Hypothesis: Resection of the gallbladder together with the dilated bile duct is the preferred treatment for pancreaticobiliary maljunction (PBM) with bile duct dilatation, whereas this treatment for PBM without bile duct dilatation is still controversial.

Design: Retrospective study of 196 patients from January 1979 to November 2004.

Setting: Two university hospitals.

Patients: One hundred ninety-six patients with PBM, 152 (78%) with and 44 (22%) without bile duct dilatation, formed the basis of this study.

Main Outcome Measures: The effects of cholecystectomy on long-term results in the patients without bile duct dilatation.

Results: Significant differences were observed in patients without bile duct dilatation: patients were older, carcinoma of the gallbladder was more prevalent (19 patients [43.2%] without dilatation vs 9 patients [5.9%] with dilatation), and pancreatic cancer and pancreatitis were also more frequent. Most of their gallbladder carcinomas were found at stage IV (63%). The outcome was very poor in stage IV, whereas 5 patients in stage I and II lived for more than 5 years after surgery. Of the 44 patients without bile duct dilatation, 23 with carcinoma of the gallbladder or pancreas died and the other 2 were lost to follow-up. The remaining 19 patients were alive at the study’s conclusion after cholecystectomy without bile duct resection. None of them had bile duct carcinoma at the time of surgery or during the mean follow-up period of 9 years after surgery.

Conclusions: Prophylactic cholecystectomy without bile duct resection is the best treatment option for patients with PBM without bile duct dilatation. Possible association of gallbladder carcinoma should be kept in mind at the time of treatment of patients with PBM when the bile duct is not dilated.

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Pancreaticobiliary maljunction (PBM) is a rare congenital anomaly where the pancreatic and biliary ducts join outside the duodenal wall, forming an abnormally long common channel. The incidence of PBM has been reported to be 3% in patients undergoing endoscopic retrograde cholangiopancreatography for various reasons and it is well known that PBM is commonly associated with congenital bile duct dilatation and carcinoma of the bile duct and gallbladder. The reason for biliary carcinogenesis in such patients has been ascribed to reflux and stagnation of bile mixed with pancreatic juice in the dilated bile duct and gallbladder. Therefore, resection of the gallbladder together with the dilated bile duct, resulting in biliary diversion, is generally recognized as the treatment of choice for PBM with bile duct dilatation. We have performed resection of the dilated extrahepatic duct and biliary diversion by a Roux-en-Y reconstruction, and previously reported long-term results after the surgical treatment for patients with PBM and bile duct dilatation.

In contrast, treatment for PBM without bile duct dilatation is still controversial. Approximately 20% to 30% of the patients with PBM do not have bile duct dilatation. Prophylactic cholecystectomy is usually indicated because of frequent association of gallbladder cancer and less frequent bile duct carcinoma in PBM without bile duct dilatation. The alternative is excision of the gallbladder together with the nondilated bile duct to ensure bile diversion to prevent carcinogenesis. However, little is known about long-term results after surgical treatment of PBM without bile duct dilatation.

The aim of this study was to compare the characteristics of patients with PBM...
with and without bile duct dilatation and to examine the effect of cholecystectomy on long-term results in patients with PBM without bile duct dilatation. Special attention was paid to associated diseases in detail.

### METHODS

From January 1979 through November 2004, 196 Japanese patients were diagnosed as having PBM by endoscopic retrograde cholangiopancreatography, percutaneous transhepatic cholangiography, and/or magnetic resonance cholangiopancreatography in our university hospitals and formed the basis of this study. The presence of PBM was defined by a common channel length longer than 15 mm on cholangiopancreatograms and by a high level of amylase in bile. This was based on the findings that the length of the common channel in healthy adults ranged from 2 to 10 mm on direct cholangiograms and 1 to 12 mm in autopsy cases. Pancreaticobiliary maljunction (PBM) was defined by a common bile duct joins the main pancreatic duct. In the P-C type the common pancreatic duct joins the common bile duct, and in the C-P type the common bile duct joins the main pancreatic duct. Clinical characteristics and associated biliary diseases were compared between the PBM patients with and without bile duct dilatation.

Next, characteristics of the patients without bile duct dilatation were carefully evaluated. Clinical and pathological staging of the gallbladder carcinoma was determined by General Rules for Surgical and Pathological Studies on Cancer of Biliary Tract. Special attention was paid to long-term outcome after the treatment of these patients, obtained by telephone interview, mail questionnaires, and/or a visit to the outpatient clinic. All values were expressed as mean ± SD. Statistical analyses were carried out using the Student t test and the χ² test. P values less than .05 were considered significant.

### RESULTS

Of 196 patients with PBM, there were 57 men and 139 women. Ages ranged from 3 months to 82 years with a mean age of 35.1 years. Of these 196 patients, bile duct dilatation was present in 152 patients (77.6%) and absent in the remaining 44 (22.4%) (Table 1). The diameter of the bile duct in the patients without bile duct dilatation ranged from 5 to 12 mm, with a mean of 9 mm. The female-male ratio of 152 patients with PBM and bile duct dilatation was 105:33 (17/27; M/F). The diameters of the bile duct in the patients without bile duct dilatation were significantly different from that of 44 patients without bile duct dilatation (27.17; P = .41). The mean age of those with bile duct dilatation was 30.0 ± 20.7 years. They were significantly younger than those without bile duct dilatation. The type of PBM could not be determined in 14 of the 152 patients with PBM and bile duct dilatation owing to the loss of detailed medical records. The C-P type was significantly more frequent in the remaining 138 PBM patients with bile duct dilatation than in those without bile duct dilatation. In contrast, the P-C type was predominant in the patients without bile duct dilatation (Table 1).

The prevalence of associated diseases was different between patients with and without bile duct dilatation (Table 1). Diseases of the gallbladder were significantly more frequent in the patients without bile duct dilatation than in those with bile duct dilatation (77.3% vs 17.8%), whereas diseases of the bile duct were less frequent in patients without bile duct dilatation (6.8% vs 19.1%). In addition to cholelithiasis, these differences were ascribed to the different rate of association of biliary tract carcinoma. Carcinoma of the gallbladder was found in 43.2% of the patients without bile duct dilatation, and in only 5.9% of the patients with bile duct dilatation. Carcinoma of the bile duct was seen only in patients with bile duct dilatation. On the contrary, diseases of the pancreas were more frequent in the patients without bile duct dilatation (20.5% vs 3.3%). Pancreatic cancer was found in 2 patients (1.3%) with bile duct dilatation and 4 patients (9.1%) without bile duct dilatation.

The clinical symptoms of the 44 patients without bile duct dilatation are presented in Table 2. The main symptoms were abdominal pain, back pain, and jaundice. Thirty-five (79.5%) of the 44 patients had abdominal pain. However, 5 patients (11.4%) had no symptoms. Three of them had a polypoid lesion of the gallbladder (the final diagnosis was gallbladder carcinoma in all 3 patients) and the remaining 2 had wall thickening and swelling of the gallbladder, incidentally found by ultrasonography.

Of the 19 patients with gallbladder carcinoma without bile duct dilatation, the stage and outcome of 1 patient could not be identified and the results of the remaining 18 patients are presented in Table 3. Twelve of the 18 patients had stage IV gallbladder carcinoma and 8 of them underwent surgical treatment. Five patients with stage I or II carcinoma were alive for more than 5 years after surgery, but the 13 patients with stage III and IV...
carcinoma all died except for 1 who underwent surgery 2 months prior to the writing of this article; their prognosis was very poor.

Of the 44 PBM patients without bile duct dilatation, carcinoma of the gallbladder or pancreas was absent in 21 patients. Two of the 21 patients were lost to follow-up (1 underwent cholecystectomy and the other did not have surgery). The long-term results after cholecystectomy in 19 patients are presented in Table 4. Of these 19 patients, laparoscopic cholecystectomy was performed in 11 patients, open cholecystectomy or extended cholecystectomy alone (cholecystectomy and gallbladder bed resection) in 3, cholecystectomy with resection of the extrahepatic bile duct and hepaticojejunostomy in 1, cholecystectomy and duodenum-preserving pancreatic head resection in 1, and cholecystectomy and choledocholithotomy with hepatectomy in 1. During the follow-up period (111.2±53.3 months), 2 patients died of unrelated diseases (respiratory disease and heart disease), but the remaining 17 patients were alive and well at the time of the paper’s writing. None of these 17 patients developed bile duct carcinoma during the follow-up period of 9.3±4.7 years (range, 21-206 months) after cholecystectomy.

The present study focused on the characteristics of the patients with PBM without bile duct dilatation and their long-term results after surgical treatment. Carcinoma of the gallbladder was frequently associated with PBM without bile duct dilatation and mostly found at the advanced stage. Except for the patients who developed gallbladder or pancreatic carcinoma, cholecystectomy gave a satisfactory result; bile duct carcinoma was not observed during the mean follow-up of 9 years. These results suggest that prophylactic cholecystectomy is the best treatment choice for patients with PBM without bile duct dilatation.

In this study, we first compared the types, characteristics, and frequency of associated diseases between 152 patients with PBM with bile duct dilatation and 44 pa-
tients with PBM without bile duct dilatation. Gallbladder diseases, especially carcinoma, were significantly more frequent in the latter group where the P-C type of PBM was predominant. No single case of bile duct carcinoma was found in the latter group during the follow-up. This result suggests that the mixing of bile and pancreatic juice is necessary but not sufficient to develop biliary tract carcinoma. Stasis of bile mixed with pancreatic juice is likely to be an additional, essential factor for carcinogenesis. In contrast, when the bile duct is dilated, stasis associated with bile duct dilatation seems to lead to carcinogenesis of both the gallbladder and bile duct.

It has been reported that the prevalence of biliary tract carcinoma in patients with PBM is significantly higher than in the general population. The age of patients with gallbladder carcinoma associated with PBM is 10 years older than that of patients with gallbladder carcinoma without PBM. Several investigators have reported that K-ras and p53 mutations may be important in the early stage of carcinogenesis in patients with PBM. We previously reported that the oxidative DNA injury might possibly be related to carcinogenesis in such patients. Thus, PBM itself is an important risk factor for biliary tract carcinogenesis, but the risk of gallbladder carcinoma and bile duct carcinoma is different in the presence or absence of bile duct dilatation. In addition, our results also suggest that the presence of pancreatic cancer should be carefully evaluated, especially in patients with PBM without bile duct dilatation.

Since the treatment procedure for patients with PBM and bile duct dilatation has been established, we have paid special attention to the patients without bile duct dilatation. In 19 patients who had no cancer of the gallbladder or pancreas, we removed the gallbladder but preserved the bile duct. Laparoscopic cholecystectomy was applied to 11 patients and open cholecystectomy in 1. Surgical procedures (Table 4) were added to cholecystectomy in the remaining 7 patients because of the presence of associated diseases and/or suspicion of carcinoma. All but 2 patients who died of unrelated diseases were alive and doing well during the mean follow-up period of 9 years (range, 21-206 months) after surgery. These results suggest that prophylactic cholecystectomy is the best treatment for patients with PBM without bile duct dilatation. Resection of the extrahepatic bile duct should be reserved for selected patients with repeated cholangitis and/or pancreatitis, which continue to occur even after cholecystectomy.

It has been recognized that the frequency of biliary tract carcinoma increases depending on the age of the patient with PBM with bile duct dilatation. Voyles et al reported that the incidence was 14% for patients aged 20 to 49 years and 50% for patients older than 50 years. The mean age of our patients with gallbladder carcinoma with PBM without bile duct dilatation was 57.2 years (range, 40-79 years). The necessity of prophylactic cholecystectomy in childhood is not clear, but laparoscopic cholecystectomy before age 40 years is recommended for patients with PBM without bile duct dilatation. Of the 18 patients with gallbladder carcinoma associated with PBM without bile duct dilatation, 5 patients were alive for more than 5 years after surgery and no recurrence had been confirmed during the writing of this article. All 5 patients had either stage I or stage II carcinoma. The remaining 13 patients had either stage III or stage IV carcinoma, and their outcomes were poor. Elnemr et al demonstrated that the patients with PBM without bile duct dilatation had more advanced malignant diseases and worse outcomes than those with bile duct dilatation. Therefore, prophylactic cholecystectomy is the preferred choice when one is diagnosed as having PBM without bile duct dilatation, even in the absence of gallbladder diseases.

We previously reported 2 cases of pancreatic carcinoma associated with PBM. In the present study, 4 (9.1%) of 44 patients with PBM without bile duct dilatation had carcinoma of the pancreas, including the 2 patients previously reported. The rate of association of pancreatic carcinoma was higher in the absence of bile duct dilatation in patients with PBM. The exact reason for this difference is not clear and remains to be investigated in the future. The possible presence of pancreatic carcinoma should be kept in mind especially in patients with PBM without bile duct dilatation.

Most patients with PBM without bile duct dilatation have no clinical symptoms during their youth, resulting in delayed diagnosis, as compared with those with bile duct dilatation. Because endoscopic retrograde cholangiopancreatography is an invasive examination and PBM without bile duct dilatation is difficult to detect by ultrasonography, magnetic resonance cholangiopancreatography should probably be employed as a screening examination in patients with wall thickening, and polyps or elevated lesions of the gallbladder.

In conclusion, prophylactic laparoscopic cholecystectomy is the best treatment for patients with PBM without bile duct dilatation. When the patients continue to have repeated episodes of cholangitis and/or pancreatitis, additional surgery should be considered, depending on the pathology and pathophysiology of associated diseases. Special attention to the possible presence of gallbladder carcinoma and pancreatic carcinoma is mandatory in patients with PBM when the bile duct is not dilated.

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Correspondence: Kazuo Chijiiwa, MD, PhD, Department of Surgery 1, Miyazaki University School of Medicine, 5200 Kihara, Kyotake, Miyazaki 889-1692, Japan (kazuochi@med.miyazaki-u.ac.jp).

Author Contributions: Study concept and design: Ohuchida, Chijiiwa, and Tanaka. Acquisition of data: Ohuchida, Chijiiwa, Hiyoishi, Kobayashi, Konomi, and Tanaka. Analysis and interpretation of data: Ohuchida. Drafting of the manuscript: Ohuchida. Critical revision of the manuscript for important intellectual content: Chijiiwa, Hiyoishi, Kobayashi, Konomi, and Tanaka. Statistical analysis: Ohuchida. Administrative, technical, and material support: Chijiiwa, Hiyoishi, Kobayashi, Konomi, and Tanaka. Study supervision: Chijiiwa, Konomi, and Tanaka.

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REFERENCES


