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Five- and 10-Year Survival Rates After Surgery for Biliary Atresia: A Report From the Japanese Biliary Atresia Registry

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Purpose: The aim of this study was to elucidate the epidemiology and short- and long-term results of biliary atresia in Japan analyzing the data of the Japanese Biliary Atresia Registry (JBAR).

Methods: In 1989, the Japanese Biliary Atresia Society started a nationwide registry, JBAR, to investigate all aspects of biliary atresia. A total of 1,381 patients, 863 girls, 507 boys, and 11 unknown, were registered between 1989 and 1999. JBAR includes an initial and follow-up questionnaires. Using these patients' data, the incidence, sex distribution, associated anomalies, the type of obstruction, the type of operation, and the surgical results were evaluated. The 5- and the 10-year results of 735 patients who were registered initially in or before 1994 also were analyzed.

Results: The incidence of biliary atresia was 1 in 9,640 live births. One hundred sixty-four patients (11.9%) had type I atresia of the common bile duct, 34 (2.5%) had type II atresia of the hepatic ducts, and 1,162 (84.1%) had type III atresia at the porta hepatis. Congenital associated anomalies were found in 19.6% of the patients including 33 cases associated with polysplenia. Impact of the age at operation on bile flow was not clear until 90 days of age, and after 90 days the bile flow rate worsened. The original Roux-en-Y procedure had been used in more than 50% of the patients since 1995. In 1999, 96% of the patients underwent the original Roux-en-Y procedure or the Roux-en-Y with an intestinal valve, and only 3 patients (3.5%) underwent other modifications. There were no significant differences in either the rate of disappearance of jaundice or the incidence of cholangitis among these 3 procedures. Of the 735 patients registered in or before 1994, 19 patients (2.6%) were lost to follow-up. The 5-year survival rates of patients registered in 1989, 1990, 1991, 1992, 1993, and 1994 were 62%, 64.5%, 61.3%, 59.0%, 58.7%, and 52.7% without liver transplantation (LTx), and 69.4%, 74.2%, 75.2%, 79.5%, 78%, and 78.3% with LTx, respectively. Although the overall 5-year survival rate changed from 69.4% to 78.3%, the difference was not statistically significant. According to the 10-year follow-up results of the 108 patients initially registered in 1989, 72 (66.7%) and 57 (52.8%) survived with and without the aid of LTx, respectively.

Conclusions: The overall 5- and 10-year survival rates were 75.3% (553 of 734) and 66.7% (72 of 108), respectively. In spite of the increasing number of survivors after LTx, there was no significant improvement in the 5-year survival rate. It was shown that the JBAR system was functioning well with only 19 patients lost to follow-up among the 743 patients registered from 1989 to 1994.

INDEXWORDS: Biliary atresia, registry, Japan.

THE KASAI OPERATION is accepted widely as the therapeutic first choice for biliary atresia, but its long-term efficacy still remains controversial. In 1989, the Japanese Biliary Atresia Registry (JBAR), a nationwide registry of children with biliary atresia in Japan, was established by the Japanese Biliary Atresia Society to investigate all aspects of biliary atresia including the long-term outcome. Each year data sheets are collected from institutions throughout Japan. In this report, we analyzed collected data with the approval of the society committee.

MATERIALS AND METHODS

The JBAR, consisting of an initial questionnaire and follow-up questionnaires, were sent to all major institutions (132 institutions)

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Table 1. Patients Registered in Each Year

Year	No.
1989	108
1990	125
1991	142
1992	122
1993	109
1994	129
1995	147
1996	129
1997	126
1998	120
1999	124
Total	1381

belonging to the Japanese Society of Pediatric Surgeons. The initial questionnaire was designed to obtain patients' information including gestational history, perinatal history, diagnosis, treatment, and early results. Once a patient is registered, the institution is obliged each year to complete and return the follow-up questionnaire including current results of treatment, further surgical treatment such as revision of Kasai operation and liver transplantation (LTx), complications, and mental and physical development. Until 1999, 1,381 patients from 93 institutions were enrolled into the JBAR. Using these patients' data, the incidence, sex distribution, associated anomalies, types of obstruction, types of operation, and surgical results were evaluated. The long-term outcome of 735 patients who were registered in or before 1994 was studied as well. The influences of the patient's age at operation, the preoperative value of serum direct bilirubin, the type of modifications, and the type of obstruction on the 5-year survival rate were also assessed. The 10-year survival rate was calculated using data from 108 patients initially registered in 1989. The disappearance of jaundice was defined as the postoperative value of total serum bilirubin less than 2.0 mg/dL. In the statistical analysis, χ^2 test for categorical variables and Student's t test for continuous variables were used, and a P value less than .05 was considered statistically significant.

RESULTS

Results of the Initial Questionnaire

The number of patients registered each year is shown in Table 1. Between 100 and 150 patients were registered every year. There was no clear tendency of increase or decrease in these 11 years. Because the total number of live births in Japan between 1989 and 1999 was 13,313,000, the incidence was 1 in 9,640 live births. The sex ratio showed a female to male predominance of 1:0.59 (863 girls and 507 boys). The family history of surgical hepatobiliary diseases was found in 3 patients, 2 siblings with biliary atresia and one sibling with choledochal cyst.

Congenital-associated anomalies were found in 19.6% of the patients. Thirty-three cases were associated with polysplenia, a common associated anomaly of biliary atresia. All except 4 patients underwent corrective operation for biliary atresia. Two patients underwent primary liver transplantation, and the other 2 underwent an exploratory laparotomy.

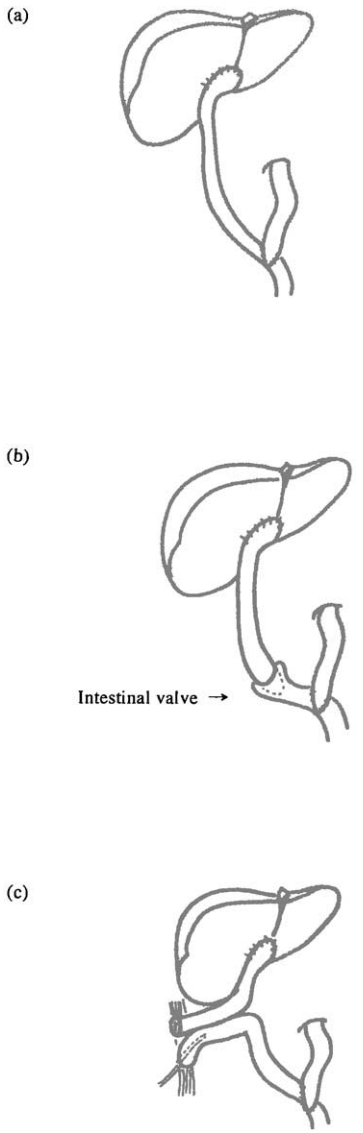

Fig 1. (A) Original Roux-en-Y procedure. (B) Roux-en-Y with an intestinal valve. To prevent cholangitis, the intestinal valve is equipped to the Roux-en-Y limb. (C) Suruga II. A total biliary conduit is created, which is to be restored at the second operation.

Table 2. The Age at Operation and Postoperative Bile Flow

Age at Operation (d)	No.	Disappearance of Jaundice (%)
<31	63	59
31-45	168	60
46-60	274	61
61-70	223	61
71-80	168	51
81-90	95	58
>90	190	48
Total	1,181	57

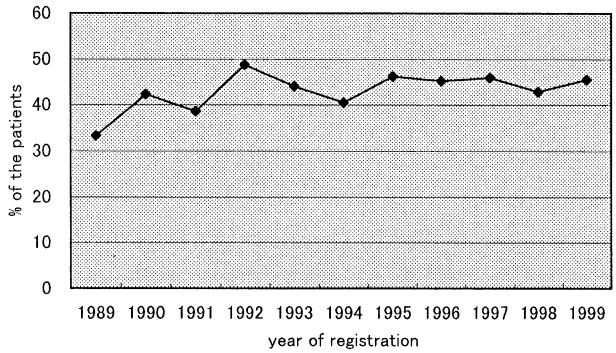

Fig 2. A trend of the patients who underwent corrective operation at the age of 60 days or before. No remarkable change was seen in the proportion of the patients who underwent corrective operation at the age of 60 days or before.

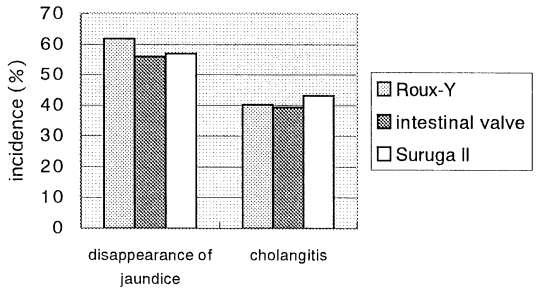

Fig 4. Disappearance of jaundice and incidence of cholangitis in each procedure. There were no significant differences in disappearance of jaundice or incidence of cholangitis among the 3 procedures, the original Roux-en Y, the Roux-en Y with an intestinal valve, and the Suruga II procedure.

Regarding the type of obstruction, 164 patients (11.9%) had type I atresia of the common bile duct, 34 (2.5%) had type II atresia of the hepatic ducts, and 1,162 (84.1%) had type III atresia at the porta hepatis. The type of obstruction of the remaining 22 was unknown.

In 1989, less than 40% of the patients underwent corrective operation by the age of 60 days. Since 1990 there had been no remarkable change in the trend of the age at operation (Fig 1). Five hundred five patients (43%) underwent corrective operation at the age of 60 days or before. Although the impact of the age at operation on bile flow was not clear until 90 days of age, after 90 days the bile flow rate worsened (Table 2).

In a number of operative modifications to prevent cholangitis, the original Roux-en-Y, the Roux-en-Y with an intestinal antireflux valve and the Suruga II were mainly used (Fig 2). The trend showed the original Roux-en-Y procedure had been used in more than 50% of the patients since 1995 (Fig 3). In 1999, 73% of the patients underwent the original Roux-en-Y procedure, 24% underwent the Roux-en-Y with an intestinal valve, and only 3 patients (3.5%) underwent other modifications.

Operative results were compared among these 3 procedures. The rate of disappearance of jaundice in the original Roux-en-Y procedure, the Roux-en-Y with an intestinal valve, and the Suruga II were 62%, 56%, and 57%, and the incidence of cholangitis were 40%, 39%, and 43%, respectively. There were no significant differences in either the rate of disappearance of jaundice or the incidence of cholangitis among the procedures (Fig 4).

Five- and 10-Year Survival Rates

Of the 735 patients, 19 (2.6%) were lost to follow-up. The 5-year survival rates of patients registered in 1989, 1990, 1991, 1992, 1993, and 1994 were 62%, 64.5%, 61.3%, 59.0%, 58.7%, and 52.7% without LTx, and 69.4%, 74.2%, 72.5%, 79.5%, 78%, 78.3% with LTx, respectively (Table 3). Although the overall 5-year survival rate rose from 69.4% to 78.3%, the difference was not statistically significant ($P = .1206$).

The age at operation and the type of obstruction had significant impacts on the 5-year survival rates without LTx. However, the preoperative value of serum direct bilirubin and the type of modifications had no influence on it (Table 4).

According to the 10-year follow-up results of the 108 patients initially registered in 1989, 72 (66.7%) and 57 patients (52.8%) survived with and without the aid of LTx, respectively. Only one patient was lost to the 10-year follow-up.

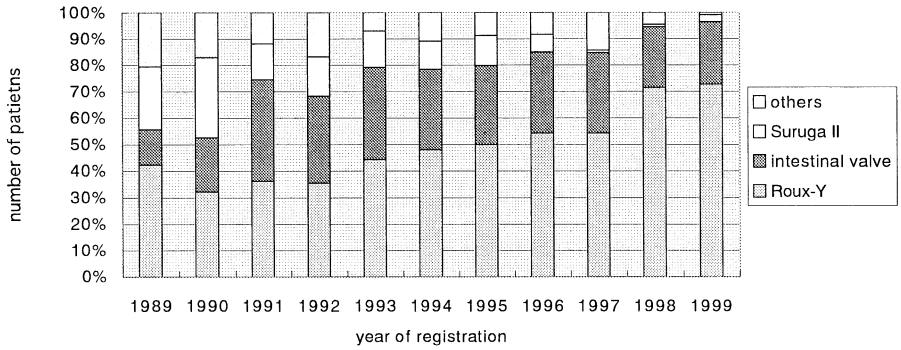

Fig 3. A trend of employed modifications of the JBAR. The original Roux-en-Y procedure had been used in more than 50% of the patients since 1995. Its frequency is increasing. In 1999, 96% of the patients underwent the original Roux-en-Y procedure or the Roux-en-Y with an intestinal valve, and only 3 patients (3.5%) underwent other modifications.

Table 3. Five-Year Survival Rates

Year of Registration	Without LTx (%)	With/Without LTx (%)
1989	62.0	69.4
1990	64.5	74.2
1991	61.3	72.5
1992	59.0	79.5
1993	58.7	78.0
1994	52.7	78.3
Total	59.7	75.3

Table 4. The Impact of Clinical Factors on the 5-Year Survival Rate Without LTx

	Five-Year Survival, mean (SD)		
	Yes	No	*P* Value
Age at operation (day)	65 (27.7)	72.7 (33)	.008
Direct bilirubin at operation (mg/dL)	7.2 (2.8)	7.15 (2.8)	.8161
Procedures			
Roux-en Y	177	99	
Intestinal valve	112	76	.7868
Suruga II	65	60	
Type of obstruction			
I	67	10	
II	13	1	< .0001
III	348	264	

DISCUSSION

A nationwide surveillance like the JBAR was carried out in US-Canada (1976 to 89),[1] France (1986 to 96),[2] and UK-Ireland (1993 to 95).[3] The JBAR is still ongoing and has become the largest one.

The incidence of biliary atresia in Japan was estimated to be 10.4 in 100,000 live births from the current study. According to the report by Chardot's et al,[2] this value is the third highest after the 32 in 100,000 live births in French Polynesia and 10.6 in 100,000 live births in Hawaii. Considering that all the patients with biliary atresia were not registered, we assumed the actual incidence to be much higher than 1 in 13,000 live births, which was reported in the earlier study.[4]

The age at operation is well known as an important prognostic factor. In this study, disappearance of jaundice was achieved in around 60% of the patients until by the age of 90 days. The advantage of early operation was not clear in terms of postoperative bile flow. The age at operation, however, had a significant impact on long-term prognosis.[5] We believe that the policy of the early diagnosis and the early operation should be kept.

The incidence of cholangitis in complex modifications such as the Roux-en with an intestinal valve and the Suruga II was not lower than that in the original Roux-en-Y procedure. It is difficult to conclude that both the intestinal valve and the biliary stoma are useless, because the severity or outcome of cholangitis was not assessed in the current study. Moreover, it is true that no antireflux procedure could successfully prevent cholangitis. Another reason the Suruga II procedure was almost abandoned was that the stoma formation affected the outcome of LTx,[6] which might be subsequently required.

Regarding the 5-year survival rate, the survival rate of 59.7% without LTx in JBAR was greater than the other reported values, which were between 24% and 48%,[7-9] and it was similar with the average rate (60.3%), which was achieved by the institutions in which more than 5 patients underwent corrective surgery for biliary ateresia as reported by McKiernan et al.[3] In spite of the increasing number of survivors after LTx, there was no significant improvement in the 5-year survival rate.

As for the 10-year survival rate without LTx, 52.8% in the JBAR was greater than reported values, 33% by Laurence et al,[10] 28% by Caccia et al,[11] and 34% by Howard et al.[9] However, the actual 10-year survival rate of 66.7% was not as good as the best reported values. Further improvement of the 10-year survival rate is expected, because LTx had become widely available in Japan since the early 1990s.

It was shown that the JBAR system was functioning well with only 19 patients lost to follow-up among the 735 patients registered from 1989 to 1994. To elucidate the real role of Kasai operation in biliary atresia, a longer follow-up study for the registered patients of the JBAR is needed.

REFERENCES

1. Karrer FM, Lilly JR, Stewart BA, et al: Biliary atresia registry, 1976 to 1989. J Pediatr Surg 25:1076-1080, 1990

2. Chardot C, Carton M, Spire-Bendelac N, et al: Epidemiology of biliary atresia in France: A national study 1986-96. J Hepatol 31:1006-1013, 1999

3. McKiernan PJ, Baker AJ, Kelly DA: The frequency and outcome of biliary atresia in the UK and Ireland. Lancet 355:25-29, 2000

4. Chiba T, Ohi R, Kamiyama T, et al: Japanese biliary atresia Registry. Biliary Atresia. 79-86, ICOM Associates Inc, Tokyo, 1991

5. Ohi R, Nio M, Chiba T, et al: Long-term follow-up after surgery for patients with biliary atresia. J Pediatr Surg 25:442-445, 1990

6. Meister RK, Esquivel CO, Cox KL, et al: The influence of portoenterostomy with stoma on morbidity in pediatric patients with biliary atresia undergoing orthotopic liver transplantation. J Pediatr Surg 28:387-390, 1993

7. Houwen RH, Zwierstra RP, Severijnen RS, et al: Prognosis of extrahepatic biliary atresia. Arch Dis Child 64:214-218, 1989

8. Gauthier F, Laurent J, Bernard O, et al: Improvement of results after Kasaioperation: The need for early diagnosis and surgery. Biliary Atresia. 91-95, ICOM Associates Inc, Tokyo, 1991

9. Howard ER, Davenport M: The treatment of biliary atresia in Europe 1969-1995. Tohoku J Exp Med 181:75-83, 1997

10. Laurent J, Gauthier F, Bernard O, et al: Long-term outcome after surgery for biliary atresia. Study of 40 patients surviving for more than 10 years. Gastroenterology 99:1793-1797, 1990

11. Caccia G, Dessanti A, Alberti D, et al: More than 10 years survival after surgery for biliary atresia. Biliary Atresia. 246-249, ICOM Associates Inc, Tokyo, 1991