Original Article

Korean J Transplant 2021;35:177-182
https://doi.org/10.4285/kjt.21.0018

KJT
KOREAN JOURNAL OF TRANSPLANTATION

pISSN 2671-8790
eISSN 2671-8804

Indications and outcomes of liver transplantation for post-Kasai biliary atresia in young adults

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Background: Some young adults have a long survival period with native liver after Kasai portoenterostomy (KPE) for biliary atresia (BA). However, a considerable proportion of these patients require liver transplantation (LT). This study aimed to analyze the indications and outcomes of LT in young adults after a long survival period with native liver after KPE.
Methods: We selected seven patients who were 18 years or older at the time of LT out of 116 BA patients who underwent primary LT from 2008 to 2019 at Asan Medical Center.
Results: The mean ages at KPE and LT were 2.1±0.9 months and 22.0±5.1 years, respectively. Mean serum total bilirubin level and model for end-stage liver disease score at LT were 7.91±7.22 mg/dL and 15.3±6.0, respectively. The main reasons for LT were liver cirrhosis with portal hypertension-associated complications in five patients and intractable cholangitis in two patients. There were five cases of living donor LT and two cases of deceased donor LT. All the seven patients are currently alive during the mean follow-up period of 74.7±40.9 months. One patient suffered from outflow graft vein obstruction requiring endovascular stenting. Another patient showed core antibody-positivity-induced de novo hepatitis B virus infection, which was well managed with antiviral therapy.
Conclusions: Young adult patients with BA are a unique group of patients requiring specialist care regarding transition from pediatric to adult services. The outcomes of LT 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; Adolescence

Received August 23, 2021
Revised September 10, 2021
Accepted September 17, 2021

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INTRODUCTION

Biliary atresia (BA) is a chronic cholangiopathy of unknown etiology presenting in the first weeks of life. In most infants with BA, the initial treatment is Kasai portoenterostomy (KPE), in which the obliterated extrahepatic bile ducts are excised and bile flow is restored through portoenterostomy. After KPE, it is reported that 40% to 45% of infant patients live to the age of 10 years [1,2]. The majority of them may grow up to adolescence and young adulthood. Although many of these long-term survivors with their native liver after KPE are asymptomatic, there is a considerable proportion of patients that have serious complications due to chronic liver diseases. If KPE is not successful or late

HIGHLIGHTS

- **Seven young adult patients underwent liver transplantation after a long survival period with native liver after Kasai portoenterostomy for biliary atresia.**
- **The outcomes of transplantation in young adult patients were excellent, thus liver transplantation should be considered in patients showing serious biliary atresia-associated complications.**

presentation of BA with established liver cirrhosis occurs, liver transplantation (LT) can be considered as a definite treatment. The most common indications for LT in adult BA patients are liver cirrhosis with cholestasis and variceal bleeding and refractory cholangitis [3,4]. This study aimed to analyze the indications and outcomes of LT in young adult LT recipients who had survived for a long period with native liver after KPE.

METHODS

The study protocol was approved by the Institutional Review Board of Asan Medical Center (IRB No. 2021-1347), and the requirement for informed consent was waived due to the retrospective nature of this study. This study was performed in accordance with the ethical guidelines of the World Medical Association and Declaration of Helsinki 2013.

This study was a retrospective analysis using single-institution LT data from the Asan Medical Center. The LT database of our institution was searched to identify patients who had been diagnosed with BA and underwent primary LT over a 12-year period from January 2008 to December 2019. During this study period, 116 patients with BA had undergone primary LT. Among them, 7 (6.0%) patients were 18 years or older at the time of LT, thus they were selected for this study (Fig. 1). The medical records of these patients were retrospectively reviewed, with all patients followed up until July 2021.

Numeric data are presented as mean with standard deviation. All statistical analyses were performed using IBM SPSS ver. 22 (IBM Corp., Armonk, NY, USA).

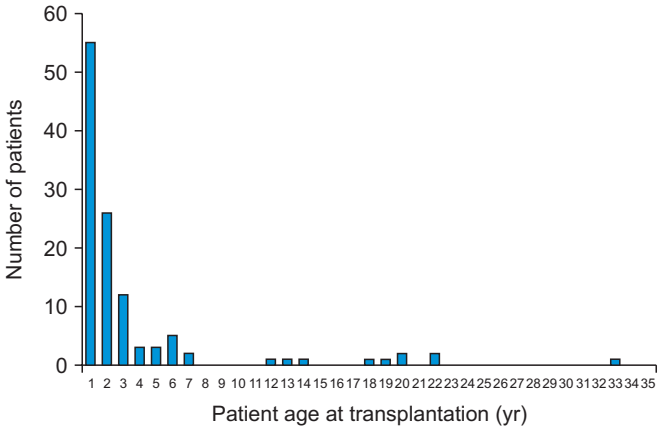

Fig. 1. Distribution of recipient age at the time of liver transplantation for biliary atresia.

RESULTS

The mean ages at KPE and LT were 2.1±0.9 months and 22.0±5.1 years, respectively. None of the patients had BA-splenic malformation syndrome at KPE with data available. One patient (case No. 1) underwent splenectomy at the age of 12 years and another patient (case No. 4) underwent partial splenectomy to decrease its size at the age of 13 years. There were five cases of living donor LT (LDLT) and two cases of deceased donor LT (DDLT). Three patients experienced variceal bleeding and one patient did hepatic encephalopathy. The mean serum total bilirubin level at LT was 7.91±7.22 mg/dL. The mean model for end-stage liver disease (MELD) score was 15.3±6.0. The laboratory data and the liver disease severity at the time of LT are summarized at Table 1.

Based on the pretransplant imaging study results, all patients showed advanced liver cirrhosis with splenomegaly and venous collaterals or intractable cholangitis (Fig. 2). The main reasons for LT were liver cirrhosis with portal hypertension-associated complications in five patients and intractable cholangitis in two patients.

Two patients underwent deceased donor whole LT in 2008 and 2016 with MELD scores of 20 and 24, respectively. After introduction of Korean MELD score-based liver allocation system in June 2016, no adult patient with BA on the waiting list in our institution has undergone DDLT.

Five patients underwent LDLT. Their donors were siblings in four patients and father in one patient. One patient (case 4) underwent ABO blood group-incompatible LDLT. The graft types were a modified right liver graft in 4 patients and an extended left liver graft in 1 patient, and their

https://doi.org/10.4285/kjt.21.0018

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)	Age at KPE (mo)	Cause of LT	VB	HE	MELD score	CTP score	Platelet count (10^3/mL)	TB (mg/dL)	Alb (g/dL)	Cr (mg/dL)	PT INR	Graft type	Donor sex	Donor age (yr)	Graft weight (g)	GRWR	Recipient survival period (mo)
1	M	18	3	PH	N	Y	24	13	179	21.0	1.7	0.40	2.46	WL	M	30	1,420	2.11	158
2	F	19	1	PH	Y	N	15	10	47	5.6	2.3	0.33	1.22	ELL	M	46	415	0.92	87
3	M	22	3	IC	N	N	12	8	368	3.9	3.7	0.71	0.96	MRL	M	23	1,060	1.31	73
4	M	20	2	PH	Y	N	8	6	59	0.8	4.1	0.71	1.10	MRL	M	21	830	1.36	68
5	F	20	1	PH	N	N	20	9	31	5.0	2.4	0.31	1.90	WL	M	66	1,400	1.73	61
6	M	33	3	PH	Y	N	19	9	73	15.0	2.2	0.63	1.33	MRL	M	25	823	1.37	42
7	F	22	2	IC	N	N	9	9	158	4.1	2.6	0.45	1.05	MRL	M	27	735	1.17	34
Mean	M=4, F=3	22.0±5.1	2.1±0.9	PH=5, IC=2	Y=3, N=4	Y=1, N=6	15.3±6.0	9.1±2.1	130.7±118.9	7.91±7.22	2.71±0.86	0.51±0.17	1.43±0.55	MRL=4, ELL=1, WL=2	M=7	34.0±16.4	954.7±364.8	1.42±0.39	74.7±40.9

LT, liver transplantation; KPE, Kasai portoenterostomy; VB, variceal bleeding; HE, hepatic encephalopathy; MELD, model for end-stage liver disease; CTP, Child-Turcotte-Pugh; TB, total bilirubin; Alb, albumin; Cr, creatinine; PT, prothrombin time; INR, international normalized ratio; GRWR, graft-to-recipient weight ratio; PH, portal hypertension; IC, intractable cholangitis; N, no; Y, yes; WL, whole liver; ELL, extended left liver; MRL, modified right liver.

Fig. 2. Peritransplant computed tomography findings of the seven young adult recipients with biliary atresia. The numbers indicate case numbers.

mean graft-to-recipient body weight ratio was 1.23±0.19. All the seven patients are currently alive during the mean follow-up period of 74.7±40.9 months.

One patient (case No. 6) who underwent LDLT using a modified right liver graft suffered from graft outflow vein obstruction. However, it was successfully managed with endovascular stenting of the graft hepatic veins and inferior vena cava.

One patient (case No. 1) underwent DDLT with a hepatitis B virus (HBV) surface antibody (anti-HBs)-positive

and core antibody (anti-HBc)-positive donor and showed de novo HBV infection at two years after LT. The recipient was anti-HBs-positive at the time of LT, thus we neglected HBV prophylaxis. The patient has shown normal liver function test and undetectable blood HBV DNA with entecavir monotherapy for 12 years.

DISCUSSION

BA is the most common indication for LT in children, particularly for those aged between 0 and 5 years (45%). On the other hand, in adolescents (11 to 17 years), its proportion deceased to 7.4%, and it occupied 4.9% in young adults (18 to 24 years) [5,6]. A meta-analysis revealed that 7.4% of BA patients who survived for more than 20 years with their native liver finally underwent LT [3]. A British single-center study reported that 36 (7%) of the 514 patients diagnosed with BA between 1977 and 2000 were listed for LT after the age of 11 years [7]. The majority of adults with BA surviving into adulthood with native liver are expected to develop 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 [3,6,8]. The main indications for LT in BA patients are cholangitis, symptomatic portal hypertension, and synthetic liver failure [4,6,8-11].

Enrollment for DDLT waiting list in young adult patients with BA has definite a disadvantage compared with pediatric BA patients because such adult BA patients have to compete with other adult LT candidates. After introduction of MELD score-based liver organ allocation system in Korea in June 2016, no adult BA patient underwent DDLT in our institution primarily because of relatively low MELD scores [12,13]. In the present study, the mean MELD score at LT was only 15.7±5.6. In contrast, more than half of pediatric LT for BA patients have been performed in the form of deceased donor split or whole LT in our institution [12,14]. Because of the serious shortage in deceased donors in the current Korean setting, LDLT should be considered for young adults with BA [9]. The posttransplant outcomes in young adult patients with post-KPE BA were excellent, as shown in the present study.

The present study is the first case series of LT for adult BA patients in Korea. The environment for LT in Korea is quite different from that of Western countries. Preliminary analysis of the Korean Organ Transplantation Registry database revealed that 25 adult patients with BA have undergone LT between 2014 and 2020, including 22 cases of LDLT and three cases of DDLT (unpublished data). We presume that the present study might reliably reflect the clinical features of Korea-nationwide experience.

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 aimed for irrespective of the institutional logistics of transition between pediatric and adult services [7]. In our institution, pediatric physicians have continuously cared for their BA patients for a long period from infancy to young adulthood. 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, they are referred 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 obtained 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 [15,16]. Thus, HBV prophylaxis with hepatitis B immunoglobulin or antiviral agent is highly recommended [17,18], but such prophylactic measures were neglected in the case No. 1. Consequently, de novo HBV infection occurred at posttransplant 2 years, which was well managed with administration of an antiviral agent.

The present study had several limitations, including its retrospective design and small sample size from a single center. Therefore, multi-center 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 regarding transition from pediatric to adult services. The outcomes of LT in young adult BA patients were excellent. Therefore, LT should be considered in patients showing serious BA-associated complications.

ACKNOWLEDGMENTS

Conflict of Interest
No potential conflict of interest relevant to this article was reported.

https://doi.org/10.4285/kjt.21.0018

Funding/Support
This study was supported by research grant from the Korean Society for Transplantation (2021-00-01009-017).

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https://doi.org/10.4285/kjt.21.0018