REVIEW ARTICLE

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Review of redo-Kasai portoenterostomy for biliary atresia in the transition to the liver transplantation era

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ABSTRACT

Portoenterostomy (PE) is the standard therapy for biliary atresia (BA). PE offers the chance of survival to children with BA. PE was the ultimate therapeutic modality for BA before liver transplantation (LT) was available. Failure of biliary drainage with PE was almost invariably fatal in children with BA. In such cases, redo-PE was performed to salvage patients following PE failure. PE remains the standard first treatment for BA despite the availability of LT. Further, redo-PE is also performed in a limited number of cases despite the development of LT as an alternative means of PE. However, there is concern that redo-PE increases morbidity at the time of subsequent LT. Laparoscopic redo-PE has recently been described. Laparoscopic redo-PE is expected to reduce complications of LT by preventing abdominal adhesion associated with repetitive surgery. In the present article, the future utility of redo-PE and the history of its changing roles are reviewed.

Keywords: biliary atresia, laparoscopic operation, portoenterostomy, reoperatio

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INTRODUCTION

Biliary atresia (BA) is a disease characterized by progressive fibroobliteration and obstruction of the biliary tree caused by inflammation of unknown etiology. BA affects approximately 1 in 10000 live births[1,2]. Failure to properly treat BA results in cholestasis leading to progressive cirrhosis and hepatic failure, with few patients surviving for more than 2 years[3].

Portoenterostomy (PE) was developed as a treatment for BA in the 1950s. This procedure is characterized by dissecting the tissue of porta hepatis, exposing residual microscopic bile ductules, and anastomosing the jejunum with Roux-Y fashion to porta hepatis to receive the exuding bile juice. PE offers the chance of survival to children with BA, though the children with BA could hardly survive before introducing PE. PE remains a standard first treatment for BA nowadays in Japan despite the introduction of liver transplantation (LT)[4]. On the other hand, the role of redo-PE changed with the development of LT with stable prognosis.

In the present article, we review the future utility of redo-PE and the history of its changing

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roles. The target articles were searched in Pubmed with "biliary atresia + portoenterostomy + reoperation" as searching words and the articles about the review of reoperation of PE in BA were chosen.

Redo-PE during the pre-transplantation period

In Japan, LT was developed as the ultimate therapeutic modality for BA in the 1990s, with PE the only option for to salvaging children with BA before this time[5]. Therefore, failure of biliary drainage following PE was almost invariably fatal in children with BA. Pediatric surgeons therefore had to struggle with redo-PE when the first PE procedures failed to achieve sufficient bile drainage.

Altman reviewed cases of redo-PE at his institution. According to his review, seven patients underwent redo-PE, with resolution of jaundice in two (29%) patients. However, its prognostic factor was not described[6]. Saito *et al.* described the outcomes of redo-PE. Twenty-nine (60%) of 48 patients with BA underwent redo-PE with good bile excretion and survival observed in 3 (10%) out of 29 cases[7].

Around this period, enterostomy tended to be created in Roux-Y limb. The amount of bile drainage could be observed in patients who underwent this procedure. Suruga *et al.* reviewed 33 (25%) redo-PE cases out of 132 cases of BA after PE cases. According to their report, 16 (48%) out of 33 patients were not observed to have bile excretion after the first PE. Only three (19%) out of 16 cases achieved complete resolution of jaundice after redo-PE and all underwent redo-PE by the age of 4 months. The remaining 17 (52%) cases had adequate bile excretion after the first PE for a certain period followed by cessation of bile flow. Four (24%) out of 17 patients achieved complete resolution of jaundice, and all four had bile flow of greater than 40 ml a day. Further analysis revealed that two conditions were required to obtain bile flow of greater than 40 ml a day: 1) bile excretion of more than 40 ml a day for more than 30 days after the first PE; and 2) redo-PE performed within 30 days after the cessation of bile flow[8]. A separate study reported 11 (46%) out of 24 cases of redo-PE, with biliary excretion of more than 50 ml per day observed in 4 (36%) out of 11 cases[9].

As the creation of an enterostomy at the Roux-Y limb is rare in the current technique, it is not possible to measure the amount of bile flow directly. Accordingly, the time required to determine the need for redo-PE may be considerable.

Redo-PE has been evaluated based on the reduction of jaundice after the first PE. Eighteen (18%) of 100 cases treater with PE underwent redo-PE. The cases of redo-PE were divided into two groups depending on whether the disappearance of jaundice was achieved after the first PE. Eight (73%) out of 11 cases whose jaundice initially resolved after the first PE achieved jaundice-free status after redo-PE, whereas only one (14%) out of seven cases where the first PE failed achieved jaundice-free status[10]. A separate study also reported similar results with 18 (5%) out of 353 cases of BA requiring redo-PE. Five (63%) out of eight patients in the jaundice clearance group achieved jaundice-free status after redo-PE and only 1 (10%) out of 10 cases in the failed group achieved jaundice-free status[11].

The results of these studies indicate that cases where jaundice does not resolve after the first PE appear to have poor outcomes. Table 1 summarizes the results of these studies from the viewpoint of whether the first PE was successful (ie, disappearance of jaundice).

Redo-PE in the era of liver transplantation

In Japan, LT from cadaveric donors had not been performed due to the lack of the donors or the cultural background. Therefore, LT from living donors has been developed as an alternative solution. In 1989, the first living donor LT for BA was performed by Nagasue[12]. Inomata *et al.*

Table 1 The success rate of redo-PE from the viewpoint of whether the first PE was successful

Reference	Redo-PE (n)	Successful redo-PE (n)	Successful first PE	Total redo-PE (n)	Successful redo-PE (n)	%	P-value
[7]	29	3	Yes	0	0		–
			No	29	3	10.3	
[8]	33	7	Yes	16	3	18.8	1
			No	17	4	23.5	
[10]	18	9	Yes	11	8	72.7	0.02
			No	7	1	14.3	
[11]	18	6	Yes	8	5	62.5	0.03
			No	10	1	10.0	
[5]	27	5	Yes	21	5	23.8	0.25
			No	6	0	0.0	
[13]	25	5	Yes	4	2	50.0	0.17
			No	21	3	14.3	
[15]	10	4	Yes	10	4	40.0	–
			No	0	0		
[18]	46	7	Yes	22	6	27.3	0.04
			No	24	1	4.2	
[19]	22	7	Yes	6	3	50.0	0.27
			No	16	4	25.0	
total	228	53	Yes	98	36	36.7	<0.0001

Almost all studies report that cases where jaundice had not disappeared by the first PE appeared to have poor outcomes. Statistical analysis was performed with Fisher's exact test.

reviewed and compared their case experience divided into two groups according to the date of the first PE. Thirty-five cases underwent PE before 1989 and 20 (57%) out of 35 cases underwent redo-PE. As a result, 3 (15%) out of 20 cases survived without transplantation. Among the cases that underwent PE after 1990, 7 (28%) out of 25 cases underwent redo-PE and 2 (29%) out of seven cases survived without transplantation. Furthermore, it was also reported that no patient survived without LT after redo-PE in cases where bile flow had not been sufficient after the first PE[5].

According to the report by Hasegawa *et al.*, 31 out of 91 cases underwent redo-PE. However, it is unclear whether the tendency toward redo-PE was changed after LT became available. In this report, 25 cases of redo-PE were reviewed. The results of the first PE was compared in these 25 cases. Four out of 25 cases achieved resolution of jaundice after the first PE and 2 (50%) out of four underwent successful redo-PE. On the other hand, only 3 (14%) out of the 21 cases with failure of the first PE became anicteric after redo-PE[13].

Bondoc *et al.* reviewed 181 cases of BA. Sixty-four out of 181 cases survived after the first PE and 24 (13%) out of 181 cases underwent redo-PE. As a result, 11 (46%) out of 24 cases achieved native liver survival[14]. According to a review by Mendoza *et al.*, 10 (10%) out of 102 cases underwent redo-PE and 4 (40%) out of 10 case achieved native liver survival[15].

Table 1 summarizes the results of these reports from the viewpoint of whether the first PE was successful. The results of these reports indicate that cases where jaundice had not disappeared

Table 2 Median age at the first PE and redo-PE from the viewpoint of whether the redo-PE was successful or not

Reference	Redo-PE (n)	Successful redo-PE (n)	Age at operation (days)			P-value
				Redo-PE		
				Success	Failure	
[6]	7	2	First PE	62	60	0.84
			Redo-PE	97.5	104	0.55
[9]	11	4	First PE	70	72.5	0.75
			Redo-PE	117.5	131	0.67
[11]	18	9	First PE	55.5	68	0.28
			Redo-PE	254.5	138.5	0.51
[15]	10	4	First PE	44	61.5	0.20
			redo-PE	161.5	106	0.52

The median age at the time of both operations had no effect on the success or failure of the redo-PE. Statistical analysis was performed with the Mann–Whitney U test using the data described in each report.

after the first PE appeared to have poor outcomes ($p < 0.0001$). Table 2 indicates the median age at the first PE and redo-PE from the viewpoint of whether the redo-PE was successful or not. The median ages at both operations appeared to have no effect on the success or failure of redo-PE.

Regarding the tendency for redo-PE in the pre-LT period, the proportion of cases requiring redo-PE has been decreasing and its success rate has been increasing. This finding is thought to be attributable to the development of LT as an alternative means of treating BA and applying redo-PE to only select cases. The indication for redo-PE is limited to cases such as acute development of jaundice after a successful first PE or cases with recurrent cholangitis.

On the other hand, previous discussion regarding redo-PE has been more focused on the impact on subsequent LT than success rate or prognostic factors as LT becomes more common. Compared with patients who did not undergo redo-PE, redo-PE cases tended to have higher blood loss per weight[16,17], higher transfusion volumes per weight[16,17], longer operative time[14,17], longer cold ischemic time[17], and more frequent bowel perforation[16,17]. However, the overall survival rate did not significantly differ[14,16,17]. These differences appeared to be due to intraabdominal adhesions after multiple surgeries.

Long term prognosis

The actual prognosis of patients following redo-PE has been described in a few articles. Nakamura *et al.* reviewed 46 cases of redo-PE from five hospitals. Their cases were divided into two groups according to whether the resolution of jaundice had been achieved following the first PE. Twenty-two cases were assigned to the successful first PE group and 6 (27%) out of 22 cases achieved anicteric survival with their native liver. The first PE failed in the remaining 24 cases. Only one out of 24 cases survived with their native liver without jaundice. However, six out of seven cases surviving with their native liver without jaundice had multiple morbidities associated with BA such as recurrent cholangitis, portal hypertension, or hypersplenism. The likelihood of anicteric survival with the native liver was reported as 37.5%, 24.8%, 21.7%, 16.2%, 10.8%, and 10.8% at 5, 10, 15, 20, 25, and 30 years after the first PE, respectively[18].

Some reports have compared the likelihood of native liver survival in redo-PE cases compared

to single PE cases. Shirota *et al.* reported a series of redo-PE cases. Three (50%) cases achieved anicteric survival with their native liver among six cases of successful first PE. Whereas 4 (25%) cases achieved anicteric survival with their native liver among 16 cases where the first PE failed. They described the likelihood of survival with the native liver in redo-PE cases as over 60% and to be comparable to the likelihood in cases without redo-PE[19]. Bondoc *et al.* reported the likelihood of survival with the native liver for redo-PE cases was higher that cases not requiring redo-PE, with survival rates of 56%, 49%, and 39% at 5, 10, and 15 years after the first PE, respectively. Whereas the corresponding rates of survival with the native liver for patients who did not undergo redo-PE were 40%, 31%, and 22%, respectively. However, no significant difference was observed between the two groups[14].

The prognosis after redo-PE in BA patients appears to vary between reports. However, redo-PE may be effective in selected cases.

Laparoscopic redo-PE and the influence for LT

Recently, some institutions have adopted laparoscopic PE for BA. A systematic review revealed that the prognosis of laparoscopic PE is worse than that of open surgery[20]. However, the results were only short-term and the evaluation of laparoscopic PE remains controversial.

On the other hand, laparoscopic redo-PE may be deemed effective if redo-PE is shown to increase the morbidity of subsequent liver LT due to abdominal adhesion associated with multiple surgeries. Murase *et al.* reported their case experience. Seven (35%) out of 20 cases of open redo-PE survived with their native liver, whereas 3 (75%) out of four cases of laparoscopic redo-PE survived with their native liver. However, this difference appeared to be due to the difference in follow-up period. Further, one patient underwent LT after laparoscopic redo-PE. Though this was a single case report, the time required for hepatectomy at LT was shorter than that of open redo-PE[21].

CONCLUSIONS

In the period when LT was unavailable, failure of the first PE was fatal for BA patients. Therefore, the struggle to perform redo-PE was only the means of saving patients. However, as LT can be performed with consistent results, the value of redo-PE may be lower than in the past. It seems worthwhile to perform redo-PE in selected cases, e.g., cases where first PE achieved jaundice clearance, as some cases maybe be able to avoid LT. Redo-PE may increase the morbidity of subsequent LT. However, laparoscopic redo-PE may be able to minimize the influence of redo-PE on LT.

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