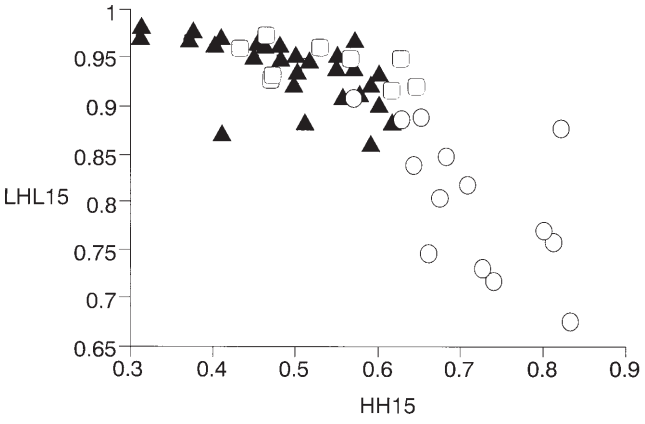

Fig. 4. The relationship between blood clearance (*HH15*) and hepatic accumulation (*LHL15*) in the ^{99m}Tc galactosyl serum albumin scintigram findings after the Kasai operation. *Triangles*, almost normal liver function; *squares*, severe portal hypertension group; *circles*, indications for a liver transplantation

cessfully predict the outcome of the Kasai procedure before performing such surgery. Doppler ultrasound,[12] urinary excretion of D-glucaric acid,[13] the macroscopic appearance at portoenterostomy,[14] and evaluation of needle biopsy of the liver[15] have all been proposed as preoperative and/or intraoperative predictors. To our regret, however, no definite conclusions have been reached.

Indications and Timing of Liver Transplantation for BA Patients

Liver transplantation is not indicated in a considerable number of unicteric patients who have neither serious sequelae nor a progressive hepatic dysfunction. However, it should be considered in patients with decompensated liver cirrhosis at referral and for patients without bile drainage after the Kasai procedure before they deteriorate. Patients with inadequate bile drainage should undergo a transplantation when developmental retardation begins or when their sequelae become uncontrollable. Patients with sufficient bile drainage could also be considered as candidates when their associated sequelae become both medically and socially unacceptable.

To decide the timing of the transplantation, we employ ^{99m}Tc galactosyl serum albumin (GSA) scintigraphy.[16] A new radiophamaceutical ^{99m}Tc-GSA binds to the asialoglycoprotein receptor on hepatocytes. The blood clearance and hepatic accumulation indices are useful for evaluating both the function and morphology of the liver from a new viewpoint of receptor-mediated accumulation. LHL15, the hepatic accumulation, and HH15, the blood clearance, are measured, calculated, and plotted (Fig. 4). The data of the patients with end-stage liver disease drop in the right and lower part of the figure, with high HH15 and with low LHL15.

Discussion and Conclusions

Our present surgical management strategy for BA is as follows: we operate on patients are early as possible, we widely dissect the portal bile duct remnant (the occluded extrahepatic bile duct at the porta hepatis) during the Kasai procedure, the Kasai procedure is performed without stoma, precise postoperative care is performed, a reoperation of the Kasai procedure is performed in only strictly selected cases, and we avoid laparotomy for the treatment of portal hypertension. Lastly, for patients with advanced liver disease, an exploratory laparotomy and/or primary liver transplantation should also be considered.

The advantages of an initial Kasai procedure versus primary liver transplantation are: (1) approximately 50% of the patients achieve an adequate liver function; (2) a further refinement of the Kasai procedure might lead to a cure rate of about 70% to 80%; (3) the native organ is preferred to a donated foreign one; (4) we presently suffer a shortage of donors in pediatric liver transplantation; and (5) last but not least, liver transplantion involves numerous hazards including serious infections and oncogenesis. The Kasai procedure combined with liver transplantation is recommended, but they both have their specific roles and limitations.

In conclusion, liver transplantation is another option in the management of BA, but the first procedure of choice for patients without progressive liver disease should be the Kasai procedure, while endeavoring to make as early a diagnosis of this condition as possible.

References

1. Ohi R, Kasai M, Takahashi T (1969) Intrahepatic biliary obstruction in congenital bile duct atresia. Tohoku J Exp Med 99:129–149
2. Ohi R, Nio M, Chiba T, Endo N, Goto M, Ibrahim M (1990) Long-term follow-up after surgery for patients with biliary atresia. J Pediatr Surg 25:442–445
3. Wood RP, Langnas AN, Stratta RJ, Pillen TJ, Williams L, Lindsay S, Meiergerd D, Shaw BW Jr (1990) Optimal therapy for patients with biliary atresia: portoenterostomy ("Kasai" procedures) versus primary transplantation. J Pediatr Surg 25:153–162
4. Sandler AD, Azarow KS, Superina RA (1997) The impact of a previous Kasai procedure on liver transplantation for biliary atresia. J Pediatr Surg 32:416–419
5. Dunn SP, Weintraub W, Vinocur CD, Billmire DF, Falkenstein K (1993) Is age less than 1 year a high-risk category for orthotopic liver transplantation? J Pediatr Surg 28:1048–1050
6. Inomata Y, Tanaka K, Okajima H, Uemoto S, Ozaki N, Egawa H, Satomura K, Kikuchi T, Yamaoka Y (1996) Living related liver transplantation for children younger than one year old. Eur J Pediatr Surg 6:148–151
7. Ohi R, Shikes RH, Stellin GP, Lilly JR (1984) In biliary atresia duct histology correlates with bile flow. J Pediatr Surg 19:467–470
8. Tan CE, Davenport M, Driver M, Howard ER (1994) Does the morphology of the extrahepatic biliary remnants in biliary atresia influence survival? A review of 205 cases. J Pediatr Surg 29:1459–1464
9. Segawa O, Miyano T, Fujimoto T, Watanabe S, Hirose M, Fujiwara T (1993) Actin and myosin deposition around bile canaliculi: a predictor for clinical outcome in biliary atresia. J Pediatr Surg 28:851–856
10. Hossain M, Murahashi O, Ando H, Iio K, Kaneko K, Ito T (1995) Immunohistochemical study of proliferating cell nuclear antigen in hepatocytes of biliary atresia: a parameter to predict clinical outcome. J Pediatr Surg 30:1297–1301
11. Kobayashi H, Puri P, O'Briain DS, Surana R, Miyano T (1997) Hepatic overexpression of MHC class II antigens and macrophage-associated antigens (CD68) in patients with biliary atresia of poor prognosis. J Pediatr Surg 32:590–593
12. Wanek EA, Horgan JG, Karrer FM, Hall RJ, Pumack CM, Lilly JR (1990) Portal venous velocity in biliary atresia. J Pediatr Surg 25:146–148
13. Fujimoto T, Ohya T, Miyano T (1994) A new clinical prognostic predictor for patients with biliary atresia. J Pediatr Surg 29:757–760
14. Davenport M, Howard ER (1996) Macroscopic appearance at portoenterostomy — a prognostic variable in biliary atresia. J Pediatr Surg 31:1387–1390
15. Azarow KS, Philips MJ, Sandler Ad, Hagerstrand I, Superina RA (1997) Biliary atresia: should all patients undergo a portoenterostomy? J Pediatr Surg 32:168–174
16. Shimaoka S, Ohi R, Nio M, Iwami D, Sano N (1997) Clinical significance of ^{99m}Tc-DTPA galactosyl human serum albumin scintigram in follow-up after Kasai operation. Tohoku J Exp Med 181:203–211