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Long-term outcomes of biliary atresia with splenic malformation☆,☆☆

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ABSTRACT

Background: We assessed the long-term outcomes of patients with biliary atresia with splenic malformation (BASM).
Methods: We retrospectively assessed outcomes of 255 patients who underwent the Kasai procedure (KP) at our hospital between 1972 and 2014. Clinical outcomes of 11 patients with BASM (group A: nine with polysplenia, two with asplenia) and 244 patients with isolated BA (group B) were compared.
Results: The incidence of early cholangitis and hepatopulmonary syndrome (HPS) was significantly higher in group A than in group B. Of the 11 group A patients, three died of severe cardiac defects during early infancy. Seven became jaundice free following KP, with three patients subsequently requiring liver transplantation (LTx). Four survived with their native livers for 2, 5, 22, and 23 years, respectively. Overall 20-year survival rates were 63.6% and 66.5% and 20-year native liver survival rates were 29.0% and 47.3% in groups A and B, respectively. No significant difference in cumulative survival rates was observed between both groups.
Conclusions: Long-term outcomes in BASM patients without lethal cardiac defects were comparable to patients with isolated BA. Careful follow-up may be required in patients with BASM because of a potentially higher risk of secondary complications such as HPS.

Biliary atresia with splenic malformation (BASM) is recognized to have a poor prognosis. However, long-term outcomes in this clinical subset of patients are yet to be fully elucidated. Therefore, we assessed long-term outcomes of patients with BASM at our hospital.

1. Materials and methods

We retrospectively analyzed 255 patients who underwent the Kasai procedure (KP) at Tohoku University Hospital between 1972 and 2014. They were divided into two groups: group A comprised 11 patients with BASM (nine with polysplenia, two with asplenia) and group B comprised 244 patients with isolated BA. Subsequently, clinical parameters, including age at surgery, postoperative bile drainage, number of episodes of early cholangitis, requirement for treatment of portal hypertension, and native liver/overall survival rates, were determined and compared between both groups (Tables 1 and 2).

Jaundice clearance was defined as the blood level of total bilirubin <2.0 mg/dl. Early cholangitis was defined as the development of cholangitis before 1 year of age.

The study protocol was approved by the Clinical Research Ethics Board of our institution.

Statistical analyses were performed using the chi-square test or Student's t test, where appropriate. The cumulative survival rates were analyzed using the Kaplan–Meier survival curves, and the statistical difference was assessed using the log-rank test. A probability (p) value of <0.05 was considered statistically significant.

2. Results

2.1. Age at surgery

The mean patient age at surgery was 56.6 days [standard deviation (SD), 28.1 days] and 66.3 days (SD, 22.2 days) in groups A and B, respectively. There was no significant difference between both groups ($p = 0.056$).

2.2. Type of obstruction

The types of extrahepatic biliary obstruction were classified according to the Japanese Society of Pediatric Surgeons [1].

All 11 patients in group A had type III biliary obstruction (atresia at the porta hepatis), whereas 41, 14, and 189 patients in group B had type I/I cyst (atresia of the common bile duct), type II (atresia of the hepatic duct), and type III, respectively ($p = 0.075$). The condition of the bile duct can be further divided into the following subtypes: subtype a, patent common bile duct; subtype b, atretic common bile duct; subtype c, absent common bile duct; and subtype d, unclassified. In group A, 1 patient, 2 patients, 7 patients, and 1 patient had subtypes a, b, c, and d, respectively. In group B, 45, 163, 16, and 19 patients had subtypes

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Table 1
Patient Characteristics.

		Group A	Group B	p
No. of Patients		11	244	
Female:Male		6:5	159:85	0.069
Age at the Kasai Procedure (days)	(mean, SD)	56.6, 28.1	66.3, 22.2	0.059
Type*	I/I cyst	0	41	
	II	0	14	0.075
	III	11	189	
Subtype*	a	1	45	<0.001
	b	2	163	
	c	7	16	
	d	1	19	

Type*: I/I cyst, atresia of common bile duct; II, atresia of hepatic duct; III, atresia at porta hepatis.
Subtype*: a, patent common bile duct; b, atretic common bile duct; c, absent common bile duct; d, unclassified.

Table 2
Clinical Course.

		Group A	Group B	p
Jaundice Disappearance	Yes	7	178	0.74
	No	4	66	
Early Cholangitis*	Yes	0	122	0.032
	No	11	122	
EIS*/EVL*		0	16	
PSE*		0	16	
ET* and PSE (both)		0	15	
HPS*/PPH*	Yes	2	8	0.013
	No	9	236	

Early Cholangitis*: cholangitis developing before the age of 1 year.
EIS*: endoscopic injection sclerotherapy.
EVL*: endoscopic variceal ligation.
PSE*: partial splenic embolization.
ET*: EIS and/or EVL.
HPS*: hepatopulmonary syndrome.
PPH*: portopulmonary hypertension.

a, b, c, and d, respectively. Subtype c was the most common in group A, and subtype b was the most common in group B. There was a significant difference in subtype distribution between both groups ($p < 0.001$).

2.3. Jaundice clearance

Jaundice clearance was achieved in seven (63%) and 178 (73%) patients in groups A and B, respectively. No significant difference between both groups was observed ($p = 0.74$).

2.4. Early cholangitis

The incidence of early cholangitis was assessed in each group. Although no patient developed early cholangitis in group A, 122 (50%) patients developed early cholangitis in group B. There was a statistically significant difference in the incidence of early cholangitis between both groups ($p = 0.032$).

2.5. Portal hypertension

Esophageal varices, hypersplenism, hepatopulmonary syndrome (HPS), and portopulmonary hypertension (PPH) were evaluated to assess portal hypertension. No patient in group A required endoscopic treatment (ET) such as endoscopic injection sclerotherapy (EIS) or endoscopic variceal ligation (EVL) for esophageal varices or partial splenic embolization (PSE) for hypersplenism. In group B, 16 patients underwent EIS/EVL, 16 underwent PSE, and 15 underwent both ET and PSE. Two patients in group A (18%) developed HPS and eight patients in group B (3.3%, six HPS and two PPH) developed conditions associated with portal hypertension ($p = 0.013$).

2.6. Patient outcomes and current status

In group A, two patients with asplenia and one with polysplenia died of severe cardiac defects in early infancy (patients #1, #2, and #4 in Table 3). Of the remaining eight patients, seven became jaundice free following KP; however, three patients subsequently required liver transplantation (LTx) at ages ranging from 18 months to 12 years. Indications for LTx were liver failure and HPS in one and two patients, respectively. Four patients survived with their native livers for 2, 5, 22, and 23 years, respectively.

In group B, a total of 159 patients (109 with native livers and 50 following LTx) survived and 185 patients died, including seven who underwent LTx. Four patients were associated with cardiac defects which were all successfully treated medically or surgically; thus, no patient died of cardiac defects in group B.

Native liver survival and overall survival rates more than a 20-year period were 29.0% and 63.6% in group A and 47.3% and 66.5% in group B, respectively. No significant difference was found in the cumulative survival rate between both groups (Figs. 1 and 2). On exclusion of the three patients with cardiac defects from group A, 20-year native liver survival and 20-year overall survival rates were found to be 40.0% and 87.5%, respectively (Fig. 3).

Currently, four (36.3%) and 109 (44.7%) patients are alive with their native liver in groups A and B, respectively. On exclusion of the three patients with cardiac defects from group A, the native liver survival rate became 50.0% (4/8), which was almost the same as that of group B.

Table 3
Outcome of Group A Patients.

No.	Current Age	Sex	Age at Kasai (days)	Type*1	Associated Anomaly*2	HPS*3	Outcome	Age at Death/LTx*4 (years)
1	*	F	69	III-b	AS, SI, MAL, CD	–	Dead	0.3
2	*	F	40	III-c	PS, SI, MAL, CD	–	Dead	0.12
3	*	F	128	III-c	PS, SI, MAL	–	Dead	1.62
4	*	M	61	III-d	AS, PDPV, MAL, CD	–	Dead	0.33
5	24.6	M	73	III-a	PS, SI	–	LTx*4	1.54
6	23.4	M	33	III-c	PS, SI, MAL	–	Native Liver	–
7	22.8	M	39	III-c	PS, SI	–	Native Liver	–
8	17.5	F	65	III-b	PS, PDPV, MAL	Yes	LTx*4	12.18
9	6.0	M	30	III-c	PS, MAL	–	Native Liver	–
10	5.3	F	45	III-c	PS, SI, MAL	Yes	LTx*4	3.35
11	2.5	F	39	III-c	PS	–	Native Liver	–

Type*1: III: type III; atresia at porta hepatis.
a: subtype a; patent common bile duct, b: subtype b; atretic common bile duct, c: subtype c; absent common bile duct, d: subtype d; unclassified.
Anomaly*2: AS: asplenia. CD: cardiac defect. SI: situs inversus. PS: polysplenia. MAL: malrotation. PDPV: preduodenal portal vein.
HPS*3: hepatopulmonary syndrome.
LTx*4: liver transplantation.