J Hepatobiliary Pancreat Sci (2010) 17:865–870
DOI 10.1007/s00534-010-0282-4

ORIGINAL ARTICLE

Pancreatobiliary reflux and the length of a common channel

Terumi Kamisawa · Masafumi Suyama · Naotaka Fujita · Hiroyuki Maguchi · Keiji Hanada · Seiyo Ikeda · Yoshinori Igarashi · Takao Itoi · Mitsuhiro Kida · Goro Honda · Jinkan Sai · Jun Horaguchi · Kuniyuki Takahashi · Takamitsu Sasaki · Kensuke Takuma · Fumihide Itokawa · Hisami Ando · Hiroo Takehara · The Committee of Diagnostic Criteria of The Japanese Study Group on Pancreaticobiliary Maljunction

Received: 18 October 2009 / Accepted: 4 March 2010 / Published online: 15 April 2010

Abstract
Background/purpose Gallbladder cancer occurs frequently in patients with pancreaticobiliary maljunction due to pancreatobiliary reflux. Pancreatobiliary reflux is also detected in some patients with a relatively long common channel. This study aimed to clarify the correlation between pancreatobiliary reflux and the length of a common channel.
Methods Two hundred and three patients, in whom both the length of a common channel and amylase level in the bile were measured, were enrolled from nine centers.
Results Bile amylase level was correlated with the length of a common channel ($P < 0.01$). The minimum length of a common channel that could induce a markedly elevated amylase level in the bile (>1,000 mg/dl) was determined as 5 mm. We redefined high confluence of pancreatobiliary ducts (HCPBD) as cases with a common channel ≥5 mm, in which the communication between the pancreatic and bile ducts was occluded with the sphincter contraction. Gallbladder cancer was found in 20% of 56 redefined HCPBD patients. Bile amylase level >1,000 mg/dl and biliopancreatic reflux were detected in 79 and 95% of the patients, respectively.
Conclusions Patients with a common channel ≥5 mm (redefined HCPBD) should be monitored for the development of gallbladder cancer, as they frequently showed significant pancreatobiliary reflux.

T. Kamisawa (✉)
Department of Internal Medicine, Tokyo Metropolitan Komagome Hospital, 3-18-22 Honkomagome, Bunkyo-ku, Tokyo 113-8677, Japan
e-mail: kamisawa@cick.jp

M. Suyama · J. Sai
Department of Gastroenterology, Juntendo University, Tokyo, Japan

N. Fujita · J. Horaguchi
Department of Gastroenterology, Sendai City Medical Center, Sendai, Japan

H. Maguchi · K. Takahashi
Center for Gastroenterology, Teine-Keijinkai Hospital, Sapporo, Japan

K. Hanada
Center of Gastroenterology, Onomichi General Hospital, Onomichi, Japan

S. Ikeda · T. Sasaki
Department of Surgery, Fukuoka University, Fukuoka, Japan

Y. Igarashi · K. Takuma
Department of Gastroenterology and Hepatology, Toho University Ohmori Medical Center, Tokyo, Japan

T. Itoi · F. Itokawa
Department of Gastroenterology, Tokyo Medical University, Tokyo, Japan

M. Kida
Department of Gastroenterology, Kitasato University, Sagamihara, Japan

G. Honda
Department of Surgery, Tokyo Metropolitan Komagome Hospital, Tokyo, Japan

H. Ando
Department of Pediatric Surgery, Nagoya University, Nagoya, Japan

H. Takehara
Department of Pediatric Surgery, Tokushima University Hospital, Tokushima, Japan

Keywords Pancreatobiliary reflux · Common channel · Gallbladder cancer · Pancreaticobiliary maljunction

Introduction

The main pancreatic duct and the common bile duct open into the duodenum either separately or via a common channel. The incidence of common channel formation ranges from 55% [1] to 82% [2, 3]. In regard to the length of the common channel, Dowdy et al. [4] reported a range from 1 to 12 mm, with an average length of 4.4 mm. Sterling [1] reported that it varied from 1.2 to 8.4 mm, averaging 4.4 mm. Rienhoff and Pickrell [5] reported that 92 (53%) of 173 cases had a common channel of 2 mm, 62 (36%) had a common channel ranging from 3 to 5 mm, and 19 (11%) had a common channel >6 mm.

The sphincter of Oddi is located at the distal end of the pancreatic and bile ducts and regulates the outflow of bile and pancreatic juice. A common channel can be so long that junction of the pancreatic and bile ducts is located outside of the duodenal wall, as occurs in pancreaticobiliary maljunction (PBM). In such cases, the action of the sphincter does not have a functional impact on the junction. Thus, biliopancreatic and pancreatobiliary reflux occurs, resulting in various pathological conditions in the biliary tract and the pancreas [6, 7]. Biliopancreatic reflux is confirmed by operative or postoperative T-tube cholangiography, and pancreatobiliary reflux is diagnosed by elevated amylase levels in the bile [7].

Apart from PBM, it is unknown whether the anatomy of the pancreaticobiliary ductal drainage into the duodenum has any significant association with the development of pancreatobiliary disease. There are some cases with a relatively long common channel that are not classified as PBM because the sphincter includes the pancreaticobiliary ductal junction. To investigate the clinical significance of a relatively long common channel, we defined high confluence of pancreaticobiliary junction (HCPBD) as a common channel ≥6 mm based on the previously reported data [1, 4, 5], in which the communication was occluded when the sphincter was contracted (Fig. 1) [7, 8]. However, there are no data available regarding correlation between pancreatobiliary reflux and the length of a common channel. To clarify the definition of HCPBD, we performed a multicenter study investigating the relationship between the length of a common channel and pancreatobiliary and biliopancreatic reflux, and the clinical implications.

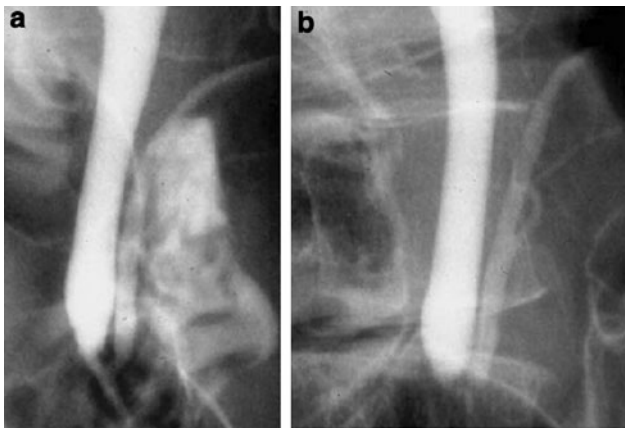

Fig. 1 Endoscopic retrograde cholangiopancreatography of a patient with high confluence of pancreaticobiliary ducts and a common channel of 9 mm in length (**a**). The communication between pancreatic and bile ducts was destroyed with sphincter contraction (**b**)

Methods

A retrospective, multicenter study was conducted using a questionnaire in nine centers in Japan. Major referral centers with established expertise in the diagnosis and management of pancreatobiliary diseases participated in the study. In the nine centers, the relationship between pancreatobiliary reflux and occurrence of gallbladder cancer has been prospectively studied independently.

To clarify the correlation between pancreatobiliary reflux and the length of a common channel, 203 patients, in whom both the length of a common channel and amylase level in the bile were measured, were enrolled in this study. The longest length of the common channel was measured from several cholangiograms during the sphincter relaxation period by endoscopic retrograde cholangiopancreatography (ERCP, $n = 186$), T-tube cholangiography ($n = 15$), and intraoperative cholangiography ($n = 2$) using a goniometer. Reflux of contrast medium into the main pancreatic duct was determined while a small amount of contrast medium was gradually injected under the least possible pressure during intraoperative cholangiography ($n = 24$) and T-tube cholangiography ($n = 24$). Amylase level was measured in the bile of the common bile duct ($n = 138$) and gallbladder ($n = 65$). Bile in the gallbladder was obtained intraoperatively, and bile in the common bile duct was collected through an indwelling T-tube or during ERCP. When the bile amylase level was ≤10 IU/l, it was regarded as 0 in the calculation of the values.

Eighty-one patients with a long common channel, in which the communication between the pancreatic and bile ducts was maintained during contraction of the sphincter of Oddi, were diagnosed as having PBM. Patients were

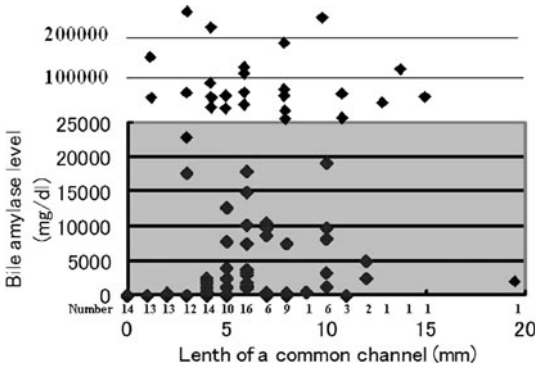

Fig. 2 Correlation between length of a common channel and bile amylase level

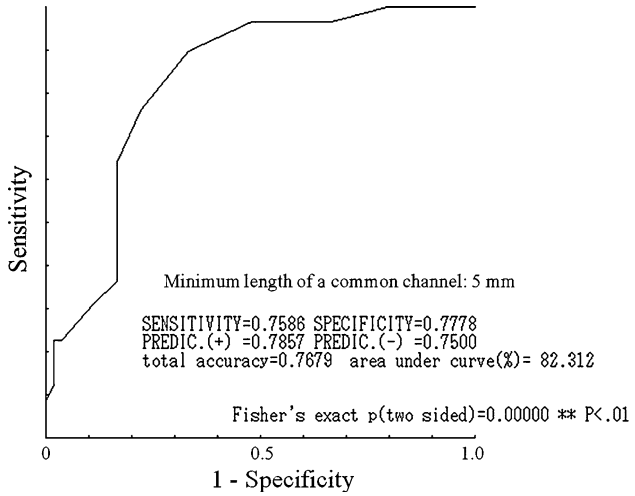

Fig. 3 The receiver operating characteristic curve determining the minimum length of a common channel that could induce a markedly elevated amylase level in the bile (more than 1,000 mg/dl)

divided into a group with biliary dilatation (maximum diameter of the bile duct >10 mm; $n = 47$) and a group without biliary dilatation ($n = 34$).

Correlation between the length of a common channel and bile amylase level was analyzed using Kendall's rank correlation coefficient under the normal upper limit of bile amylase level (150 mg/dl) based on the normal upper limit of serum amylase level (150 mg/dl). Since bile amylase level was elevated more than 1,000 mg/dl in 34 (97%) of 35 gallbladder cancer patients with bile amylase level >150 mg/dl, we defined 1,000 mg/dl as a cutoff level of markedly elevated amylase in the bile. To determine the length of a common channel cutoff value that could induce the markedly elevated amylase level in the bile, receiver operator characteristic (ROC) curves were used.

For other statistical analyses, Mann–Whitney *U* test and Fisher's exact test were employed, and $P < 0.05$ was considered significant. When repeated comparisons were made, the significant level was adjusted by the Bonferroni method.

Results

Correlation between amylase level in the bile and the length of a common channel

In 122 non-PBM patients, amylase level in the bile was correlated with the length of a common channel (Fig. 2, $P < 0.01$). According to the ROC curve, the minimum length of a common channel that could induce a markedly elevated amylase level in the bile (more than 1,000 mg/dl) was 5 mm. Using this cutoff value, sensitivity was 75.8%, specificity was 77.8%, and the area under the curve was 0.82 (Fig. 3).

Comparison between patients with common channel ≥5 mm (redefined HCPBD), PBM patients with or without biliary dilatation, and controls

Clinical features

Based on the data from the ROC curve, we redefined HCPBD as cases with a common channel ≥5 mm, in which the communication between the pancreatic and bile ducts was occluded when the sphincter was contracted. Fifty-six patients were diagnosed as having redefined HCPBD. The other 66 patients without redefined HCPBD or PBM were used as controls. Age at the diagnosis was significantly older in redefined HCPBD patients than in patients with PBM with biliary dilatation ($P < 0.01$). There was no difference between genders in redefined HCPBD patients, while PBM occurred predominantly in females (Table 1).

Biliary and pancreatic complications

Gallbladder cancer was associated in 11 (20%) patients with redefined HCPBD, while the incidence of gallbladder cancer was significantly higher in those with PBM without biliary dilatation ($P < 0.01$). Gallbladder stones and acute pancreatitis were detected in 23 (41%) and 11 (20%) of redefined HCPBD patients, being more frequent than in PBM (Table 1).

Radiological features, and pancreatobiliary and biliopancreatic reflux

Length of a common channel was significantly shorter in redefined HCPBD patients than in PBM ($P < 0.01$). Diameter of the common bile duct was similar in redefined

Table 1 Clinical features of redefined HCPBD, PBM, and controls

	Redefined HCPBD	PBM with biliary dilatation	PBM without biliary dilatation	Controls	*P* value
Number of patients	56	47	34	66	
Age at diagnosis (years, mean ± SD)	58.5 ± 16.5	47.8 ± 18.4	54.1 ± 15.3	59.8 ± 17.1	0.001[a]
Male/female	27/29	13/34	9/25	30/36	0.042[a]
					0.048[b]
Gallbladder cancer	11 (20%)	8 (17%)	16 (47%)	5 (8%)	0.004[b]
Bile duct cancer	0	3 (6%)	0	4 (7%)	NS
Gall stones	23 (41%)	6 (13%)	6 (18%)	22 (33%)	0.001[a]
					0.026[b]
Bile duct stones	10 (18%)	3 (6%)	4 (12%)	16 (28%)	NS
Acute pancreatitis	11 (20%)	2 (4%)	1 (2%)	1 (2%)	0.033[a]
					0.026[b]
					0.001[c]
Chronic pancreatitis	2 (4%)	1 (2%)	0	1 (2%)	NS

P values were data of redefined HCPBD compared with [a] PBM with biliary dilatation, [b] PBM without biliary dilatation, and [c] controls

NS not significant

Table 2 Radiological features and pancreatobiliary and biliopancreatic reflux

	Redefined HCPBD	PBM with biliary dilatation	PBM without biliary dilatation	Controls	*P* values
Length of common channel (mm, mean ± SD)	7.8 ± 3.1	16.3 ± 8.4	12.6 ± 7.4	2.1 ± 1.4	<0.001[a,b,c]
Diameter of common bile duct (mm, mean ± SD)	9.4 ± 3.0	24.3 ± 11.7	8.4 ± 1.7	8.5 ± 2.8	<0.001[a]
Bile amylase level >150 mg/dl	50 (89%)	46 (98%)	31 (91%)	17 (30%)	<0.001[c]
Bile amylase level >1,000 mg/dl	44 (79%)	46 (98%)	31 (91%)	14 (25%)	0.002[a]
					<0.001[c]
Bile amylase level (mg/dl, mean ± SD)	26,635 ± 49,970	172,988 ± 295,932	93,898 ± 143,224	13,077 ± 37,910	<0.001[a,b,c]
Biliopancreatic reflux	20/21 (95%)	10/10 (100%)	6/6 (100%)	0/11 (0%)	<0.001[c]

P values were data of redefined HCPBD compared with [a] PBM with biliary dilatation, [b] PBM without biliary dilatation, and [c] controls

HCPBD patients and patients with PBM without biliary dilatation. In redefined HCPBD patients, amylase level in the bile >150 mg/dl was detected in 50 (89%) patients and amylase level in the bile >1,000 mg/dl was detected in 44 (79%) patients. However, mean amylase level in the bile (26,635.8 ± 49,970.5 mg/dl) in redefined HCPBD patients was significantly lower than in PBM patients ($P < 0.01$). Biliopancreatic reflux assessed by intraoperative or T-tube cholangiography was observed in 95% of redefined HCPBD patients (Table 2).

Gallbladder cancer associated with redefined HCPBD and PBM with and without biliary dilatation

Gallbladder cancer associated with redefined HCPBD and PBM was rarely associated with gallstones. Bile amylase level in cases of gallbladder cancer associated with redefined HCPBD was significantly lower than that of gallbladder cancer associated with PBM without biliary dilatation ($P < 0.05$) (Table 3).

Discussion

Pancreaticobiliary maljunction is generally accepted as a condition that predisposes patients to the development of gallbladder cancer due to pancreatobiliary reflux via a markedly long common channel in which the action of the sphincter of Oddi does not affect the pancreaticobiliary junction [6, 7]. Prophylactic cholecystectomy is recommended for patients with PBM without biliary dilatation before malignant change can take place in the gallbladder [9]. However, little is known about the clinical significance of a relatively long common channel.

To investigate the clinical significance of a relatively long common channel, we defined HCPBD as a common

Table 3 Gallbladder cancer associated with redefined HCPBD and PBM with or without biliary dilatation

	Redefined HCPBD	PBM with biliary dilatation	PBM without biliary dilatation
Number of patients	11	8	16
Age at diagnosis (years, mean ± SD)	66.8 ± 9.0	63.0 ± 3.5	60.5 ± 11.5
Male/female	5/6	3/5	2/14
With gall stones	1 (9%)	1 (13%)	1 (6%)
Bile amylase level (mg/dl, mean ± SD)	17,922 ± 27,105*	62,716 ± 62,449	72,543 ± 92,359

* $P = 0.038$ compared with PBM without biliary dilatation

channel length ≥6 mm, in which the communication was occluded when the sphincter was contracted [7, 8]. In our recent study of 65 HCPBD patients in a single center, gallbladder cancer was found in 7 (11%). Reflux of contrast medium into the pancreatic duct was detected in 12 (86%) of 14 patients with HCPBD who underwent postoperative T-tube cholangiography. Amylase level of the bile in seven HCPBD patients was elevated to an average 47,774 IU/l. Hyperplastic change in the gallbladder mucosa with increased epithelial cell proliferative activity was detected in HCPBD patients. Furthermore, K-ras mutations of the noncancerous epithelium of the gallbladder were detected in 5 (28%) of 18 patients with HCPBD [10, 11].

By demonstrating elevated levels of pancreatic enzymes in bile sampled from the common bile duct or gallbladder, or by MRCP evidence of biliary duct dilatation after secretin injection, it has been recently recognized that pancreatobiliary reflux can occur with a normal pancreaticobiliary junction [12–14]. A high bile trypsin level was also reported in patients with bile duct stones [12]. Horaguchi et al. [13] reported that high biliary amylase level was observed in 46 (26%) of 178 patients with a normal pancreaticobiliary junction, and the prevalence of elevated biliary amylase level was high in patients with gallbladder cancer. Sai et al. [14] demonstrated enhanced visualization of the intrahepatic and extrahepatic bile ducts and gallbladder with increased maximum diameter of the extrahepatic bile duct and short axis of the gallbladder on secretin-stimulated dynamic MRCP in 4 (5%) of 74 patients who had a normal pancreaticobiliary junction on ERCP. The bile amylase level was markedly elevated in all four patients, and three of these four patients had gallbladder cancer. These reports would suggest that there is a relationship between pancreatobiliary reflux in individuals with a normal pancreaticobiliary junction and gallbladder cancer.

In this study, it became clear that bile amylase level was correlated with the length of a common channel. The most significant problem in these cases with a relatively long common channel is the association with cancer of the gallbladder. Since bile amylase level was elevated more than 1,000 mg/dl in 97% of gallbladder cancer patients with bile amylase level >150 mg/dl, we defined 1,000 mg/dl as a cutoff level of markedly elevated amylase in the bile. Therefore, using ROC curves, we determined that 5 mm is the minimum length of a common channel that induces marked elevation of bile amylase levels. Subsequently, we redefined HCPBD as a length of the common channel ≥5 mm, in which the communication was occluded when the sphincter was contracted. In redefined HCPBD patients, gallbladder cancer was found in 20%, and pancreatobiliary and biliopancreatic reflux was observed in 89 and 95%, respectively. Although it is reported that 40–70% of gallbladder cancers are generally associated with gall stones [15], the incidence of gall stones in conjunction with cancer of the gallbladder associated with both redefined HCPBD and PBM was lower.

Although the degree or incidence was different, pathophysiological conditions due to pancreatobiliary and biliopancreatic reflux appear to occur in both PBM and also in redefined HCPBD. However, as shown in our previous data [7, 8], there were several differences in gender, age at diagnosis, bile amylase level, and incidence of associated gallbladder cancer between redefined HCPBD and PBM patients. Pancreatobiliary reflux can also occur in cases of sphincter dysfunction [16], periampullary diverticula [17], as well as after endoscopic sphincterotomy [18] or endoscopic papillary balloon dilatation [19]. Itokawa et al. [20] reported that the amylase level in the bile obtained during ERCP was higher than the serum amylase level in 22 (26%) of 86 patients with a normal pancreaticobiliary junction, and the incidence of an elevated amylase level in the bile was significantly higher in patients who were elderly, had a dilated common bile duct, and in those who had choledocholithiasis. Pancreatobiliary reflux in some cases of normal pancreaticobiliary junction seems to be caused by dysfunction of the sphincter of Oddi. Anderson et al. [21] reported that the bile amylase level obtained through an indwelling T-tube was higher than the serum amylase level in 21 (81%) of 26 patients with biliary tract disease, and the bile amylase level fluctuated considerably in the same patient. According to Paulino-Netto et al. [22],

biliopancreatic reflux during T-tube cholangiography was detected when the sphincter was relaxed in instances with high confluence of the pancreatic and bile ducts. It would seem that, unlike in PBM, pancreatobiliary reflux in cases with a normal pancreaticobiliary junction occurs not continuously but transiently. Apart from the degree of reflux of pancreatic enzymes, another factor that induces cell injury and resultant carcinogenesis appears to be the long-term local stasis of bile intermingled with refluxed pancreatic juice. In cases with a relatively long common channel, the pancreatic juice refluxes into the common bile duct and is cleared rapidly without stasis; therefore the occurrence of cancer of the gallbladder where bile stasis occurs poses a problem in these cases. Although the incidence of associated gallbladder cancer in HCPBD is lower than that in PBM, a relatively long common channel appears to be an important risk factor for the development of gallbladder cancer. We think that redefined HCPBD should currently be treated as a separate entity from PBM, but clinicians should be vigilant regarding the development of gallbladder cancer in redefined HCPBD patients.

There are some limitations in this study. First, this is a retrospective multicenter study. The method of measurement of a common channel may differ somewhat among centers. Second, amylase level was measured in the bile of the common bile duct or gallbladder. Some investigators [20, 23] reported a difference in amylase level in the gallbladder or the common bile duct; however, in this study, amylase levels in the common bile duct were higher than those in the gallbladder in 9 (56%) of 17 cases and were lower in 7 cases (44%). Third, there was bias in the cases enrolled in this study, as subjects chosen for the study were patients who underwent ERCP or intraoperative or T-tube cholangiography. In redefined HCPBD patients, there were many patients with gall stones and acute biliary pancreatitis, which may have been induced by this bias. To clarify the clinical significance of redefined HCPBD including the place of prophylactic cholecystectomy in these cases, further prospective studies are needed.

In conclusion, patients with a common channel $\geq$5 mm (redefined HCPBD) should be monitored for the development of gallbladder cancer, as they frequently showed significant pancreatobiliary reflux as indicated by marked elevation of bile amylase levels.

References

1. Sterling JA. The common channel for bile and pancreatic ducts. Surg Gynecol Obstet. 1954;98:420–4.
2. Suda K, Miyano T, Hashimoto K. The choledocho-pancreatico-ductal junction in infantile obstructive jaundice diseases. Acta Pathol Jpn. 1980;30:187–94.
3. Suda K, Miyano T, Konuma I, Matsumoto M. An abnormal pancreatico-choledocho-ductal junction in cases of biliary tract carcinoma. Cancer. 1983;52:2086–8.
4. Dowdy GS, Waldron GW, Brown WG. Surgical anatomy of the pancreaticobiliary ductal system. Arch Surg. 1962;84:229–46.
5. Rienhoff WF, Pickrell KL. Pancreatitis: an anatomic study of the pancreatic and extrahepatic biliary systems. Arch Surg. 1945;51:205–19.
6. The Japanese Study Group on Pancreaticobiliary Maljunction. Diagnostic criteria of pancreaticobiliary maljunction. J Hepatobiliary Pancreat Surg. 1994;1:219–21.
7. Kamisawa T, Okamoto A. Biliopancreatic and pancreatobiliary refluxes in cases with and without pancreaticobiliary maljunction: diagnosis and clinical implications. Digestion. 2006;73:228–36.
8. Kamisawa T, Amemiya K, Tu Y, Egawa N, Sakaki N, Tsuruta K, et al. Clinical significance of a long common channel. Pancreatology. 2001;2:122–8.
9. Sugiyama M, Atomi Y. Anomalous pancreaticobiliary junction without congenital choledochal cyst. Br J Surg. 1998;85:911–6.
10. Kamisawa T, Funata N, Hayashi Y, Egawa N, Nakajima H, Tsuruta K, et al. Pathologic changes in the non-carcinomatous epithelium of the gallbladder in patients with a relatively long common channel. Gastrointest Endosc. 2004;60:56–60.
11. Kamisawa T, Kuwata G, Chen PY, Tu Y, Fujiwara T, Endoh J, et al. Precancerous lesions in the gallbladder of patients with a long common channel. Dig Endosc. 2006;18:192–5.
12. Vracko J, Wiechel KL. Trypsin level in gallbladder bile and ductitis and width of the cystic duct. Hepatogastroenterology. 2000;47:115–20.
13. Horaguchi J, Fujita N, Noda Y, Kobayashi G, Ito K, Takasawa O, et al. Amylase levels in bile in patients with a morphologically normal pancreaticobiliary ductal arrangement. J Gastroenterol. 2008;43:305–11.
14. Sai JK, Suyama M, Kubokawa Y, Tadokoro H, Sato N, Maehara T, et al. Occult pancreatobiliary reflux in patients with a normal pancreaticobiliary junction. Gastrointest Endosc. 2003;57:364–8.
15. Ohta T, Nagakawa T, Ueno K, Maeda K, Ueda N, Kayahara M, et al. Clinical experience of biliary tract carcinoma associated with anomalous union of the pancreaticobiliary ductal system. Jpn J Surg. 1990;20:36–43.
16. Peveretos P, Polydorou A, Golematis P, Golematis B. The role of the pancreatic enzymes in the pathogenesis of cholelithiasis. Mt Sinai J Med. 1988;55:369–73.
17. Sugiyama M, Atomi Y. Periampullary diverticula cause pancreatobiliary reflux. Scand J Gastroenterol. 2001;36:994–7.
18. Sugiyama M, Atomi Y. Does endoscopic sphincterotomy cause prolonged pancreatobiliary reflux? Am J Gastroenterol. 1999;94:795–8.
19. Sugiyama M, Atomi Y. Endoscopic papillary balloon dilatation causes transient pancreatobiliary and duodenobiliary reflux. Gastrointest Endosc. 2004;60:186–90.
20. Itokawa F, Itoi T, Nakamura K, Sofuni A, Kakimi K, Moriyasu F, et al. Assessment of occult pancreatobiliary reflux in patients with pancreaticobiliary disease by ERCP. J Gastroenterol. 2004;39:988–94.
21. Anderson MC, Hauman RL, Suriyapa C, Schiller WR. Pancreatic enzyme levels in bile of patients with extrahepatic biliary tract disease. Am J Surg. 1979;137:301–6.
22. Paulino-Netto A, Paulino F. Pancreatic ductal reflux. Am J Dig Dis. 1963;8:666–72.
23. Aoki T, Tsuchida T, Kasuya K, Endo M, Kitamura K, Koyanagi Y. Is preventive resection of the extrahepatic bile duct necessary in cases of pancreaticobiliary maljunction without dilatation of the bile duct? Jpn J Clin Oncol. 2001;31:107–11.