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Impact of Age of Patient and Experience of Surgeon on the Outcome after Kasai Portoenterostomy: Can We Delay the Surgery?

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Abstract

Introduction Age of patient and experience of biliary atresia (BA) center are well-known factors associated with early jaundice clearance (EJC) after Kasai portoenterostomy (KPE) in infants with BA. This study focused on the impact of age and surgeon factor on the short-term outcome after KPE within a single center.

Materials and Methods Fifty-four consecutive infants (18 boys and 36 girls) who underwent KPE from January 2010 to January 2020 were reviewed. KPE was performed in the earliest available operative session once the initial work-up was completed. In group A ($n = 41$), KPE was performed by surgeon A. In group B ($n = 13$), KPE was performed by specialists under the supervision of surgeon B (who is the mentor of surgeon A) when surgeon A was not available for operation. The demographics of patients, the EJC (total bilirubin <20 μmol/L within 6 months of KPE), and 2-year native liver survival (NLS) between the two groups were studied.

Results The median age at operation was 52 days (range 26–135 days). The overall EJC rate and 2-year NLS were 85.2 and 89.4%, respectively. Group A ($p = 0.015$) and male gender ($p = 0.029$) were statistically associated with EJC but not the age at operation ($p = 0.101$). Group A was also statistically associated with superior 2-year NLS ($p = 0.047$).

Conclusion Balancing between the impact of age at operation and the experience of surgeon on the outcome after KPE, our result suggested that KPE may be deferred until a more experienced surgeon to operate.

Keywords

- biliary atresia
- Kasai portoenterostomy
- jaundice clearance
- native liver survival
- centralization

Introduction

Biliary atresia (BA) is the most common cause of neonatal cholestasis.[1,2] It is a lethal disease until the introduction of portoenterostomy by Kasai in 1959.[3] Early jaundice clearance (EJC) after Kasai portoenterostomy (KPE) is a good prognostic factor for long-term native liver survival (NLS) in patient with BA.[4–6] On the contrary, infant with poor bile drainage after KPE will require early liver transplantation to avoid liver failure and mortality.[4,5]

Many factors may have impact on the EJC and NLS. These factors include the type of BA, the presence of splenic malformation, the cytomegalovirus status, and the degree of liver fibrosis at the time of KPE.[4–11] However, these factors are not modifiable. Conversely, the age of patient at operation and the experience of BA center are two modifiable or improvable factors for EJC.[4] BA is rare disease and a high-volume center is usually defined as a center that performed at least four to five KPE per year.[12] Centralization of BA surgery has resulted in an improvement in jaundice

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clearance and NLS in England and Finland.[12,13] On the contrary, despite there is no consensus on the best timing for KPE, the efficacy of early KPE has been repeatedly reported.[4,7]

Our center adopted a standardized perioperative management regimen since 2007. We have reported our EJC was 81% after reintroduction of open KPE.[14] We performed KPE in the earliest available operation session to avoid the potential detrimental effect of progressive fibrosis in delaying the operation, which may worsen the EJC after KPE.[4] However, there is a dilemma whether the operation should be delayed in case the more experienced surgeon is not available to operate. Since there is no report on the impact on individual surgeon in a single center on the outcome after KPE in the literature, in this study, we aimed to review our latest EJC after KPE with focus on the surgeon factor on the outcome under this "as early as possible" policy.

Materials and Methods

Study Design

From January 2010 to January 2020, 54 consecutive infants with BA underwent KPE in our center. No patient with BA underwent primary liver transplantation within the study period. Diagnostic work-up for prolonged neonatal jaundice by ultrasonography and hepatobiliary scintigraphy scans was performed in all the patients. KPE was scheduled in the earliest elective operation session once the work-up was completed. In our center, KPE was performed in the presence of experienced surgeons including surgeon A or surgeon B. Surgeon B is the mentor of surgeon A. Operative surgeon in this study was defined as the surgeon who dissected the fibrous cone and fashioned the portoenterostomy. The patients were divided into two groups according to the operative surgeon to study the surgeon factor. In group A, the operative surgeon was surgeon A only. In group B, KPE was performed by two different specialists under the close supervision by surgeon B. KPE in group B was performed when surgeon A was not available to perform the operation.

The age, sex of the patient, the bilirubin level before the operation, operative surgeon, the operative time, the EJC, and the 2-year NLS were reviewed. EJC was defined as the total bilirubin <20 µmol/L within 6 months of KPE. Patient who underwent redo-KPE within 6 months of KPE was defined as failure to achieve EJC. Possible preoperative and operative factors affecting EJC and the outcome between groups A and B were studied. Ethical approval was obtained from our Institutional Review Board (CRE Ref. No. 2019.548).

Surgical Technique

The operation was started with diagnostic laparoscopy. The technique of laparoscopic-assisted cholangiogram had been described before.[15] The operation was then converted to a laparotomy with a rooftop incision. Lysis of the triangular ligaments and falciform ligament was made. The liver was delivered outside the abdominal cavity. The distal common bile duct (if present) was first ligated and divided. Atretic gallbladder was then dissected from gallbladder fossa. Dissection of the fibrous cone was extended over the bifurcation of the portal vein. The portal vein tributaries were ligated between 6 "O" ligatures (►Fig. 1A). The fibrous cone was dissected at the level flush with the liver capsule, started at 10 o'clock of the portal plate toward 2 o'clock. After dissection, a semitransparent layer of tissue was seen over the portal plate (►Fig. 1B). Electrocautery was not used for hemostasis at porta unless there was a branch of aberrant hepatic artery entering into the center of portal plate. In this scenario, bleeding could only be controlled by electrocautery.

A 40-cm Roux-en-Y jejunal loop was then fashioned without any intussuscepted or spur valve. The Roux loop was delivered to liver hilum through the transverse mesocolon by a retrocolic route. End-to-side portoenterostomy was performed with 6 "O" interrupted sutures. The sutures were placed on the edge of the portal plate but not on the liver parenchyma. The suture bites were tiny and shallow. Usually, 12 to 14 sutures were needed on the posterior layer and 10 to 12 sutures over the anterior layer of the portoenterostomy. No drain was inserted.

Postoperatively, all infants started receiving oral prednisolone at 4 mg/kg 1 week after the operation. The dosage of steroid was adjusted weekly (4, 2, and 1 mg/kg/d). Ursodeoxycholic acid (20–30 mg/kg/d), meropenem (20 mg/kg/d), and fat-soluble vitamins were prescribed to all patients. The postoperative care decisions were made jointly by surgeons A and B.

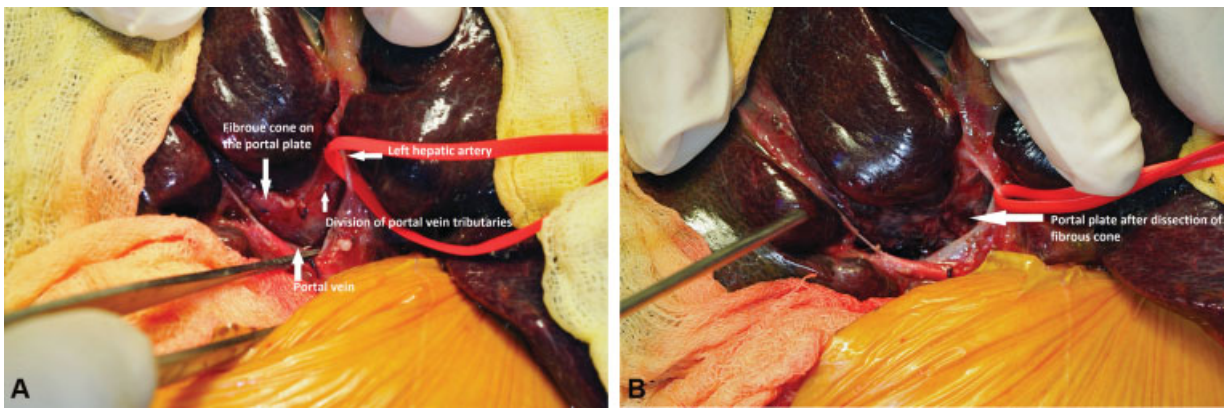

Fig. 1 (**A**) The extent of exposure of portal plate after division of portal vein tributaries. (**B**) The semitransparent appearance of portal plate after dissection of fibrous cone.

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Table 1 Demographics and the impact of clinical factors on EJC

	With EJC ($n = 46$)	Without EJC ($n = 8$)	*p*-Value
Age at Kasai, d (median, range)	52 (26–135)	48.5 (35–69)	0.101
Sex, male:female	18:28	0:8	0.030[a]
Preoperative bilirubin, μmol/L (median, range)	132.5 (84–400)	129 (83–233)	0.711
Cystic biliary atresia	8.7% (4/46)	12.5% (1/8)	0.732
Congenital malformation	4.3% (2/46)	12.5% (1/8)	0.353
Surgeon factor, group A:group B	38:8	3:5	0.006[a]
Operative time (median, range)	215 (165–355)	245 (185–305)	0.510

Abbreviation: EJC, early jaundice clearance.
Note: EJC was defined as the total bilirubin <20 μmol/L within 6 months after Kasai portoenterostomy.
[a]$p < 0.05$ was considered statistically significant.

Statistical Methods

Statistical analysis was accomplished using the SPSS program for Windows, version 22.0 (SPSS, Chicago, Illinois, United States). The Mann–Whitney's *U* test was used to compare the continuous data. Fisher's exact test was used to compare the categorical data. A binary logistic regression was used to predict EJC. Independent variables included operative surgeon, sex, age, malformation, cystic change, preoperative bilirubin level, and operation time. The survival curve was established according to the Kaplan–Meier's method and compared by the log-rank test. A $p < 0.05$ was considered statistically significant.

Results

All patients had type III BA including five with cystic BA. No patient in this study had BA splenic malformation, but three patients had other unusual congenital anomalies. One patient had congenital diaphragmatic hernia (CDH), one patient had sacral meningocele, and one patient was dysmorphic with chromosomal anomalies. The patient with CDH had cystic BA.

The median age at operation was 52 days (range: 26–135 days). The median preoperative bilirubin was 132.5 μmol/L (range: 83–400 μmol/L). The median operative time was 215 minutes (range: 163–355 minutes). The median follow-up time was 72 months (range: 4–120 months). There was no lost to follow-up in this study. The overall EJC rate was 85.2% (46/54). All male patients ($n = 18$) achieved EJC. The 2-year NLS rate was 89.4% (42/47).

►Table 1 shows the potential factors associated with EJC. Group A ($p = 0.015$) and male sex ($p = 0.029$) were associated with EJC but not the age at operation ($p = 0.101$) and preoperative bilirubin level ($p = 0.711$).

A comparison of demographics between groups A and B was performed and the results are shown in ►Table 2. There was no statistical difference on the age of operation ($p = 0.769$) and preoperative total bilirubin level ($p = 0.066$). Operative time in group A was statistically shorter ($p = 0.003$). Since there was statistical difference on gender between the two groups ($p = 0.022$), further subanalysis was performing on female patient only. Although the difference did not reach statistical significance, group A was trended toward better EJC ($p = 0.062$) in female patient. A binary logistic regression analysis was used to predict the EJC; sex was excluded from the analysis because all male patients achieved EJC. Surgeon A had an odds ratio of 21.5 for EJC (confidence interval: 1.7–259.3, $p = 0.016$). The 2-year NLS in group A was 94.4% (34/36) and was statistically superior to 72.7% (8/11) in group B ($p = 0.046$) (►Fig. 2).

Discussion

This study reported the early outcome of infant with BA after KPE with standardization of surgical technique and postoperative adjuvant therapy. As cited by other reports, the EJC

Table 2 Clinical characteristics and outcome in group A and group B

	Group A ($n = 41$)	Group B ($n = 13$)	*p*-Value
Age at Kasai, d (median, range)	52 (26–135)	52 (40–89)	0.769
Sex, male:female	17:24	1:12	0.024[a]
Preoperative bilirubin, μmol/L (medians, range)	128 (83–400)	155 (91–233)	0.066
Operative time (median, range)	210 (163–280)	250 (210–320)	0.003[a]
EJC	92.7% (38/41)	61.5% (8/13)	0.006[a]
EJC in female only	87.5% (21/24)	58.3% (7/12)	0.047[a]

Abbreviation: EJC, early jaundice clearance.
Note: EJC was defined as the total bilirubin <20 μmol/L within 6 months after Kasai portoenterostomy.
[a]$p < 0.05$ was considered statistically significant.

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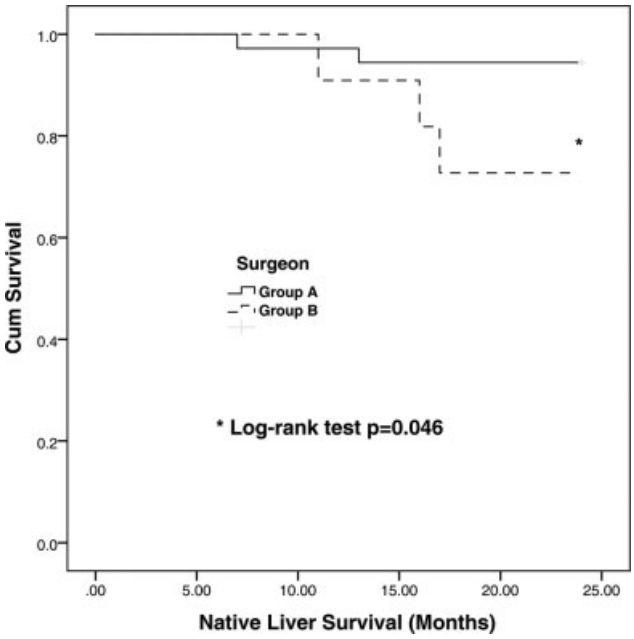

Fig. 2 Two-year native liver survival rate after Kasai portoenterostomy.

rate in high-volume centers ranged from 55 to 75%.[12,16,17] Our EJC rate of 85.2% represented the most updated and one of the best results after open KPE reported in the literature.

BA is characterized by progressive fibrosclerosing cholangiopathy.[18] It is generally believed KPE should be performed as early as possible to avoid progressive fibrosis or obliteration of intrahepatic duct. If the intrahepatic ducts are obliterated, bile flow cannot be restored even after KPE.[4,5] However, there was controversy on the impact of age of KPE and outcome reported in the literatures.[4,5,19–22] Kasai suggested KPE should be performed before 60 days of life, while other suggested the outcome was still satisfactory before 90 days of life.[4,5,7,19]

As far as we know, there is no recommendation to delay KPE in patient with suspected BA for whatever reason. In our institute, KPE was performed "as early as possible" with the presence of either surgeon A or surgeon B. We observed the median age of patient with EJC (52 days) was older than those without EJC (48.5 days), although the difference did not reach statistical significant. In this study, the oldest patient without EJC was only 69 days old. On the contrary, all eight (15%) patients older than 70 days who were operated could achieve EJC. Our results differ from most of the reports which demonstrated the older the age of patient, the poorer the outcome.[4,7] Of course, this observation may be attributed by the small number of cases included in this study and the small number of patients who failed EJC. A recent study from Korea also demonstrated that the impact of age at the time of KPE on operative outcomes became less significant over time with the increase in the single surgeon's experience.[16] We believed, besides the impact of age at operation, the presence of surgical expertise and standardized management did have a significant impact on the outcome.

Our findings should not be interpreted as early diagnosis of BA is not important.[23,24] In our region, jaundice screening was performed at 1 month of age during the government vaccination program. Thus, by the time, finishing the work-up for prolonged jaundice and surgical arrangement, our median age at operation was only 52 day, which was younger than most of the recent reports.[11,12,16] Even by deferring the operation for 1 week or 2 to have surgical expertise present, KPE would be performed well before 90 days of life. It should not affect the outcome as studies showed the outcome was still satisfactory when KPE was performed before 90 days of life.[7,22] We believe our results back up the feasibility of centralization of BA surgery in a big country.[12,13] Patients may need to travel a long distance for surgery, but the "delay" in surgery should not affect the outcome in the presence of surgical expertise.

KPE demands high level of technical precision and dexterity. KPE is one of the most technical demanding operations in pediatric surgery and the learning curve in performing open KPE has been studied.[25] In the literature, there were different techniques describing the dissection of fibrous cone and portoenterostomy.[26–28] We suggest the dissection of fibrous cone should be flushed with the liver capsule. If the dissection is too shallow, the fibrous tissue will obscure the small bile ductules. If the dissection is too deep into the liver parenchyma, bleeding and scarring may lead to fibrosis at porta.[26] There was report advocated dissection at porta until extravasation of bile.[27] In our experience, bile was not necessary seen after dissection of the fibrous cone. Even some yellowish fluid was seen, it was difficult to differentiate whether it was bile or just bile stained lymphatic fluid at porta after dissection. Besides dissection at the porta, fashioning of the portoenterostomy is also a technical demanding procedure. We placed the sutures at the edge of the transected plate and the suture bites were tiny and shallow. Other suggested the bites should be on the liver parenchyma and not on the transected plate, while some suggested the bites should be deep.[27,28]

It is a universally agreed that the more the experience of the surgeon, the more favorable the surgical outcome will be. Our result demonstrated the operative time in group A was significantly shorter than group B (►**Table 2**). However, with regard to BA surgery, the most important outcome measure is on the EJC after KPE since patients who failed to achieve EJC will require liver transplantation for continuation of life.[4] In this study, the 2-year NLS rate and EJC rate were comparable, with nearly 90% of patients could live with their native liver. Although this study did not report the long-term NLS, our previous report has shown that the 10-year NLS rate after KPE was also comparable with the EJC rate.[29]

Despite all surgeons who performed KPE in this study followed the teaching from the same mentor (surgeon B), it is reasonable to assume variation in the microelement of the surgical technique because of the difference in surgical experience. For example, the dissection of the fibrous cord may be deeper than expected or the placement of sutures may not be as wide as standard teaching. Despite less favorable outcome in group B in this study, more than 60% of EJC were achieved. It is important to point out that the result in group B should not be interpreted as below standard. On the contrary, the result was comparable with results in other well-known BA centers.[5]

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This study echoed with the importance of surgical expertise in BA surgery via centralization or collaboration on the outcome after KPE.[12,13,30,31] In many high-volume centers, there was only one or two surgeons performing KPE.[16,32] Within a dedicated team of experience surgeons in a high-volume center, individual surgeon may produce different outcome. To the best of our knowledge, the influence of the experience of individual surgeon on the outcome of KPE has not been reported before. The current study has demonstrated the presence of a surgical expertise did have a significant impact on the outcome after KPE. More than 90% of EJC after KPE could be achieved in modern era.

The impact of sex on EJC was an unexpected and interesting result we observed. BA is a female predominant disease but better EJC in male sex has never been reported in the literature.[2] All male infants in this study could achieve EJC, although 94% of KPE in male were performed by surgeon A. We could not find any explanation of this result except the possible impact by the operative surgeon and sampling bias as a result of small case volume. Further study on EJC and sex is warranted in future.

We admitted there are limitations in this study. This is a retrospective study and inherited all faults in a retrospective study. Despite retrospective data collection, all patients who were referred to our center for suspected and subsequent confirmed BA were included. We did not exclude patient with cystic or other malformation. We also performed KPE in infants with "old" age or poor hepatic function instead of referring them to a transplant center for primary liver transplantation. With this strategy, we believe by including all patients, we can reflect the real situation without bias, and thus, results are more representative. Despite our center is defined as a high-volume center for BA surgery, the case number was not comparable with other studies.[16,19,33,34] It reflected the rare incidence of BA. Multicenter study or prolonged the study period would increase the case number and the drawback including variation of surgical techniques and perioperative management.[14,33,34] The statistical comparison is also weakened by the different sizes of the cohorts and the small size of group B.

Conclusion

We have provided evidence that the surgeon factor but not the age at KPE had the impact on the EJC and 2-year NLS in our center. Our results reflected there is no rush to perform KPE as early as possible. Conversely, to achieve a better EJC, we suggest KPE may be deferred until the surgeon with more experience to perform the operation. Our finding supports the concept of centralization of BA service. We advise BA surgeons should regularly audit their own results in KPE. Surgeons with less experience may start to take up this technically demanding procedure in male patient under close supervision.

Conflict of Interest

None declared.

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