



# Laparoscopic Kasai portoenterostomy is advantageous over open Kasai portoenterostomy in subsequent liver transplantation

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## Abstract

**Background** Native liver survival after laparoscopic Kasai portoenterostomy (Lap-PE) for biliary atresia (BA) is controversial. We examined whether a jaundice-free native liver survival rate is comparable between conventional Kasai portoenterostomy (Open-PE) and Lap-PE. Then, the impact of the two types of PE on subsequent living-donor liver transplantation (LTx) was addressed in this study.

**Methods** The jaundice-free rate in 1- and 2-year-old patients who underwent Open-PE and Lap-PE from January 2006 to December 2017 was investigated. Additionally, perioperative data (duration from the start of surgery to the completion of hepatectomy and others) of patients aged 2 years or younger who underwent LTx after either Open-PE or Lap-PE from 2006 to 2017 were evaluated.

**Results** Thirty-one (67%) out of 46 Open-PE patients and 23 (77%) out of 30 Lap-PE patients showed native liver survival with jaundice-free status at 1 year of age ( $p=0.384$ ); 29 (63%) out of 46 Open-PE patients and 19 (70%) out of 27 Lap-PE patients showed native liver survival with jaundice-free status at 2 years of age ( $p=0.524$ ); there were no significant differences. Additionally, there were 37 LTx cases after PE within 2 years of birth, including 29 Open-PE and 8 Lap-PE cases. The patients in the Lap-PE group had fewer adhesions and significantly shorter durations of surgery up to the completion of the recipient's hepatectomy and durations of post-LTx hospital stay compared to the Open-PE group. There were no differences in blood loss or duration of stay in intensive care unit between the Lap-PE and Open-PE groups.

**Conclusions** Jaundice-free native liver survival rate has been comparable between Open-PE and Lap-PE. Lap-PE resulted in fewer adhesions, contributing to better outcomes of subsequent LTx compared to Open-PE.

**Keywords** Biliary atresia · Laparoscopic Kasai portoenterostomy · Liver transplantation · Adhesion · Revision of Kasai portoenterostomy

Endoscopic surgery can provide significant benefits to patients, including fast postoperative recovery, less pain than open surgery, and minimal adhesions. It is broadly used even

for pediatric surgeries with high technical difficulty, such as those for congenital esophageal atresia or common bile duct dilatation, for which favorable outcomes have been reported [1, 2]. In contrast, endoscopic surgery had not been widely applied to the treatment of biliary atresia (BA), since a lower native liver survival rate was reported after laparoscopic portoenterostomy (Lap-PE) compared to conventional Kasai portoenterostomy (Open-PE) [3, 4]. The number of Lap-PE cases has been gradually accumulating, and they demonstrate outcomes comparable to those of Open-PE, including native liver survival rate. The critical end point of PE, which is jaundice-free native liver survival rate, has been comparable between Open-PE and Lap-PE [5–7].

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Kasai portoenterostomy (PE) is regarded as the standard initial therapy for BA. Nevertheless, the success rate of Kasai PE as a sole method to resolve BA has not improved for more than 20 years, resulting in 35–60% of the patients requiring liver transplantation (LTx) after PE [8–10]. Moreover, 80% of these patients undergo LTx within 2 years of birth [11–13]. Since the interval between the last PE and subsequent LTx is relatively short, it is important to evaluate the impact of PE on LTx. However, there are only few reports comparing Lap-PE and Open-PE with regard to the impact on subsequent LTx surgery [4, 13, 14]. Additionally, adhesions, whose minimal occurrence is one of the most important advantages of Lap-PE, were evaluated in a very limited number of cases in comparison with Open-PE, precluding adequate statistical analysis [13].

If the native liver survival rate is comparable between Lap-PE and Open-PE, it is better to select the procedure with lower impact on subsequent LTx. Initially, we evaluated the jaundice-free native liver survival rate between Open-PE and Lap-PE and thereafter determined the impact of Lap-PE on LTx, which is performed in more than 30% of patients receiving PE [15, 16].

## Materials and methods

### Patients

We obtained approval from the institutional ethics board of Nagoya University Graduate School of Medicine, Nagoya, Japan, for a retrospective review of the medical records of patients diagnosed with BA (approval number: 2015-0094) and progressive study of Lap-PE (approval number: 2014-0400) and consent from patients or their parents.

The jaundice-free native liver survival rate was investigated in 76 1-year-old and 73 2-year-old patients who underwent Open-PE and Lap-PE at our institution from January 2006 to December 2017.

Additionally, we evaluated the perioperative data of 37 patients (13 male and 24 female) who underwent LTx after PE, aged within 2 years between 2006 and 2017. The following parameters were measured: time elapsed between the start of surgery and the completion of the hepatectomy, blood loss, total duration of surgery, complications during surgery, days of intensive care unit (ICU) stay, and length of post-LTx hospital stay. Because living-donor LTxs were performed, in some cases, the time from the start of surgery to the completion of hepatectomy included the time of waiting for the donor's liver to be removed. In such cases, the waiting time was subtracted from the analysis. Patients were required to have a diagnosis of BA based on a combination of radiographic findings, uncorrectable surgical findings, and liver histology. Patients with total serum bilirubin

(T-bil) levels of 1.2 mg/dl or lower were regarded as having achieved a jaundice-free status.

### Laparoscopic Kasai portoenterostomy

All manipulations of the hilar region are done using 3-mm forceps and 5-mm microbipolar forceps. The area between the right porta hepatis, in which the right anterior branch of the hepatic artery and portal vein enter the hepatic parenchyma, and the left porta hepatis, in which the left branch of the portal vein enters the parenchyma, is dissected for anastomosis. The fibrous tissue in the hilar plate is dissected just before exposing the liver parenchyma. The fibrous tissue is not completely resected and is held lightly on the hilar plate after dissection, which is the issue of Kasai portoenterostomy that we are most concerned about. After creating a Roux-en-Y limb with exteriorization via the umbilical incision, end-to-side portoenterostomy is performed laparoscopically [17].

### Kasai portoenterostomy revision

We have been actively performing revision of Kasai PE for cases that have lower tendency for jaundice after initial surgery but are not completely jaundice-free. In patients included in the recurrent jaundice or cholangitis group who underwent successful initial PE, we also are on the indication of revision. Cases of intractable ascites and liver failure that show abnormal coagulation are not indicated for revision.

### Statistical analysis

Statistical analyses were performed using  $\chi^2$  test and Wilcoxon rank sum test for continuous variables with SAS version 9.4 (SAS Institute, Cary, NC, USA). A *p* value < 0.05 was considered statistically significant.

## Results

During the study period, PE was conducted in 78 cases at our institution, including 47 Open-PE and 31 Lap-PE cases. We excluded one case from each group. One case with severe congenital heart disease resulting in a hospital transfer was excluded from the laparotomy group. We also excluded cases in which laparoscopy had been converted to laparotomy during reoperation. All other reoperations (revision Kasai PE) were performed in the same manner as that of the initial surgery.

In December 2013, laparoscopic surgery became the standard procedure for BA, and all cases were henceforth performed laparoscopically. Lap-PE was performed in 31

patients by December 2017, and there was an instance when 25 cases reached jaundice-free status after Lap-PE. Thirty-one (67%) out of 46 Open-PE patients and 23 (77%) out of 30 Lap-PE patients showed native liver survival with jaundice-free status at 1 year of age ( $p=0.384$ ); 29 (63%) out of 46 Open-PE patients and 19 (70%) out of 27 Lap-PE patients showed native liver survival with jaundice-free status at 2 years of age ( $p=0.524$ ); there were no significant differences (Table 1). Eighteen Open-PE (39%) and 8 Lap-PE (27%) cases required subsequent LTx within 2 years of birth. Comparing the Lap-PE group with the Open-PE group, the age of surgery was significantly higher, the operation time was shorter, and the amount of bleeding was greater in the Open-PE group. The meal start time and drain removal time were significantly earlier in the Lap-PE group. This comparison may have been somewhat influenced by the historical background, as the old cases were open and the new ones were laparoscopic (Table 1).

Of the 30 patients who underwent Lap-PE, 9 underwent revision Lap-PE, of whom 8 reached jaundice-free status.

LTx was carried out in 3 cases in the revision Lap-PE group, including 1 case without jaundice-free status, 1 case with initially decreased but subsequently increased jaundice, and 1 case with repeated cholangitis.

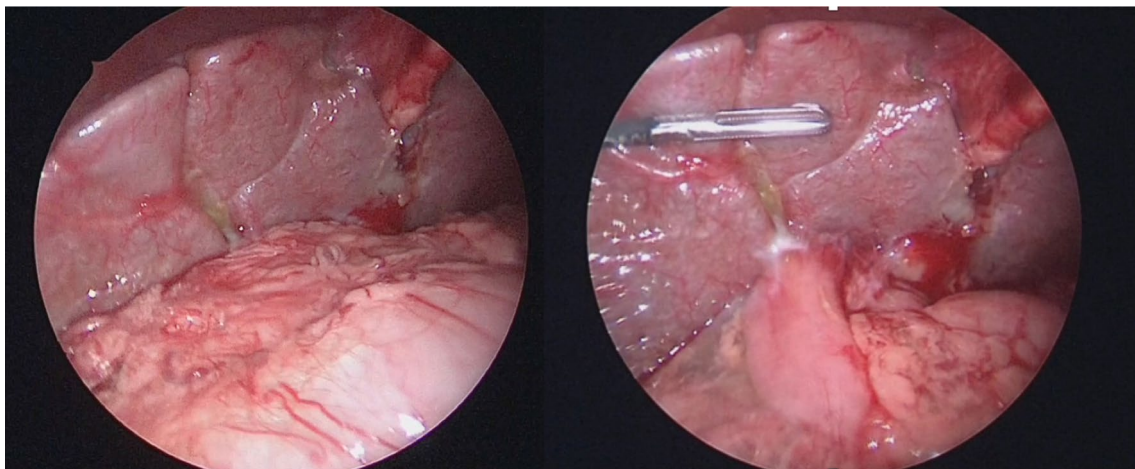
During the study period, 38 patients underwent LTx within 2 years of birth, including 11 patients who underwent PE at another hospital. We excluded one case of conversion from laparoscopy to laparotomy. Among the 37 cases included, 29 patients underwent LTx after Open-PE and 8 patients underwent LTx after Lap-PE. Lap-PE cases exhibited fewer adhesions and had significantly shorter durations of surgery up to the completion of the recipient's hepatectomy (median 136 min; range 117–210 min) compared with to Open-PE cases (median 232 min; range 141–334 min;  $p=0.0003$ ; Figs. 1, 2). The duration of post-LTx hospital stay was significantly shorter in the Lap-PE

**Table 1** Comparison of patient characteristics variables and PE between the Open-PE and Lap-PE groups

	Open-PE	Lap-PE	<i>p</i>
Patients	46	30	
Sex (male)	20 (43%)	9 (30%)	0.237
Age at PE (days)	67 (35–144)	53 (28–80)	<b>0.0003</b>
Revision	9 (20%)	9 (30%)	0.296
Operation time	249 (167–377)	315 (242–479)	<b>&lt; 0.0001</b>
Blood loss (ml)	72.5 (5–363)	23 (3–160)	<b>&lt; 0.0001</b>
Days at drain removal (post operative day)	7 (4–15)	5 (3–7)	<b>&lt; 0.0001</b>
Days at feeding (post operative day)	6 (3–11)	3 (2–6)	<b>&lt; 0.0001</b>
Jaundice-free native liver survival at 1 year	31/46 (67%)	23/30 (77%)	0.384
Jaundice-free native liver survival at 2 years	29/46 (63%)	19/27 (70%)	0.524

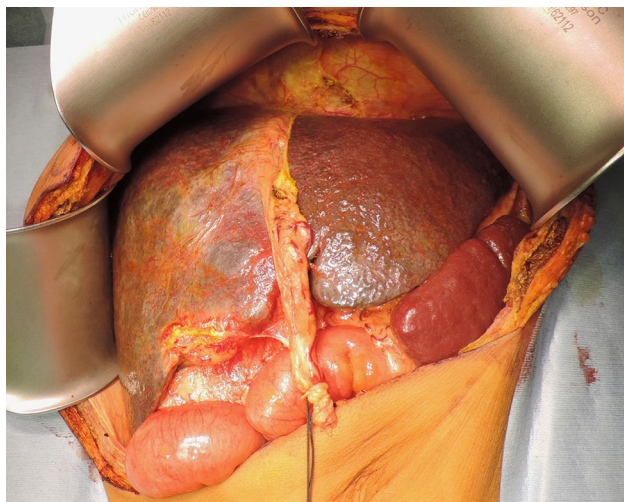
Bold values indicate significant differences

Values are presented as *n* (%) or median (range)



**Fig. 1** Site of revision in laparoscopic portoenterostomy (PE). During laparoscopic reoperation, it was not difficult to reach the PE region because there was almost no adhesion in the abdominal cavity.

Because there was no adhesion at the PE area, the operation procedure at the redo PE was not complicated



**Fig. 2** Liver transplantation after laparoscopic portoenterostomy. There were almost no adhesions seen. transplantation; ICU intensive care unit

cases (median 47 days; range 29–138 days) than in the Open-PE cases (median 87 days; range 30–384 days;  $p = 0.022$ ). There were no significant differences in blood loss or duration of ICU stays between the Lap-PE (median 598 ml; range 161–2472 ml, and median 6 days; range 2–43 days, respectively) and the Open-PE groups (median 1337 ml; range 145–5684 ml, and median 5 days; range 1–62 days, respectively). There was one intraoperative complication, inferior vena cava injury, in the Open-PE group. There were no intraoperative complications in the Lap-PE group (Table 2).

Revision Open-PE was performed in 9 of 29 patients who underwent open surgery. Open-PE in revision patients had significantly longer durations of surgery up to the completion of the recipient's hepatectomy (median 263 min; range 144–291 min) in contrast to Open-PE without revision cases (median 219 min; range 141–334;  $p = 0.043$ ; Table 3). Revision Lap-PE was performed in 3 out of the 8 patients who underwent laparoscopic surgery. There were no significant differences between the Lap-PE

**Table 2** Comparison of patient characteristics and LTx operation parameters between the Open-PE and Lap-PE groups

	Open-PE	Lap-PE	<i>p</i>
LTx within 2 years of age	29	8	
Body weight at the time of LTx (kg)	6.9 (4.3–10.7)	7.0 (4.8–8.8)	0.796
Age at LTx (days)	234 (139–608)	218 (158–569)	0.671
Revision	9 (31%)	3 (38%)	
Duration up to completion of hepatectomy (min)	232 (141–334)	136 (117–210)	<b>0.0003</b>
Post-LTx hospital stay (days)	87 (30–384)	47 (29–138)	<b>0.022</b>
Blood loss (ml)	1337 (145–5684)	598 (161–2472)	0.065
ICU stay (days)	5 (1–62)	6 (2–43)	0.766
Intraoperative complications	1 (IVC injury)	0	

Bold values indicate significant differences

Values are presented as *n* (%) or median (range)

**Table 3** Comparison of patient characteristics and LTx surgery parameters between Open-PE cases with and without revision

	Open-PE with revision	Open-PE without revision	<i>p</i>
LTx within 2 years of age	9	20	
Body weight at the time of LTx (kg)	6.5 (5.6–10.7)	7.0 (4.3–9.0)	0.962
Age at LTx (days)	270 (149–608)	231 (139–579)	0.494
Duration up to completion of hepatectomy (min)	263 (144–291)	219 (141–334)	<b>0.043</b>
Post-LTx hospital stay (days)	88 (46–319)	83 (30–384)	0.814
Blood loss (ml)	1337 (257–4691)	1260 (145–5684)	0.888
ICU stay (days)	5 (1–43)	5 (1–62)	0.943
Intraoperative complications	0	1	

Bold value indicates significant difference

Values are presented as *n* or median (range)

**Table 4** Comparison of patient characteristics and LTx surgery parameters between Lap-PE cases with and without revision

	Lap-PE with revision	Lap-PE without revision	<i>p</i>
LTx within 2 years of age	3	5	
Body weight at the time of LTx (kg)	7.3 (6.9–8.8)	7.0 (4.8–8.2)	0.297
Age at LTx (days)	382 (262–569)	183 (158–242)	<b>0.025</b>
Duration up to completion of hepatectomy (min)	125 (121–210)	140 (117–185)	0.882
Post-LTx hospital stay (days)	52 (29–65)	42 (30–138)	0.655
Blood loss (ml)	569 (161–1233)	627 (182–2472)	0.655
ICU stay (days)	2 (2–7)	6 (2–43)	0.285
Intraoperative complications	0	0	

Bold value indicates significant difference

Values are presented as *n* or median (range)

with revision (median 125 min; range 121–210 min) and Lap-PE without revision groups (median 140 min; range 117–185 min; Table 4) in terms of the duration of surgery up to the completion of the recipient's hepatectomy.

To exclude the effects of adhesions due to double open surgery, we compared Open-PE with revision and Lap-PE with revision as well as Open-PE without revision and Lap-PE without revision. Lap-PE without revision

patients had significantly shorter durations of surgery up to the completion of the recipient's hepatectomy (median 140 min; range 117–185 min) in contrast to Open-PE without revision patients (median 219 min; range 141–334 min;  $p = 0.003$ ) (Table 5). Lap-PE with revision patients had significantly shorter durations of surgery up to the completion of the recipient's hepatectomy (median 125 min; range 121–210 min) in contrast to Open-PE with

**Table 5** Comparison of patient characteristics between cases of Open-PE and Lap-PE without revision

	Open-PE without revision	Lap-PE without revision	<i>p</i>
LTx within 2 years of age	20	5	
Body weight at the time of LTx (kg)	7.0 (4.3–9.0)	7.0 (4.8–8.2)	0.759
Age at LTx (days)	231 (139–579)	183 (158–242)	0.126
Duration up to completion of hepatectomy (min)	219 (141–334)	140 (117–185)	<b>0.003</b>
Post-LTx hospital stay (days)	83 (30–384)	42 (30–138)	0.174
Blood loss (ml)	1206 (145–5684)	627 (182–2472)	0.221
ICU stay (days)	5 (1–62)	6 (2–43)	0.373
Intraoperative complications	1 (IVC injury)	0	

Bold value indicates significant difference

Values are presented as *n* or median (range)

**Table 6** Comparison of patient characteristics between cases of Open-PE and Lap-PE with revision

	Open-PE with revision	Lap-PE with revision	<i>p</i>
LTx within 2 years of age	9	3	
Body weight at the time of LTx (kg)	6.5 (5.7–10.7)	7.3 (6.9–8.8)	0.518
Age at LTx (days)	270 (149–608)	382 (262–569)	0.309
Duration up to completion of hepatectomy (min)	263 (144–291)	125 (121–210)	<b>0.021</b>
Post-LTx hospital stay (days)	88 (46–319)	52 (29–65)	0.034
Blood loss (ml)	1337 (257–4691)	569 (161–1233)	0.116
ICU stay (days)	5 (1–43)	2 (2–7)	0.574
Intraoperative complications	0	0	

Bold value indicates significant difference

Values are presented as *n* or median (range)

revision patients (median 263 min; range 144–291 min;  $p=0.021$ ; Table 6).

## Discussion

LTx for BA has dramatically improved patient survival rates [18]. Treatment of BA always includes the possibility of LTx. Nevertheless, it is best for the patient to survive with a native liver without jaundice. Therefore, it is important to perform surgery that does not interfere with future LTx while also avoiding LTx to the greatest extent possible. This premise is indispensable in determining the treatment protocol for BA, including laparotomy, laparoscopy, or revision PE. We hypothesized that if the result of Lap-PE is not different from that of Open-PE, the former would be better for BA by allowing subsequent LTx to be easier due to reduced adhesions and more rapid recovery. Thus, we conducted this study to analyze this hypothesis. Since this study aimed to evaluate the influence of PE on LTx, the period from PE to LTx was compared in cases where surgery was performed in patients younger than 2 years of age. Oetzmann von Sochaczewski et al. [16] compared the impact on subsequent LTx between 11 Open-PE cases and 8 Lap-PE cases and reported no differences in their end points, including the surgical duration up to the completion of the recipient's hepatectomy. In contrast, our evaluation demonstrated a significantly shorter duration for hepatectomy [16]. The outcome of Lap-PE for BA has remained controversial [3, 5, 6, 13, 19]. Although there are some reports in the literature arguing against the effectiveness of Lap-PE, its outcome has compared favorably with that of Open-PE at our institution and also in other standard Open-PE reports [8]. We encountered 76 Open-PE cases at our hospital during the period from 1996 through 2013, in which a jaundice-free native liver survival rate was 63% (48/76 cases). Revision PE was required in 7 out of 48 cases [20]. The jaundice-free rate in our hospital was generally comparable with other reports, although direct comparison is impossible due to differences in study design [8, 15]. In this study, we compared the results of Open and Lap-PE surgeries from 2006 to 2017 in our hospital. There was a significant difference in the age at which surgery was performed between the two groups. Since 2011, stool color information was added in maternal handbooks in Japan for early detection of BA. This information makes it faster for visiting hospital. As laparoscopic surgery became the standard procedure for BA since December 2013, all cases were henceforth performed laparoscopically; hence, the patients in the Open-PE group were older than those in the Lap-PE group, making age difference an unsuitable basis for comparison of surgical results. However, according to a study of 3160 patients with BA in Japan by Nio [21], the results of surgery up to the age of 80 days are not affected by

the age at surgery. Comparison of the Lap-PE group (with 37 patients, excluding 9 patients who were 80 days or older) with the Open-PE group revealed no significant difference in the jaundice-free native liver survival rates between the two groups at 1 year and 2 years of age (at 1 year of age: Open-PE, 27/37, 73%; Lap, 23/30, 77%,  $p=0.730$ ; at 2 years of age: Open, 25/37, 68%; Lap, 19/27, 70%,  $p=0.811$ ).

The standard treatment algorithm for patients with BA consists of PE followed by LTx if PE fails; revision of PE has tended to be viewed negatively because of the possibility of future LTx [22–24]. In our review, the transplant surgeon reported that adhesions were mild, even in cases where revision was performed in the Lap-PE group. For Open-PE patients, but not in Lap-PE cases, the effects of revisions were observed at the time of completion of hepatectomy. This may help challenge the common belief that revision hinders LTx and should not be done. Although it is a short-term result, in the Lap-PE group, 6 (67%) out of 9 patients survived jaundice-free with a native liver after revision; therefore, there is a possibility that the adoption of revision surgery may be expanded by applying Lap-PE. Future research is needed to confirm the advantage of Lap-PE seen in the current study and also to ascertain that this advantage is retained even if revision is performed.

## Limitations

Several limitations of the current study should be considered. First, no objective evaluation procedure for the severity of adhesions is available; therefore, the severity of adhesions in this study was determined based on the operative record alone. Since adhesions affect the duration of surgery up to the completion of the recipient's hepatectomy, the association between the adhesions and the period to hepatectomy completion was objectively evaluated. However, this evaluation may not accurately reflect the severity of the adhesions. Second, no established indicators of revision PE efficacy exist, and the revision could potentially influence the LTx outcomes. Finally, since Lap-PE was introduced relatively recently, the follow-up period was limited, precluding the capability to evaluate potential long-term complications, warranting further long-term and thorough evaluation with a larger study size.

## Conclusions

In this study, jaundice-free native liver survival rate has been comparable between Open-PE and Lap-PE. Lap-PE cases had a significantly shorter surgical duration up to the completion of the recipient's hepatectomy during LTx in comparison to Open-PE cases. This study demonstrated that

Lap-PE has a favorable advantage over Open-PE in terms of subsequent LTx, possibly due to reduced adhesions.

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### Compliance with ethical standards

**Disclosures** Drs. Chiyoee Shirota, Naruhiko Murase, Yujiro Tanaka, Yasuhiro Ogura, Hideya Kamei, Nobuhiko Kurata, Masahiro Nakatochi, Akinari Hinoki, Takahisa Tainaka, Wataru Sumida, Kazuki Yokota, Satoshi Makita, Kazuo Oshima, and Hiroo Uchida have no conflicts of interest or financial ties to disclose.

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