

The application of SpyScope® technology in evaluation of pre and post liver transplant biliary problems

Karaciğer transplant öncesi ve sonrası safra yolu problemi olan hastalarda SpyScope teknolojisinin kullanımı

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Background/aims: Peroral cholangioscopy with its limitations led to further research regarding development of SpyScope® technology. The aim of this retrospective study was to investigate the efficacy of a new device and the application of this device in our Liver Transplant Center. **Methods:** Charts of patients who had undergone evaluation with SpyScope® were retrospectively reviewed. Indications included pre-transplant as well as post-transplant evaluation of biliary strictures. If strictures or filling defects were noted by cholangiogram, SpyScope® was performed. Biopsy was obtained under direct visualization if necessary with SpyBite® biopsy forceps. Demographic features, indications for SpyScope® evaluation, results, and histopathological diagnoses were recorded. **Results:** Ten patients (6 male, 4 female; median age: 55) had undergone SpyScope® procedure between August 2007 and January 2008. Six out of 10 cases were in the pre-transplant work-up period, referred to as Group I, while the remaining four were post-transplant patients, referred to as Group II. In Group I, 4 of 6 cases had undergone the procedure for work-up of primary sclerosing cholangitis prior to orthotopic liver transplantation. In Group II, indications were either strictures noted during the previous endoscopic retrograde cholangiopancreatography (n=2) or common bile duct stones with elevated total bilirubin levels and stones with long segment biliary stricture (n=2). In the patient with anastomotic stricture, the biliary lithiasis was eventually exposed just above the anastomotic stricture, after abundant lavage was applied at that level. All SpyBite® biopsy specimens were reported to be adequate samples for histopathological examination. No malignancy was detected among 4 patients with primary sclerosing cholangitis and patients with elevated CA 19-9. **Conclusions:** SpyScope® allows direct visualization of biliary strictures and SpyScope®/SpyBite® were found to be technically superior to conventional cholangiogram with better sampling than brushing obtained by endoscopic retrograde cholangiopancreatography. Prospective, multicenter, large volume studies are warranted to identify its sensitivity and specificity.

Key words: SpyScope®, SpyBite®, liver transplantation, primary sclerosing cholangitis, biliary stricture

Amaç: Peroral kolanjiyoskopinin uygulanmasının sınırlı olması SpyScope teknolojisinin gelişmesine sebep olmuştur. Bu retrospektif çalışmanın amacı SpyScope'un etkinliği ve Transplant Kliniğimizde uygulama alanlarının belirlenmesidir. **Yöntem ve Gereç:** Hastaların kayıtları retrospektif olarak değerlendirilmiştir. Endikasyonlar nakil öncesi (Grup I) ve nakil sonrası (Grup II) safra yolu darlıklarının değerlendirilmesi şeklindedir. Gerekliğinde SpyBite biyopsi forsepsi ile direk görüş altında biyopsi alınmıştır. Demografik özellikler, SpyScope endikasyonlarının değerlendirilmesi, sonuçlar ve histopatolojik tanımlar kayıt edilmiştir. **Bulgular:** Ağustos-2007 ile Ocak-2008 tarihleri arasında SpyScope uygulanan 10 hasta (6 erkek 4 kadın ortalama yaş 55) değerlendirilmeye alınmıştır. On hastanın 6 sı Grup I de kalanı Grup 2 de idi. Grup I de, 6 hastanın 4 ü ortotopik karaciğer nakli öncesi rutin olarak değerlendirilen primer sklerozan kolanjitli (PSC) hastalardı. Grup II de, endikasyonlar hem önceki endoskopik retrograd kolanjiyopankreatografi sonucuna göre darlık olan hastalar (n=2), hem de total bilirubin seviyesi yüksek olan ana safra kanalı taşları olan hasta ile uzun segment safra yolu darlığı ile birlikte olan safra yolu taşları olan hasta idi (n=2). SpyBite ile alınan tüm biyopsi örnekleri yeterli örnekleme olarak bildirildi. Dört primer sklerozan kolanjit hastasının ve CA19-9 yüksekliği olan hastaların hiçbirinde maligniteye rastlanmadı. **Sonuç:** SpyScope safra yolu darlıklarını direk görüşle değerlendirir, bu yöntem teknik olarak konvansiyonel kolanjiyografiye ve retrograd kolanjiyopankreatografi de fırçalama yöntemi ile alınan biyopsilere göre üstündür. Prospektif, çok merkezli ve daha çok hasta sayısı içeren çalışmalarla sensitivitesi ve spesifitesi hakkında bilgi sahibi olunabilir.

Anahtar kelimeler: SpyScope, SpyBite, karaciğer nakli, primer sklerozan kolanjit, safra yolu darlığı

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INTRODUCTION

Cholangiogram by endoscopic retrograde cholangiopancreatographic (ERCP) approach is the standard of practice for biliary evaluation in Liver Transplant Centers, either pre- or post-operatively. Brushing is performed during ERCP for cytological evaluation for possible abnormalities of the biliary system. Because of the limited efficacy of indirect radiological visualization of the common bile duct (CBD), novel procedures offering visualization of the biliary epithelium have been researched. Peroral cholangioscopy was initially introduced with that intention. However, its limitations in routine clinical application were fragility, restricted scope movement and requirement of two endoscopists working simultaneously. This led to further research regarding the development of SpyScope® technology, which is easier to perform by a single operator (1).

The aim of this retrospective study was to investigate the efficacy of a new device and the application of this device in our Liver Transplant Center.

MATERIALS AND METHODS

Following the local Institutional Review Board (IRB) approval, charts of patients who had undergone evaluation with SpyScope® were retrospectively reviewed. Indications included pre-transplant (Group I) as well as post-transplant (Group II) evaluation of biliary strictures. All procedures were performed by a single experienced hepatologist/endoscopist. Moderate sedation was achieved with intravenous (IV) midazolam and fentanyl, both administered by the endoscopist. Depending on the general medical condition of the patient, general anesthesia was also administered in some cases by the anesthesiologist. All procedures were performed with side viewing duodenoscope (Olympus TGF 160F, Olympus America Inc., Center Valley, PA, USA). Following the identification of the sphincter of Oddi, cannulation of the ampulla was performed by a taper-tip cannula. Sphincterotomy was performed if it had not been done previously. If strictures or filling defects were noted on cholangiogram, the guide wire was advanced to pass the stricture, to be followed by advancement of the SpyScope® cannula (Spyglass Direct Visualization System; Microvasive Endoscopy, Boston Scientific Corp, Natick, MA, USA) through the 4.2 mm working channel of the duodenoscope. The SpyScope® diameter is 10F and it has 4 channels, through which the SpyProbe® and SpyBite® forceps are passed. Technically, the

SpyProbe is 231 cm in length, with a maximum diameter of 0.9 mm. Biliary ducts were fully inspected during the withdrawal process of the SpyScope®. Biopsy was obtained under direct visualization if necessary with SpyBite® biopsy forceps (cable diameter: 0.039 inches, jaw outer diameter: 1.0 mm with jaw opening: 4.1 mm and 55°) placed through a 1.2 mm working channel of the SpyScope®.

Demographic features, indications for SpyScope® evaluation, results, and histopathological diagnoses were recorded.

RESULTS

Ten patients (6 male, 4 female; median age: 55 years) underwent the SpyScope® procedure between August 2007 and January 2008 at Nazih Zuhdi Transplant Institute, Integris Baptist Medical Center, Oklahoma City, Oklahoma. Six out of 10 cases were in the pre-transplant work-up period, referred to as Group I, and the remaining four were post-transplant patients, referred to as Group II (Table 1).

General anesthesia was given to 2 out of 6 patients in Group I, whereas it was performed to all patients in Group II. Moderate sedation was administered with midazolam (8-14 mg IV) and fentanyl (100-300 µg IV) in the 4 remaining patients in Group I.

In Group I, 4 out of 6 cases had undergone the procedure for work-up of primary sclerosing cholangitis (PSC) prior to orthotopic liver transplantation (OLTx). The indications of SpyScope® for these patients were: i) solely elevated CA 19-9 (n=2, Patients #5, #6), ii) elevated liver function tests with elevated CA 19-9 (n=1, Patient #2), and iii) decreased caliber of confluence of the hepatic ducts at previously performed ERCP with elevated CA 19-9 (n=1) (Figure 1).

In Group I, other SpyScope® indications were i) cystic lesion compressing part of the main right and the posterior right hepatic ducts (Caroli's disease) in a patient with hepatitis C virus (HCV) cirrhosis and ii) an asymmetrical stricture in the CBD with elevated CA 19-9 level (Patient #3) (aim was to differentiate PSC from a potential stone disease) (Figure 2).

In Group II, indications were either strictures noted during the previous ERCP (n=2, Patients #1, #3) (1 month, 9 months after OLTx) or CBD stones with elevated total bilirubin levels (4.1 mg/dl) and stones with long segment biliary stricture (10

Table 1. Demographic features of the patients

Group	Patient #	Age	Sex	Diagnosis	Indications For SpyScope
I	1	65	M	HCV Cirrhosis	Cystic lesion in the bile duct (CAT)
	2	66	M	PSC	Elevating Liver function test numbers Elevated CA 19-9 (138 U/mL)
	3	40	F	SSC	Biliary stricture Elevated CA 19-9 (62 U/mL)
	4	30	F	PSC	Decreased caliber of the confluence and Elevated CA 19-9 (70 U/mL)
	5	58	M	PSC	Elevated CA 19-9 (147 U/mL)
	6	51	M	PSC	Elevated CA 19-9 (44 U/mL)
II	1	56	F	S/P OLTx for HCV Cirrhosis 1 month following OLTx	Distal CBD stricture
	2	53	M	S/P OLTx for HCV Cirrhosis 10 months following OLTx	Elevated Bilirubin (4.1 mg/dL)
	3	60	M	S/P OLTx for A1AT def. 9 months following OLTx	Anastomotic stricture
	4	33	F	S/P OLTx for Wilson Disease 14 years following OLTx	Long segment biliary stricture

Group I: Pre OLTx cases, Group II: Post OLTx cases, HCV: Hepatitis C Virus, CAT: Computerized axial tomography, PSC: Primary sclerosing cholangitis, SSC: Secondary sclerosing cholangitis, S/P OLTx: Status post orthotopic liver transplantation, CBD: Common bile duct, A1AT: Alpha-1 Antitrypsin

months and 14 years after OLTx, respectively) (n=2, Patients #2, #4) (Figure 3). Stones were removed by either abundant washout or endoscopic basket technique. In the patient with anastomotic stricture (Patient #3), the biliary lithiasis was eventually exposed just above the anastomotic stricture, after abundant lavage had been applied at that level. This stone had not been noticed during the cholangiogram that was performed initially. This unanticipated stone was easily washed

out with the SpyScope® system, into the duodenum.

Balloon dilatations and/or stent applications were performed on all patients with strictures, in both groups. No complications were encountered in either group of patients.

Tissue sampling was obtained in 5 out of 10 patients. Biopsies were obtained from all patients with PSC. No malignancy was detected among 4

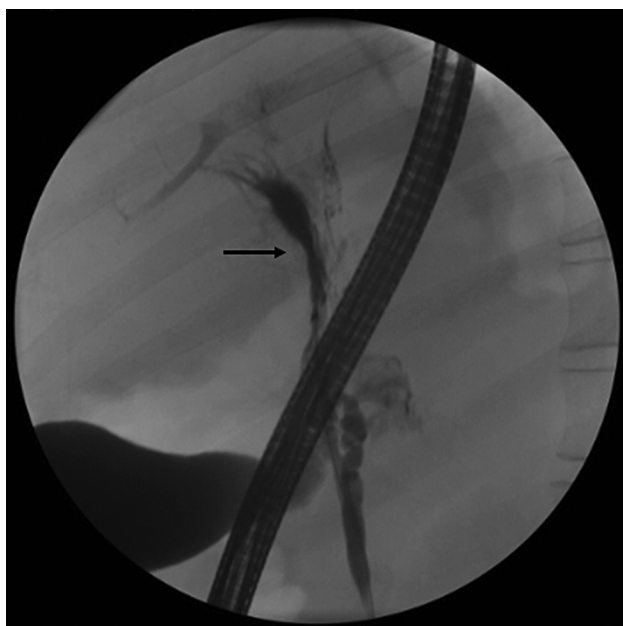


Figure 1. ERCP image of decreased caliber of confluence of the hepatic ducts (arrow).

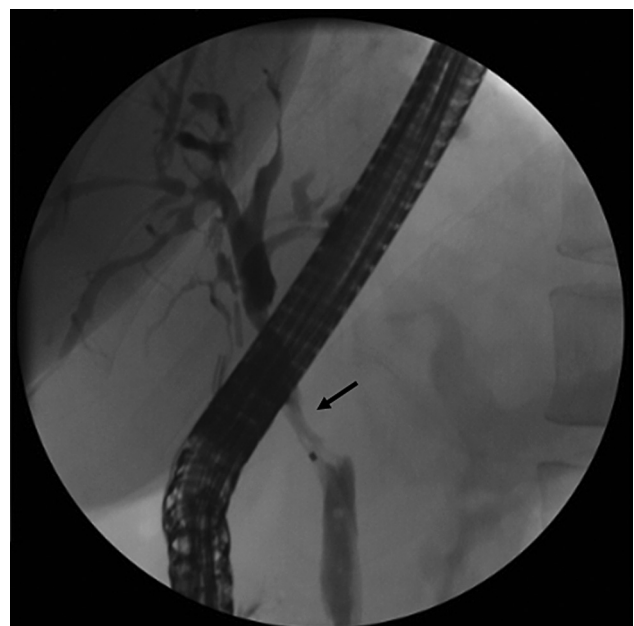


Figure 2. ERCP image of the asymmetrical stricture in the common bile duct of patient #3 (arrow).

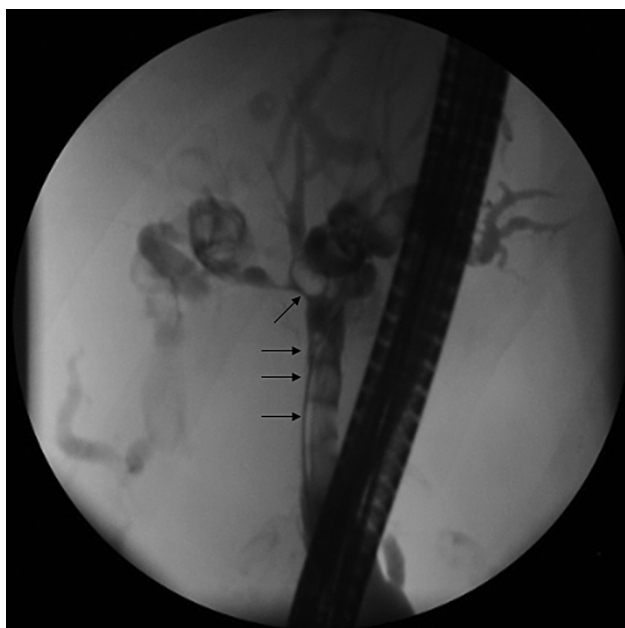


Figure 3. ERCP image of the patient with biliary stones and long segment biliary stricture.

patients with PSC and CA 19-9 level elevations (44, 70, 138, 147 U/ml, normal value <37 U/ml). Chronic inflammatory changes were detected in the biopsy of one 30-year-old PSC patient with decreased caliber at the confluence of the hepatic ducts. Acute inflammation was noticed in histopathological examination of the biliary stricture in one post-OLTx patient. There was no indication to obtain SpyBite® biopsy for the remaining 5 patients. Similarly, there was no need to obtain biopsy from the patient with asymmetrical stricture in the CBD with CA 19-9 elevation (62 U/ml), because of normal-looking mucosa. All SpyBite® biopsy specimens were reported to be adequate samples for histopathological examination.

DISCUSSION

Biliary problems are a known cause of morbidity in both pre- and post-OLTx patients (2). Every effort should be performed for definitive diagnosis of bile duct abnormalities, which is essential in the planning of therapy in this setting.

Identifying the causes of biliary strictures by peroral cholangiopancreatography (CP), another advanced technique of ERCP that allows direct visualization of the biliary and/or pancreatic ductal system, promises to facilitate accurate tissue sampling and therapeutic intervention (3). The efficacy and the feasibility of using peroral CP have been noted in several reports (4-8). However, there are some reported limitations associated with

peroral CP, i.e. i) requirement of two endoscopists working simultaneously, ii) limited tip deflection of cholangioscope, and iii) suboptimal irrigation capabilities (3). Therefore, a novel technology, SpyScope® system, was introduced with its highly effective biliary access capability, visualization and biopsy in all quadrants (1). The efficacy of this new system's feasibility was subsequently published in a 35-patient series (3).

Differential diagnosis of benign versus malignant strictures is particularly important for patients with PSC, since approximately 10% of patients with PSC develop cholangiocarcinoma (9), the second most common cause of mortality after liver failure for patients with PSC (10). Tumor markers, i.e. CA 19-9 and CEA, have been accepted as screening/follow-up criteria for patients with PSC, especially for early detection of *de-novo* cholangiocarcinoma, although these markers were found to be unreliable for such cases (10). ERCP, magnetic resonance cholangiopancreatography (MRCP) and endoscopic ultrasound (EUS) can supply state-of-the-art technology for clarification of biliary abnormalities and their effectiveness; however, their use is still limited and questionable. Therefore, improved evaluation of biliary strictures and selection of the appropriate therapeutic intervention have remained major diagnostic challenges (1). Thus, direct visualization of the biliary ducts with a flexible system is crucial.

Since early diagnosis of cholangiocarcinoma in patients with PSC is necessary, the novel technology should be performed during the work-up period of PSC patients for OLTx. Although it is difficult to examine the specificity and sensitivity of this technique due to the limited number of patients, it can be easily emphasized that direct visualization and eventual better sampling from the suspicious area are considered to be superior to conventional brushing techniques.

In this retrospective review, SpyScope® was also performed on four patients who had presented with biliary stricture following OLTx. In fact, strictures following OLTx are reported to be the commonest biliary problems, with incidences reported as 5-15% for non-anastomotic strictures and 4-9% for anastomotic strictures (11-13,15). The conventional approach to the management of biliary stricture is endoscopic dilatation followed by stenting (14). The success rate of this application is 50% to 100%, depending on the location and length of the stricture (15). The failure of the con-

ventional approach is usually due to unsuccessful cannulation of the strictured area by the endoscopist. Since the blind approach has been eliminated by SpyScope®, eventual increase in the success rate of stricture passage is anticipated. No difficulties were encountered by the endoscopist for cannulation of the biliary tree in our limited experience with four patients.

Procedure-related complications have been reported as 6%, namely, ascending cholangitis and cholangitis with intrahepatic abscess (3). No complications were encountered among the 10 patients in this review. Tissue sampling was obtained from 5 out of 10 patients, and all samples were reported to be adequate by the histopathologist.

To our knowledge, this is the first English-language series of SpyScope® technology, reported from a Liver Transplant Center. In conclusion, SpyScope® allows direct visualization of biliary strictures, in both pre- or post-OLTx settings, with no complications being encountered thus far. This limited review suggests SpyScope®/SpyBite® to be technically superior to conventional cholangiogram. Merits of this new technology include better sampling than brushing obtained by ERCP. Further clinical investigation is needed to identify its sensitivity and specificity for the work-up of biliary strictures encountered in both pre- and post-OLTx patients. Prospective, multicenter, large volume studies are warranted.

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