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Biliary Atresia: Current Management and Outcome

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MURAJI, T., NISHIJIMA, E., HIGASHIMOTO, Y. and TSUGAWA, C. *Biliary Atresia: Current Management and Outcome.* Tohoku J. Exp. Med., 1977, **181** (1), 155-160 —— Between 1986 and 1994, 42 patients with BA were treated at the Kobe Children's Hospital. These patients underwent a wider excision of the hilar fibrous remnant with Roux-Y reconstruction (with or without intussuscepted valve) without stoma. Corticosteroids were used postoperatively when the stool was acholic or unsteadily cholic. The daily dose was reduced from 20 mg/day by half down. The patients were divided into two groups; in Group I ($n=17$, before October 1990), a single course of corticosteroid therapy was employed. In Group II ($n=25$, from November 1990 on), this regimen was repeated whenever the stool appeared less cholic. The bile flow improved significantly (excellent in 29% and 60%, and poor in 71% and 32% in Groups I and II, respectively.) Corticosteroids were used in 15 Group I patients with good response in 10 and in 21 Group II patients, 15 of whom had multiple courses. Sixteen of the 21 Group II patients had a good response. The incidence of the cholangitis was not significantly different between the 19 patients with valve and the 23 patients without valve. A 5 year survival significantly improved from 70% in Group I to 96% in Group II. In both groups, the survival rate significantly increased, when compared with the survival rate figured out with an assumption of OLT survivors as dead. On the same assumption, the survival rate of Group II is significantly more than that of the Group II. These suggest a positive contribution of liver transplantation and an aggressive corticosteroid therapy on better survival of Group II. ——
biliary atresia; corticosteroid; liver transplantation

In the late 1980's, we introduced a lateral extension of the dissection of the porta hepatis (Endo et al. 1983), postoperative corticosteroid therapy (Karrer and Lilly 1985) to our management of the patients with biliary atresia (BA), as well as an orthotopic liver transplantation (OLT) as a last resort. Since 1990, we have

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achieved a significant improvement in outcome with more liberal use of corticosteroids. This paper summarizes our current management and outcome of our patients.

Patients and Method

During the period between August 1986 and June 1994, 42 patients with BA were treated at the Kobe Children's Hospital. In 17 patients treated before October 1990 (Group I), a single course of corticosteroid was employed in a fashion described below. From November 1990 on, this regimen was repeated whenever the stool appeared less cholic even if the previous dose had not yet been discontinued(Group II). Their ages at operation were 65.2 ± 13.2 days (mean $\pm$ S.D., median: 62) in Group I and 73.1 ± 21.2 days (mean $\pm$ S.D., median: 67) in Group II. There was one patient with I-cyst type, so called correctable type of porta hepatis in Group I, while the remaining 41 were type III, so called uncorrectable type.

Surgical technique. The porta hepatis is dissected, preserving the fibrous remnant between the right and left branches of the portal vein. The depth of excision of the fibrous remnant in the liver hilus is kept at the transitional level between the fibrous tissues and the liver parenchyma. In addition to the "portal" level approach (Kimura et al. 1979), wider excision into the lateral sides of the fibrous tissue at the liver hilum, extending up to the umbilical point on the left and the bifurcation of the anterior and posterior branches of the right portal vein on the right.

Reoperation was performed when there was no bile drainage or diminution of bile excretion in each group.

Postoperative management consisted of adequate hydration and prophylactic antibiotics via intravenous access for the first month on an in-patient basis. Corticosteroids were used; prednisolone was started 6-8 days postoperatively when the stool was acholic or unsteadily cholic, with an initial dose of 20 mg/day (4 mg/kg). The daily dose was reduced by half down to 5.0 or 2.5 mg/day. The degree of bile flow was defined as "excellent" when the stool is fully cholic and serum bilirubin decreased to below 1.0 mg/100 ml 6 months after surgery, defined as "poor" when the stool is acholic and/or re-vision of portoenterostomy was performed, and defined as "fair" for the others.

Statistical analysis was made using Fisher exact test and the Kaplan-Meier survival curve and Cox-Mantel test. A p value of less than 0.05 was considered significant.

Results

There was no operative death related to the Kasai procedure. Table 1 summarizes the results. Twelve out of 17 Group I patients survived, 4 with OLT and 24 of the 25 Group II survived, 4 with OLT. Postoperative bile drainage was

TABLE 1. *The degree of bile drainage and survivors and dead in each group*

Group	Excellent	Fair	Poor	Survivor (OLT)	Dead
I	5	0	12	12	5
($n=17$)	(29%)		(71%)	(4)	(1)
II	15	2	8	24	1
($n=25$)	(60%)	(8%)	(32%)	(4)	(0)

The distribution of the patients with each degree of bile drainage is significantly different between the two groups (Fisher exact test, $p=0.03$).

excellent in 5 Group I patients (29%), 15 Group II patients (60%). Bile drainage was poor in 12 Group I patients (71%), in 8 Group II patients (32%). This distribution of patients is significantly different between the two groups (Fisher exact test, $p=0.03$). The incidence of cholangitis was not significantly different between the 19 patients with valve and the 23 patients without valve (Fisher exact test, $p=0.89$). Corticosteroids were used in 15 patients with good response in 10.

Of these 10, 7 alive (3 with portal hypertension and 4 without portal hypertension). Corticosteroids were used in 21 Group II patients, 15 of whom had multiple courses repeated until the bile flow was stabilized. Sixteen of the 21 patients had a good response. All these 16 patients are alive at the time of follow-up; 2 after OLT, 3 with portal hypertension, 11 with "normal" life, free of jaundice and portal hypertension.

A 5 year survival significantly improved from 70% in Group I to 96% in Group II (Fig. 1). In both groups, the survival rate significantly increased, when compared with the survival rate figured out with an assumption of OLT survivors as dead at the time of OLT ($p<0.05$, Figs. 2, 3). This suggests a positive impact of liver transplantation on survival. Similarly, provided that OLT survivors are

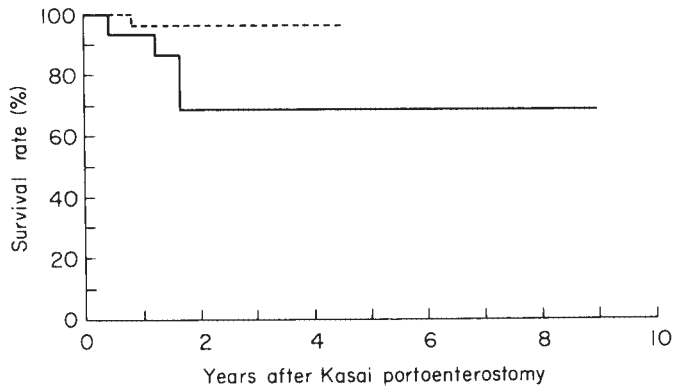

Fig. 1. Kaplan-Meier survival curve of each group.
A 5-year survival is 70% and 96% in group I (——) and Group II (------), respectively and is significantly different between the two groups (Cox-Mantel test, $p<0.01$).

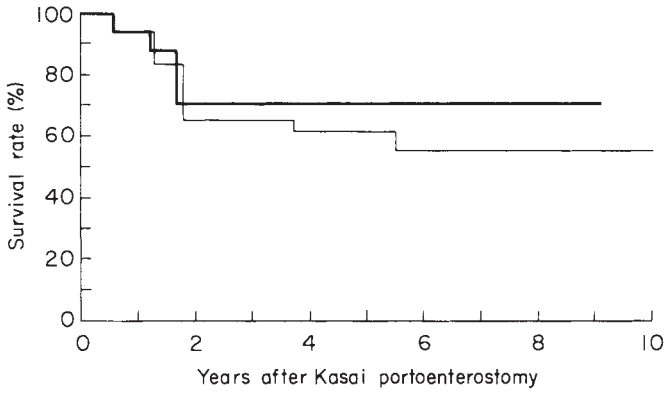

Fig. 2. Kaplan-Meier survival curve of Group I.
OLT survirors as alive (——) and OLT survivors as dead (——).
The survival rate is compared with the one calculated out with an assumption of OLT survivors as dead. It is significantly different between the two groups (Cox-Mantel test, $p<0.05$).

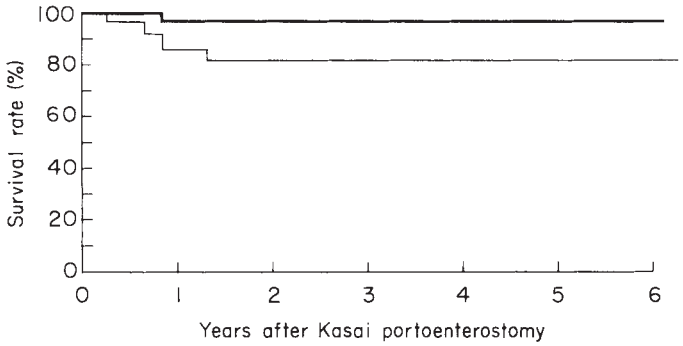

Fig. 3. Kaplan-Meier survival curve of Group II.
OLT survivors as alive (——) and OLT survivors as dead (——).
The survival rate is compared with the one calculated out with an assumption of OLT survivors as dead. It is significantly different between the two groups (Cox-Mantel test, $p<0.05$).

regarded as dead at the time of OLT in Group I and II, the survival rate of Group II is significantly more than that of the Group II ($p<0.01$, Fig. 4). This suggests a positive contribution of an aggressive corticosteroid therapy on better survival.

Discussion

Survival has remarkably improved in our recent patients with BA, especially when combined with liver transplantation for those who failed. However, for pediatric surgeons, surgery and an early postoperative management are in our hands, and it is important for us to make an effort to minimize the number of patients to be sent to OLT. Two surgical modifications, a valve and a lateral extension of portal dissection, were made in this series. A level and an extent of transection of the hilar fibrous remnant are essentially and critically important. The Kasai operation is certainly a delicate surgical procedure, requiring a skillfullness and experiences. We might have improved our surgical technique, affecting

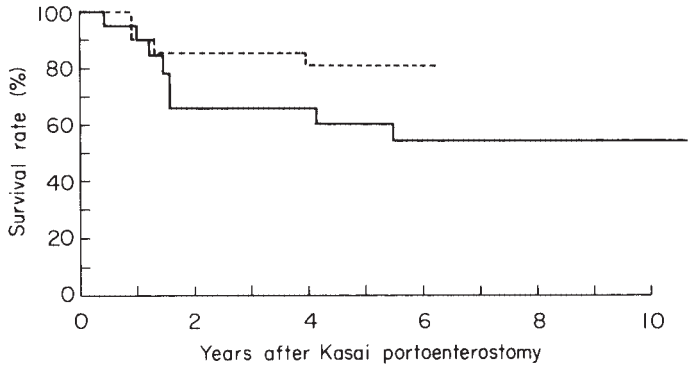

Fig. 4. Kaplan-Meier survival curve of Group I (——) and II (------).
The survival rate calculated out with an assumption of OLT survivors as dead is compared between Group I and II. It is significantly different between the two groups (Cox-Mantel test, $p<0.01$).

the better outcome in Group II. However, it is difficult to draw any conclusion regarding an impact of surgical techniques on survival from this study except for the role of valve. A valve does not seem to be responsible for this improvement. The effort in the postoperative management, on the other hand, includes a careful monitoring of degree of bile drainage and early treatment of cholangitis when it occurs. Adequate hydration and prophylactic antibiotics are essential in the first month, and even more important is an aggressive use of corticosteroid to promote bile drainage, usually starting 7 days after surgery. It is particularly important to maintain a good bile flow in the first month, during which time the microscopic communicating ducts are formed into the epithelialized fistula (Lilly et al. 1989). In our experiences, prednisolone is effective with a dose of 2 to 4 mg/kg and is as effective as oral administration of prednisone as long as it is given in similarly high doses. At our institution, there is no stoma in patients. An each stool is collected in a transparent petri dish by a nurse every day. Careful monitoring of the color of the stool is an important component of our rounds. Steroid dose is manipulated according to the color. Even before the previous dose is discontinued, the dose of steroid is re-bolused whenever the stool appears less cholic. Using this approach bile drainage gradually becomes steady in a significant number of patients. A stoma is not mandatory for this purpose.

Although "cure" of this disease by the Kasai operation remains unclear, multiple corticosteroid therapy during an early postoperative period is promising.

Conclusion

1. Our current management achieved 96% of survival when combined with liver transplant. 2. An aggressive corticosteroid therapy improved bile drainage and outcome. 3. A valve in the Roux-Y limb did not decrease the incidence of cholangitis.

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