Liver transplantation for young adult patients with post-Kasai portoenterostomy biliary atresia: Analysis of Korean Organ Transplantation Registry database

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Background: Some young adults with native liver after Kasai portoenterostomy (KPE) for biliary atresia (BA) have a long survival period. However, a considerable number of them finally require liver transplantation (LT) due to various BA-associated complications. This study aimed to analyze the outcomes of LT in adult patients with post-KPE BA using Korea Organ Transplantation Registry (KOTRY) database.

Methods: This study was a retrospective analysis of multi-center data using KOTRY database, including 14 adult patients who underwent LT in six institutions during a 7-year period from January 2014 to December 2020.

Results: All 14 patients underwent KPE at around 1 year of age. The mean ages at LT were 25.0±5.9 years. The mean model for end-stage liver disease score was 13.5±4.6. The main reasons for LT were advanced liver cirrhosis in nine and intractable cholangitis in five. All patients received living-donor LT. The mean graft-to-recipient body weight ratio was 1.21%±0.31%. All 14 patients are currently alive during the mean follow-up period of 32.3±17.1 months. Adult BA patients were being cared for by pediatric gastroenterologists in 3 institutions, by adult gastroenterologists in 1 institution, and undetermined in 2 institutions.

Conclusion: Young adult patients with BA are a unique group of patients requiring specialist care during the transition from pediatric to adult services. Living donor LT has been the main type of LT for these patients because of donor shortage in Korea. Similar to our previous single-center study, in the present study, LT outcomes in young adult BA patients were excellent. Therefore, LT should be considered in patients showing serious BA-associated complications.

Keywords: Portal hypertension; Cholangitis; Liver cirrhosis; Portoenterostomy; Adolescent

INTRODUCTION

Biliary atresia (BA) is a chronic cholangiopathy of unknown etiology presenting in the first weeks of life. The initial treatment for the majority of infants with BA is Kasai portoenterostomy (KPE), in which the obliterated extrahepatic bile ducts are excised and bile flow is restored. After KPE, it is reported that 40%–45% of infant patients live to the age of 10 years [1,2]. The majority of them also grow up to adolescence and young adulthood. Many of these long-term survivors with their native liver are asymptomatic, but they may suffer from chronic liver disease-associated complications. Liver transplantation (LT) can be considered for patients with unsuccessful KPE or late presentation of BA with advanced liver cirrhosis. The most common indications for LT in adult BA patients include liver cirrhosis with cholestasis and variceal bleeding, and refractory cholangitis [3-5]. A single-center experience of seven adult LT cases with post-KPE BA was presented previously [5]. This study aimed to analyze the outcomes of LT performed in adult patients with post-KPE BA using the Korean Organ Transplantation Registry (KOTRY) database.

PATIENTS AND METHODS

This study was a retrospective analysis of multi-center data using the KOTRY LT database. The KOTRY LT database was searched to identify patients aged 19 years or older who underwent LT following BA diagnosis during a 7-year period from January 2014 to December 2020. Finally, 14 patients registered from six institutions were selected for this study. The diagnosis of BA at infancy was confirmed through a review of institutional medical records. The database records of these patients were collected and reviewed in October 2021. A questionnaire was sent to six institutions to inquire whether adult BA patients are cared by pediatricians or adult physicians.

The study protocol was approved by the Institutional Review Board of our institution (No. 2014-0898 and 2021-1347), and the requirement for informed consent was waived due to because informed consent had already been obtained at the time of registration to KOTRY database. This study was performed in accordance with the ethical guidelines of the World Medical Association Declaration of Helsinki 2013. Numeric data are presented as mean with standard deviation. All statistical analyses were performed using SPSS version 22 (IBM Corp., Armonk, NY, USA).

RESULTS

All 14 patients underwent KPE at around 1 year of age. The mean ages at LT were 25.0 ± 5.9 years. None of the patients had BA-splenic malformation syndrome at KPE with data available. One patient underwent partial splenectomy to decrease its size at the age of 13 years. The mean and median serum total bilirubin level at LT was 8.3 ± 10.4 mg/dL and 5.3 mg/dL (range, 0.8–38.7 mg/dL), respectively. The mean and median model for end-stage liver disease (MELD) scores were 13.5 ± 4.6 and 14 (range, 8–23), respectively. The laboratory data and the liver disease severity at the time of LT are summarized in Table 1.

Based on the pretransplant clinical profiles, all the patients showed either advanced liver cirrhosis with splenomegaly and venous collaterals or intractable cholangitis. The main reasons for LT were liver cirrhosis with portal hypertension-associated complications in nine (64.3%) patients and intractable cholangitis in five (35.7%) patients.

All the 14 patients received living-donor LT (LDLT). The graft types were modified right liver graft in seven patients, right liver graft in six patients, and extended left graft in one patient. The donor-recipient relationship was living-related in 13 cases and unrelated in one case. There was no case of ABO blood group-incompatible LDLT. The mean graft-to-recipient body weight ratio was $1.21 \pm 0.31\%$. All 14 patients are currently alive during the mean follow-up period of 32.3 ± 17.1 months. Two patients received a partial liver graft from a hepatitis B virus (HBV) core antibody (anti-HBc)-positive donor, thus HBV prophylaxis with hepatitis B immunoglobulin was performed.

A questionnaire regarding the charge physicians caring for adult BA patients revealed that these patients were cared for by pediatric gastroenterologists continuously in 3 institutions, by adult gastroenterologists in 1 institution, and undetermined in 2 institutions. These feedbacks present the transitional position of young adult BA patients from the pediatric to adult caring system.

DISCUSSION

BA is the most common indication for LT in children. BA occupied 45% of LT cases for pediatric patients aged between 0 and 5 years. The proportion of BA in LT recipients has reduced to 7.4% in adolescents aged 11–17 years, and 4.9% in young adults aged 18–24 years [6,7]. A meta-analysis revealed that 7.4% of adult BA patients who survived for more than 20 years with their native liver finally underwent

Table 1. Peritransplant profiles and survival outcomes of young adult patients who underwent liver transplantation for biliary atresia

Case no.	Recipient sex	Recipient age at LT (yr)	Recipient body weight (kg)	Rea-son for LT	MELD score	CTP score	Total bilirubin (mg/dL)	Albumin (g/dL)	Creatinine (mg/dL)	PT INR	Graft type	Donor age (yr)	Donor sex	Graft weight (g)	GRWR (%)	Survival (mon)
1	F	18	53	LC	18	9	38.7	3.1	2.35	1.46	RL	22	F	557	1.04	60
2	M	22	81	LC	12	7	3.9	3.7	0.70	0.96	MRL	24	M	1,060	1.31	59
3	M	20	61	IC	8	5	0.8	4.1	0.70	1.10	MRL	22	M	930	1.53	56
4	F	33	52	IC	9	6	1.5	3.4	0.51	1.11	ELL	35	M	414	0.79	48
5	M	24	54	LC	16	7	12.7	4.6	0.76	0.94	RL	50	F	640	1.19	33
6	M	33	60	LC	19	9	15.3	2.2	0.63	1.27	MRL	25	M	883	1.46	31
7	F	30	78	LC	15	10	5.5	2.6	0.50	1.25	RL	56	F	835	1.07	29
8	F	33	64	IC	8	7	0.8	4.1	0.53	1.13	MRL	38	M	681	1.06	28
9	F	19	72	LC	15	8	5.3	2.8	0.41	1.19	RL	48	F	623	0.87	25
10	M	22	56	LC	14	7	5.3	3.9	0.79	1.17	MRL	25	F	696	1.24	24
11	F	31	72	LC	23	10	18.3	1.9	0.30	1.69	RL	36	F	856	1.18	24
12	M	18	67	IC	10	5	1.7	4.6	0.97	1.13	MRL	26	M	618	0.92	13
13	M	26	52	LC	14	9	5.5	3.1	0.59	1.14	RL	39	F	692	1.34	12
14	M	21	64	IC	8	5	0.9	4.0	0.68	1.20	MRL	52	M	1,265	1.98	10
Incidence and mean	M=8, F=6	25.0±5.9	63.3±9.7	LC=9, IC=5	13.5±4.6	9.1±2.1	8.3±10.4	3.4±0.9	0.74±0.49	1.20±0.19	RL=6, MRL=7, ELL=1	35.6±12.0	M=7, F=7	767.9±220.5	1.21±0.31	32.3±17.1

LT, liver transplantation; MELD, model for end-stage liver disease; CTP, Child-Turcotte-Pugh; PT INR, prothrombin time international normalized ratio; GRWR, graft-to-recipient weight ratio; M, male; F, female; LC, liver cirrhosis; IC, intractable cholangitis; RL, right liver; MRL, modified right liver; ELL, extended left liver.

LT [3]. A British single-center study reported that 36 of the 514 patients (7.0%) diagnosed with BA between 1977 and 2000 were listed for LT after the age of 11 years [8]. The majority of adult BA patients with native liver are expected to develop various serious complications including cholangitis and symptomatic portal hypertension. These two complications are reported to be the most significant prognostic factors for long-term native liver survival [3,5,7,9]. The main indications for LT in BA patients are cholangitis, symptomatic portal hypertension, and synthetic liver failure [4,5,7,9-12].

The present study is the first multi-center study of LT for adult BA patients in Korea. None of the adult BA patients underwent deceased-donor LT (DDLT) in the present study, which implicates that the environment for LT in Korea is quite different from that of Western countries. Our precedent single-center study included five cases of LDLT and two cases of DDLT [5]. The DDLT cases were performed before the introduction of MELD score-based liver organ allocation system in Korea in 2016. After the MELD score-based liver organ allocation system was implemented, the possibility of DDLT allocation to adult BA patients was very low because of relatively low MELD scores [13,14]. In the present study, the mean MELD score at LT was only 13.5 ± 4.6 , which was much lower than that of patients who underwent DDLT after 2016 [14,15].

Enrollment for DDLT waiting list in young adult BA patients has a definite disadvantage compared with pediatric BA patients because such adult BA patients have to compete with other adult LT candidates with high MELD score. For instance, more than half of LT for pediatric BA patients have been performed in the form of deceased donor split or whole LT in Korea [13,16,17]. Because of the serious shortage in deceased donors in the current Korean setting, LDLT should be considered for young adults with post-KPE BA [10,14]. The posttransplant outcomes in young adult patients with post-KPE BA were excellent, as shown in the present and our previous studies [5].

Close collaboration between pediatric and adult physicians and surgeons taking care of adolescent and young adult patients with BA is essential to ensure that subtle changes in their condition are monitored closely. Seamless and timely referral for LT assessment should be a major objective irrespective of the institutional logistics of transition between pediatric and adult services [8]. In the current Korean setting, pediatric physicians have continuously cared for their BA patients for a long period from infancy to young adulthood, and then gradually handed them over to adult

physicians. Close follow-up is required for those with advanced liver disease in order to evaluate and determine the optimal timing for LT. If young adult BA patients require LT, it is reasonable to refer them to the adult LT team instead of the pediatric LT team because they are regarded as adult patients regardless of the disease entity.

A liver graft recovered from an anti-HBc-positive donor carries a considerable risk of de novo HBV infection because an anti-HBc-positive liver could have occult HBV load in the liver graft [18,19]. Thus, HBV prophylaxis with hepatitis B immunoglobulin or antiviral agent is highly recommended regardless of anti-HBs antibody status [20,21]. In the current Korean setting, either hepatitis B immunoglobulin or antiviral agent for posttransplant HBV prophylaxis is permitted by the social insurance policy.

The present study had several limitations, including its retrospective design and small sample size. Because of the nature of cohort database study, detailed patient information was limitedly available. Further follow-up studies including a larger number of patients are necessary to validate the results of the present study.

In conclusion, young adult patients with BA are a unique group of patients requiring specialist care during the transition from pediatric to adult services. LDLT has been the main type of LT in Korea for young adult patients with BA. Similar to our previous study, in the present study, LT outcomes in young adult BA patients were excellent. Therefore, LT should be considered in patients with serious BA-associated complications.

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CONFLICT OF INTEREST

All authors have no conflicts of interest to declare.

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AUTHORS' CONTRIBUTIONS

Conceptualization: SH. Data curation: WHK, SH. Methodology: MSK, JGL, NJY, YRC, DSK, YWN, JMK. Visualization: SH. Writing - original draft: WHK, SH. Writing - review & editing: All.

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