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Reappraising the portoenterostomy procedure according to sound physiologic/anatomic principles enhances postoperative jaundice clearance in biliary atresia.

RUNNING TITLE

Kasai portoenterostomy

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ABSTRACT

Background: The portoenterostomy (PE) procedure for treating biliary atresia (BA) has been so repeatedly modified that it currently hardly resembles Kasai's original PE (KOPE). Now PE involves an extended lateral dissection and a wide anastomosis (extended PE: EPE). We reappraised KOPE and created our-KOPE (OKOPE) by adhering strictly to its principles and techniques. We compared outcome of EPE and OKOPE.

Methods: We reviewed 24 consecutive cases of PE for BA performed at our institution from 2005-2011. 13 had EPE, 11 had OKOPE. Body weight, serum total bilirubin, age at PE, total steroid dosage required for jaundice clearance (JC: total bilirubin ≤1.2mg/dL), JC ratio, time taken for JC, survival rate with the native liver (SNL), and SNL after JC (SNL+JC) were compared at 16months (shortest mean follow-up). Postoperative management protocols were identical for both groups.

Results: The JC ratio was significantly higher for OKOPE (90.9%) than EPE (46.2%) (p=0.02). Both SNL and SNL+JC were significantly higher for OKOPE (90.9% and 72.7%) than EPE (30.8% and 30.8%) (p=0.003 and p=0.04, respectively). All other variables were similar for both groups.

Conclusions: Jaundice clearance following OKOPE would appear to be better than after EPE.

Keywords: biliary atresia, Kasai, portoenterostomy, jaundice clearance

INTRODUCTION

The portoenterostomy (PE) procedure for biliary atresia (BA) has been so repeatedly modified in order to achieve better rates of jaundice clearance (JC) and survival with a native liver (SNL) since it was originally performed by Kasai, that it now hardly resembles his original PE (Kasai's original PE: KOPE). Now it involves an extended lateral dissection with a very wide anastomosis (extended PE: EPE) [1-8]. We recently reviewed an original video of Kasai performing KOPE [9] and found his portal dissection was actually quite shallow and limited, resulting in a narrow PE anastomosis, with sutures deliberately placed shallowly at 2 and 10 o'clock where the original right and left bile ducts would have been, probably to minimize micro bile duct injury. We reappraised KOPE to develop our own version of KOPE (our-KOPE or OKOPE) and compared it with EPE.

MATERIALS AND METHODS

We retrospectively reviewed the medical records of 24 consecutive cases of PE for BA performed at our institution from 2005-2011. We began performing OKOPE in 2009. Thus, 13 of our cases had EPE, while 11 had OKOPE. Duration of follow-up for EPE ranged from 33 to 79 months (mean: 59 months) and for OKOPE ranged from 2 to 29 months (mean: 16 months). We used the shorter mean follow-up period of 16 months in the OKOPE group as the point of reference to compare body weight, serum total bilirubin, age at PE, total steroid dosage required for jaundice clearance (JC: total bilirubin $\leq$1.2mg/dL), time taken for JC, incidence of cholangitis, ratio of patients requiring liver transplantation (LTx), survival rate with the native liver (SNL), and SNL after JC (SNL+JC).

Extended portoenterostomy (EPE)

In EPE, dissection of the porta hepatis is not confined to the area around the base of the fibrous biliary remnant mass [11, 12] (Figure 1). The hepatic ducts usually form a cone-shaped fibrous mass cranial to the bifurcation of the portal vein. Several small vessels bridging the portal vein to the fibrous cone are divided after being ligated. The posterior aspect of the fibrous cone is freed completely. The anterior aspect of the fibrous cone and the quadrate lobe of the liver are dissected free. The fibrous biliary remnant cone must be dissected as far as the entrance of the anterior branch of the right hepatic artery on the right side and as far as the umbilical point of the left portal vein on the left. The fibrous cone is transected at the level of the posterior surface of the portal vein, and is removed from the entire dissected area; in other words, the fibrous cone has an extensive transected surface that makes the PE very wide. During PE anastomosis, as much as possible of the transected surface, including all potentially usable remnants of the intrahepatic ducts in the area between and beneath the branches of the right and left portal veins is incorporated and the right and left portal veins and hepatic arteries must either be taped or retracted in order to both transect the biliary remnant widely and to perform a wide PE. The jejunum is anastomosed to the liver parenchyma around the transected fibrous biliary remnant with interrupted 5/0 or 6/0 monofilament absorbable sutures placed deeply to prevent leakage around the anastomosis, even at the 2 and 10 o'clock positions.

Figure 1

Our version of Kasai's original portoenterostomy (OKOPE)

In both KOPE and OKOPE, dissection of the porta hepatis is confined to the area

Figure 1

around the base of the fibrous biliary remnant (Figure 1) which is transected shallowly, thus limiting the extent of the transected surface. As a result, the PE anastomosis is much narrower than in EPE. There is no need to either tape or retract the right and left portal veins and hepatic arteries, because, as in KOPE, transection is shallow and the anastomosis is also not wide. In KOPE, as observed from the video of Professor Kasai himself performing PE mentioned earlier, continuous sutures are placed in the edges of the transected biliary remnant, however, at the 2 and 10 o'clock positions where the original right and left bile ducts would have been, sutures seems to be placed shallowly, that is, only to the connective tissues at the porta hepatis, not to the edges of the transected biliary remnant [9, 10]. In OKOPE, we do not place sutures in the edges of the transected surface of the biliary remnant, and the jejunum is sutured to the liver parenchyma around the outer edge of the transected biliary remnant, except at the 2 and 10 o'clock positions, to minimize micro bile duct injury within the transected biliary remnant. These sutures are placed shallowly, but deep enough to prevent leakage. We also do not place sutures in the liver parenchyma at 2 and 10 o'clock for the same reason; but place them in the connective tissue at the porta hepatis around the outer edge of the transected biliary remnant instead, i.e., in the hepatoduodenal ligament or connective tissue over the right and left hepatic arteries at 2 and 10 o'clock, which is actually similar to KOPE.

In our cases (both EPE and OKOPE), PE anastomosis was end-to-end if possible, end-to-side otherwise, and no intussusception antireflux valves were created in the Roux-en-Y loop in any case. All PE in this series were performed under the supervision of a single surgeon (AY).

Postoperative management

Postoperative management protocols for steroid dosage, antibiotic therapy, and choice of cholagogues were identical for both groups. Specifically, a decreasing dose regime of prednisolone is administrated intravenously once C-reactive protein falls below 1.0mg/dL. Each dose is given for 3 days each, commencing with an initial dose of 4mg/kg/day, then 3mg/kg/day, 2mg/kg/day, 1mg/kg/day, and finishing with 0.5mg/kg/day. This 15 day cycle can be repeated up to 4-5 times if jaundice persists (total bilirubin > 1.2mg/dL) and there is evidence that there is clinical benefit (i.e., lower serum bilirubin or improvement in stool color). However, if jaundice persists without evidence of clinical benefit, then only 3 cycles are administered and the patient is actively considered for LTx. An important aspect of this protocol is if stools begin to turn pale, the cycle is either recommenced from the beginning or the previous dose is re-administered, depending on the situation. Double agent antibiotic therapy, usually a cephalosporin and an aminoglycoside, is routine and ceased once C-reactive protein is less than 0.3mg/dL. An intravenous cholalogue (usually dehydrocholic acid) is commenced on day 2 after PE and continued until jaundice clears. Oral cholalogues such as ursodeoxycholic acid or aminoethylsulfonic acid are administered once oral feeding is commenced, generally on day 5 after PE and continued thereafter.

Postoperative cholangitis, defined as elevated serum bilirubin (>2.5 mg/dL), leukocytosis, and normal to acholic stools in a febrile patient (>38.5^{o}C) is treated with intravenous antibiotics. Once resolved, a prophylactic antibiotic such as sulfamethoxazole/trimethoprim is administered orally.

The Student's *t*-test and chi-squared test were used for statistical analysis. P value <.05 was considered significant.

This study was approved by the Ethics Committee of Juntendo University School of Medicine and complies with the Helsinki Declaration of 1975 (revised 1983).

RESULTS

Our results are summarized in Table 1.

Table 1

Body weight at PE was 4.1±0.9kg for OKOPE and 5.4±1.8kg for EPE (p=0.05) which was not statistically significant. Age at PE was 66.9±24.1 days for OKOPE and 63.8±22.8 days for EPE (p=0.8). JC ratio was significantly higher for OKOPE (90.9%: 10/11) than EPE (46.2%: 6/13) (p=0.02). Time taken for JC was similar for OKOPE and EPE: 45.2±14.6 days for versus 41.3±18.2 days which was not statistically significant (p=0.65). The steroid dosage required for JC was lower for OKOPE (52.2±32.5mg/kg) than EPE (73.5±22.6mg/kg) but was not statistically significant (p=0.7). Incidence of cholangitis was not significantly different between OKOPE (36.4%: 4/11), and EPE (28%: 5/13) (p=0.9). The LTx ratio was significantly lower for OKOPE (9.1%: 1/11) than EPE (69.2%: 9/13) (p=0.003). SNL was significantly higher for OKOPE (90.9%: 10/11) than EPE (30.8%: 4/13) (p=0.003). SNL+JC was also significantly higher for OKOPE (72.7%: 8/11) than EPE (30.8%: 4/13) (p=0.04).

DISCUSSION

Although there are various published techniques for PE, none address the issues of location and depth of suture placement during PE specifically. In this study we attempted to assess if location and depth of suturing actually has any effect on outcome, and as such we believe this is the first report that focuses on this aspect of PE.

As mentioned in the introduction, while viewing an original video of Kasai

performing KOPE [9, 10] we saw that he transected the fibrous biliary remnant quite shallowly, resulting in a more limited transected surface. As a result, his PE anastomosis was much narrower than in EPE. Also, sutures placed at 2 and 10 o'clock at the porta hepatis, where the original right and left hepatic ducts would have been, were placed shallowly, probably to prevent injury to minute bile duct remnants that might still be present at these positions although Professor Kasai never made any reference to this in any of his publications. Incidentally, in the video, the transected surface of the biliary remnant in KOPE appears to be localized more centrally at the porta hepatis. However, since the mid-late 1980's, many Japanese, English and American pediatric surgeons became preoccupied with more extensive lateral dissection at the porta hepatis to enhance KOPE, thus EPE came to be.

We believe OKOPE has 2 distinct features that would appear to be advantageous. The first is the edges of the transected surface of the biliary remnant are not sutured to prevent ischemia and potential injury to minute bile ducts that might be present in the transected biliary remnant. The second is sutures are deliberately and intentionally placed shallowly at 2 and 10 o'clock around the outer edge of the transected biliary remnant, but not directly in the parenchyma. Thus, OKOPE could minimize the risk for damage to micro bile ducts around the porta hepatis, while the full potential for possible injury to micro bile ducts during deep suturing as performed during EPE can be fully appreciated Although depth of suturing in such a delicate area should be of concern, no surgeon, even Professor Kasai, has ever made mention of the possible importance of depth/placement of sutures during PE in any publication, and there is no general consensus among EPE practitioners about the depth of suturing.

In our series, OKOPE resulted in significantly higher JC ratios, SNL, and

SNL+JC than EPE and we believe this could be attributed to the depth/placement of sutures at 2 and 10 o'clock, where the original bile ducts would have been, a fact that we were not fully aware of until one of the authors (AY) watched a video of Professor Kasai performing his PE. In other words, the extended lateral dissection in EPE could actually cause more injury to micro bile ducts simply because the area of dissection is bigger, and any extension of lateral dissection could in fact only worsen the risk for injury. Interestingly, during a question and answer discussion after a presentation about the efficacy of OKOPE at the 36th Japanese Society of Biliary Atresia in 2009 [13], Professor Ohi confided that extended lateral dissection could potentially cause injury to the liver parenchyma itself, which could subsequently scar; an accurate explanation for the poor outcome that often follows initially good JC in EPE cases. Supporting this is a report from Tohoku University [14] that describes JC ratios falling from 70.0% for the KOPE era (1981 to 1990) to 61.0% for the EPE era (1991 to 2000), but improving again to 80% for 2001 to 2010 as PE performed are closer to KOPE than EPE. Thus, a PE with a narrower more physiological anastomosis based on sound anatomic principles would seem to be more appropriate for achieving reliable JC and OKOPE could be as good as or better than KOPE for achieving bile excretion, while EPE would appear to be inferior as a procedure.

The authors are fully aware that this study could be biased because of the difference in duration of mean follow-up and to minimize this, we chose to use the mean length of follow-up in the OKOPE group (16 months) as the point of reference for comparison between the two groups. However, mid-term and long-term results should be compared in the future to confirm if outcome of OKOPE is consistent and whether there is any change in JC ratios over time.

In conclusion, as OKOPE is associated with higher jaundice clearance in general and significantly higher jaundice clearance in patients with native livers in the short term, it could contribute to improved outcome in postoperative BA patients.

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FIGURE LEGEND

Figure 1: Comparison of suturing between EPE, KOPE, and OKOPE

Deep interrupted sutures (bold broken lines) placed in the liver parenchyma around the transected biliary remnant even at 2 and 10 o'clock [EPE].

A continuous suture (looped lines) placed along the edge of the transected biliary remnant, not the liver parenchyma, except at 2 and 10 o'clock where sutures (dotted lines) are placed in the connective tissues, not the edges of the transected biliary remnant [KOPE].

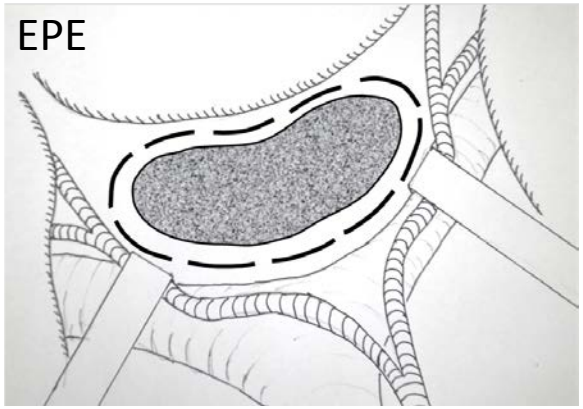
Interrupted shallow sutures (thin broken lines) placed in the liver parenchyma around the transected biliary remnant except at 2 and 10 o'clock where sutures (thin dotted lines) are deliberately placed shallowly to the connective tissues.

EPE: extended portoenterostomy

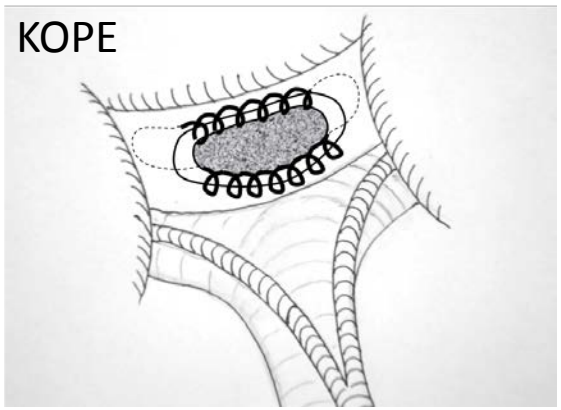
KOPE: Kasai original portoenterostomy

OKOPE: our-KOPE.

EPE



KOPE



OKOPE

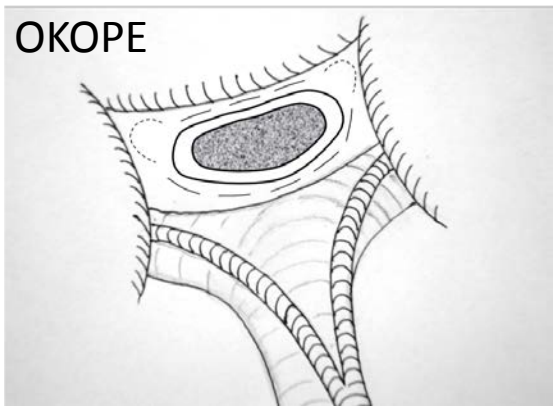


Table 1 Outcome of OV-KOPE vs DEPE

	OV-KOPE	DEPE	P value
Body weight (kg)	4.3 ± 0.5	5.4 ± 1.8	p=0.2
Age at PE (days)	73.0 ± 23.5	63.8 ± 22.8	p=0.4
Jaundice-free ratio (%)	100 (7/7)	46 (6/13)	p=0.02*
Time taken to become jaundice-free (days)	49 ± 8.9	41.3 ± 18.2	p=0.4
Steroid dosage required until patients got jaundice free (mg/kg)	55.0 ± 36.4	78.7 ± 31.2	p=0.2
Total steroid dosage (mg/kg)	55.0 ± 36.4	124.3 ± 123.0	p=0.06
Liver transplantation ratio (%)	14 (1/7)	69 (9/13)	p=0.03*
Jaundice-free ratio for patients with native livers (%)	86 (6/7)	31 (4/13)	p=0.045*
Frequency of cholangitis (%)	57 (4/7)	28 (5/13)	p=0.17

PE : portoenterostomy

OV-KOPE : our version of the Kasai original PE

DEPE : deep extended PE