Effect of Repeat Kasai Hepatic Portoenterostomy on Pediatric Live-Donor Liver Graft for Biliary Atresia

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Abstract

Objectives: Treatment for patients with biliary atresia is a Kasai hepatic portoenterostomy; however, the efficacy of repeat Kasai hepatic portoenterostomy is unclear. This study sought to examine the effect of a prior Kasai hepatic portoenterostomy, especially a repeat Kasai hepatic portoenterostomy, on the outcomes of living-donor liver transplant.

Materials and Methods: One hundred twenty-six of 170 children that underwent a living-donor liver transplant between May 2001, and March 2010, received a living-donor liver transplant for biliary atresia. These patients were divided into 2 groups according to the number of previous portoenterostomies: 1 (group A, n=100) or 2 or more Kasai hepatic portoenterostomies (group B, n=26). Portoenterostomy was performed twice in 24 patients in group B, 3 times in 1, and 4 times in 1. Preoperative, operative factors, mortality, morbidity, and survival rates were examined and compared between groups.

Results: The surgical factors such as operative time, blood loss per weight, cold ischemia time, and weight of the native liver were significantly greater in group B than they were in group A. The patient survival rates were comparable in the 2 groups (94.5% in group A and 93.3% in group B), and the difference was not statistically significant. No statistically significant difference was observed between the groups with regard to vascular complications, biliary complications, and other factors including postoperative variables. Bowel perforation requiring surgical repair was more frequent in group B than it was in group A.

Conclusions: Repeat Kasai hepatic portoenterostomy might have a negative effect on patients who undergo living-donor liver transplant for biliary atresia patients with potential lethal complications such as bowel perforation. More biliary atresia patients could have a liver transplant, with improved survival and better life expectancy, if they have inadequate biliary drainage after the initial Kasai hepatic portoenterostomy.

Key words: Biliary atresia, Kasai hepatic portoenterostomy, Repeat hepatic portoenterostomy, Pediatric living-donor liver transplant

Introduction

The standard first choice treatment for patients with biliary atresia (BA) is the Kasai hepatic portoenterostomy (HPE).1-5 Despite technical refinement in the HPE technique since the induction of this procedure in the 1950s, only 15% to 20% of patients can achieve long-term survival after HPE.5-10 Subsequent liver transplant (LT) is required if the patients fail to achieve adequate long-term biliary decompression after the initial HPE or if they develop progressive liver failure despite a functioning HPE.7-14 Primary LT without the Kasai procedure is one of the therapeutic options for BA, but is controversial owing to a shortage of organs for children, higher morbidities compared to adult cases, and the necessity for long-term immunosuppressive treatment. Therefore, HPE can provide potential palliation to avoid a subsequent LT.7-11 However, even patients who achieve long-term biliary drainage may have progressive portal hypertension and liver failure, because BA has...
potential pathogenesis for liver failure with a progressive panhepatic inflammatory process of the biliary ducts despite an initially successful HPE.8-14

The efficacy of repeat HPE for BA after an unsuccessful initial HPE is unclear. Although previous reports note that a repeat HPE is not generally accepted3,12,15-19, it accounts for 30% of the patients who undergo HPE in Japan.13,20,21 Some articles20,21 have shown that multiple previous HPEs might have a negative short-term effect in patients who undergo LDLT for BA patients, but further investigation is required. This study examined the effect of prior HPE, especially repeat HPE on the outcome of LDLT.

Materials and Methods

One hundred and seventy children underwent an LDLT at Jichi Medical University Hospital during the 10 years from January 2001 to March 2010. One hundred twenty-six of those patients (74.1%) received an LDLT for BA. Left lateral segmentectomy for living-donor graft was the most usual procedure (n=95, 75.4%), followed by a left lobectomy (n=25, 19.8%), and extended left lobectomy (n=6, 4.8%). Donor hepatectomy and the recipient’s operation time, and postoperative factors were compared using the chi-square test or the Fisher exact test. Continuous variables were expressed as the mean ± standard deviation and compared using the t test. When a normal distribution was not present, they were expressed as the median and range, and compared using the Mann-Whitney U test. The patient and graft survival rates were estimated using the Kaplan-Meier method and log rank test was used compare survival. Differences of P < .05 were considered to be statistically significant. All protocols were approved by the ethics committee of the institution before the study began, and the protocols conformed with the ethical guidelines of the 1975 Helsinki Declaration.

Results

The perioperative factors, postoperative complications, and outcomes of the cases are summarized in Tables 1, 2, 3, and Figure 1. There were no significant differences between the groups in age, sex, body weight, total bilirubin, albumin, prothrombin, international normalized ratio, serum creatinine, or pediatric model for end-stage liver disease score (Table 1). However, some surgical factors such as operative time (P = .012), blood loss per weight (P = .026), cold ischemia time (P = .015), and weight of the native liver (P = .032) were significantly greater in group B than in group A (Table 2). There was no significant difference in the patient and graft survival rates at 5 years after LDLT in the groups: 94.5% and 92.1% in group A and 93.3% and 90.3% in group B (P = .442, P = .394; Figures 1 and 2). In addition, there was no significant difference in vascular complications, such as hepatic arterial thrombosis, portal venous thrombosis, hepatic vein stenosis, and biliary complications such as bile leakage and bile duct stenosis (P = .05). Other factors including

| Table 1. Preoperative Characteristics of Recipients With a Single Hepatic Portoenterostomy (Group A) and a Repeat Hepatic Portoenterostomy (Group B) Before Living-Donor Liver Transplant |
|-----------------------------------------------|-----------------|-----------------|-----------------|
| Parameter                                | Group A (n=100) | Group B (n=26)  | P Value         |
| Age at LT (mo)                           | 36.6 ± 45.8     | 57.5 ± 64.1     | .86             |
| Sex (female/male)                       | 27/73           | 8/18            | .70             |
| Bodyweight (kg)                          | 12.8 ± 10.1     | 16.8 ± 13.6     | .079            |
| Total bilirubin (μmol/L)                 | 189.8 ± 174.4   | 186.4 ± 159.0   | .94             |
| Preoperative prothrombin international normalized ratio | 1.36 ± 0.38     | 1.41 ± 0.40     | .56             |
| Preoperative prothrombin                 | 32.3 ± 5.8      | 30.9 ± 5.3      | .69             |
| Albumin (g/L)                            | 1.9 ± 1.6       | 1.9 ± 1.6       | .35             |
| Serum creatinine (μmol/L)                | 11.2 ± 9.34     | 12.8 ± 8.23     | .21             |

Abbreviations: LT, liver transplant; PELD, pediatric model for end-stage liver disease

Parametric variables are expressed as the mean ± standard deviation (SD).

*P value < .05 was considered statistically significant.
postoperative status such as acute rejection, overall relaparotomy rate, retransplant rate, and duration of hospital stay were not significantly different between the groups. However, bowel perforation that required surgical repair was more frequent in group B (11.5%) than it was in group A (1.0%; \( P = .035 \) (Table 3).

**Discussion**

The basic purpose of HPE for BA is to make fistulas of small bile ducts at the hepatic hilum to the intestinal lumen.\(^1\)-\(^6\) Kasai hepatic portoenterostomy is the treatment of choice for BA patients; however, refractory cholangitis can easily occur owing to obstruction of this fistula, because BA has potential pathogenesis for liver failure because of progressive panhepatic inflammatory process of the biliary ducts, despite an initially successful HPE.\(^7\)-\(^15\) A previous report noted that if BA patients with obvious cirrhosis, portal hypertension, and refractory cholangitis at the time of the initial HPE, they should be referred for LT.\(^7\)-\(^15\) On the other hand, some reports described the effectiveness of repeated HPE to avoid LT. The aim of repeated HPE is an extensive and sufficient resection to achieve reopening of the small bile ducts on hepatic hilum, but it is unclear whether repeat HPE should be performed for BA patients after an unsuccessful initial HPE.\(^3\)-\(^13\),\(^16\)-\(^21\) The current study investigated whether repeated HPE increased the morbidity and mortality or both at the time of LDLT.

Many authors recommend that HPE should continue to be the initial surgical procedure performed. Although 70% to 80% will fail, HPE allows a period of growth for small, malnourished BA patients, but it seems necessary to consider HPE as serving only as bridging surgery until LT can be performed.\(^7\),\(^14\),\(^18\)-\(^20\),\(^22\)-\(^25\) Published reports of the results after PE reflect a wide spectrum of results, largely reflecting significantly shorter transplant-free survival

| Table 3. Postoperative Characteristics for Recipients With Single Hepatic Portoenterostomy (Group A) and Repeated Hepatic Portoenterostomy (Group B) Before Living-Donor Liver Transplant |
|-----------------------------------------------|-----------------|-----------------|-----------------|
| **Vascular complications**                     | **Group A**     | **Group B**     | **P Value**     |
| Hepatic arterial thrombosis                    | 10              | 3               | .95             |
| Portal vein thrombosis/stenosis                | 17              | 2               | .89             |
| Hepatic vein stenosis                         | 5               | 2               | .38             |
| **Biliary complications**                      | **Group A**     | **Group B**     | **P Value**     |
| Bile leakage                                   | 6               | 0               | .44             |
| Bile duct stenosis                             | 20              | 6               | .73             |
| Relaparotomy rate (%)                         | 1.0             | 11.5            | .035*           |
| Replantation rate (%)                         | 16.0            | 15.4            | .95             |
| Duration of hospital stay (d)                 | 59.5 ± 38.8     | 54.1 ± 27.4     | .25             |

Parametric variables are expressed as the mean ± SD.

\* \( P \) value < .05 was considered to be statistically significant.
in the United States\(^{16}\) and Europe\(^{14}\) compared with Japan.\(^{13,14}\) Despite the persistent optimism in some Japanese centers that HPE might lead to a “cure rate of approximately 70% to 80%” with further technical refinements,\(^{13}\) most institutions have achieved only approximately 15% to 20% long-term survival without transplant.\(^{5-10,14}\) Although centralization to high-volume centers can improve outcomes,\(^{6}\) transplant-free survival after HPE ranges from just 30% to 50% at 5 years in western countries.\(^{26}\) In fact, the majority of long-term survivors (more than 10 years) after HPE will go on to require LT.\(^{3}\) There is accumulating evidence that BA is a panhepatic inflammatory process.\(^{8-14}\) Because extrahepatic bile duct obstruction is only a portion of the problem, the disease typically progresses despite surgical restoration of bile flow. Cholangitis also appears to have a detrimental effect on the maintenance of long-term liver function. Efforts to predict which patients will respond well to HPE have been disappointing.

Patients who never achieve adequate biliary drainage after the initial HPE are unlikely to improve with a reoperation, and these patients should be referred for LT.\(^{3}\) A repeat HPE has a low chance of yielding sufficient amounts of bile in cases of poor bile drainage. However, good candidates for repeat HPE are cases where active bile flow is achieved in the first HPE and only those patients who experience adequate biliary drainage and have a sudden decrease or cessation of bile flow will benefit from a re-exploration of their HPE.\(^{13,20,21}\) These criteria are obscure and lack a persuasive background to indicate whether repeated HPE should be performed for each case.\(^{5-12,18}\) The presence of adequate biliary drainage does not ensure long-term success, and these patients must be closely monitored for developing chronic liver failure at which time they should receive an LT. Whether the degree of native liver fibrosis as a predictor for the timing of LT remains controversial, it has been reported by some authors. In this study, there was no significant difference between single and repeated HPE groups on METAVIR scoring systems at LDLT. It may indicate that patients with BA already had damaged native livers because of congenital and/or acquired progressive panhepatic inflammatory changes, despite the repeated surgical attempts of biliary decompression.\(^{27-29}\)

Multiple laparotomies for revision of the HPE can cause intestinal complications because of extensive dissection of the tenacious adhesions between the intestine, native liver, and the abdominal wall.\(^{7-14,18-21}\) As noted in previous reports,\(^{18}\) there was a significant difference in the incidence of bowel perforation between single and multiple previous HPE in the current series. Bowel perforation after LT is a potentially fatal complication with a high mortality rate of 30% to 50%, and the duration of the operative procedure (including adhesiolysis) is independent risk factor for bowel perforation.\(^{22-25}\) Careful and gentle adhesiolysis is required to prevent bowel perforation in an LT for BA patients after HPE, but previous repeat HPE can cause a high rate of bowel perforation and lethal postoperative complications. Therefore, repeat HPE should be avoided even in patients who experience long-term biliary drainage after initial HPE followed by progressive portal hypertension, retractable cholangitis, and liver failure.\(^{12,19-21}\)

Previous articles have shown that repeat HPE can be a negative factor in an LT in addition to operative time, intraoperative estimated blood loss, and postoperative complications.\(^{18,19}\) They recommend that repeating HPE more than 2 times should be avoided, if possible. Current results show that repeat HPEs increase morbidity, but not mortality associated with LDLT in pediatric recipients. Therefore, technical refinements and perioperative management strategies can help to overcome lethal complications, although even experienced transplant teams may still have patients who experience severe intra-abdominal adhesions. However, BA patients who fail to achieve adequate biliary decompression after the initial HPE should be referred for an LT to avoid increased morbidity and potential mortality.

In conclusion, repeat HPE might have negative effects in patients who undergo LDLT for BA patients with potential lethal complications such as a bowel perforation. More BA patients are likely to need an LT with an improving survival and better life expectancy if they have inadequate biliary drainage following the initial HPE.

References


