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Review Article

Clinical Application and Progress of Cholangiopancreatoscopy in Pancreatobiliary Diseases

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Abstract

Cholangiopancreatoscopy with the SpyGlass system is a direct and minimally invasive examination method in which the lesions in the pancreatic bile tract can be observed directly by inserting an ultra-fine endoscope through the biopsy channel of a duodenoscope. Compared with endoscopic retrograde cholangiopancreatography (ERCP), enhanced computed tomography, magnetic resonance imaging, and endoscopic ultrasonography, cholangiopancreatoscopy with the SpyGlass system has unique advantages for observing and identifying lesions originating in the pancreatic bile duct. In recent years, with the upgrading of endoscopic equipment and the improvement of operating technology, the application of cholangiopancreatoscopy is becoming more and more widespread. This article reviews the use of cholangiopancreatoscopy with the SpyGlass system for the diagnosis and treatment of pancreaticobiliary disease.

Introduction

Traditional imaging techniques such as endoscopic retrograde cholangiopancreatography (ERCP), magnetic resonance imaging, and enhanced computed tomography are valuable tools for the evaluation and treatment of pancreatic and biliary diseases; specifically, ERCP is currently the first choice for the diagnosis and evaluation of pancreatic biliary diseases.[1,2] However, its limitation lies in that when diagnosing pancreatic and bile duct diseases, endoscopists can only observe the pancreatic and bile duct structure indirectly through fluoroscopy, and the imaging quality is also unsatisfactory.[3] In addition, the sensitivity and accuracy of brush cytology and biopsy are also limited due to the fact that the lesions cannot be observed under direct vision. Currently, with the introduction and upgrade of the SpyGlass system, cholangiopancreatoscopy has been proven to be a reliable and effective method for assessing pancreaticobiliary disease.[4] In particular, the introduction of the second-generation SpyGlass system has provided a higher imaging quality and a wider field of view.[5]

Keywords: Clinical application; Cholangiopancreatoscopy; Pancreatobiliary diseases.
Abbreviations: CT, computed tomography; ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasonography; MRI, magnetic resonance imaging; IPMN, pancreatic intraductal papillary mucinous neoplasm.
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History of cholangiopancreatoscopy

A peroral pancreatoscope was first reported and applied clinically by Katagi *et al*. in 1974.[6] It was mainly applied for diagnosing lesions in the pancreatic and bile duct due to its advantage of directly observing the condition of the pancreatobiliary duct. However, because of its complex equipment, high operation difficulty, complications, small operation area, and poor imaging quality, it has not been promoted in clinical diagnosis and treatment.[7] In the 1980s, with the development of digital imaging technology and endoscopic manipulation, cholangiopancreatoscopy was able to detect subtle lesions in the pancreatic or bile ducts. In addition, the improvement of auxiliary equipment also enabled the operation of endoscopic lesion biopsy or treatment. In 2007, Boston Scientific (Natick, MA, USA) released the first-generation SpyGlass system, which is a reusable single-operator fiberoptic scope with a mother-baby system including a channel for accessory instruments and irrigation capabilities. With an external diameter of 3.3 cm and a length of 230 cm, the SpyGlass system can be used in combination with a duodenoscope, overcoming several weaknesses of previous pancreaticos-

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copy, including vulnerability, low image quality, and operation difficulty.[8–10] A study consisting of 300 patients performed by 15 medical centers demonstrated that the SpyGlass system had an improved diagnostic accuracy in patients with pancreatic and biliary disease.[4] Hence, in 2009, the U.S. Food and Drug Administration approved the SpyGlass system for the diagnosis and treatment of pancreatic biliary disease.[11] The second-generation SpyGlass system was introduced in 2015, and compared with the first-generation SpyGlass system, the new SpyGlass system has a further improved image resolution and operational vision field.[12] Moreover, a recent study was designed to compare the effects of fiberoptic and digital cholangiopancreatoscopy. The results showed a considerable increase in utilization rates of cholangiopancreatoscopy in pancreatic biliary disease, indicating that the technology improvement in the SpyGlass system made the use of cholangiopancreatoscopy more widespread.[13]

Clinical application

In the diagnosis and treatment of pancreatic and biliary diseases, the use of endoscopy can shorten the examination distance through the natural cavity. Additionally, the application of endoscopy has been shown to improve the diagnosis rate and treatment effect of diseases.[14] The SpyGlass system has advantages over ERCP and has been increasingly used in cholangiopancreatography in recent years.[15–17] The following sections describe the application of cholangiopancreatoscopy in the treatment of pancreatic biliary system diseases.

Biliary tract diseases

Recent studies have demonstrated that the SpyGlass system is beneficial for patients with difficult or undiagnosed bile duct stones.[18–20] When a stone is embedded in the cystic duct or attached to the duct wall, it is difficult to show the stone position clearly with conventional cholangiography. The SpyGlass system, however, can detect stones under direct vision and remove them by placing a guide wire.[14] Furthermore, for patients with recurrent cholangitis, significant dilation of the bile duct, and missed biliary stones, the SpyGlass system can also be used to directly explore the bile duct to find lesions.[21] A single-center study consisting of 39 patients with biliary stones indicated that the use of the SpyGlass system successfully removed biliary stones in 82.1% of patients.[22] The advantage of the SpyGlass system is that it clearly shows the extrahepatic and proximal intrahepatic bile ducts.

In addition to biliary stones, the SpyGlass system also has advantages in the diagnosis of biliary strictures, especially those with undiagnosed benign or malignant lesions.[23,24] Due to the limited sensitivity and positive rate of ERCP with brush cytology and biopsy, studies have shown that the postoperative pathology of some patients with biliary stenosis was not a malignant tumor.[25] However, surgery for a biliary malignant tumor usually involves great trauma, many complications, and a long recovery time. Therefore, the accurate diagnosis of benign or malignant biliary stenosis is of great importance for the clinical treatment of patients.

De Oliveira *et al.* recruited 283 patients in 6 studies and concluded that the use of the SpyGlass system for the diagnosis of malignant biliary stenosis had a sensitivity, specificity, and accuracy of 94%, 95%, and 94%, respectively.[26] Moreover, a prospective randomized multicenter trial indicated that the SpyGlass choledochoscopy system was more sensitive than ERCP for the histological diagnosis of unclear bile duct stenosis.[27] The application of the SpyGlass system allowed direct examination of biliary stenosis and a more accurate biopsy under direct vision; these benefits also have been reported in several case reports of bile duct cancer treatment.[28–30] In addition to the previously mentioned direct vision and tissue biopsy for bile duct stenosis, the SpyGlass system could resolve bile duct lesions via radiofrequency ablation as well.[31] As described in a bile duct stenosis case report, the patient underwent SpyGlass-guided radiofrequency ablation for recurrent bile duct carcinoma, and radiofrequency ablation was performed in multiple bile duct stenosis segments under cholangioscopy with direct vision.[32] The patient recovered well after the operation. Another patient had a resectable intraductal papilloma in the bile duct and opted for endoscopic treatment. After the physicians performed the biopsy for the lesion, the patient underwent a lesion radiofrequency ablation operation and was discharged normally.[33]

Choledochoscopy with the SpyGlass system also has demonstrated advantages for diagnosing hemobilia.[34] Traditional ERCP and magnetic resonance cholangiopancreatography methods can identify hemobilia; however, they cannot unveil the underlying pathogenesis of biliary bleeding. Choledochoscopy can help to detect the exact source of bleeding, and biopsy under direct vision via the SpyGlass system can obtain a pathological diagnosis. A previous case report describes a patient with biliary hemorrhage, and the pathogenesis could not be determined by magnetic resonance cholangiopancreatography. Therefore, cholangioscopy with the SpyGlass system was performed. It was found that the cause of the patient's bleeding was due to biliary vascular dysplasia, which is a rare type of hemobilia.[35]

Pancreatic neoplasms

With advances in endoscopic manipulation, the use of the SpyGlass system also has been reported in pancreatic diseases, especially in pancreatic cancer, intraductal papillary tumors, and pancreatic duct stenosis.[14,36] Previous studies have demonstrated that the sensitivity and specificity of conventional examination methods, including computed tomography, ERCP, and endoscopic ultrasonography, have been significantly improved in the diagnosis of pancreatic tumors, while the sensitivity for tumors with a diameter of less than 2 cm is still unsatisfactory.[37,38] Therefore, it is crucial to use the SpyGlass system, which takes a direct view into the pancreatic duct for these patients. A pancreatic intraductal papillary mucinous neoplasm (IPMN) can be divided into the main pancreatic duct (MD-IPMN), branching pancreatic duct (BD-IPMN), and mixed type according to the range of lesions involved, which mainly grow along the pancreatic duct in a multifocal or skip growth way.[39] Fritz *et al*. retrospectively analyzed the data of 287 surgically resected IPMN patients, among which 51 patients (17.8%) had multifocal lesions.[40] In addition, He *et al*. found that the postoperative recurrence rate of IPMN patients was about 17%,[41] and the recurrence risk was time-cumulative, with recurrence rates of 4%, 25%, and 62% at 1, 5, and 10 years after surgery, respectively. For IPMNs, the pancreatic duct lesions can be observed and biopsied under direct vision by the SpyGlass system. Therefore, the diagnostic value of the SpyGlass system for IPMNs is better than that of traditional imaging examination. Hara *et al*. have reported that the accuracy rates of MD-IPMN and BD-IPMN diagnosis by oral pancreatoscopy were 88% and 67%, respectively, and the pancreatic duct lesions observed by pancreatoscopy were classified into the following five categories: granular mucosa, seed-like protrusion without covered vessels, seed-like protru-

sion with covered vessels, villous protrusion, and florid papillomatosis, among which the latter three categories were more malignant.[37] The SpyGlass system can also be used to assess the extent of IPMN involvement before surgery. For example, Tyberg *et al*. analyzed the data of 13 patients who underwent preoperative pancreaticoscopy, among which 8 patients changed their surgical plan due to pancreaticoscopy, 4 patients expanded the surgical scope, and 4 patients narrowed the surgical scope, but 2 of the 4 patients obtained positive surgical margins.[42] According to existing reports, preoperative oral pancreaticoscopy with the SpyGlass system for IPMN detection could obtain good diagnostic results; however, the guiding effect for the surgical resection scope was inadequate. Currently, there are few studies describing the application of intraoperative pancreatoscopy for IPMN patients. Kaneko *et al*. have reported cases of intraoperative pancreatoscopy for IPMN resection and found that the sensitivity, specificity, and accuracy of intraoperative pancreatoscopy were all 100%, superior to ERCP and endoscopic ultrasonography.[43] Moreover, a recent study by Wei *et al*. recruited 10 patients with MD-IPMN. All of the patients underwent intraoperative pancreatoscopy with the SpyGlass system. The examination results revealed that four patients had positive surgical margins, which required the surgeon to expand the resection scope. The application of intraoperative pancreatoscopy is still limited; however, a pancreaticoscope can be directly inserted into the pancreatic duct during the operation and help surgeons to determine the margin of pancreatic duct lesions under direct vision to achieve the surgical resection. Hence, compared with other imaging examination methods, pancreaticoscopy with the SpyGlass system still has unique advantages.

Complications

Although there have been limited reports of complications related to cholangiopancreatoscopy with the SpyGlass system, endoscopic treatment is generally considered to be a safe procedure with few complications.[9] Postoperative complications of pancreaticoscopy with the SpyGlass system include pancreatitis, celialgia, cholangitis, biliary tract infection, and duodenal perforation. In a clinical study consisting of 36 biliary stenosis patients who underwent pancreaticoscopy with the SpyGlass system, only one patient developed mild pancreatitis and two patients developed cholangitis during a follow-up period of at least one month, both of whom recovered with medication.[44] Duodenal perforation is also a rare complication, and conservative treatment is recommended.

Conclusions

Cholangiopancreatoscopy with the SpyGlass system provides better image resolution and enables surgeons to observe lesions under direct vision as well as to obtain biopsied tissue for pathological examination. Previous studies have demonstrated the SpyGlass system to be cost-effective, and cholangiopancreatoscopy is becoming an effective tool for the diagnosis and treatment of pancreatic biliary diseases. With the further development of digital technology, the introduction of the third-generation SpyGlass system will provide cholangiopancreatoscopy with a higher resolution and a wider vision field. In conclusion, cholangiopancreatoscopy with the SpyGlass system is an exciting technology and treatment method that will play a more important role in pancreatic biliary diseases in the future.

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Conflict of interest

One of the authors, Prof. Yi Miao, has been an editorial board member of *Cancer Screening and Prevention* since March 2022. The authors declare no other competing interests.

Author contributions

YM and KRJ designed and conceived the project. HY, GSC, LZ, and SQF collected the related articles. BX drafted the manuscript.

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