

Percutaneous transluminal forceps biopsy in patients suspected of having malignant biliary obstruction: factors influencing the outcomes of 271 patients

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Abstract

Objectives To evaluate predictive factors for false-negative diagnosis of percutaneous forceps biopsies in patients suspected of having a malignant biliary obstruction

Methods Two hundred seventy one consecutive patients with obstructive jaundice underwent percutaneous forceps biopsy. In each patient, three to five specimens (mean, 3.5 specimens) were collected from the lesion. The final diagnosis for each patient was confirmed with pathologic findings at surgery, additional histocytologic data, or clinical and radiologic follow-up. Univariate and multivariate logistic regression analysis was used to identify risk factors associated with false-negative diagnosis.

Results One hundred ninety four of 271 biopsies resulted in correct diagnoses of malignancy, while 20 biopsy diagnoses were proved to be true-negative. There were 57 false-negative diagnoses and no false-positive diagnoses. The diagnostic performance of transluminal forceps biopsy in malignant biliary obstructions was as follows: sensitivity, 77.2%; specificity, 100%; and accuracy, 78.9%; positive predictive value, 100%, negative predictive value; 25.9%. Periapillary segment of common bile duct, intrahepatic bile duct and metastatic disease were the significant risk factors of false-negative diagnosis.

Conclusions Percutaneous forceps biopsy provides relatively high accuracy in the diagnosis of malignant biliary obstructions. The predictive factors of false-negative biopsy were determined to be biopsy site and origin of primary tumour.

Key Points

- Percutaneous forceps biopsy provides relatively high accuracy in diagnosis of malignant biliary obstructions.
- The predictive factors of false-negative biopsy were biopsy site and origin of primary tumour.
- The procedure-related complications were low.

Keywords Biopsy · Diagnostic technique, surgical · Cholangiocarcinoma · Bile duct diseases · Radiography, interventional

Abbreviations

CI Confidence interval

Introduction

Major advances in the diagnosis of malignant biliary obstruction have been made over the past few decades. The site of obstruction in the bile duct can be identified quickly and accurately using non-invasive imaging systems, such as ultrasound scanning (US), computed tomography (CT), and magnetic resonance cholangiopancreatography (MRCP) [1]. However, tumours that affect the bile duct are often too small to have specific imaging findings. Moreover, malignant obstructions cannot be easily distinguished from benign obstructions [2, 3]. Therefore, histological confirmation for correct diagnosis is often required from both a therapeutic and a prognostic viewpoint.

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Percutaneous transhepatic biliary drainage (PTBD) is a well-established interventional radiologic procedure used in patients with obstructive jaundice. It can be used to provide access to the bile duct for various biopsy instruments. Forceps biopsy via the PTBD tract has become a popular method for diagnosing biliary tumours since it was first reported in 1980 [4]. Four recent large studies that included more than 50 patients suggested that histological diagnosis with forceps biopsy was more successful than that with bile cytology and fine-needle aspiration biopsy (FNAB), with a reported sensitivity of 78%–93% [5–8]. However, most of the previous studies have focused on the results of the technique [5–8], and no studies have been performed to analyze outcome-associated factors in a large study population. Therefore, additional studies are needed to identify factors associated with the outcome. The purpose of the current study was to evaluate the diagnostic accuracy of percutaneous transluminal forceps biopsy in 271 patients suspected of having a malignant biliary obstruction and to identify predictive factors associated with technical outcomes.

Materials and methods

Patients

Institutional review board approval was obtained before the initiation of this retrospective study. We retrospectively examined a total of 291 consecutive patients with obstructive jaundice who underwent percutaneous transluminal biopsy of the bile duct with a 50-cm, 5.4-F flexible biopsy forceps (Cordis, Miami, FL, USA) between February 1995 and October 2014 at our institution. Twenty patients were excluded due to inadequate image quality of the CT images or short follow-up duration. All cases were performed by one of two interventional radiologists (G.S.J, G.H.K) through a PTBD tract during or after the procedure for bile duct decompression. One hundred and thirty of the 271 patients were also included in a previous study performed at our institution [8]. This previous article focused on the results of the technique, whereas in this manuscript we evaluate predictive factors for false-negative diagnosis.

Suspicion of a malignant obstruction was the main indication of the biopsy. The medical records, surgical reports, histopathologic reports, and diagnostic imaging reports of each patient were retrospectively reviewed. The following information was recorded from patient records: age, sex, technical success of the biopsy procedure, approach route for the biopsy (right- or left-side approach), site of the lesion, length of stenosis, operator, complications and their treatment, final diagnosis and means of establishing the final diagnosis, histopathologic results, biopsy sample adequacy, radiological follow up, and clinical follow-up. The length of the stenosis was

evaluated in only 131 of the 271 study participants because multiplanar reformatted CT images or digital cholangiography images during the procedure were not available in the remaining 140 patients.

Technical success of the biopsy procedure was defined as successful access to the lesion site and successful acquisition of tissue samples. The samples were considered successful if the histopathologist had sufficient material to render a diagnosis from the sample provided.

All patients underwent abdominal computed tomography (CT) and ultrasonography before the interventional procedure. Radiology reports identified biliary dilatation in all cases.

Procedure

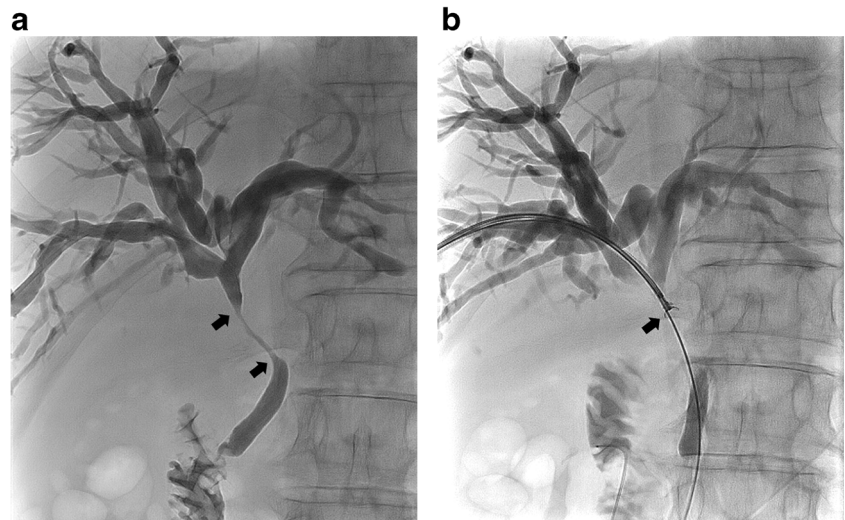
For conscious sedation, 1–2 mg of lorazepam (Ativan; Wyeth-Korea, Gunpo, South Korea) was administered intravenously before the procedure. All procedures were performed under local anaesthesia at the puncture site. Percutaneous transhepatic cholangiography and biliary drainage were performed with the standard technique as previously described [9]. The biopsies were performed as previously discussed [10, 11]. Briefly, after passage of a 145-cm, 0.035-inch guide wire (Radiofocus M, Terumo, Tokyo, Japan or Amplatz Superstiff, Med-tech/Boston Scientific, Watertown, MA, USA) through the lesion into the common bile duct or down to the duodenum, a 25-cm, 8-F sheath (Cook, Bloomington, IN, USA) was advanced over the guide wire, with its tip positioned within the stricture area. Subsequently, the dilator was removed and the outer sheath and guide wire were left in place. The biopsy forceps was then inserted through the sheath to the proximal margin of the stricture, and biopsy was performed with fluoroscopic guidance (Fig. 1). In each patient, three to five biopsy specimens (mean, 3.5 specimens) were taken from the lesion and were fixed with formalin to be sent for histopathologic examination.

The final diagnosis for each patient was rendered with histological analysis at surgery or other histological or cytological studies (i.e., FNAB, ascitic fluid). In the absence of histological or cytological studies, the final diagnosis was of malignancy if there was an increase in size of the lesion and/or development of a metastasis on follow-up imaging studies.

Statistical evaluation

Sensitivity, specificity, positive and negative predictive values, and accuracy were calculated for the biopsy technique. For statistical purposes, a pathologic result reported as “inadequate” or as “suspicious”, but not definitely diagnostic for a malignant tumour was regarded as a negative result. Univariate and multivariate logistic regression analysis were

Fig. 1 Image obtained in a 70-year-old man with jaundice **(a)** Percutaneous transhepatic cholangiogram shows a stricture (*arrows*) in the common hepatic duct. **(b)** Percutaneous transhepatic cholangiogram shows the biopsy forceps (*arrow*), which is inserted through a sheath to enable biopsy of the region of the stricture



performed to identify independent prognostic factors that were associated with a false-negative result. The factors that were found to be statistically significant by using univariate analysis were entered into multivariate models to gauge their independent predictive value on false negative diagnosis. Statistical analysis was performed with SPSS software, version 19.0 (IBM, Chicago, IL). A P value < 0.05 was considered to indicate a significant difference.

Results

All biopsy procedures were technically successful. Biopsies were performed with a right-sided approach in 191 patients and with a left-sided approach in 80 patients.

The lesions involved the common bile duct ($n = 106$), common hepatic duct ($n = 60$), hilum ($n = 5$), periampullary segment of common bile duct ($n = 31$), and right or left IHD duct ($n = 15$). A stricture located within the distal 2 cm of the common bile duct and extending down to the level of the ampulla of Vater was considered to be a stricture of the periampullary segment of the common bile duct.

The final diagnosis was malignant disease in 251 patients. The disease included cholangiocarcinoma ($n = 180$), pancreatic carcinoma ($n = 25$), GB cancer ($n = 6$), hepatocellular carcinoma ($n = 3$), Ampulla of Vater cancer ($n = 6$), duodenal cancer ($n = 1$) and metastatic carcinoma ($n = 30$) from stomach cancer, cervical cancer, lymphoma, anal cancer and lung cancer.

Malignant tumours were classified into two groups according to the origin of primary tumour: Cholangiocarcinoma ($n = 180$) and metastatic disease ($n = 71$) which is a malignant tumour other than cholangiocarcinoma. Metastatic disease includes pancreatic carcinoma, GB cancer, hepatocellular carcinoma, duodenal cancer and metastatic carcinoma.

The diagnosis of malignant disease was confirmed with a pathologic finding at surgery ($n = 81$); with histological or

cytological findings after FNAB, sampling of ascitic fluid or bile acid ($n = 36$), or evidence of increase in size of the lesion or development of a metastasis at radiologic follow-up ($n = 134$). The final diagnosis in the remaining 20 patients was benign disease. Seven of 20 patients with benign diseases were confirmed with surgical biopsy results. In the absence of surgical biopsy results, the final diagnosis of benign disease was based on follow-up at a minimum of 12 months with clinical course and imaging showing no evidence of disease progression.

The histological results of forceps biopsy are shown in Table 1. One hundred and ninety-four of 271 biopsies resulted in a correct diagnosis of malignancy. A specific histological diagnosis was made in 186 cases. The remaining eight cases were definitely carcinoma, although the exact histological type was not determined. There were 20 true negative diagnoses. The remaining 57 diagnoses at biopsy were considered to be false-negative and included chronic inflammation ($n = 46$), findings suspicious for carcinoma ($n = 6$), and inadequate samples ($n = 5$). In the five cases of inadequate sampling, necrotic or fibrinous materials were obtained from the specimens. For the diagnosis of malignant biliary obstruction, transluminal forceps biopsy had a sensitivity of 77.2% and a specificity of 100%. Although the positive predictive value

Table 1 Histologic results of forceps biopsy in 271 patients

Histologic result	No. of patients (%)
Adenocarcinoma	180 (66.4)
Squamous cell carcinoma	2 (0.7)
Lymphoma	2 (0.7)
Hepatocellular carcinoma	2 (0.7)
Carcinoma, type undetermined	8 (3)
Suspicious for carcinoma	6 (2.2)
Chronic inflammation	66 (24.4)
Inadequate sample	5 (1.8)

Table 2 Baseline characteristics of 271 patients and univariate analysis of risk factors for a false-negative diagnosis

Factors	All patients (<i>n</i> =271)	False-negative diagnosis (<i>n</i> =57)	Univariate analysis	
			Odds ratio (95% CI)	<i>P</i> value
Age (years)	64 ± 11.53	63±11.07	0.990 (0.066 - 1.015)	0.435
Male (female)	179 (92)	36 (21)	1.175 (0.639 - 2.160)	0.604
Operator				
Operator 1	228	46	1	
Operator 2	43	11	1.360 (0.638 - 2.901)	0.426
Approach site				
Right	191	42	1	
Left	80	15	0.837 (0.424 - 1.580)	0.551
Biopsy number	3 ± 1.08	3 ± 1.18	0.674 (0.500 - 0.910)	0.009
Length of the stenosis ^b	2 ± 0.98	1.9 ± 0.90	0.734 (0.330 - 1.636)	0.450
Site of the lesion				
CBD	106	19	1	
Periampullary segment	31	13	6.58 (2.298 - 16.504)	<0.001
CHD	60	13	1.232 (0.557 - 2.725)	0.607
Hilar	59	7	0.574 (0.226 - 1.460)	0.244
IHD	15	5	3.045 (0.871 - 10.646)	0.081
Origin of primary tumour				
Cholangiocarcinoma	186	33	1	
Metastatic disease ^a	65	24	2.714(1.447 - 5.089)	0.002

^a Metastatic disease includes pancreatic carcinoma, GB cancer, hepatocellular carcinoma, duodenal cancer, stomach cancer, cervical cancer, lymphoma, anal cancer and lung cancer.

^b Length of the stenosis was evaluated in only 131 of the 271 study population

CBD = common bile duct; CHD = common hepatic duct; IHD = intrahepatic bile duct

was 100%, the negative predictive value was only 26%. The overall accuracy of forceps biopsy for correct diagnosis of all biliary lesions was 78.9% (214 of 271 cases).

The univariate logistic analysis was used to identify the predictive factors associated with false-negative biopsy and included age, sex, operator, approach site for the biopsy (right- or left-side approach), site of the obstruction, type of the primary tumour, and number of biopsy specimens. Univariate logistic analysis showed that false-negative results were associated with a number of biopsy specimens, site of the obstruction and type of primary tumour (Table 2). Multivariate logistic analysis revealed that metastatic disease (odds ratio 2.626, 95% CI 1.288-5.354, *P* = .008), periampullary segment of the common bile duct (odds ratio 4.355, 95% CI 1.651-11.490, *P* < .001) and intrahepatic bile duct (odds ratio 4.051, 95% CI 1.077-15.246, *P* = .039) were independent prognostic factors for false-negative results (Table 3). Other factors were not related to the false-negative results.

Eleven patients (4%) experienced complications, which included hemobilia (*n* = 9) and biloma (*n* = 2). Eight cases of hemobilia were transient and resolved within 24 hours. One case of hemobilia lasted for two days and was successfully

treated by transarterial embolization. The two cases of biloma were successfully treated with percutaneous catheter drainage.

Table 3 Multivariate predictive factors for a false-negative diagnosis

Factors	Multivariate analysis	
	Odds ratio (95% CI)	<i>P</i> value
Biopsy number	0.737 (0.542 - 1.001)	0.051
Site of the lesion		
CBD	1	
Periampullary segment	6.811 (2.420 - 19.166)	<0.001
CHD	1.483 (0.646 - 3.408)	0.353
Hilar	0.887 (0.327 - 2.407)	0.814
IHD	4.051 (1.077 - 15.246)	0.039
Origin of primary tumour		
Cholangiocarcinoma	1	
Metastatic disease [*]	2.626 (1.288 - 5.354)	0.008

Metastatic disease includes pancreatic carcinoma, GB cancer, hepatocellular carcinoma, duodenal cancer, stomach cancer, cervical cancer, lymphoma, anal cancer and lung cancer.

CBD = common bile duct; CHD = common hepatic duct;

IHD = intrahepatic bile duct

Discussion

Currently, various transluminal techniques for acquiring tissue from biliary tumours are performed through a PTBD tract. Because most tumours of the bile duct arise from ductal epithelium, tissue obtained through the bile duct from an abnormal segment seems to be the most appropriate for pathologic examination. Collection of bile for cytological examination is a simple technique but is rarely used because of its poor results [12]. Brush cytology sampling performed during PTBD or endoscopic retrograde cholangiopancreatography has been proven to be safe and effective, but several reports showed it to have a low sensitivity of 35%–61% and superficial sampling nature [5, 13, 14]. In an attempt to further increase the diagnostic value of biopsy of the bile duct, a transluminal biopsy technique has been developed that incorporates the use of biopsy forceps, which were reported to have relative high sensitivity of 78–93% and specificity of 100% [5–8]. In addition, percutaneous cholangioscopic transluminal forceps biopsy of the bile duct offers the greatest chance to obtain malignant cells because it enables more accurate targeting and direct inspection of the lesion; its reported sensitivity in the diagnosis of cholangiocarcinoma is 96% [15]. However, this technique is more difficult, time consuming, and expensive than other transluminal techniques because the PTBD tract must be dilated to accommodate the cholangioscope (10). Moreover, the utility of cholangioscopic forceps biopsy in the diagnosis of extrabiliary malignancy remains limited. Peroral cholangioscopic forceps biopsy is another method that enables more accurate targeting and direct inspection of the lesion, but several reports showed it to have a low sensitivity of 49%–77% [16–19]. Peroral cholangioscopic forceps biopsy has an inherent limitation that relates to the smaller cup size compared with percutaneous transluminal forceps biopsy [17]. IDUS has been reported to be a useful modality to demonstrate the longitudinal extent of bile duct cancer [20]. Transpapillary biopsy under the guidance of IDUS may further improve the diagnostic accuracy [21]. Therefore, the combination of IDUS and transpapillary biopsy could be used as an alternative to percutaneous transhepatic cholangioscopy and biopsy for accurate targeting of the lesion and increasing the diagnostic efficacy of the biopsy technique [21].

This large series study shows that transluminal forceps biopsy of biliary tumours is highly accurate in the diagnosis of malignant biliary obstruction. The overall accuracy of forceps biopsy was 79%, with sensitivity of 77.4% and a specificity of 100%. Several studies [5, 7, 8, 22] in relatively large groups of patients obtained results comparable to ours (i.e., overall sensitivities of 78%–93% were observed in 40–130 patients).

Multivariate logistic analysis showed that false-negative results were associated with the origin of a primary tumour and with the site of obstruction. Metastatic disease was a significant independent factor of false-negative results. Many

extrabiliary cancers may cause biliary obstruction by metastasizing to the lymph nodes around the extrahepatic bile duct, through direct neoplastic invasion of the biliary tree, or by compressing the biliary tree without direct invasion [23–25]. Sato et al. found that, in percutaneous transhepatic cholangioscopy-guided forceps biopsy of the bile duct, biopsy specimens were obtained from only the mucosa and superficial part of the fibromuscular layer of the duct [26]. They suggested that forceps biopsy is therefore less helpful for detecting extrinsic tumours or tumours in the deep part of the bile duct wall. Our study showed that the sensitivity of forceps biopsy in patients with malignant metastatic disease (61.9%) was significantly lower than its sensitivity in patients with cholangiocarcinoma (83.3%). Terasaki et al. [27] reported a sensitivity of 100% for forceps biopsy, even in five patients with extrinsic malignancy. We surmise that biopsy results of metastatic disease were dependent on the depth of infiltration of the bile duct wall by the extrinsic malignancy.

In our study, location of the lesion in the periampullary segment of the common bile duct and IHD were also the significant independent factor for false-negative results. The thirteen of 31 cases of periampullary segment showed false-negative results, which including seven cases of metastatic cancer, four cases of ampulla of Vater cancer and two cases of cholangiocarcinoma. Obstructions in the distal part of the common bile duct were difficult to satisfactorily sample at biopsy because the forceps jaws frequently faced the sidewall of the duct rather than the wall of the obstructed region due to angulation in that area. These factors could explain false-negative results in the periampullary segment. Five of 15 cases of IHD showed false-negative results, including four cases of cholangiocarcinoma and one case of metastatic cancer. Three out of the four cases of cholangiocarcinoma represented intrahepatic mass-forming cholangiocarcinoma. We hypothesized that the three cases of intrahepatic mass-forming cholangiocarcinoma may have caused biliary obstruction by extrinsic compression rather than by bile duct invasion.

Endoscopic transpapillary forceps biopsy is another method used to obtain tissue samples of malignant biliary obstruction, and has a wide range of sensitivity from 30 to 88% [28–30]. This ERCP-based technique is also a significantly higher sensitive method in bile duct cancer but not in tumours outside the bile duct, such as pancreatic cancer [28, 29]. Endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) can be used as an alternative sampling technique. Researchers have reported that EUS-FNA has a high sensitivity for suspected malignant biliary obstruction, when endoscopic forceps biopsy showed negative results [31]. Therefore, tissue sampling for periampullary tumours or metastatic disease by using the EUS-FNA might be a better method than forceps biopsy [29, 30].

One recent large study including 241 patients with biliary strictures suggested that a stricture length ≥ 30 mm was a

significant indicator of positive diagnosis by forceps biopsy [28, 29]. However, stricture length was not associated with a false-negative diagnosis in our study, in which tissue samples were obtained at the stricture margin. We surmise that differences in sampling method explained this discrepancy.

The number of passes with the biopsy forceps was related to the amount of specimens. The small amount of biopsy specimens does pose significant issue for the pathologist. In our study, the number of biopsy specimens was a significant factor for the false-negative results in univariate logistic analysis (odds ratio 0.674, CI 0.500 - 0.910, $p = 0.009$), and was a marginal trend in multivariate logistic analysis (odds ratio 0.737, CI 0.542 - 1.001, $p = 0.051$). The number of passes with the biopsy forceps was left to the operator's discretion. During the study period, the number of passes with biopsy forceps was usually three times. When a biopsy sample was thought to be inadequate (i.e., bloody sample, necrotic debris, small sample size), an additional sample was taken. Mean number of biopsy specimens was 3.5. Based on the findings of the present study, however, a minimum of five samples have been routinely obtained since then.

The complication rate was low (4%); eleven patients experienced complications of hemobilia or biloma. In one case of hemobilia, transarterial embolization was required. The theoretic risks of performing transluminal biopsy of the bile duct wall include injury to an adjacent blood vessel or development of a bile leak. However, such complications have not been reported in the literature. In our study, two cases of biloma were thought to be caused by the drainage process rather than by the biopsy procedure, because the bilomas occurred in subcapsular locations far from the biopsy site.

This study is not without limitations. Clinical data collected after the procedure were retrospective in nature. There was the lack of confirmative histological diagnoses in a large number of patients (53%). Moreover, the thirty-three cases of benign histological results were included in our study, having the final diagnosis was rendered on the basis of follow-up only. Nevertheless, we thought that a clinical follow-up period of longer than 12 months would be sufficient to exclude other potential diagnoses.

In conclusion, percutaneous transluminal forceps biopsy provides relatively high accuracy in the diagnosis of malignant biliary obstructions and has a low number of complications. The predictive factors of false-negative biopsy were determined to be the biopsy site and the origin of the primary tumour.

Compliance with ethical standards

Guarantor The scientific guarantor of this publication is Gyoo-Sik Jung, MD.

Conflict of interest The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

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Informed consent Written informed consents were obtained from all subjects (patients) in this study.

Ethical approval Institutional Review Board approval was obtained.

Study subjects or cohorts overlap Some study subjects or cohorts have been previously reported in Radiology. Jung G, Huh J, Lee SU, Han BH, Chang H, Cho YD (2002) Bile duct: analysis of percutaneous transluminal forceps biopsy in 130 patients suspected of having malignant biliary obstruction. *Radiology* 224:725-730.

Methodology

- Retrospective
- Diagnostic study
- Performed at one institution

References

1. Changhua L, Huajie M, Qinghua W et al (2011) Diagnostic performance of magnetic resonance cholangiopancreatography in malignant obstructive jaundice. *Cell Biochem Biophys* 61:383–388
2. Baron RL, Stanley RJ, Lee JK et al (1982) A prospective comparison of the evaluation of biliary obstruction using computed tomography and ultrasonography. *Radiology* 145:91–98
3. Hall-Craggs MA, Lees WR (1986) Fine-needle aspiration biopsy: pancreatic and biliary tumors. *AJR Am J Roentgenol* 147:399–403
4. Elyaderani MK, Gabriele OF (1980) Brush and forceps biopsy of biliary ducts via percutaneous transhepatic catheterization. *Radiology* 135:777–778
5. Tapping C, Byass O, Cast J (2012) Cytological sampling versus forceps biopsy during percutaneous transhepatic biliary drainage and analysis of factors predicting success. *Cardiovasc Intervent Radiol* 35:883–889
6. Kim CS, Han YM, Song HY, Choi KC, Kim DG, Cho BH (1992) Percutaneous transhepatic biliary biopsy using gastrofiberscopic biopsy forceps. *J Korean Med Sci* 7:325–332
7. Patel P, Rangarajan B, Mangat K (2015) Improved accuracy of percutaneous biopsy using “Cross and push” technique for patients suspected with malignant biliary strictures. *Cardiovasc Intervent Radiol* 38:1005–1010
8. Jung G, Huh J, Lee SU, Han BH, Chang H, Cho YD (2002) Bile duct: analysis of percutaneous transluminal forceps biopsy in 130 patients suspected of having malignant biliary obstruction. *Radiology* 224:725–730
9. Günther R, Schild H, Thelen M (1988) Review article: percutaneous transhepatic biliary drainage: Experience with 311 procedures. *Cardiovasc Intervent Radiol* 11:65–71
10. Donald JJ, Fache JS, Burhenne HJ (1993) Percutaneous transluminal biopsy of the biliary tract. *Can Assoc Radiol J* 44:185–188
11. Savader SJ, Prescott CA, Lund GB, Osterman FA (1996) Intraductal biliary biopsy: comparison of three techniques. *J Vasc Interv Radiol* 7:743–750
12. Savader SJ, Lynch FC, Radvany MG et al (1998) Single-specimen bile cytology: a prospective study of 80 patients with obstructive jaundice. *J Vasc Interv Radiol* 9:817–821
13. Ponchon T, Gagnon P, Berger F et al (1995) Value of endobiliary brush cytology and biopsies for the diagnosis of malignant bile duct

- stenosis: Results of a prospective study. *Gastrointest Endosc* 42: 565–572
14. Weber A, von Weyhern C, Fend F et al (2008) Endoscopic transpapillary brush cytology and forceps biopsy in patients with hilar cholangiocarcinoma. *World J Gastroenterol* 14:1097–1101
 15. Nimura Y (1993) Staging of biliary carcinoma: cholangiography and cholangioscopy. *Endoscopy* 25:76–80
 16. Chen YK, Parsi MA, Binmoeller KF et al (2011) Single-operator cholangioscopy in patients requiring evaluation of bile duct disease or therapy of biliary stones (with videos). *Gastrointest Endosc* 74: 805–814
 17. Hartman DJ, Slivka A, Giusto DA, Krasinskas AM (2012) Tissue yield and diagnostic efficacy of fluoroscopic and cholangioscopic techniques to assess indeterminate biliary strictures. *Clin Gastroenterol Hepatol* 10:1042–1046
 18. Chen YK, Pleskow DK (2007) SpyGlass single-operator peroral cholangiopancreatography system for the diagnosis and therapy of bile-duct disorders: a clinical feasibility study (with video). *Gastrointest Endosc* 65:832–841
 19. Siddiqui AA, Mehendiratta V, Jackson W, Loren DE, Kowalski TE, Eloubeidi MA (2012) Identification of cholangiocarcinoma by using the spyglass spyscope system for peroral cholangioscopy and biopsy collection. *Clin Gastroenterol Hepatol* 10:466–471
 20. Nakazawa T, Naitoh I, Hayashi K (2012) Usefulness of intraductal ultrasonography in the diagnosis of cholangiocarcinoma and IgG4-related sclerosing cholangitis. *Clin Endosc* 45:331–336
 21. Noda Y, Fujita N, Kobayashi G et al (2008) Intraductal ultrasonography before biliary drainage and transpapillary biopsy in assessment of the longitudinal extent of bile duct cancer. *Dig Endosc* 20: 73–78
 22. Ierardi AM, Mangini M, Fontana F et al (2014) Usefulness and safety of biliary percutaneous transluminal forceps biopsy (PTFB): Our experience. *Minim Invasive Ther Allied Technol* 23: 96–101
 23. Lee BH, Chin SY, Kim SA, Kim KH, Do YS (1995) Obstructive jaundice in gastric carcinoma: cause, site, and relationship to the primary lesion. *Abdom Imaging* 20:307–311
 24. Thomas JH, Pierce GE, Karlin C, Hermreck AS, MacArthur RI (1981) Extrahepatic biliary obstruction secondary to metastatic cancer. *Am J Surg* 142:770–773
 25. Lee J, Gwon DI, Ko G, Kim JW, Sung K (2016) Biliary intraductal metastasis from advanced gastric cancer: radiologic and histologic characteristics, and clinical outcomes of percutaneous metallic stent placement. *Eur Radiol* 26:1649–1655
 26. Sato M, Inoue H, Ogawa S et al (1998) Limitations of percutaneous transhepatic cholangioscopy for the diagnosis of the intramural extension of bile duct carcinoma. *Endoscopy* 30:281–288
 27. Terasaki K, Wittich GR, Lycke G et al (1991) Percutaneous transluminal biopsy of biliary strictures with a biptome. *AJR Am J Roentgenol* 156:77–78
 28. Naitoh I, Nakazawa T, Kato A et al (2016) Predictive factors for positive diagnosis of malignant biliary strictures by transpapillary brush cytology and forceps biopsy. *J Dig Dis* 17:44–51
 29. Chen W, Wei K, Chen Y et al (2016) Transpapillary biliary biopsy for malignant biliary strictures: comparison between cholangiocarcinoma and pancreatic cancer. *World J Surg Oncol* 14:1
 30. Navaneethan U, Njei B, Lourdasamy V, Konjeti R, Vargo JJ, Parsi MA (2015) Comparative effectiveness of biliary brush cytology and intraductal biopsy for detection of malignant biliary strictures: a systematic review and meta-analysis. *Gastrointest Endosc* 81: 168–176
 31. Ogura T, Hara K, Hijioka S et al (2012) Can endoscopic ultrasound-guided fine needle aspiration offer clinical benefit for tumors of the ampulla of Vater? -an initial study. *Endosc Ultrasound* 1:84–89