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Original article

Outcome of gallbladder polyps in patients with primary sclerosing cholangitis

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Background: The American Association for the Study of Liver Disease (AASLD) guideline recommends cholecystectomy for GB polyps of any size in patients with PSC without strong supporting evidence.
Objective: Evaluate the predictors of malignancy and outcomes of PSC patients with GB polyps.
Methods: We identified 86 patients with PSC and GB polyps at the Mayo Clinic, Rochester, MN between January 1, 2000 and August 31, 2009 using a computerized record system. Twenty-six patients were excluded due to indefinite diagnosis or inadequate follow up data.
Results: Of the 2281 patients with PSC, 60 patients (2.6%) were diagnosed as having GB polyps with a median age of 49.8 years; 67% were male. The median follow up from the diagnosis of GB polyps to the last follow-up was 3.5 years. Thirty-one patients (52%) subsequently underwent cholecystectomy and eight of 31 patients (25.8%) developed malignant GB lesions. Low-grade dysplasia of the GB was seen in two (6.4%). Twenty-nine patients without cholecystectomy had a median follow up of 4.8 years and none of them developed a malignant GB lesion during follow-up. By multivariable logistic analysis, the size of GB polyps at baseline was associated with malignant GB lesions or GB dysplasia (OR = 7.0; 95%CI 2.0-25.1).
Conclusions: One third of GB polyps in patients with PSC who underwent cholecystectomy become malignant or developed dysplasia. A GB polyp at first diagnosis of at least 1 cm in size was a good predictor for malignant lesions of GB or GB dysplasia. In PSC patients with comorbidities who had GB polyp size at first diagnosis less than 1 cm, careful monitoring of the progression of GB polyp size over time with periodical assessment by ultrasound may be an option.

Keywords: Gallbladder polyps, outcome, primary sclerosing cholangitis

Abbreviations
ALP = alkaline phosphatase
ALT = alanine transaminase
AST = aspartate aminotransferase
DB = direct bilirubin
PSC = primary sclerosing cholangitis
TB = total bilirubin

The frequency of hepatobiliary malignancies is increased in patients with primary sclerosing cholangitis (PSC) and one-third of the cancers were diagnosed within one year of the diagnosis of PSC [1]. Gallbladder cancer can also complicate PSC. Gallbladder polyps or masses were observed in 4% to 6% of PSC patients or 14% of patients with PSC receiving cholecystectomy [2-4]. In our previous study, the histological findings from 72 gallbladders (GB) of PSC patients with liver explants and cholecystectomies included GB dysplasia (37%) and GB adenocarcinoma (14%) [5]. GB adenocarcinoma was associated with intrahepatic bile duct dysplasia, cholangiocarcinoma (CCA), inflammatory bowel disease (IBD) and older age [5]. Recently, case reports from New Zealand showed that four patients with PSC and GB polyps developed malignancy [6]. The size of GB polyp in this study varied from 7 to 25 mm on imaging and the authors suggested that any GB polyp in a patient with PSC should be considered for cholecystectomy, regardless of size (6). Zielinski et al. [7] studied risk factors for GB malignancy in 79 patients with GB polyps and found that history of

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PSC, local invasion, vascularity, and size of GB polyps at least 6 mm based on pre-operative ultrasonography were risk factors. However, this study was limited by including only seven patients with PSC and only two of them had GB neoplasia. Recently, the American Association for the Study of Liver Disease (AASLD) guideline recommends cholecystectomy for gallbladder polyps of any size in patients with PSC without strong evidence of back-up studies [8]. We aimed to evaluate the predictors of neoplastic lesions of the gallbladder and outcomes of PSC patients with gallbladder polyps.

Patients and methods

This was a longitudinal, retrospective study of patients diagnosed with PSC over a nearly 10-year period between January 1, 2000 and August 31, 2009. Primary sclerosing cholangitis was defined as present when all the following criteria were met, 1) chronic cholestatic disease of at least six months' duration, 2) elevation of serum alkaline phosphatase (ALP), 3) retrograde, operative, percutaneous or magnetic resonance cholangiography demonstrating intrahepatic and/or extrahepatic biliary duct obstruction, beading or narrowing consistent with PSC, and 4) exclusion of secondary sclerosing cholangitis or other causes of cholestatic liver diseases [8]. The diagnosis of a GB polyp was based on ultrasonography as a lesion projecting into the lumen of the GB which did not cast an acoustic shadow and did not move with the position of the patient [9]. A GB polyp in patients with PSC was identified by using HICDA codes (05756-21 with 05760-31) and radiological diagnosis codes of GB polyp/mass (760.3104) at the Mayo Clinic, Rochester, MN. We identified 86 patients during the study period.

Inclusion Criteria

We included PSC patients who had no cholecystectomy at baseline, and had at least two serial US examinations with diagnosis of a GB polyp or one US examination as well as pathological diagnosis for patients who underwent cholecystectomy. Cholecystectomy cases include open or laparoscopic cholecystectomy. All included patients must have had at least one visit after the first diagnosis of GB polyps.

Exclusion Criteria

Of the 2281 patients with PSC, 86 identified patients were diagnosed as having GB polyps. Twenty-six patients were excluded due to the indefinite diagnosis of PSC or GB polyp (n = 22), known cases of cholangiocarcinoma (n = 2) and incomplete follow up (n = 2). All medical records of the remaining 60 patients were retrospectively reviewed. A detailed history and physical examination was recorded by a health care provider using standardized protocols. Clinical information, date of cholecystectomy, preoperative and follow-up radiographic findings, and pathological findings of GB polyps were reviewed. A GB polyp was defined by at least two serial reports of radiological diagnosis. Mayo risk score at baseline was calculated to obtain survival estimates up to 4 years of follow-up (10) and it can be accessed from the web site, http://www.mayoclinic.org/gi-rst/mayomodel3.html. The study was approved by the Institutional Review Boards of the Mayo Clinic and all participants provided permission for their medical information to be used for research.

Follow-up data

The diagnosis of malignant GB lesions or GB dysplasia was based on pathological findings in patients who underwent cholecystectomy or the clinical outcomes at the end of follow-up or at the time of the primary endpoints occurred. The primary endpoints were the occurrence of the malignant lesions of GB including cancer or dysplasia, death or undergoing liver transplantation. The grading of histopathological findings of GB cancer was defined by the classification of Henson et al, as follows: grade 1; "well-differentiated", grade 2; "moderately differentiated" , grade 3; "poorly differentiated", and grade 4; "undifferentiated"(11). Follow-up time was calculated from the time between the dates of GB polyp diagnosis (i.e., baseline) to the last date of follow-up or death or date of diagnosis of malignant lesion of the GB or GB dysplasia.

Statistical Analyses

Statistical analyses were performed with SPSS version 15.0 software. Subjects were categorized by the presence of a malignant lesion of the GB. Continuous variables were presented as mean ± standard deviation (SD) or median (±interquartile range [IQR]) as appropriate. Comparisons between the two groups were performed using independent *t*-test if values were normally distributed or using the Wilcoxon rank sum test if the distribution was not normal. Categorical data were presented as numbers (percentage) and were

compared by Fisher exact test or Chi-square test where appropriate. All tests were two sided, and the chosen level of significance was p <0.05. Logistic regression analysis was used to identify the factors significantly associated with the presence of a malignant lesion of the GB in PSC patients. Only those variables with p <0.2 by univariate analysis were included in multivariate analysis. We estimated receiver operating characteristics (ROC) of related variables for detection of the malignant lesions of GB in patients with PSC to maximize the area under the curve (AUC).

Results

Clinical features at presentation

Of the 2281 patients with PSC, 60 patients (2.6%) were diagnosed as having GB polyps with median age (interquartile range; IQR) of 49.8 years (39.3, 58.6); 67% were male. Forty-nine patients (82%) were diagnosed with GB polyps at age of less than 60 years. Median (IQR) Mayo risk score at baseline was 0.33 (-0.11, 1.36). Seventy-five percent of patients were Child–Pugh A cirrhosis, 22% were Child–Pugh B and 3% were Child–Pugh C. Fifty-one patients (85%) had a history of inflammatory bowel disease mostly ulcerative colitis (96%). Eleven patients (18%) were obese and five patients (8%) had a history of diabetes. GB polyps were initially diagnosed by ultrasonography in 58 patients (97%), CT scanning in 1.5% and MRI in 1.5%. At baseline, 36% of PSC patients with GB polyps had at least two polyps and 70% of patients had GB polyps with size less than 0.6 cm as shown in **Table 1**. Gallstones were found in 11 patients (18%). Six patients with PSC (10%) had history of GB polyps before the diagnosis of PSC with a median (IQR) interval of 0.2 (0, 5.2) months while 54 patients (90%) were diagnosed with GB polyps after the diagnosis of PSC with a median (IQR) interval of 5.9 (2.2, 11.6) years.

Six of 60 patients (10%) were symptomatic including biliary colic in four, nausea with vomiting in one and acute cholecystitis in one. Four of six patients developed symptoms before the diagnosis of GB polyps (range of interval from 1 day to 5 months) while two patients who were diagnosed as having GB polyps developed symptoms later with an interval of 29 and 33 months. The median (IQR) interval from the diagnosis of GB polyps to cholecystectomy was 0.7 months (0.2, 33.5 months). The remaining 54 patients (90%) were asymptomatic. The laboratory tests at baseline are summarized in **Table 2**. The average values of ALT and AST levels were one and a half times higher than the normal range while mean values of alkaline phosphatase (ALP) was two times higher than the normal range.

Table 1. Patient characteristics and data of GB polyps at baseline of 60 patients with PSC

Variables Median (Interquartile range; IQR) or number (%)	Total (n = 60)	Symptomatic patients (n = 6)	Asymptomatic patients (n = 54)	*p* value
Patients Characteristics				
Age at GB polyp diagnosis (years)	49.8 (39.3, 58.6)	53.1 (38.7, 61.6)	49.3 (38.9, 58.5)	0.6
Gender, % male	40 (67)	5 (83.3)	35 (65)	0.4
Race, % white	55 (92)	6 (100)	49 (91)	0.4
Presence of advanced liver fibrosis at baseline	17 (28.3)	6 (100)	37 (68.5)	0.1
Mayo risk score at baseline	0.33 (-0.11, 1.36)	-0.06 (-0.52, 0.51)	0.33 (-0.07, 1.46)	0.2
Patients with history of IBD	51 (85)	5 (83.3)	46 (85.2)	0.9
Presence of obesity (BMI >30 kg/m^2)	11 (18.3)	2 (33.3)	9 (16.7)	0.3
History of receiving immunosuppressive drugs	14 (23.3)	1 (16.7)	13 (24.1)	0.7
History of current alcohol drinking	11 (18.3)	1 (16.7)	10 (18.5)	0.8
History of diabetes	5 (8.3)	1 (16.7)	4 (7.4)	0.4
History of current smoking	2 (3.3)	0 (0)	2 (3.7)	0.5
Data of gallbladder polyps at baseline				
Presence of gallstone	11 (18.3)	2 (33.3)	9 (16.7)	0.3
Number of patients with several GB polyps (>2 polyps)	20 (36)	2 (33.3)	18 (36)	0.9
Number of patients with GB polyp size <0.5 cm	42 (70)	2 (33.3)	40 (74)	0.04
Size of GB polyp (cm)	0.2 (0.2, 0.7)	1.6 (0.3, 2.3)	0.2 (0.2, 0.6)	0.01
Duration from the diagnosis of PSC to the presence of GB polyp (years)	5.9 (2.2, 11.6)	0.3 (0.1, 17.1)	5.9 (2.3, 10.8)	0.4

Table 2. Laboratory tests at baseline of 60 patients with PSC and GB polyps

Variables Median (IQR) or number (%)	Total (n = 60)	Symptomatic patients (n = 6)	Asymptomatic patients (n = 54)	*P* value
ALT (U/L)	64 (36, 103)	32 (24, 117)	70 (36, 103)	0.2
AST (U/L)	60 (33, 100)	32 (24, 58)	62 (37, 102)	0.06
Albumin (g/dL)	4.0 (3.6, 4.3)	4 (3.5, 4.3)	3.9 (3.5, 4.3)	0.6
Total bilirubin (mg/dL)	1.1 (0.7, 2.2)	0.7 (0.4, 1)	1.2 (0.7, 2.6)	0.03
Direct bilirubin (mg/dL)	0.3 (0.2, 0.9)	0.2 (0.1, 0.4)	0.4 (0.2, 1)	0.04
ALP (U/L)	340 (174, 679)	226 (119, 574)	371 (183, 709)	0.3
Glucose (mg/dL)	92 (85, 99)	91 (88, 100)	92 (85, 98)	0.8
Creatinine (mg/dL)	1.0 (0.8, 1.1)	1.1 (1, 1.2)	1 (0.8, 1.1)	0.1
Cholesterol (mg/dL)	190 (175, 239)	194 (181, 272)	190 (169, 239)	0.8
Triglyceride (mg/dL)	103 (62, 142)	122 (70, 155)	97 (62, 142)	0.5
CA 19-9 (normal <55 U/ml)	14 (10.9, 20.1)	13.7 (11.3, 14)	14.2 (11, 20.9)	0.3
Hemoglobin (g/dL)	13.6 (12.5, 14.7)	13.7 (13.4, 14.3)	13.6 (12.3, 14.7)	0.6
White cell count (X 10^3/L)	6.6 (4.3, 8.2)	6.3 (4.4, 9.0)	6.7 (4.3, 8.2)	0.8
Platelet (X 10^9/L)	248 (157, 309)	232 (201, 269)	251 (154, 311)	0.8
INR	1.0 (0.9, 1)	0.9 (0.9, 1)	1.0 (0.9, 1.1)	0.2

Clinical outcomes and predictors for neoplastic lesion of GB

Table 3 summarizes the clinical outcomes at the end of follow-up of 60 patients with PSC with the median (IQR) follow up from the diagnosis of GB polyps to the last follow-up at an average of 3.5 years (1.2, 7.0). Thirty-one patients (52%) subsequently underwent cholecystectomy. The pathological findings of the removed GB with GB polyps in 31 patients (6 symptomatic patients and 25 asymptomatic patients) were adenocarcinoma of the GB (n = 8) with median GB polyps' size of 2.1 cm (range1-4 cm), low grade dysplasia of the GB (n = 2) with GB polyps' size of 1 and 3.5 cm, GB wall thickening (n = 14), hyperplastic polyp (n = 3), tubular adenoma (n = 2), papillary adenoma (n = 1), and cholesterosis (n = 1).

Table 3. Clinical outcomes at the end of follow-up of 60 patients with PSC and GB polyps

Clinical outcomes Median (IQR) or number (%)	Total (n = 60)	Symptomatic patients (n = 6)	Asymptomatic patients (n = 54)	*P* value
Cholecystectomy	31 (52)	6 (100)	25 (46.3)	0.01
Presence of GB cancer or low grade GB dysplasia at the end of follow up	10 (16.7)	3 (50)	7 (13)	0.02
All-cause mortality	6 (10)*	0 (0)	6 (10)	0.4
Liver transplantation	9 (15)	0 (0)	9 (16.7)	0.3
Lost to follow-up	8 (13.3)**	1 (16.7)	7 (13)	0.8
Duration from the diagnosis of GB polyps to cholecystectomy (months)	-	0.7 (0.2, 33.5)	13.8 (0.6, 26.9) (N = 25)	-
Duration from the diagnosis of PSC to first presence of death, liver transplantation, or last follow-up date (years)	9.6 (5.3, 16.3)	8.6 (3.4, 19.6)	9.9 (5.8, 16.3)	0.8

*****liver related complications; hepatocellular carcinoma, hepatic encephalopathy and hepatic hydrothorax (n = 3), sepsis post chemotherapy for lymphoma (n = 1), metastatic GB cancer to liver (n = 1) and GB dysplasia with unknown cause of death (n = 1). **Eight patients were lost to follow up and had no results of GB polyps were excluded from the multivariate analysis

Ten of the 31 patients who underwent cholecystectomy, with the histological finding of the adenocarcinoma of the GB or low-grade dysplasia had the median age (range) of 58 (34, 68) years. Seventy percent of them were younger than 60 years. The grading of histopathological findings of adenocarcinoma of GB in 8 patients were grade 1 in one, grade 2 in five, and grade 3 in two. The median (IQR) interval from the diagnosis of GB polyps to cholecystectomy of these 10 patients was 0.3 months (0.1, 2 months). Nine patients had interval abdominal imaging studies at 6-months or less and one patient at 6 to 12-month intervals between exams. At the end of follow-up, four of 10 patients with malignant GB lesions or GB dysplasia were lost to follow-up. The median (IQR) follow up from the diagnosis of GB polyps to the last follow-up of the remaining six patients was 73 months (months) including four patients alive with continued follow-up and two patients who died, one from metastatic GB cancer after cholecystectomy and of unknown cause in the other.

The remaining 21 patients who underwent cholecystectomy and the removed GB had no malignant GB lesions or GB dysplasia, had the indications of cholecystectomy of prophylactic cholecystectomy in nine, cholecystectomy as part of liver transplantation in nine and enlarging GB polyps in three. The median (IQR) interval from the diagnosis of GB polyps to cholecystectomy of these 21 patients was 2.3 months (0.8, 4 months). Thirteen patients had interval abdominal imaging studies at 6-months or less and five patients at 6 to 12-month intervals between exams. At the end of follow-up, three of them (14%) were lost to follow-up. The median (IQR) follow up from the diagnosis of GB polyps to the last follow-up of the remaining 18 patients was 2.3 years (0.2, 7.7 years) including nine patients alive with continued follow-up and nine patients who received a liver transplant. No patients developed malignant GB lesions or GB dysplasia during the follow-up period.

For 29 patients without cholecystectomy, five of them were lost to follow-up (17%). The median (IQR) follow up from the diagnosis of GB polyps to the last follow-up of the remaining 24 patients was 4.8 years (2.2, 7.0 years) including 20 patients alive with continued follow-up and four patients who died. The causes of death of four patients were liver related complications, hepatocellular carcinoma, hepatic encephalopathy, and hepatic hydrothorax (n = 3) and sepsis post chemotherapy for lymphoma (n = 1). The median (IQR) interval of follow up abdominal imaging study was six (4, 8.6) months. Eleven patients (46%) had interval abdominal imaging studies at six months, 11 patients (46%) at 12 months, and two patients (8%) had more than 12 months intervals between exams. All 24 patients were asymptomatic from GB polyps during the follow-up. No patients developed malignant GB lesions or GB dysplasia during the follow-up period.

Of the 60 patients, eight of them were excluded from the multivariate analysis due to lost to follow-up. Of 52 patients with PSC and GB polyps, 38 of them (73%) had polyps of 0.5 cm or less. Eight from 38 patients (21%) showed progression on the size of GB polyps with serial imaging study. Five of eight patients with enlarged GB polyps underwent cholecystectomy. Four of five patients had primary endpoints including two patients who died from disease progression of the malignant GB lesions or GB dysplasia after cholecystectomy, one patient who received a liver transplant, and one alive patient with malignant GB lesions. The remaining three patients without cholecystectomy were alive and continued follow-up

Table 4 shows the comparison of clinical characteristics of 52 patients with PSC and GB polyps with or without malignant GB lesions or GB dysplasia. By univariate analysis, patients with malignant GB lesions or GB dysplasia were older, had significantly larger size of GB polyps at first diagnosis, more % change in size of GB polyps, and more symptomatic patients, and less use of ursodeoxycholic acid than those with benign GB lesions. By multivariable logistic analysis, model 2 was the best fit model and showed that the size of GB polyps at baseline was associated with malignant GB lesions or GB dysplasia (OR = 7.0; 95%CI 2.0-25.1) as can be seen in **Table 5**. By using the ROC curve, GB polyp size ≥1 cm had a sensitivity of 70%, specificity of 92.5%, a negative predictive value of 92.5% and a positive predictive value of 70%, with an area under the curve of 80% for predicting malignant GB lesions. To summarize our results, we conclude an algorithm for the outcomes of 60 patients with PSC and GB polyps (**Figure 1**).

Table 4. Comparison of clinical characteristics of 52 patients* with PSC and GB polyps categorized by with or without malignant lesion of GB or GB dysplasia

Clinical characteristics, Median (IQR) or number (%)	Without malignant lesion of GB (n = 42)	With malignant lesion of GB (n = 10)	*P* value
Gender, % male	28 (66.7)	9 (90)	0.14
Age at GB polyp diagnosis (years)	47.6 (36.6, 55)	58.5 (44.7, 62.7)	0.05
Presence of multiple GB polyps at baseline	14 (33.3)	5 (50)	0.23
Use of ursodeoxycholic acid	34 (81)	3 (30)	0.001
Size of GB polyp at baseline (cm)	0.2 (0.2, 0.3)	1.8 (0.2, 2.4)	0.001
% change in size of GB polyps during the follow-up	0 (-14, 8)	440 (-75, 787)	0.01
Presence of biliary pain or cholecystitis	2 (4.8)	3 (30)	0.02

*Eight of 60 patients were excluded from the analysis due to lost to follow-up. $p < 0.05$ for patients with benign versus malignant GB lesion and those variables with $p < 0.1$ by univariate analysis were included in multivariate analysis.

Table 5. Multivariate analysis model showing the association of PSC patients with malignant lesions of GB

Multivariate analysis	*P* value	OR	95% CI
Model 1*			
- Size of GB polyp at baseline (cm)	0.03	9.2	1.2-67.8
- %Change in size of GB polyps per year of the follow-up	0.35	1.001	0.99-1.002
Model 2**			
- Size of GB polyp at baseline (cm)	0.003	7.0	2.0-25.1
- %Change in size of GB polyps per year of the follow-up	0.01	1.01	1.002-1.02
- Interaction between size of GB polyp at baseline and %change in size of GB polyps during the follow-up	0.05	0.996	0.992-1.0

Model 1*without interaction among 5 included variables; age at GB polyp diagnosis, size of GB polyp at baseline (cm), use of ursodeoxycholic acid , %change in size of GB polyps during the follow-up, presence of biliary pain or cholecystitis.
Model 2**added variables of interaction between size of GB polyp at baseline and % change in size of GB polyps during the follow-up into model 1.

Discussion

Our study indicates that the detection rate of GB polyps in patients with PSC was low with a frequency of 2.6%, which was similar to previous studies of 4% to 6% [2-4]. Most were diagnosed with GB polyps at an average of 6 years after the diagnosis of PSC. We also found that one third of GB polyps in patients with PSC receiving cholecystectomy become malignant or developed dysplasia and the size of GB polyps at first diagnosis of at least 1 cm was a good predictor for malignant lesions of GB or GB dysplasia (OR = 7). The age and sex of patients with PSC and GB polyps in our study were different from previous studies of GB polyps in the general populations [12, 13]. However, it was similar to those reported in patients with PSC [2, 3]. Seventy percent of our PSC patients with malignant lesions of the GB were less than 60 years whereas only 17% of patients in a non-PSC population were less than 60 years [14]. Two-thirds of our patients with PSC were male while a previous study showed that the incidence rate of GB cancer among women was three times higher than men [12]. Thus, the differences in the nature of underlying disease and patient selection may explain the difference in baseline demographic data. All of our patients with malignant lesions of the GB had histological findings of adenocarcinoma and 88% of these patients were moderately to poorly differentiated which was similar to a previous study [12]. Even though we had incomplete information for TNM

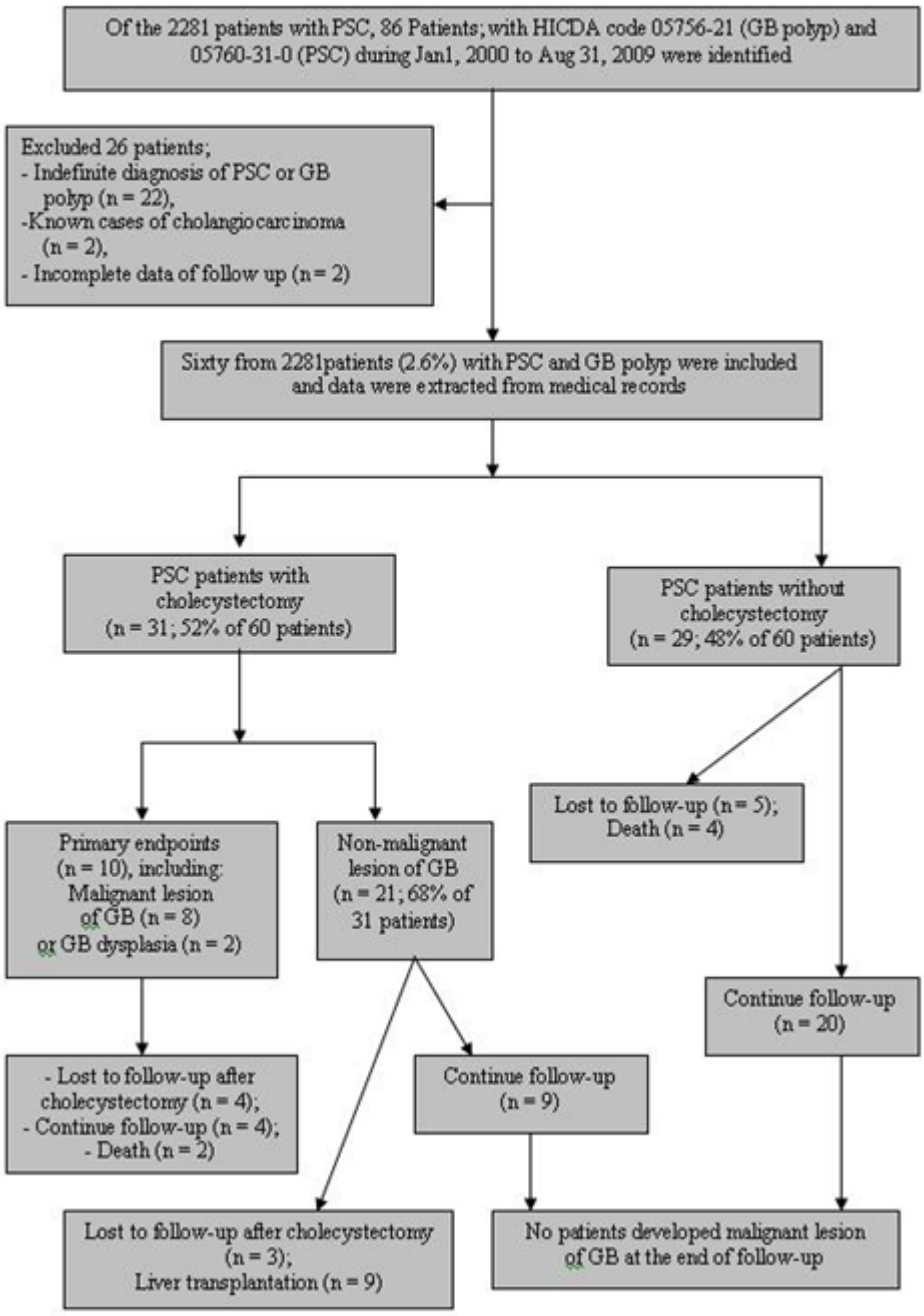

Figure 1. Outcomes of 60 patients with PSC and GB polyps

staging; but we had the results of histological grading which was useful in predicting survival for adenocarcinomas [15]. Previous studies showed that the staging of GB cancer in general populations and history of receiving surgery with adjuvant therapy were associated with survival [13, 16]. A previous study reported that the 5-year survival of patients with GB cancer was closely associated with tumor staging and patients with stage 3 to 4 disease had survival rate less than 5% [14]. Thus, the screening measure for early diagnosis of GB cancer is important to ensure better outcomes especially in high-risk patients. Currently, there is no standard surveillance protocol for detecting malignant lesions of the GB in patients with PSC. The recommendation for initial follow-up of general patients with GB polyp is 3 to 6-monthly ultrasonography examination [17] which may be applicable in patients with PSC. The study of appropriate duration of follow-up had not been performed. However, our 31 patients with PSC and

GB polyps received cholecystectomy had interval abdominal imaging studies at 6-months in 71% and 12-months in 19% whereas those patients without cholecystectomy had interval abdominal imaging studies at 6-months in 46%, and 12-months in 46%. Ultrasonography is considered as the most effective and available modality to screen for GB cancer [18]. MRI with MRCP is also considered as an accurate modality for assessment of the local and regional extent of GB cancer in general patients [19, 20]. Previous study showed that a laparoscopic cholecystectomy in cirrhotic patients with Child's class A and B was safe and showed no mortality; however the rate of complications was significantly higher in cirrhosis patients (12.5%) than those in non-cirrhotic patients (4.2%) [21]. Recently, Delis et al. [22] reported that cirrhotic patients with preoperative MELD score above 13 showed a higher complication rate postoperatively and higher conversion to open cholecystectomy. Our study had only two patients with Child–Pugh C cirrhosis. Both of them underwent cholecystectomy as part of liver transplantation and had no complications.

The main strengths of our study are 1) the inclusion of the large number of PSC patients with GB polyps and 2) the available information of clinical data, imaging studies and the pathological findings, which were useful for assessment of outcomes. Our study has some limitations and the first one is the incomplete information of long-term follow-up for GB cancer risk. Our study showed that 21 patients receiving cholecystectomy who had no malignant GB lesions or GB dysplasia had limited intervals of follow up of 2.3 years while the remaining 20 patients without cholecystectomy had the average duration of follow up of 4.8 years. Although, no patients in both groups developed malignant GB lesions or GB dysplasia during the follow-up period but the duration of follow-up period was too short to make a firm conclusion. With a large proportion of patients having no standardized method of follow-up or detecting GB polyps, further prospective study and longer-term follow-up should be performed. Second, the intervals of surveillance ultrasonography for detecting malignant lesions of the GB in patients with PSC in our study had varied from 6-months to 12-months because of its retrospective nature. Currently, there is no standard surveillance protocol for detecting malignant lesion of the GB in PSC patients with GB polyp and thus further prospective study of the appropriate interval of follow-up abdominal ultrasonography is needed. Last, the decision making for treating patients with cholecystectomy or followed up in our study depended on doctors' opinion but the major reason for surgery was the progression in polyp size and symptomatic patients. However, there was some overlap with the non-surgical group. Thus, our results are difficult to use as a basis for determining policy. They may be useful as a guideline for a standard surveillance protocol to detect malignant lesion of the GB in PSC patients with GB polyp for the further prospective study.

Laparoscopic cholecystectomy should not be recommended in all patients with PSC as well as with the presence of gallbladder polyps of any size. It should be considered in patients with PSC and GB polyps of at least 1 cm for prevention of GB cancer based on the evidence in our study. However, careful monitoring of the progression of GB polyp size over time with periodical assessment by ultrasound may be an option for selected patients such as Child–Pugh C patients or patients with comorbidities who had GB polyp size at first diagnosis less than 1 cm.

In conclusion, one third of GB polyps in patients with PSC who underwent cholecystectomy become malignant or developed dysplasia. A GB polyp at first diagnosis of at least 1 cm in size was a good predictor for malignant lesions of GB or GB dysplasia. In PSC patients with comorbidities who had GB polyp size at first diagnosis less than 1 cm, careful monitoring of the progression of GB polyp size over time with periodical assessment by ultrasound may be an option.

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