

SpyGlass® single-operator peroral cholangioscopy in the evaluation of indeterminate biliary lesions: a single-center, prospective, cohort study

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Abstract

Background SpyGlass® single-operator peroral cholangioscopy appears to be a promising technique to overcome some limitations of conventional peroral cholangioscopy. We aimed to prospectively evaluate the SpyGlass system in a cohort of patients with indeterminate biliary lesions.

Methods Patients with indeterminate strictures or filling defects at endoscopic retrograde cholangiopancreatography (ERCP) were consecutively enrolled. After SpyGlass visual evaluation, targeted biopsies were taken with the SpyBite® and histopathological assessment was made by two experienced gastrointestinal pathologists. SpyBite-targeted biopsy results were evaluated by assessing agreement with surgical specimens and by evaluation of final, clinical follow-up-based diagnosis.

Results Fifty-two patients participated in the study. In 7 cases, definite diagnosis (stones, varices) was made by SpyGlass endoscopic evaluation. In 42 of the remaining 45 cases, material suitable for histopathology assessment was provided by the SpyBite. Overall, a definite diagnosis was made in 49 (7 + 42; 94 %) cases. Agreement of SpyBite biopsy results with surgical specimen diagnosis was found in 38/42 (90 %) cases; sensitivity, specificity, and positive and negative predictive values were 88, 94, 96, and 85 %, respectively. Procedure-related complications consisted of one case of mild cholangitis and one case of mild pancreatitis.

Conclusions In our series, the SpyGlass system allowed adequate biopsy sampling and definite diagnosis with high accuracy in the vast majority of patients with indeterminate biliary lesions. Its use was associated with a low complication rate. Further refinements of the technique are warranted, but the SpyGlass system has the potential to become a diagnostic standard for the assessment of indeterminate biliary lesions.

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Despite refinements in imaging techniques, differential diagnosis of biliary strictures and filling defects can prove difficult. At surgery, benign findings are found in 15 % of patients undergoing intervention without a preoperative histological diagnosis [1]. Biliary brushing is a relatively inexpensive and widely available method to obtain samples from the biliary tract but the diagnostic accuracy of blind sampling remains low [2].

Cholangioscopy, allowing direct visualization of the biliary tract with targeted biopsy sampling of suspicious lesions, is a promising diagnostic tool in those instances in

which a definite diagnosis cannot be obtained by means of endoscopic retrograde cholangiopancreatography (ERCP) or other imaging modalities [3, 4]. Recent technical advances in this field, such as the SpyGlass® single-operator peroral cholangioscopy system (Microvasive Endoscopy, Boston Scientific Corp., Natick, MA, USA), has overcome several limitations of conventional cholangioscopy (requirement of two experienced endoscopists, limited maneuverability, inadequate irrigation, small instrument channel, equipment cost) [5, 6]. According to preliminary reports, the SpyGlass system appears to be a useful diagnostic tool for the characterization of intraductal biliary lesions [5, 6]. However, further data are needed to establish the role of the SpyGlass system in clinical practice.

Our aim was to prospectively assess the diagnostic yield of the SpyGlass system in a cohort of patients with indeterminate biliary lesions.

Patients and methods

Adult patients referred for evaluation of indeterminate biliary strictures and filling defects at endoscopic cholangiopancreatography (ERCP) were asked to participate in the study after receiving a careful and detailed explanation of the goal of the investigation. A signed informed consent form was obtained from all patients before entering the study. Indeterminate findings consisted of indeterminate strictures or filling defects with inconclusive/unsuitable brush cytology as assessed by a gastrointestinal pathologist (LM). The study protocol was approved by our Institutional Review Board. Patients with ampullary lesions involving the distal part of the common bile duct were excluded.

SpyGlass system procedures were carried out according to previously published criteria [5, 6]. The system consists of a pump, a light source, a monitor, and three disposable devices: (1) optical probe (SpyGlass, a 231 cm-long, 6,000-pixel fiber-optic bundle) that enters the biliary tree through the SpyScope catheter and provides a 70° field of view; (2) access-and-delivery catheter (SpyScope), a 10-F-diameter, 230-cm-long device with a handle with two knobs that allows four-way steering of the catheter; this four-lumen catheter has an optical channel for accommodating the SpyGlass probe, a 1.2 mm accessory channel, and two independent irrigation channels; (3) biopsy forceps (SpyBite®), with jaws that open to 4.1 mm, designed to obtain histological samples. At SpyGlass endoscopic evaluation (RM, RC), lesions were defined as malignant (presence of intraluminal vegetation), suspicious (irregular nodulations with or without erosion), or benign (smooth nodulations, erythematous mucosa with or without erosion). Targeted biopsy sampling was carried out using the SpyBite, and histopathological evaluation was

performed by two experienced gastrointestinal pathologists (LM, VV). SpyBite biopsy results were compared with the final diagnosis, the latter being based on (1) consensus pathological assessment (LM, VV) of surgical specimens for lesions provisionally considered malignant, or (2) at least 1-year clinical follow-up for lesions provisionally considered benign.

Statistical analysis

The sample size was calculated on the assumption that additional diagnostic information of 30 % or more could be clinically significant. It was calculated that with a power of 80 % and at a significance level of 0.05, a cohort of 49 patients was required. Descriptive statistics consisted of the mean, standard deviation (SD), range, agreement, sensitivity, specificity, and positive and negative predictive values.

Results

Between January 2009 and December 2011, a total of 1,354 patients underwent ERCP procedures at our center. Fifty-two patients had an indeterminate stricture or filling defect. A SpyGlass assessment was completed in all 52 patients. The main baseline characteristics and the procedures carried out are reported in Table 1.

Targeted biopsy sampling was not attempted in seven patients since small stones (4 cases) or varices (3 cases) were detected at SpyGlass endoscopic evaluation. In the remaining 45 patients, biopsy samples could not be taken in two cases because the biopsy forceps could not exit the operative channel of the SpyScope, and in one case the material obtained was judged unsuitable for pathologic

Table 1 Baseline characteristics

Total no. of patients	52
Age (years) [mean ± SD (range)]	51 ± 12 (36-81)
Male/female	38/14
Location of lesion	
Intrahepatic	6
Hilar	11
Common bile duct	35
Procedures at the time of SpyGlass cholangioscopy (>1 may apply)	
Sphincterotomy	9
Extension of previous sphincterotomy	44
Stent placement	45
Balloon dilation	12
Procedure time, min, mean ± SD (range)	38 ± 12 (17–70)

Table 2 Specific histopathological diagnoses

	SpyBite	Surgical specimen
Cholangiocarcinoma	11	18
Pancreatic cancer	2	4
Gallbladder cancer	0	1
Undetermined malignancy	10	–

Table 3 Agreement between SpyBite-targeted biopsy results and final diagnosis

	SpyBite	Final diagnosis
Malignancy	23	22
Benign lesions	19	16
Overall agreement: 38/42 (90 %)		
SpyBite sensitivity: 88 %		
SpyBite specificity: 94 %		
SpyBite positive predictive value: 96 %		
SpyBite negative predictive value: 85 %		

diagnosis. Because there was a strong suspicion of malignancy by SpyGlass endoscopic evaluation, these three cases all underwent surgical intervention that confirmed malignancy. Histopathologic assessment was carried out in 42 of the remaining 45 (93 %) cases. At SpyGlass endoscopic evaluation, 20 lesions were considered malignant, 8 suspicious for malignancy, and 14 benign. Overall, the SpyGlass evaluation agreed with the histopathologic evaluation of the SpyBite-targeted biopsies in 32/42 (76 %) cases. Thus, by using the SpyGlass system we were able to make a definite diagnosis in 49 (7 + 42) (94 %) patients. All patients with a diagnosis of malignancy by SpyBite-targeted biopsy underwent surgical intervention and the diagnosis of malignancy was confirmed by histopathologic assessment of surgical specimens in 22/23 cases. The specific diagnosis from the surgical specimen was cholangiocarcinoma in 18 cases, infiltrating pancreatic cancer in 4 cases, and gallbladder cancer in 1 case (Table 2). In the 19 patients with a SpyBite-targeted biopsy diagnosis of benign disease, malignancy was diagnosed in 3 cases at the 12–42 months clinical follow-up (median = 24 months). The final diagnosis was cholangiocarcinoma in 21 cases, infiltrating pancreatic cancer in 4 cases, gallbladder cancer in 1 case, and benign lesion in 16 cases. As far as diagnosis of malignant or benign disease is concerned, Table 3 compares the SpyBite-targeted biopsy results with the final diagnosis; overall, agreement was found in 38/42 (90 %) cases with good sensitivity, specificity, and positive and negative predictive values.

With respect to complications of the SpyGlass procedure, cholangitis that resolved with antibiotic treatment

developed in one patient and mild pancreatitis developed in one patient. No other complications were observed.

Discussion

In the present study we assessed the diagnostic accuracy of the SpyGlass system in 52 consecutive patients referred to our center for indeterminate biliary lesions at ERCP and inconclusive/unsuitable brush cytology during a 3-year period. In seven cases, SpyGlass endoscopic evaluation provided definite diagnosis (stones, varices) requiring no biopsy. Targeted biopsy samples obtained by the SpyBite allowed pathological diagnosis in 42 of 45 (93 %) cases. The final diagnosis was based on pathological assessment of surgical specimens for lesions considered malignant or a 12–42 month clinical follow-up for lesions considered benign. We found that the SpyGlass system has high sensitivity and specificity, with a 96 % positive predictive value and an 85 % negative predictive value in comparison with surgical specimens. A few mild complications, apparently not related to the SpyGlass but rather to the ERCP procedure, were registered.

Despite significant advances in pancreatobiliary imaging, the characterization of intraductal biliary lesions remains a diagnostic challenge, even in high-volume centers with significant ERCP expertise, and a histological diagnosis can prove extremely useful in a diagnostic work-up. Peroral cholangioscopy has distinct advantages over ERCP for the exploration of the biliary tree [7], allowing direct visualization. Moreover, targeted biopsy sampling with histopathology evaluation can prove significantly advantageous when compared with ERCP-guided brushing with cytology assessment. The diagnostic specificity of brush cytology is reportedly high but the diagnostic sensitivity is relatively modest and frequently hampered by inadequate specimens. The SpyGlass system allows targeted biopsy sampling by means of the SpyBite and, theoretically, targeted biopsies should improve the cancer detection rate in malignant biliary strictures by allowing sampling of the site that appears suspicious. According to our findings and of those reported in very recent studies [8–12], an accurate diagnosis of malignant and benign lesions of the biliary tree can be provided by the SpyGlass system in the vast majority of cases and the management plan of the patient can be significantly altered by this procedure. For instance, an accurate estimate of the distance from the hepatic hilum in cases of intraluminal common bile duct malignant lesions allows the distinction of type I from type II Klatskin tumors, with the latter being unfit for surgical resection. Furthermore, detection of varices in patients with suspected malignancy of the common bile duct may allow the patient to remain on the waiting list for liver transplantation.

A few limitations of this study should be acknowledged. We based SpyGlass visual evaluations on the assessment done by two experienced endoscopists according to previous published criteria [5, 6] and found a good agreement with SpyBite-targeted biopsy results, but validation of classification criteria warrants further studies. The mean time required to complete visual evaluation and biopsy sampling was relatively high but could be reduced with further experience. The SpyGlass system is costly: we have calculated an additional cost of \$3,000 per patient, but we believe that such an additional cost is justified in the clinical setting of suspected malignancy, given the high diagnostic yield shown by our results. Our study was not randomized; however, similar results can be provided by observational studies and randomized, controlled trials [13, 14].

In conclusion, our results show that the SpyGlass system has a high accuracy for diagnosing or excluding malignancy in patients with indeterminate strictures or equivocal ERCP findings. Further refinements of the technique are warranted but taking into account the relatively low rate of complications, the SpyGlass system has the potential to become the diagnostic standard for the assessment of indeterminate biliary lesions.

Disclosures Drs. Raffaele Manta, Marzio Frazzoni, Rita Conigliaro, Livia Maccio, Gianluigi Melotti, Emanuele Dabizzi, Helga Bertani, Mauro Manno, Danilo Castellani, Vincenzo Villanacci, and Gabrio Bassotti have no conflicts of interest or financial ties to disclose for the present study.

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