

Effectiveness of cholangioscopy using narrow band imaging for hepatobiliary malignancies

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Purpose: Recently, cholangioscopy using narrow band imaging (NBI) has been used as a diagnostic modality for better visualization in hepatobiliary malignancies; however, there are few reports on it. Our aim is to evaluate the effectiveness of cholangioscopy using NBI in hepatobiliary malignancies.

Methods: Between January 2007 and December 2016, 152 cholangioscopies using percutaneous approach were conducted in total 123 patients. Among these, 36 patients were suspicious of hepatobiliary malignancies. Thirteen patients with an ambiguous margin on endoscopic retrograde cholangiopancreatography (ERCP) or magnetic resonance cholangiopancreatography (MRCP), for whom NBI tipped the balance in diagnosis of lesion and decision of lesion extent by adding NBI, were involved in our study.

Results: Underlying diseases were all malignant in 13 patients (11 bile duct cancers, 1 liver cancer, 1 pancreas cancer with common bile duct invasion). In 7 cases with papillary type tumor, minute superficial spreading tumor was detected by NBI more easily, and NBI provided a better visualization of tumor vessel and margin evaluation in 4 cases with infiltrative tumor. In 2 cases with mucin-hypersecreting tumor, NBI showed better penetration through the mucin and gave us a much clearer image. Nine patients ultimately underwent surgical resection. The margins predicted by NBI cholangioscopy were consistent with the pathological margins on the resected specimens.

Conclusion: In conclusion, cholangioscopy using NBI is very useful for evaluation of suspected hepatobiliary malignancies with an ambiguous margin on ERCP or MRCP. It can give us an accurate pathologic mapping, and this information seems to be essential before deciding on a treatment strategy.

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Key Words: Cholangiography, Narrow band imaging

INTRODUCTION

Cholangioscopy, though invasive, seems to have several advantages when compared with other diagnostic modalities. It can be useful for the differential diagnosis of focal stricture of the biliary tree [1,2], especially in the intrahepatic ducts [3], as well as for determining the extent of superficial spread of bile duct tumors, especially up to the proximal margin [4,5]. In addition, targeted biopsy specimens can provide an accurate histologic diagnosis, and therapeutic maneuvers can be chosen based on accurate histologic mapping [6-8].

Narrow band imaging (NBI) is a new technology aimed to improve the quality and utility of endoscopic images that helps to differentiate malignant from benign lesions [9]. Cholangioscopy using NBI has been attempted, which provides more characteristic endoscopic imaging of mucosal structures and mucosal vessels in bile duct lesions to differentiate benign from malignant lesions compared with conventional white-light imaging [10]. However, there is few data on percutaneous cholangioscopy using NBI.

We therefore analyzed patients with suspected hepatobiliary malignancies in whom cholangioscopy using NBI played a

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crucial role in diagnosis and decision of treatment plan.

METHODS

Patients

Between January 2007 and December 2016, 152 cholangioscopies using percutaneous approach were conducted in a total of 123 patients. Among these, 36 patients were suspicious of hepatobiliary malignancies. Thirteen patients with an ambiguous margin on endoscopic retrograde cholangiopancreatography (ERCP) or magnetic resonance cholangiopancreatography (MRCP), for whom NBI tipped the balance in diagnosis of lesion and decision of lesion extent by adding NBI, were involved in our study. All enrolled patients had undergone ERCP or MRCP; however, these were inadequate in determining the extent of the lesions or in differentiating malignant from benign. According to previous literature, our group categorized hepatobiliary malignancies as nodular, papillary, or infiltrative types based on cholangioscopic findings [11]. Operability was evaluated in all enrolled patients. If the patient underwent surgical resection, then the pathological margin was compared with the preoperatively evaluated margin.

All patients provided a written informed consent for cholangioscopy using percutaneous approach. The study protocol was approved by the Institutional Review Board of our center.

Techniques

Cholangioscopic examination was performed via a percutaneous transhepatic tract. For cholangioscopy using percutaneous approach, initial percutaneous transhepatic biliary drainage (PTBD) was carried out by using a pigtail catheter (7.5F to 8.0F; Cook, Bloomington, IN, USA) under fluoroscopic guidance. Before PTBD, meperidine (50 mg) and midazolam (3 to 5 mg) were given intravenously for control of pain and anxiety. Local anesthesia of the skin and intercostal space was obtained by the injection of 2% lidocaine. Two or 3 days after PTBD, the tract was dilated up to 16F or 18F. Cholangioscopy using percutaneous approach was then performed 7 to 10 days after tract dilatation. This waiting period is required for stabilization and maturation of the wall of the dilated tract.

Cholangioscopy was carried out by using a cholangioscope (CYF 240A, Olympus Optical Ltd., Tokyo, Japan). During cholangioscopy, white-light imaging was done at first, after which NBI was used again to evaluate the same biliary lesion. Multiple targeted biopsies were taken with a forceps under direct cholangioscopic visualization.

Statistical analysis

Data were reported as mean and standard deviation for continuous variables, and as relative frequencies for categorical variables. The chi-square test, or the Fisher test when necessary,

was used to compare relative frequencies. P-values of less than 0.05 were considered to indicate statistical significance. All analyses were performed using SPSS 18.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Baseline characteristics of 13 enrolled patients

The baseline characteristics of 13 patients who received cholangioscopy using NBI are shown in Table 1. They included 8 men and 5 women, with a mean age of 62.7 years (standard deviation, ± 10.3). Underlying diseases were all malignant in the 13 patients (11 bile duct cancers, 1 liver cancer, 1 pancreas cancer with common bile duct invasion). Whereas 9 patients showed strictures, 4 showed filling defects on ERCP or MRCP. The median follow-up period was 545 days (range, 117 to 1,234 days).

The effectiveness of cholangioscopy using NBI according to the categorized tumor types

Among the 13 included patients, 7 patients showed papillary tumors on ERCP or MRCP. They showed strictures or filling defects in the tumor-involved site. However, one side of the tumor margins was ambiguous in determining the extent of the lesion. Therefore, cholangioscopy using NBI was performed to evaluate the exact margin of the tumors. Minute superficial spreading of the papillary tumors was observed in the area with strictures or filling defects. After NBI, minute papillary changes were detected more easily not only in the area with strictures or filling defects but also on the area which appeared to be normal on ERCP or MRCP. They changed the treatment plan such as to the extent of surgical resection due to newly detected lesions after cholangioscopy using NBI (Fig. 1).

Table 1. Baseline characteristics of the enrolled 13 patients

Characteristic	Value
Age (yr)	62.7 \pm 10.3
Sex, male:female	8:5
Underlying diseases	13
Bile duct cancer	11
Liver cancer	1
Pancreas cancer with common bile duct invasion	1
ERCP or MRCP findings	
Stricture	9
Filling defect	4
Follow-up period (day)	545 (117–1,234)

Values are presented as mean \pm standard deviation, number, or median (range).

ERCP, endoscopic retrograde cholangiopancreatography; MRCP, magnetic resonance cholangiopancreatography.

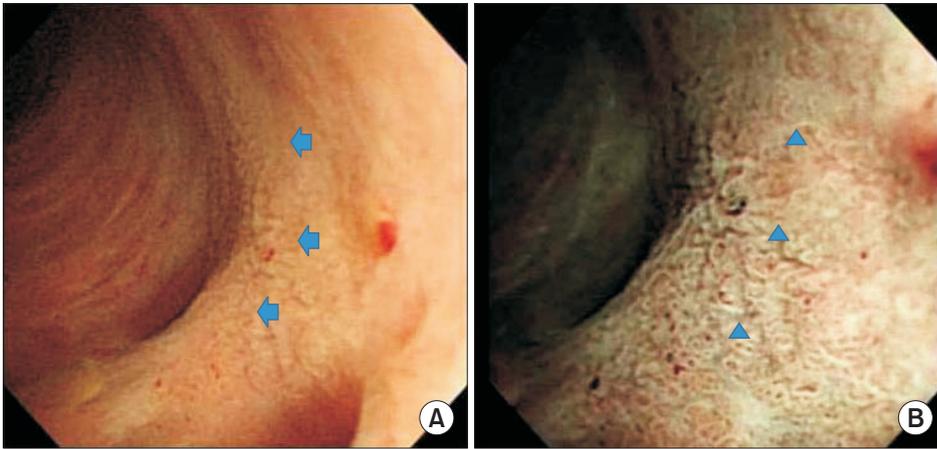


Fig. 1. Papillary type cancer. (A) Minute papillary mucosal changes (arrows) were suspected at this level of bile duct. But, the border of lesion was ambiguous. (B) With narrow band imaging, a prominent papillary lesion (arrowheads) was noted at the same level.

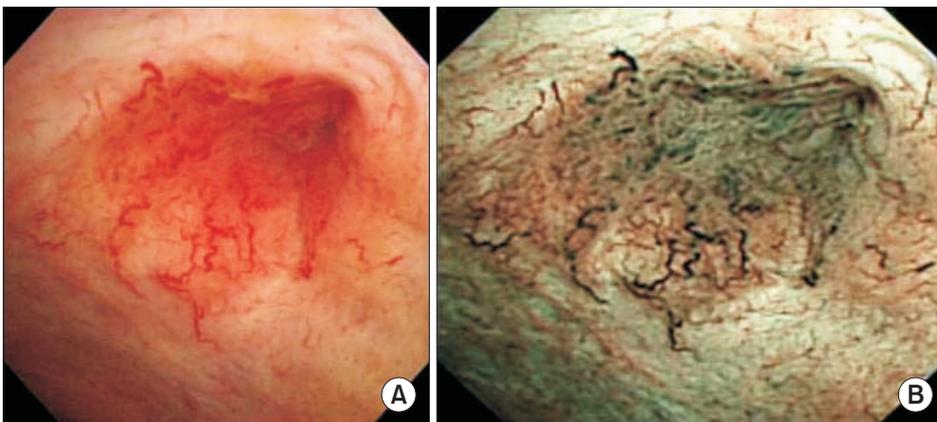


Fig. 2. Infiltrative type cancer. (A) Conventional white-light imaging showed a tapered, luminal narrowing of the common hepatic duct and neovascularization of its surface. (B) After narrow band imaging, more irregular mucosal surface, color change on the tumor vessel, and more vascular changes especially on the tumor margin were noted.

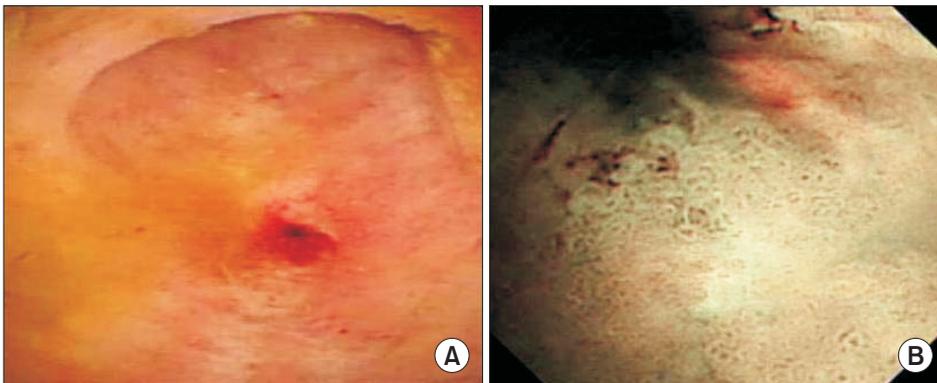


Fig. 3. Mucin-hypersecreting type tumor. (A) White-light imaging showed floating mucinous material, however, we could not identify any mucosal change because of the large amount of mucin. (B) On narrow band imaging, both mucin and the tumor mass were clearly visible.

In 4 cases with infiltrative tumor, a definite mucosal mass is not present and the tumors appear as strictures on ERCP or MRCP. During cholangioscopy using NBI, white-light imaging usually showed a tapered luminal narrowing of the bile duct and neovascularization of its surface. NBI cholangioscopy showed a more irregular mucosal surface and color change of the tumor vessel from red to black, and more vascular changes, especially on the tumor margin (Fig. 2).

In 2 cases with mucin-hypersecreting tumor, ERCP or MRCP showed a marked bile duct dilatation. Mucin-like material was

also observed in 2 patients who underwent ERCP. However, the extent of the tumor in the mucosa may not correspond to the segments of the duct that are dilated because the development of mucin plugs also results in dilatation. During cholangioscopy, conventional white-light imaging showed floating mucinous materials, but mucosal changes were difficult to evaluate because of the large amount of mucin. After NBI, both mucin and tumor mass were clearly visualized (Fig. 3).

Table 2. Comparison between margin status evaluated radiologically/endoscopically and margin documented pathologically in 9 patients with surgical resection

Patient	Diagnosis	Margin evaluated by CT/MRCP ± ERCP	Margin reevaluated by NBI cholangioscopy	Surgery	Pathological margin
1	CCC	Only CBD	CBD, Rt. IHD	Rt. hepatectomy + BDR + hepaticojejunostomy	CBD, Rt. IHD
2	CCC	Only CBD	CBD, Rt. IHD, Lt. IHD	Rt. hepatectomy + BDR + hepaticojejunostomy	CBD, Rt. IHD, Lt. IHD
3	CCC	Only CBD	CBD, Lt. IHD	Lt. hepatectomy + BDR + hepaticojejunostomy	CBD, Lt. IHD
4	CCC	Only CBD	CBD, Rt. IHD	Rt. hepatectomy + BDR + hepaticojejunostomy	CBD, Rt. IHD
5	CCC	Only CBD	CBD, Lt. IHD	Lt. hepatectomy + BDR + hepaticojejunostomy	CBD, Lt. IHD
6	CCC	CBD, Rt. IHD	CBD, Rt. IHD, Lt. IHD	Rt. hepatectomy + BDR + hepaticojejunostomy	CBD, Rt. IHD, Lt. IHD
7	CCC	Only CBD	CBD, Rt. IHD	Rt. hepatectomy + BDR + hepaticojejunostomy	CBD, Rt. IHD
8	Pancreas cancer	Pancreas head	Pancreas head, distal CBD	PPPD	Pancreas, CBD
9	CCC, mucin-producing type	CBD, Rt. IHD, Lt. IHD	Only CBD	BDR + hepaticojejunostomy	CBD

MRCP, magnetic resonance cholangiopancreatography; ERCP, endoscopic retrograde cholangiopancreatography; NBI, narrow band imaging; CCC, cholangiocarcinoma; CBD, common bile duct; Rt., right; Lt., left; IHD, intrahepatic duct; BDR, bile duct resection; PPPD, pylorus-preserving pancreaticoduodenectomy.

Surgical resection and comparison between the preoperatively evaluated margin and the pathological margin

Nine of the 13 enrolled patients ultimately underwent surgical resection. Of the 4 patients who did not undergo surgical resection, 2 patients were transferred to their hometown hospitals for surgery, and 1 patient with a mucin-producing tumor refused surgical resection because of old age and underlying comorbidities. The 1 remaining patient with cholangiocarcinoma was initially scheduled to undergo surgical resection, but NBI cholangioscopy showed a more diffuse involvement of the cancer into both intrahepatic ducts than the extents evaluated by CT and ERCP.

The pathological margins of the 9 patients who underwent surgical resection were compared with their preoperatively evaluated margins. The margin status predicted by NBI cholangioscopy was consistent with the pathological margin in all 9 cases. These results are summarized in Table 2.

DISCUSSION

It is important with bile duct lesions to determine whether filling defects or strictures are benign or malignant because of differences in the approach to treatment. Especially, in resectable cases, preoperative diagnosis and determination of tumor extent are essential before deciding on the extent of resection. In this study, we investigated whether cholangioscopy using NBI was effective for the identification of hepatobiliary malig-

nancies. Our results suggested that the depiction ability of the margin of lesions and identification of vessels by NBI is superior to conventional white-light imaging.

While peroral cholangioscopy is a promising method due to recent remarkable developments, technical difficulty and high cost still remain problems to be solved. Also, during bile duct imaging, compared to percutaneous approach, there are limitations on proximal margin evaluations of the tumor; also it is still of poor image quality, it is hard to use separate irrigation channels, and there are limits on therapeutic application [12]. There have been some reports [10,13] demonstrating the utility of NBI for diagnosis of bile duct disease using peroral cholangioscopy, but few studies evaluating NBI utility in cholangioscopy using percutaneous approach.

In papillary tumor, numerous papillary mucosal projections are the characteristic findings [14]. However, the papillary lesions are sometimes very minute and intermingled with pus and sludge. These minute papillary changes seemed more prominent after NBI. In mucin-hypersecreting tumor, the extent of the tumor in the mucosa may not correspond to the segments of the duct that are dilated because the development of mucin plugs also results in dilatation. After NBI, mucin is clearly distinguished from the original tumor mass. The most difficult tumor to diagnose was infiltrative tumor. Because this tumor exhibits intramural spread of tumor cells, there may not be any prominent changes in the surface of bile duct. However, with NBI, subtle mucosal elevations and neovascularizations are noted. In cases without applying NBI, tumors can be diagnosed

accurately by white-light imaging and white-light imaging guided biopsy. In these groups of patients, the tumor extent evaluated by white-light imaging and NBI was not significantly different.

Although not all enrolled patients underwent surgical resection, the pathological margins of the patients who did undergo surgical resection were consistent with the margins evaluated by NBI cholangioscopy. The addition of NBI to cholangioscopy gave a more precise extent of the lesion for the clinician than the expected extent provided by CT, MRCP, or ERCP.

Our study has some limitations. It includes a small number of only 13 patients. In addition, NBI is not just purely NBI because we evaluated all the lesions with white-light imaging first. If there is unclear imaging, we added NBI imaging. Therefore, the

result of cholangioscopy using NBI was actually produced by combined white-light imaging and NBI.

In conclusion, cholangioscopy using NBI is very useful for evaluation of suspected hepatobiliary malignancies with an ambiguous margin on ERCP or MRCP. It can give us an accurate pathologic mapping by clarifying the fine surface structure of lesions and mucosal vessels, and this information seems to be essential before deciding on a treatment strategy.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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