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ORIGINAL ARTICLE——LIVER, PANCREAS, AND BILIARY TRACT

What is the appropriate method of pathological specimen collection for cholangiocarcinoma detection in primary sclerosing cholangitis?

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Abstract

Background In primary sclerosing cholangitis (PSC), it is important to understand the cholangiographic findings suggestive of malignancy, but it is difficult to determine whether cholangiocarcinoma is present due to modifications caused by inflammation. This study aimed to clarify the appropriate method of pathological specimen collection during endoscopic retrograde cholangiopancreatography for surveillance of PSC.

Methods A retrospective observational study was performed on 59 patients with PSC. The endpoints were diagnostic performance for benign or malignant on bile cytology and transpapillary bile duct biopsy, cholangiographic findings of biopsied bile ducts, diameters of the strictures and upstream bile ducts, and their differences.

Results The sensitivity (77.8% vs. 14.3%, $P=0.04$), specificity (97.8% vs. 83.0%, $P=0.04$), and accuracy (94.5% vs. 74.1%, $P=0.007$) were all significantly greater for bile duct biopsy than for bile cytology. All patients with cholangiocarcinoma with bile duct stricture presented with dominant stricture (DS). The diameter of the upstream bile ducts (7.1 (4.2–7.2) mm vs. 2.1 (1.2–4.1) mm, $P<0.001$) and the diameter differences (6.6 (3.1–7) mm vs. 1.5 (0.2–3.6) mm, $P<0.001$) were significantly greater in the cholangiocarcinoma group than in the noncholangiocarcinoma group with DS. For diameter differences, the optimal cutoff value for the diagnosis of benign or malignant was 5.1 mm (area under the curve = 0.972).

Conclusion Transpapillary bile duct biopsy should be performed via localized DS with upstream dilation for the detection of cholangiocarcinoma in patients with PSC. Especially when the diameter differences are greater than 5 mm, the development of cholangiocarcinoma should be strongly suspected.

Keywords Primary sclerosing cholangitis · Cholangiocarcinoma detection · Endoscopic retrograde cholangiopancreatography · Bile cytology · Transpapillary bile duct biopsy

Introduction

Primary sclerosing cholangitis (PSC) is characterized pathologically by chronic inflammation and fibrosis and clinically by chronic biliary stasis [1]. As the disease progresses, diffuse stricture and wall thickening appear in the bile ducts inside and outside the liver. There are no drugs that have been shown to be effective at treating this disease, and liver transplantation is the only curative therapy. On the other hand, 5–15% of patients with PSC develop cholangiocarcinoma [2, 3], and attention should be given to the development of cholangiocarcinoma after the diagnosis of PSC. Cholangiocarcinoma in PSC is often diagnosed at an advanced stage [4–6] and is associated with poor clinical outcomes [7]. It has been reported that 80% of patients with cholangiocarcinoma in PSC die within 1 year [8], thus highlighting the expectation that early detection could lead to improved prognosis.

The development of cholangiocarcinoma in patients with PSC is often indicated by blood test abnormalities

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such as liver dysfunction, jaundice, and elevated tumor marker levels and is frequently triggered by abnormal findings in imaging studies, including abdominal ultrasound, computed tomography (CT) scans, and magnetic resonance cholangiopancreatography (MRCP) examinations. However, the presence of cholangiocarcinoma is challenging to determine based on the results of pathology from endoscopic retrograde cholangiopancreatography (ERCP) examinations. Therefore, it is extremely important to understand the findings suggestive of malignancy in the cholangiography during ERCP and to collect pathology specimens at those sites for early detection of cholangiocarcinoma. However, it is not easy to accurately identify cholangiocarcinoma on cholangiography because of the background modification of inflammation by PSC. It is often difficult to determine which part of the bile duct should be biopsied to detect cholangiocarcinoma. Furthermore, it is not clear whether cytology or histology should be used to collect pathological specimens. Therefore, we conducted this study to clarify the appropriate method of pathological specimen collection during ERCP for cholangiocarcinoma surveillance in PSC patients.

Methods

Patients

A retrospective observational study was conducted on patients with PSC diagnosed at Nagoya University Hospital between August 2006 and March 2022. The exclusion criteria were as follows: patients with bile duct stones confirmed by ERCP during the study, patients who were followed in our department for less than 1 month after PSC diagnosis, patients who underwent balloon dilation of the stricture, patients who had already had a biliary drainage tube placed at the time of PSC diagnosis, patients who were followed up in our department after liver transplantation, and patients who were followed up in our department after PSC-based cholangiocarcinoma surgery. The presence of a bile duct stone itself can cause upstream bile duct dilation, and in many patients with stones, there is a stricture downstream that prevents stone removal, resulting in bile duct stenting. Because of the multiple factors that may affect the diameter of the bile duct, we excluded patients with bile duct stones from this study. We also excluded patients with balloon dilation because the procedure changes the diameter of the bile duct, and biopsies were performed after dilation in many patients, which may have affected the imaging of the bile duct at the biopsy site. In addition, patients who had already had a biliary drainage tube placed at the time of PSC diagnosis were also excluded from this analysis because the drainage tube may affect the diameter of the bile duct. The starting date of observation was the date of PSC diagnosis. Patients who were still being followed at our department were measured for the observation period until March 31, 2023. For patients who died during the observation period, the date of death was used as the observation end date. For patients who were transferred to other hospitals during the observation period, the date of transfer was used as the observation end date. This study was approved by the Ethics Committee of Nagoya University Hospital (approval number 2016–0032) and was conducted in accordance with the Declaration of Helsinki (clinical research registration number UMIN000025631). In addition, an opt-out format was posted on the hospital website, giving the opportunity to refuse to participate in this study.

Procedure of ERCP

All patients in this study were diagnosed with PSC after ERCP, and each patient had undergone at least one session of ERCP. Although there were cases in which multiple ERCPs were performed on the same patient, the second and subsequent ERCPs were performed when the patient had development of cholangitis, worsening liver injury, periodic biliary stent replacement, or worsening bile duct images on other exams. The examiner decided whether to perform cytology and biopsy at the time of ERCP, but they were collected if there was concern about the development of cholangiocarcinoma, such as a relatively localized lesion. Bile cytology was performed either by aspiration cytology during ERCP or by cytology under endoscopic nasobiliary drainage (ENBD) tube placement. For aspiration cytology, 5–10 ml of bile was aspirated from the catheter and stored at room temperature in a sterile spit, and the spit was submitted for cytology immediately after the ERCP procedure. For ENBD cytology, an ENBD tube of 5–7 Fr was placed, and 10–20 ml of bile was collected from the ENBD tube for single or multiple cytological examinations. For transpapillary bile duct biopsy, biopsy forceps (Radial Jaw 4P; Boston Scientific Japan, Tokyo, Japan) were pressed against the stricture to collect tissue under fluoroscopic guidance. Bile duct biopsies were targeted to transitional areas of the stricture and upstream dilation, and biopsies were not performed from areas suspected of having nonmalignancy, such as areas that had uniformly spread beaded appearances or band-like strictures. All biopsies analyzed were performed with the aim of detecting cancer. Mapping biopsies intended to determine the extent of cancer progression were not included in this study. Endoscopic sphincterotomy (EST) was not performed in all ERCPs.

Outcome measurements and definition

The endpoints were the diagnostic performance for benign or malignant lesions on bile cytology and transpapillary bile duct biopsy, the cholangiographic findings of the biopsied bile ducts, diameters of the strictures and upstream bile ducts, and their differences. The diameter of the stricture was measured on the cholangiography at the biopsy site, and the diameter of the upstream bile ducts was measured in the most dilated bile duct within 1 cm upstream of the biopsy site. The measurement point of the upstream bile duct was defined as within 1 cm because the bile duct strictures observed in PSC are characterized by short strictures such as band-like strictures and because the biopsies are basically taken from the stricture-dilation transition site. Cholangiography showing good contrast of both the biopsied bile duct and the upstream bile duct was used to measure the diameter of the bile ducts. The diameter of the strictures and upstream bile ducts was adopted median of five manual measurements by a single gastroenterologist (YK, the first author) using a random sequence of images in which the clinical information was hidden and in which blinding as to whether the image was cancerous was undertaken, but the personnel had information of the biopsy site. The diameter difference was defined as the difference between the diameter of the stricture and the diameter of the upstream bile duct. A dominant stricture (DS) was defined cholangiographically as a stricture less than 1.5 mm diameter in the common bile duct, or less than 1 mm in the left or right main hepatic ducts, as previously reported [9].

The diagnosis of PSC was based on the 2016 primary sclerosing cholangitis diagnostic criteria [10]. The differentiation between benign and malignant lesions during follow-up was based on bile cytology and/or transpapillary bile duct biopsy. Malignancy or suspicion of malignancy was defined as malignant and atypical or negative as benign in both cytology and histology. The CCA group was defined as patients who were diagnosed with cholangiocarcinoma at the final diagnosis, and the non-CCA group was defined as those who were not diagnosed with cholangiocarcinoma during follow-up. The final diagnosis was made based on the pathological results of the resected specimen in the resected patients and on clinical follow-up for at least 1 year in the nonresected patients, and the results were compared with those of cytological and histological diagnoses. Adverse events of ERCP were evaluated according to the Consensus Guidelines of Cotton et al. [11]. When considering the timing of blood tests, for the non-CCA group, we used the most recent measurements from the time of PSC diagnosis, while for the CCA group, we adopted the most recent measurements from either the ERCP or surgery that served as the basis for the final cancer diagnosis. In cholangiography during ERCP, "occlusion" was defined as no visible upstream bile ducts even when contrast medium was injected from the downstream side using a balloon catheter, "stricture" was defined as narrow bile ducts with visible upstream bile ducts, and “filling defect” was defined as an immobile defect.

Statistical analysis

To evaluate differences in patient background, all continuous variables were subjected to the Mann–Whitney *U* test due to the lack of a normal distribution. For categorical variables, all variables were subjected to Fisher’s exact test. For comparisons of sensitivity, specificity, and accuracy for bile cytology and bile duct biopsy, Fisher’s exact test or the chi-square test was performed depending on the number of comparison groups. All comparisons of bile duct diameters were subjected to the Mann–Whitney U test due to the lack of a normal distribution. Receiver operating characteristic (ROC) curves were generated to determine the optimal cutoff value for diagnosing benign or malignant lesions in the stenosis-dilation diameter difference. The significance level was set at 5% in all tests. EZR (version. 1.56) software was used for statistical analysis [12].

Results

A total of 59 patients were diagnosed with PSC during the study period. Of these patients, 24 were excluded for the following reasons: ten patients with bile duct stones confirmed by ERCP during the study, six patients who were followed in our department for less than 1 month, three patients who underwent balloon dilation of the stricture, two patients who had already had a biliary drainage tube placed at the time of PSC diagnosis, two patients who were followed up in our department after liver transplantation, and one patient who was followed up in our department after PSC-based cholangiocarcinoma surgery. Finally, 35 patients were included in the analysis of this study (Fig. 1). Of the 35 patients analyzed, 33 were diagnosed with a definitive diagnosis, 2 were diagnosed with a probable diagnosis based on the 2016 primary sclerosing cholangitis diagnostic criteria [10], and 4 developed cholangiocarcinoma [median 2.1 (range 0–16.5) years]. One patient diagnosed with cholangiocarcinoma at the initial ERCP had multiple strictures on ERC images, and surgical pathology confirmed the presence of PSC in the background. The four patients with cholangiocarcinoma included three patients with perihilar cholangiocarcinoma and one patient with distal cholangiocarcinoma. In one of the three patients with perihilar cholangiocarcinoma, carcinomas were detected from three independent sites within the perihilar bile duct. In this study, there were no cases of intrahepatic cholangiocarcinoma. Two of the four patients

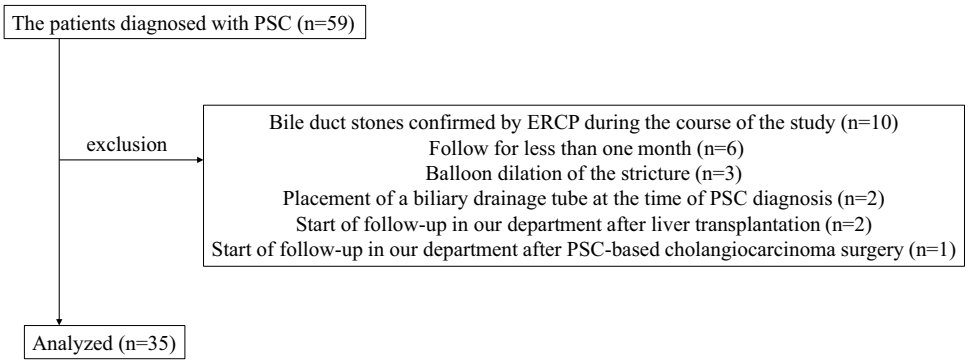

Fig. 1 Flow chart of patients recruited in this study

with cholangiocarcinoma underwent surgery, and they did not experience recurrence during follow-up at our institution. The remaining two patients were followed up due to poor liver function and numerous comorbidities, and both patients died of cancer. In the background of patients in the CCA group (n = 4) and non-CCA group ($n = 31$), there was a statistically significant difference in the CA19-9 levels, but no significant differences were observed in any of the other parameters (Table 1).

A total of 72 sessions of ERCP were performed (8 sessions in the CCA group and 64 sessions in the non-CCA group). Bile cytology was performed a total of 54 times (15 times for aspiration bile cytology and 39 times for ENBD bile cytology). In the CCA group, all bile cytology was performed only at the last ERCP when the diagnosis of malignancy was obtained. At the ERCPs prior to the last ERCP, bile cytology was not performed because the development of cholangiocarcinoma was not suspected. ENBD bile cytology was performed 1–3 times per session (median 2 times) in the CCA group and 1–8 times per session (median 2 times) in the non-CCA group. Bile duct biopsy was performed a total of 55 times (9 times for the CCA group and 46 times for the non-CCA group). In all patients in the CCA group, bile duct biopsies were performed only at the time of the last ERCP. All 9 biopsies in the CCA group were performed from the site where the cancer was present and included

Table 1 Baseline characteristics of the patients ($n = 35$)

	Overall ($n = 35$)		*P* value
	CCA ($n = 4$)	non-CCA ($n = 31$)	
Age, median, (range), years	70.5 (55–73)	40 (18–79)	0.146
Sex, male (%)	4 (100)	20 (64.5)	0.285
Smoking, *n* (%)	2 (50)	6 (19.4)	0.218
Drinking alcohol, *n* (%)	1 (25)	7 (22.6)	1
Liver cirrhosis, n (%)	1 (25)	6 (19.4)	1
IBD, *n* (%)	0 (0)	11 (35.5)	0.285
ALP (U/L), median, (range)	662.5 (190–1221)	519 (225–2205)	0.98
γ-GTP (U/L), median, (range)	308 (72–984)	281 (13–1827)	0.816
T-bil (mg/dL), median, (range)	1.45 (0.8–3)	1.2 (0.3–12.4)	0.795
CEA (ng/mL), median, (range)	3.2 (2.2–20.7)	2 (0.5–4.5)	0.067
CA19-9 (U/mL), median, (range)	376 (35–1801)	15 (1.9–2780)	0.031
Observation period, median, (range), days	1446 (918–8040)	2204 (389–13,320)	0.822
Method of final diagnosis (operation/biopsy/cytology/observation)	2/2/0/0	1/16/5/9	0.053
ERCP, median, (range), sessions	2 (1–3)	1 (1–17)	0.193
Adverse events of ERCP, n (%)	1 (25)	2 (6.5)	0.313
Pancreatitis	1 (mild)	1 (mild)	
Cholangitis	0	1 (mild)	
Perforation	0	0	

CCA patients who were diagnosed with cholangiocarcinoma at the final diagnosis, *non-CCA* those who were not diagnosed with cholangiocarcinoma during follow-up, *IBD* inflammatory bowel disease, *ERCP* endoscopic retrograde cholangiopancreatography

multiple biopsies from the same site. Bile duct biopsies were performed 1–4 times per session (median 2 times) in the CCA group and 1–4 times per session (median 2 times) in the non-CCA group. The details of each pathological result are shown in Tables 2 and 3. In terms of diagnostic performance for benign or malignant lesions on bile cytology and transpapillary bile duct biopsy, the sensitivity (14.3% vs. 77.8%, $P=0.04$), specificity (83.0% vs. 97.8%, $P=0.04$), and accuracy (74.1% vs. 94.5%, $P=0.007$) were all significantly greater for biopsy than for cytology. In all cases of bile duct biopsy, biopsy was possible from the intended site. The patients who had adverse events of ERCP included 1 patient (25%) with mild pancreatitis in the CCA group, 1 patient (3.23%) with mild pancreatitis and 1 patient (3.23%) with mild cholangitis in the non-CCA group (Table 1).

The cholangiographic findings and the bile duct diameters at each biopsy site were compared between the CCA group (9 sites) and the non-CCA group (46 sites). The cholangiographic findings were not significantly different between the CCA and non-CCA groups for the presence of occlusion and filling defect, and the types of stricture (Table 4). In the CCA group (9 sites), there were 1 site with a filling defect and 8 sites with strictures. Since all biopsy sites in CCA patients with bile duct strictures (8 sites) had DS, the bile duct diameters were compared between the CCA group and the non-CCA group limited to patients with DS (8 sites in CCA group vs. 18 sites in non-CCA group). As a result, the diameters of the strictures were 0.5 (0.2–1.1) mm vs. 0.8 (0.5–1.4) mm ($P=0.019$), the diameters of the upstream bile ducts were 7.1 (4.2–7.2) mm vs. 2.1 (1.2–4.1) mm ($P<0.001$), and the diameter differences were 6.6 (3.1–7) mm vs. 1.5 (0.2–3.6) mm ($P<0.001$) (Table 4). For the diameter differences, the optimal cutoff value for the diagnosis of benign or malignant lesions was 5.1 mm (area under the curve [AUC] = 0.972), with a sensitivity of 87.5% and a specificity of 100%. Representative bile duct images of cases with and without cholangiocarcinoma are shown in Fig. 2.

Table 3 Pathology results of bile duct biopsy

	Positive	Negative
Bile duct biopsy (55 biopsies)		
CCA	7 (suspicious of malignancy:1)	2 (atypical:1)
Non-CCA	1 (suspicious of malignancy:1)	45 (atypical:7)

CCA patients who were diagnosed with cholangiocarcinoma at the final diagnosis, *non-CCA* those who were not diagnosed with cholangiocarcinoma during follow-up

Discussion

In this study, we examined the appropriate method of pathological specimen collection during ERCP for cholangiocarcinoma surveillance in PSC patients. It was suggested that if a localized DS with upstream dilation, especially a DS with diameter differences of 5 mm or more, is observed, cholangiocarcinoma should be suspected, and transpapillary bile duct biopsy should be conducted.

According to the results of this study, in terms of diagnostic performance for benign or malignant lesions on bile cytology and transpapillary bile duct biopsy, the sensitivity, specificity, and accuracy were all significantly greater for biopsy than for cytology. Furthermore, a relatively high percentage of false positives was observed via bile cytology (8 of 47 times; 17%) (Table 2), and one patient was misdiagnosed with cholangiocarcinoma and underwent surgery; this patient was considered to have undergone over surgery. Based on these results, we believe that bile duct biopsy should be performed to detect cholangiocarcinoma in PSC patients if both bile cytology and bile duct biopsy are available at the facility.

A PubMed search of ERCP-based diagnostic methods for the diagnosis of cholangiocarcinoma in patients with PSC from 1978 to 2022 revealed reports of bile duct brush cytology, fluorescence in situ hybridization (FISH), confocal laser endoscopy, and cholangioscopic biopsy but no reports of

Table 2 Details of the pathology results of bile cytology

	Positive	Negative
Total of bile cytology (54 times)		
CCA	1	6 (atypical:1)
Non-CCA	8 (suspicious of malignancy:8)	39 (atypical:15)
Aspiration bile cytology (15 times)		
CCA	0	1
Non-CCA	5 (suspicious of malignancy:5)	9 (atypical:3)
ENBD bile cytology (39 times)		
CCA	1	5 (atypical:1)
Non-CCA	3 (suspicious of malignancy:3)	30 (atypical:12)

CCA patients who were diagnosed with cholangiocarcinoma at the final diagnosis, *non-CCA* those who were not diagnosed with cholangiocarcinoma during follow-up, *ENBD* endoscopic nasobiliary drainage

Table 4 Details of the ERC images and bile duct diameters

	ERC images	CCA (9 sites)	Non-CCA (46 sites)	*P* value
	Filling defect			
Filling defect	Presence/absence	1/8	0/46	0.359
	Occlusion			
Occlusion	Presence/absence	0/9	0/46	1

ERC images	CCA (8 sites)	non-CCA (46 sites)	*P* value
Stricture			
Smooth/irregular	1/7	6/40	1
Symmetry/asymmetry	1/7	6/40	1
Bilateral/unilateral	8/0	46/0	1
Diameter of the stricture, median, (range), mm	0.5 (0.2–1.1)	2.1 (0.5–6.9)	< 0.001
Diameter of the upstream bile duct, median, (range), mm	7.1 (4.2–7.2)	3.2 (1.2–7)	< 0.001
Diameter difference, median, (range), mm	6.6 (3.1–7)	0.7 (0.1–3.6)	< 0.001

ERC images	CCA (8 sites)	non-CCA with DS (18 sites)	*P* value
Diameter of the stricture, median, (range), mm	0.5 (0.2–1.1)	0.8 (0.5–1.4)	0.019
Diameter of the upstream bile duct, median, (range), mm	7.1 (4.2–7.2)	2.1 (1.2–4.1)	< 0.001
Diameter difference, median, (range), mm	6.6 (3.1–7)	1.5 (0.2–3.6)	< 0.001

ERC images endoscopic retrograde cholangiography images, *CCA* patients who were diagnosed with cholangiocarcinoma at the final diagnosis, *non-CCA* those who were not diagnosed with cholangiocarcinoma during follow-up

conventional bile cytology or transpapillary bile duct biopsy. A meta-analysis [13] examining studies of bile duct brush cytology, FISH, confocal laser endoscopy, and cholangioscopic biopsy concluded that cholangioscopic biopsy has the highest accuracy rate. However, it should be noted that while the overall specificity and accuracy of the four studies on cholangioscopic biopsy were high (97% and 96%, respectively), the sensitivity was low (65%), and the proportion of cholangiocarcinoma patients was low. Furthermore, when a cholangioscope is used, the inflammatory stricture caused by the PSC may hinder the insertion of the cholangioscope into the target site. In fact, it has been reported that the insertion of a cholangioscope was more difficult in patients with PSC than in those without PSC (2% vs. 15%, $P = 0.015$) [14]. Cholangioscopy is also associated with the risk of complications such as pancreatitis and cholangitis. Therefore, transpapillary bile duct biopsy without cholangioscopy may be useful as an ERCP-based diagnostic method for detecting cholangiocarcinoma in PSC patients. However, a meta-analysis [15] that evaluated the diagnostic performance of bile duct biopsy for cholangiocarcinoma without PSC showed a sensitivity of 48% and a specificity of 99%, indicating low sensitivity. This study showed a relatively high sensitivity of 77.8%, but the results remain unsatisfactory. In bile duct biopsy for cholangiocarcinoma without PSC, there have been reports focusing on the number of biopsy specimens [16], the presence of EST or endoscopic biliary stenting (EBS) [17], and immunostaining [18] of biopsy specimens; moreover, bile duct biopsy in carcinogenesis from PSC also needs to be improved to increase sensitivity.

According to the results of the present study, all the cholangiocarcinoma patients with PSC had bilateral strictures rather than unilateral strictures, which was different from those without PSC. This may be due to the presence of inflammation caused by PSC in the background. On the other hand, it has been reported that approximately 10–62% of patients with PSC develop DS at some stage after disease onset [19, 20]. In this study, all biopsy sites in the CCA patients with bile duct strictures (8 sites) presented with DS, and 18 sites (39.1%) of those in the non-CCA patients (46 sites) presented with DS. In a 25-year observational study in the UK comparing PSC patients with DS to those without DS, cholangiocarcinomas developed only in the group of patients with DS [19]. Therefore, it can be inferred that PSC patients present with DS during follow-up and subsequently develop cholangiocarcinoma from DS. In this study, we compared the diameter of the bile ducts in the CCA group with bile duct stricture and the non-CCA group with DS; the upstream bile ducts of DS were significantly more dilated in the CCA group. Furthermore, for differences in bile duct diameter, the optimal cutoff value for the diagnosis of benign or malignant lesions was 5.1 mm (AUC = 0.972). Therefore, to detect cholangiocarcinoma in patients with PSC, we should first focus on the presence or absence of localized DS during ERCP; if DS is present, the development of cholangiocarcinoma should be suspected if the upstream bile ducts are dilated, and transpapillary bile duct biopsy should be performed at the stricture-dilation

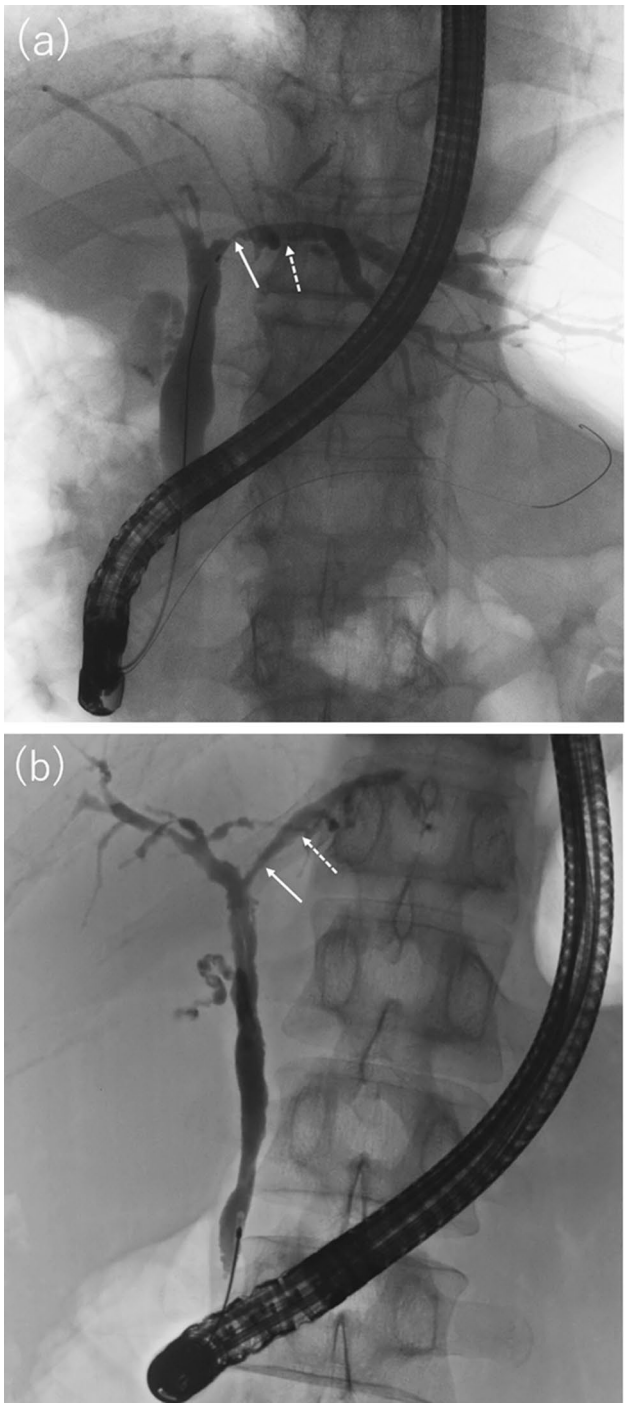

Fig. 2 **a** A case of cholangiocarcinoma. The diameter of the stricture (arrow) is 0.8 mm, the diameter of the upstream bile duct (broken arrow) is 5.9 mm, and the diameter difference is 5.1 mm. Biopsy of the stricture (1 specimen) revealed adenocarcinoma. **b** A case of non-cholangiocarcinoma. The diameter of the stricture (arrow) is 1.4 mm, the diameter of the upstream bile duct (broken arrow) is 4.7 mm, and the diameter difference is 3.3 mm. Biopsies from the stenosis (3 specimens) were all negative

transition site. In particular, if a DS with a diameter difference of 5 mm or more is observed, cholangiocarcinoma should be strongly suspected. We believe that such recognition will lead to early detection of cholangiocarcinoma in PSC patients, which will ultimately contribute to improved prognosis. The DS of which the upstream bile ducts are not so dilated may be a precancerous lesion, such as bilIN; therefore, even if a diagnosis of cholangiocarcinoma is not obtained when DS appears during PSC follow-up, it is necessary to follow the patient more closely, keeping in mind the possibility of subsequent development of cholangiocarcinoma.

On the other hand, MRCP might also be useful to estimate the cholangiographic findings and determine the indication of ERCP plus bile duct biopsy. However, in the present study, many cases were judged to require ERCP based on CT findings, and MRCP was performed before ERCP in only five (6.9%) of a total of 72 ERCPs. Therefore, it is difficult to assess the usefulness of MRCP in the present study. In addition, MRCP images tend to have lower resolution than ERCP images, which might make it difficult to precisely measure the diameter of the stricture and the upstream bile duct. Nevertheless, in the future, we consider that it is necessary to verify whether the findings obtained in this study can be utilized in MRCP using higher-resolution images.

A limitation of this study is that it is a single-center, retrospective study of a relatively small number of patients. However, PSC itself is a relatively rare disease, and the number of cases of carcinogenesis among them is even smaller, making large-scale studies at a single institution difficult. Conversely, this single-center study provided detailed information on each patient, which is an advantage of this study. Therefore, future prospective studies with many patients at multiple centers are warranted. Another limitation of this study is that the examiner was left to determine whether a localized stricture was present and whether bile cytology or bile duct biopsy should be performed.

Although the appropriate method of pathological specimen collection for detecting cholangiocarcinoma in patients with PSC is unclear, the results of this study suggest that when a localized DS with upstream dilation, especially a DS with a diameter difference of 5 mm or more, is found, cholangiocarcinoma should be suspected, and transpapillary bile duct biopsy should be performed. In the future, it is necessary to utilize these findings and prospectively examine whether cholangiocarcinoma can be detected at an early stage, not only with ERCP but also with MRCP.

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Declarations

Conflict of interest The authors declare that they have no conflict of interest.

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