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Usefulness and safety of endoscopic retrograde cholangiopancreatography in children with pancreaticobiliary maljunction

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ABSTRACT

Background: To assess the diagnostic ability and safety of endoscopic retrograde cholangiopancreatography (ERCP) in in-depth preoperative examination of children patients with pancreaticobiliary maljunction (PBM).
Methods: In 63 patients with a definite diagnosis of PBM, the ability to visualize the bile and main pancreatic ducts was compared between ERCP, which was performed in 63 patients with a definite diagnosis of PBM, and magnetic resonance cholangiopancreatography (MRCP), which was performed before ERCP in 29 patients. For ERCP, its complications were also evaluated.
Results: The intrahepatic bile ducts could be visualized using ERCP in 44 patients (69.8%) and using MRCP in 18 (62.1%). The extrahepatic bile ducts could be visualized using ERCP in 59 patients (93.7%) and using MRCP in 29 (100%). The rates of the visualization of the main pancreatic duct and pancreaticobiliary ductal union were significantly higher in using ERCP than in using MRCP (96.8 vs. 41.4% and 90.5 vs. 37.9%, respectively; $P < 0.0001$). As complications, hyperamylasemia developed in 12 patients (19%), but no other severe complications such as pancreatitis were observed.
Conclusions: ERCP as part of an in-depth preoperative examination of children with PBM is useful and safe.
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Pancreaticobiliary maljunction (PBM) is a congenital anomaly defined as "junction of the pancreatic and bile ducts located outside the duodenal wall" in which the action of the sphincter of Oddi, which prevents the mixture of pancreatic juice and bile, does not functionally affect the junction [1]. As a result, reflux of pancreatic juice into the biliary tract due to the higher pressure within the pancreatic duct than the bile duct induces biliary mucosal injury. In addition, stasis of the mixture of pancreatic juice and bile induces various pathological conditions such as pancreatitis and pancreatic stones, and also increases the incidence of biliary tract cancer in a wide age range from the young to adults [2]. Preventive surgery for PBM is performed even in children. Therefore, an early accurate diagnosis is necessary.

It has been reported that information for determining the necessity of cholangiopancreatic pediatric surgery in children with PBM can only be obtained using endoscopic retrograde cholangiopancreatography (ERCP) or intraoperative cholangiography [3]. With the recent advances in diagnostic imaging techniques, there have been many studies on the diagnostic ability of magnetic resonance cholangiopancreatography (MRCP) in children with PBM. In these studies, MRCP was compared with ERCP or direct cholangiography such as intraoperative cholangiography [4]. The diagnostic rate of MRCP varied markedly (40%–80%) among the studies [5] and remains inadequate. ERCP is an invasive procedure with a risk of complications such as pancreatitis, and its use requires a careful evaluation even in adults. Many studies have shown that ERCP can be safely performed in children and adults in special institutions with experienced endoscopists [6]. In this study, we evaluated the safety and ability of ERCP to visualize the pancreaticobiliary areas to obtain necessary pre-operative information.

1. Patients and methods

Between April 2002 and March 2012, 67 consecutive patients with suspected PBM were referred to our department from the Department of Pediatric Surgery for an in-depth preoperative examination. Of the 67 patients, 63 who were diagnosed with PBM using ERCP were included in the study. These patients comprised 18 boys and 45 girls with an age range of 4 months to 13 years (mean, 3.9 ± 3.5 years) at the time of examination (Fig. 1). All operations were performed by one surgeon (H.A.). Extrahepatic bile duct resection and bilio-jejunal anastomosis were performed in all 63 cases. Of the 31 patients with intrahepatic bile duct stenosis, the duct was resected or reconstructed from inside the lumen of the common hepatic duct, and the procedures were

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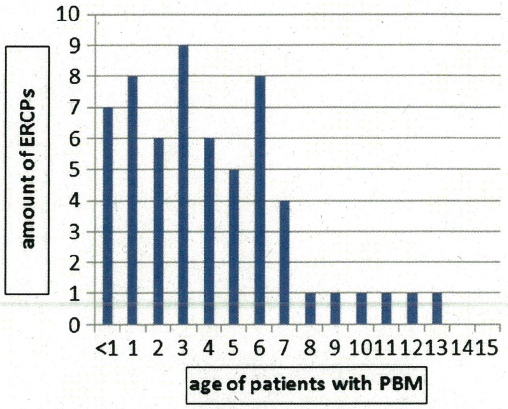

Fig. 1. Age distribution of patients with PBM. The age of patients with pancreaticobiliary junction was distributed mainly between 1 and 6.

successful in all cases. Symptoms that led to the detection of PBM and the diagnostic modalities that were used prior to ERCP were evaluated in all 63 patients. The rates of visualization of the following areas, which need to be visualized as part of the preoperative assessment for PBM conducted by pediatric surgeons, were also evaluated retrospectively: 1) intrahepatic bile ducts, 2) extrahepatic bile ducts, 3) main pancreatic duct, and 4) pancreaticobiliary ductal union. MRCP and ERCP images were compared to examine the quality of the images of the pancreaticobiliary ductal union, which is the most important in the diagnosis of PBM.

According to the diagnostic criteria of the Japanese Clinical Practice Guidelines for Pancreaticobiliary Maljunction proposed by the Japanese Study Group on Pancreaticobiliary Maljunction in August 2012 [1], the following condition must be met to define PBM: "an abnormally long common channel and/or an abnormal union between the pancreatic and bile ducts must be evident by direct cholangiography, such as ERCP, PTCD, or intraoperative cholangiography".

Visualization of the intrahepatic bile ducts was defined as visualization of both the bifurcation of the anterior (segment 5 plus 8) and posterior (segment 6 plus 7) segmental ducts along with the bile ducts of segments 2 and 3. The visualization of the main pancreatic duct was defined as continuous visualization of the main pancreatic duct from the pancreatic head to the body. Visualization using MRCP was evaluated in 29 patients after excluding cases with unclear details of the imaging conditions, or those that underwent imaging at < 1.5 T. All patients required sedation during MRCP, such as chloral hydrate (30–50 mg/kg, rectally) and/or triclofos sodium (20–80 mg/kg, orally) and/or midazolam (0.15–0.30 mg/kg, intravenous injection), and the MRCP visualization rates of the same anatomical areas assessed in ERCP were evaluated. MRCP was performed using Avanto 1.5 T (Siemens) or Visart (Toshiba). For statistical analysis, the χ^2 test was used and all analyses were performed using the SPSS version 20 software (IBM Japan Inc., Tokyo, Japan). *P* values < 0.0001 were considered statistically significant.

Post-ERCP pancreatitis was the main complication that was evaluated. Post-ERCP pancreatitis was defined as the presence of pancreatic pain persisting for ≥ 24 h and a serum amylase level ≥ 3 times the normal level (37–125 IU/L) 18 h after ERCP, and its diagnosis was made by experienced pediatricians [7]. ERCP was carried out under general anesthesia, which was performed by staff in the Department of Anesthesiology. For endoscopy, PJF 7.5 (tip outer diameter, 7.8 mm; channel diameter, 2.0 mm; Olympus) and JF240 (tip outer diameter, 12.6 mm; channel diameter, 3.2 mm; Olympus) were used for infants and for school children, respectively. This study was approved by the Institution Review Board of Nagoya University Graduate School of Medicine.

Table 1
Sensitivity of ERCP and MRCP in pediatric PBM.

	ERCP (n = 63)	MRCP (n = 29)	*p*
Intrahepatic bile duct	44 (69.8%)	18 (62.1%)	0.460
Extrahepatic bile duct	59 (93.7%)	29 (100.0%)	0.213
Main pancreatic duct	61 (96.8%)	12 (41.4%)	<.0001
Pancreaticobiliary ductal union	57 (90.5%)	11 (37.9%)	<.0001
Mean age (range)	3 y, 10 mo (4 mo–13 y)	3 y, 9 mo (6 mo–13 y)	
Minimum age for visualization of PBM	4 mo	2 y, 3 mo	

2. Results

All 63 patients had a definite diagnosis of PBM. With regard to symptoms that led to the detection of PBM, abdominal pain was the most frequently observed (48 patients, 76.2%), followed by vomiting (32 patients, 50.8%), jaundice (18 patients, 28.6%), fever (10 patients, 15.9%), an abdominal mass (9 patients, 14.3%), and whitish stools (8 patients, 12.7%). Clinical symptoms such as abdominal pain were evident only in patients who could verbalize. Other symptoms/signs could be analyzed objectively by palpation and examination. Patients with abdominal pain included one patient who had undergone surgery for biliary tract perforation and one who had undergone endoscopic lithotripsy for common bile duct stones combined with endoscopic sphincterotomy (total of two patients).

With respect to diagnostic modalities that were employed prior to ERCP, use of MRCP was the most common (59 patients, 93.7%), followed by abdominal ultrasonography (34 patients, 54.0%), and computed tomography (18 patients, 28.6%). As shown in Table 1, ERCP was performed in 63 patients and MRCP in 29. Of the 59 patients who underwent MRCP, 30 were excluded from analysis because the details of the imaging conditions were unclear, as was mentioned in the Patients and Methods section. The duration of the MRCP procedure ranged from 22 to 59 min (mean ± SD, 38.84 ± 12.14 min), and the duration of the ERCP procedure ranged from 3 to 32 min (mean ± SD, 14.08 ± 9.15). The duration of the MRCP procedure was calculated from the start to completion of the final scan, and the duration of the ERCP procedure was calculated from the time of insertion of the endoscope to the time of endoscope withdrawal.

The intrahepatic bile ducts were visualized in 44 patients (69.8%) using ERCP and in 18 (62.1%) using MRCP. The extrahepatic bile ducts were visualized in 59 patients (93.7%) using ERCP and in 29 (100.0%) using MRCP ($P = 0.213$). The intra- or extrahepatic bile duct visualization rate did not significantly differ between ERCP and MRCP. The rates of visualization of the main pancreatic duct and pancreaticobiliary ductal union were significantly higher with ERCP than with MRCP (96.8% vs. 41.4% and 90.5% vs. 37.9%, respectively; $P < 0.0001$). ERCP was adopted as the gold standard for 57 cases (90.5%) and intraoperative cholangiography was adopted as the gold standard for the remaining 6 cases. Four months was the youngest age at which detailed anatomy of the PBM was demonstrable in our ERCP series. On the other hand, detailed anatomy of the PBM was not demonstrable by MRCP in patients younger than 2 years and 3 months in our MRCP series.

With respect to complications, an increase in serum amylase level was observed in 12 patients (20.0%). These patients showed a mean serum amylase level of 198.3 IU/L (132–392 IU/L) but none of them developed pancreatitis that fulfilled the definition of post-ERCP pancreatitis. Severe complications such as cholangitis or bleeding did not occur.

With respect to the characteristics of the pancreaticobiliary ductal union in MRCP images, all 11 patients in whom the pancreaticobiliary ductal union could be visualized using MRCP showed a common channel length ≥ 10 mm (mean, 20.5 mm; 12.8–31.9 mm) in the ERCP images. Of 18 patients in whom the pancreaticobiliary ductal union could not be visualized using MRCP, 8 showed a common channel length < 10 mm (mean, 7.0 mm; 2.7–9.5 mm) in the ERCP images

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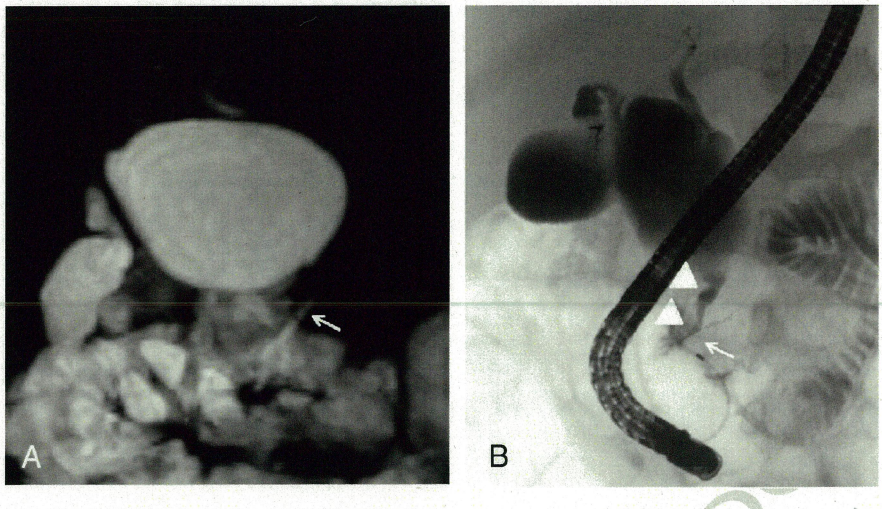

Fig. 2. A male aged 2 years and 7 months. MRCP (A) suggested a common channel (arrow), but the pancreaticobiliary union was not visualized, and a definite diagnosis of PBM could not be made. ERCP (B) showed pancreaticobiliary maljunction with a 6.7-mm common channel (arrow) and a narrow segment (arrowheads), providing a definite diagnosis.

(Fig. 2.). Six of the other 10 patients showed a common channel length ≥ 10 mm (mean, 16.6 mm; 13.2–22.4 mm). In 5 of the 6 patients, the presence of protein plugs was confirmed in the common channel during ERCP (Fig. 3). Of these 5 patients, 3 underwent stenting during ERCP because of persistent cholangitis symptoms, which resulted in symptomatic improvement and avoidance of an emergency operation.

3. Discussion

In an in-depth preoperative assessment of children with PBM, detailed information on the following areas, which were evaluated in the present study, should be available: 1) intrahepatic bile ducts, 2) extrahepatic bile ducts, 3) main pancreatic duct, and 4) pancreaticobiliary ductal union. With regard to the intra- and extrahepatic bile ducts, the presence of localized extrahepatic bile duct dilation accompanied by localized intrahepatic bile duct dilation indicates the presence of relative stenosis at a site of the hepatic hilar bile duct. If biliary tract reconstruction is performed in the presence of stenosis, recurrent postoperative cholangitis and intrahepatic stones may occur [8]. Therefore, it is very important to detect stenosis preoperatively [8]. In the present study, the intra- or extrahepatic bile duct visualization rate did not significantly differ between ERCP and MRCP. Complications other than hyperamylasemia did not develop in any patient. However, the injection of contrast medium at a high dose into markedly dilated bile ducts is associated with the risk of cholangitis and cholangiovenous reflux. To avoid these complications, we aspirated contrast medium as much as possible after imaging and avoided excessive injection of contrast medium. Because no significant difference was observed between ERCP and MRCP, it is necessary to reach a careful preoperative diagnosis by comparing the ERCP findings with the MRCP findings in these areas depending on individual cases. Intraoperative cholangiography may be necessary for safe surgery and to reduce the risks of postoperative cholangitis, intrahepatic stones and intrahepatic cholangiocarcinoma.

The pancreaticobiliary ductal union is located above the common channel and is a frequent site of protein plugs that are considered to cause symptoms such as abdominal pain, vomiting, jaundice and hyperamylasemia in patients with PBM. Kaneko et al. [9] reported that an increase in pressure within the pancreaticobiliary tract due to protein plug impaction in the common channel, or pressure surrounding the pancreatic and bile ducts such as narrowing of segments, induces obstructive symptoms. [10] Therefore, the use of various imaging techniques to obtain detailed information on the area around the pancreaticobiliary ductal union is important for making a definite diagnosis of PBM and to detect protein plugs that can sometimes cause

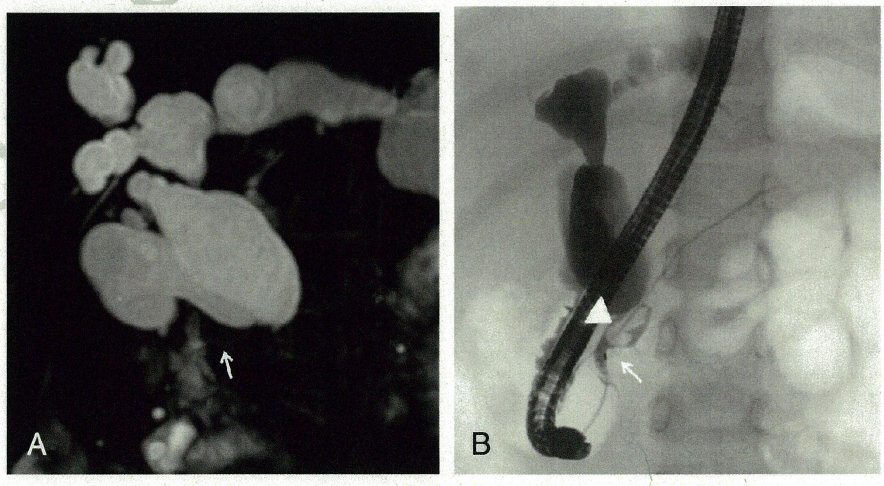

Fig. 3. A female aged 4 years and 2 months. MRCP (A) visualized the duct of Santorini (arrow), but not the common channel, pancreaticobiliary ductal union, or the main pancreatic duct. ERCP (B) showed a 13.3-mm common channel (arrow) and a protein plug (arrowhead) in the pancreaticobiliary ductal union, leading to a diagnosis of pancreaticobiliary maljunction.

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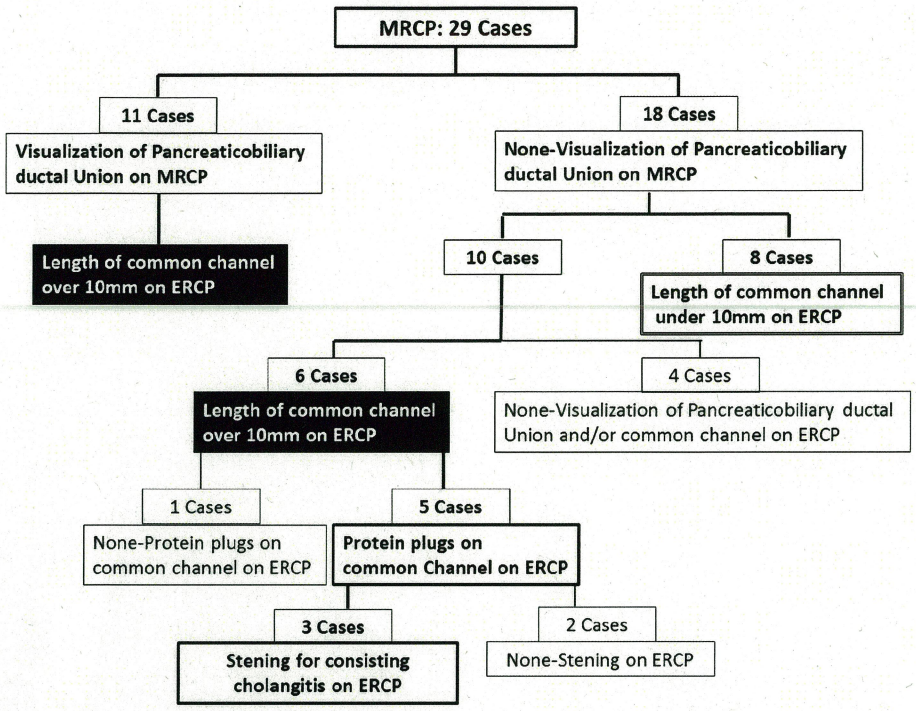

Fig. 4. Detailed description of patients with applicable MRCP images. 29 cases divided into two categories: 11 visualization of pancreaticobiliary ductal union and 18 no visualization of pancreaticobiliary ductal union cases. Details are shown in this figure.

biliary tract perforation [11]. Patient age was an important factor that influenced the failure rate in MRCP. However, many studies have shown the usefulness of MRCP for visualizing the pancreaticobiliary ductal union [5]. With respect to conditions for the diagnosis of PBM using MRCP, Sugiyama et al. [11] suggested that the common channel should be ≥ 15 mm long, while Kamisawa et al. [12] suggested that visualization of the pancreaticobiliary ductal union in patients with PBM with a short common channel is difficult using MRCP.

Fig. 4 shows a detailed description of patients with MRCP images. In our hospital, all 11 patients in whom the pancreaticobiliary ductal union could be visualized had a common channel length ≥ 10 mm on ERCP images. Of 18 patients in whom the union could not be visualized using MRCP, 8 had a common channel length < 10 mm on ERCP images. Indeed, Sugiyama et al. [11] and Kamisawa et al. [12] reported the difficulties in demonstrating the pancreaticobiliary ductal union using MRCP in adults, children and infants with a short common channel. However, their reports dealt with patients of all ages as one group and the data from children and infants were not considered separately. We are the first to report findings that are focused on children and infants, and found that ERCP was superior to MRCP in visualization of the pancreaticobiliary ductal union, especially in cases with a short common channel. Of the remaining 10 patients, 6 had a common channel length ≥ 10 mm. Of the 6 patients, 5 showed protein plugs in the common channel during ERCP. Of the 5 patients, 3 underwent stenting during ERCP because of persistent symptoms of cholangitis. As a result of stenting, the symptoms improved and an emergency operation was avoided. Thus, even in cases with a common channel that was 10 mm or longer, there might be difficulties in the visualization of the pancreaticobiliary ductal union if the common channel contains a protein plug, or if symptoms of cholangitis are present. ERCP, which does not overlook such patients, provides detailed information on the pancreatic duct, pancreaticobiliary ductal union and common channel, and allows simultaneous procedures such as stenting. ERCP is therefore indispensable in the in-depth preoperative examination of PBM.

Severe complications such as post-ERCP pancreatitis, cholangitis or bleeding did not occur during ERCP in our study. However, the length of radioactive exposure should be shortened as much as possible during the ERCP procedure, and the risks of general anesthesia should be taken into account. An acceptable trade-off between the stress of the procedure on patients and obtaining information on detailed anatomy for surgical procedures needs to be considered. With regard to the duration of procedures, ERCP required less time than MRCP in this study. ERCP provided more details on the anatomy of the pancreaticobiliary union than MRCP in a short amount of time. Fortunately, we had no post-ERCP pancreatitis in this series but we must bear in mind the potential risk of post-ERCP pancreatitis. We should be careful in selection of the appropriate method (ERCP or MRCP) for each patient.

Although our retrospective study has limitations, the findings are valuable and provide further insight into this rare condition. Our study confirmed that ERCP under general anesthesia for the in-depth preoperative examination of children with PMB is useful and safe, and provides more accurate images of the pancreatic and bile ducts compared with MRCP.

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