Per oral cholangiopancreatoscopy in pancreatico biliary diseases - Expert consensus statements

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Abstract

AIM: To provide consensus statements on the use of per-oral cholangiopancreatoscopy (POCPS).

METHODS: A workgroup of experts in endoscopic retrograde cholangiopancreatography (ERCP), endosonography, and POCPS generated consensus statements summarizing the utility of POCPS in pancreaticobiliary disease. Recommendation grades used validated evidence ratings of publications from an extensive literature review.

RESULTS: Six consensus statements were generated: (1) POCPS is now an important additional tool during ERCP; (2) in patients with indeterminate biliary strictures, POCPS and POCPS-guided targeted biopsy are useful for establishing a definitive diagnosis; (3) POCPS and POCPS-guided lithotripsy are recommended for treatment of difficult common bile duct stones when standard techniques fail; (4) in patients with main duct intraductal papillary mucinous neoplasms (IPMN) POPS may be used to assess extent of tumor to assist surgical
Pancreatobiliary diseases are commonly encountered in day to day clinical practice. Endoscopic retrograde cholangiopancreatography (ERCP) and magnetic resonance cholangiopancreatography (MRCP) are performed to further delineate the pancreatobiliary anatomy and establish a diagnosis in these patients. But these imaging modalities have limitation in that they are often only suggestive but not diagnostic of the disease. Per-oral cholangio-pancreatoscopy (POCPS) was introduced in 1970. It provides direct visualization of the biliopancreatic system and thus offers the possibility for accurate diagnoses. POCPS may also effectively guide interventions. With new developments in cholangioscopic systems including high resolution video-cholangioscopes, incorporation of narrow band imaging and availability of a single operator cholangiopancreatoscope there is renewed interest among endoscopists to perform POCPS more routinely.

There are no established guidelines about the utility of POCPS including relatively new technologies. This review provides consensus statements by experts about indications for POCPS based on available literature.

**MATERIALS AND METHODS**

A modified Delphi process was performed to establish the consensus. The procedure was based on combination of the principles of evidence-based medicine through extensive review of literature, face to face meeting and voting. A planning group panel (DNR, MR, SL, MT) made a list of statements which was sent to all consensus members. The statements were divided into the topics of indications of POCPS including diagnostic and therapeutic uses of POCPS. These statements were proposed to the Consensus Group panel for discussion, revision, and voting. A password- secured Web site was populated with relevant literature assembled by the literature review team (DNR and MR). A comprehensive literature search was conducted in the Medline/PubMed and EMBASE databases.

**RESULTS**

Both databases were searched for 16 search terms: Direct endoscopic cholangioscopy, Duodenoscope assisted cholangioscopy, Peroral cholangioscopy, Cholangioscopy tissue sampling, Cholangioscopy endoscopic biopsy, Direct pancreatoscopy, Pancreatoscope, Cholangioscopy biliary stone, Cholangioscopy lithotripsy, Spyglass, SpyScope, SpyBite, Direct visualization biliary, Direct visualization pancreatic, Digital cholangioscopy, and Digital pancreatoscopy.

Only articles published in English were included. One article was a methodologic publication[1]. Excluded were articles representing interim reports, in vitro studies or animal studies, and editorials and letters. A total of 92 articles were retrieved per this search, out of which 18 were selected for review. Seventy-four (74) articles were excluded because they were not relevant to search objectives (36), articles reporting on less than 10 patients (34), or review articles without original data (4). A few exceptions of articles reporting on less than 10 patients were included in cases in

**INTRODUCTION**

Pancreatobiliary diseases are commonly encountered in day to day clinical practice. Endoscopic retrograde cholangiopancreatography (ERCP) and magnetic resonance cholangiopancreatography (MRCP) are performed to further delineate the pancreatobiliary anatomy and establish a diagnosis in these patients.
POCPS is now an important additional tool during ERCP. Consensus statement 1
Recommendation Grade B
Quality of evidence: 2++
Direct visualization and the ability to sample and treat lesions aids in the care of patients by providing the correct diagnosis and allowing definitive treatment of lesions.
Cholangiopancreatoscopy through an ERCP catheter is a simple, safe and effective procedure for diagnosing pancreatobiliary diseases.
Intraductal peroral cholangioscopy and pancreatoscopy-sampling techniques appear to offer an advantage over fluoroscopy-guided ERCP sampling techniques for the diagnosis of pancreatobiliary lesions.

Table 1  Detailed evidence levels of respective references are provided for each consensus statement

<table>
<thead>
<tr>
<th>Consensus statement</th>
<th>Evidence level distribution</th>
<th>Recommendation grade</th>
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<tr>
<td>1</td>
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<td>2</td>
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POCPS: Peroral cholangiopancreatoscopy; ERCP: Endoscopic retrograde cholangiopancreatoscopy.

for establishing a definitive diagnosis; (3) POCPS and POCS-guided lithotripsy is recommended for treatment of difficult common bile duct (CBD) stones when standard techniques fail; (4) in patients with main duct intraductal papillary mucinous neoplasms (IPMN) peroral pancreatoscopy (POPS) may be used to assess the extent of tumor to assist surgical resection; (5) in difficult pancreatic ductal stones, POPS-guided lithotripsy may be useful in fragmentation and extraction of stones; and (6) additional indications for POCPS include selective guidewire placement, unexplained hemobilia, assessing intraductal biliary ablation therapy, and extraction of migrated stents.

Consensus statement 1
Table 2 provides a capsule summary of the first consensus statement, namely that POCPS is now an important additional tool during ERCP.

When ERCP was introduced in 1970 followed by endoscopic sphincterotomy in 1974, there was a quantum advance in the diagnosis and treatment of pancreatobiliary disorders. However, in some instances direct endoscopic visualization of the biliary and pancreatic ducts may be needed to evaluate equivocal fluoroscopic findings during ERCP, for definitive pathologic diagnosis or to provide therapeutic interventions and cholangiopancreatoscopy provides that direct visualization[2-8]. A comprehensive technology status evaluation was reported by the American Society of Gastrointestinal Endoscopy in 2008[9].

Cholangioscopy was first used in clinical medicine and described in the literature in the mid-1970s using fiber optics and was later advanced into video imaging as described in several review articles[2,8-11]. Clinical implementation of cholangiopancreatoscopy for direct visualization and examination of the bile ducts, pancreatic ducts, tissue sampling and therapeutic intervention has been slow due to limitations in the available technology. Recent advancements in the technology hold promise as an advanced technique for cases that elude successful diagnosis or treatment by conventional ERCP or other imaging modalities[2,12,13]. POCPS can be performed as a relatively safe and
In patients with indeterminate biliary strictures, POCPS and POCPS-guided targeted biopsy is useful for establishing a definitive diagnosis.

Recommendation Grade B

Quality of evidence: 2++

Technical success: Technical success for POCPS with or without POCPS-guided biopsy is reported to be 66% to 95% when defined as ability to reach the targeted lesion and, if desired, obtain a biopsy adequate for histopathology.

Diagnostic accuracy: Diagnostic measures of POCPS with or without POCPS-guided biopsy for malignancy were explicitly reported for a total of 980 cases in 11 studies. Reported sensitivity ranged from 49% to 100% and specificity ranged from 77% to 100%. In three prospective trials reporting separately on POCPS alone and on POCPS-guided biopsy and representing 297 patients, the weighted average sensitivity and specificity were 83% and 96% for POCPS alone and were lower at 56% and 81% for POCPS-guided biopsy.

Intrusive vs extrinsic strictures: POCPS-guided biopsy is significantly higher for intrusive than extrinsic tumors, and may be particularly useful in PSC patients prior to liver transplantation.

POCPS findings in indeterminate strictures: Findings of POCPS such as tortuous and irregularly dilated vessels, intraductal nodules or masses, infiltrative or ulcerated strictures, and papillary or villous mucosal projections are reported to be associated with malignancy. Generally POCPS is reported to improve yield of associated ERCP-guided biopsy. POCPS with NBI was reported to significantly improve diagnostic accuracy over white light POCPS.

Altered patient management: Changed patient management following POCPS is reported in as many as 2/3 of patients when measured. Impact of POCPS on pre-operative diagnosis may impact a surgical decision. POCPS combined with IDUS was reported useful in guiding patient management in portal biliopathy. POCPS was also reported useful for assessment of anastomotic strictures after liver transplantation.

Complications: Reported overall complication rates range from 6.6% to 9. The most common complication is cholangitis, reported in approximately 5% of cases. There is one report of fatal cholangitis.

POCS: Peroral cholangioscopy; PSC: Primary sclerosing cholangitis; ERCP: Endoscopic retrograde cholangiopancreatography; NBI: Narrow band imaging; IDUS: Intraductal ultrasonography.
it is likely that the utilization of cholangioscopy will increase.\(^{[27]}\)

Recommendation Grade: B. Quality of evidence: 2++. 

**Consensus statement 2**

Table 3 provides a capsule summary of the second consensus statement, namely that POCS and POCS-guided targeted biopsy is useful for establishing a definitive diagnosis.

**Technical success**: Technical success is typically defined as ability to reach and visualize the targeted area and additionally, in cases of POCS-guided biopsy, ability to obtain biopsies adequate for histology. Explicitly reported technical success levels for POCS of indeterminate strictures or filling defects without biopsy\(^{[22,24,26,34]}\) were 83%, 85%, 93%, and 100%, and with biopsy\(^{[21]}\) was 87%. Overall procedural success in this indication in the largest prospective series\(^{[21]}\) was 89% (202/226) with 140 cases with and 86 cases without POCS-guided biopsy.

Recommendation Grade: B. Quality of evidence: 2++. 

**Diagnostic accuracy**: A well-conducted review\(^{[34]}\) summarizes several studies on POCPs and reports mean POCS-guided tissue sampling to have 92% sensitivity, 93% specificity, 89% positive predictive value, and 95% negative predictive value for the diagnosis of malignancy. This is in line with diagnostic accuracy measures reported from four prospective studies\(^{[12,13,21,35]}\) all using the SpyGlass system, and reporting on respectively 226, 36, 35 and 52 cases in which POCS was used to assess indeterminate strictures with POCS-guided biopsy with one year of follow-up. Sensitivity and specificity of visual POCS impression only were 78% and 82%, 95% and 79%, and 100% and 77% respectively.\(^{[12,13,21]}\). Sensitivity and specificity of POCS-guided biopsy were 49% and 98%, 82% and 82%, 71% and 100% and 88% and 94%, respectively.\(^{[12,13,21,35]}\) In a prospective series of 62 cases\(^{[14]}\) using Olympus or Pentax cholangioscopes, sensitivity and specificity of POCS with or without biopsy were 89% and 96%. Several retrospective series\(^{[15,16,22,26]}\) on POCS in indeterminate strictures or filling defects respectively 130, 97, 89, and 30 cases were studied. Associated sensitivity and specificity of POCS with or without biopsies for diagnosis of malignancy were respectively 66% and 98%, 98% and 90%, 57% and 100%, and 77% and no reported specificity. A prospective study of 144 patients with peroral video cholangioscopy (PVCS)\(^{[37]}\) reported 99% sensitivity, 96% specificity, 99% positive predictive value, and 95.8% negative predictive value for the diagnosis of malignancy. Another prospective study of 33 patients\(^{[38]}\) reported the sensitivity and specificity, were 100% and 92%, for the PVCS visual findings and 38% and 100%, for the cholangioscopy-guided forceps biopsy findings. A prospective multicenter study of 87 patients in Japan\(^{[39]}\) with biliary tract diseases who underwent PVCS reported the accuracy rate of PVCS to evaluate the presence or absence of mucosal cancerous extension by endoscopic retrograde cholangiography (ERC) alone, ERC with PVCS, and ERC with PVCS+biopsy were 74%, 84%, and 93%, respectively. Table 4 provides a summary of diagnostic accuracy parameters reported in relevant references.

Recommendation Grade: B. Quality of evidence: 2++. 

**Intrinsic vs extrinsic strictures**: The sensitivity of POCS alone and of POCS-guided biopsy in 45 patients with confirmed malignancy\(^{[21]}\) was respectively 84% and 66% for intrinsic lesions (32) and was respectively 62% and 8% for extrinsic lesions. A comprehensive review\(^{[6]}\) of POCPs also reported that intraductal tissue sampling in the hands of experienced endoscopists, increases diagnostic yield particularly in cholangiocarcinoma. A large retrospective series\(^{[36]}\) identified the need for a special handling protocol for small intraductal biopsies of intrinsic lesions. POCS was reported\(^{[40–43]}\) to be useful for assessing
POCS and POCS-guided lithotripsy is recommended for treatment of difficult CBD stones when standard techniques fail.

POCS: Peroral cholangioscopy; CBD: Common bile duct; ERCP: Endoscopic retrograde cholangiopancreatography.

Table 5 Consensus statement 3

| POCS and POCS-guided lithotripsy is recommended for treatment of difficult CBD stones when standard techniques fail | Recommendation Grade A |
| Technical success: Technical success for POCS and POCS-guided lithotripsy for the treatment of difficult CBD stones when standard techniques fail range from 71%-100% |
| Direct visualization advantage: One of the key therapeutic benefits of POCS is the capacity to directly visualize and treat large intraductal stones. |
| Studies show that nearly all bile duct stones which failed conventional endoscopic removal (5%-10% of patients) could be removed non-surgically using POCS and POCS-guided lithotripsy |
| Residual stone detection: The diagnosis of small bile duct stones can be difficult with an ERCP. In those cases, POCS is able to detect residual stones missed on routine ERCP. |
| Complications: The most common complication reported is cholangitis (4.0%). Reported overall complications rates range from 3.8% to 13.3% |
| The results support the non-surgical management of difficult bile duct stones, particularly in patients at high risk for surgery |

POCS findings in indeterminate strictures:

Several publications report on correlations between various POCS findings and relative risk for malignancy. Reported findings include tumor vessels stated to be irregularly dilated and tortuous(8,13,34). They also include intraductal nodules or masses, infiltrative or ulcerated strictures, and papillary or villous mucosal projections(13,34). On the other hand, smooth mucosa without neovascularization or homogenous granular mucosa without a mass seemed associated with benign conditions(13). Direct correlation between such findings and a firm diagnosis is not perfect, and is hampered by imperfect inter-observer agreement(44).

One study specifically reported(31) on POCS to assess the presence and extent of intraepithelial tumor spread prior to surgical resection. Correlations were discussed between nodular-type carcinoma, papillary-type carcinoma and POCS findings of irregular fine granular patterns and fish-egg-like patterns with small red nodules, while non-cancerous mucosa appeared as white flat normal mucosa and hyperplastic mucosa had a scale-like appearance. POCS-guided biopsy was attempted. Conclusions were that diagnostic accuracy of POCS-guided biopsy was higher than ERCP findings, but that the cholangioscope could not be passed through the tumor sites in approximately 15% of cases. One publication(45) reported that the ability of POCS using narrow band imaging (NBI) to document surface structure was significantly better using conventional white light imaging. The study specifically reported improved visualization of vessels and improved ability to pre-operatively identify proximal and distal extent of cancerous lesions.

Recommendation Grade: C. Quality of evidence: 2++.

Altered patient management: A large prospective trial(21) reported that diagnostic POCS was deemed by attending investigators to have altered patient management in 63% (143/226) of cases. In a retrospective review of POCS cases from four centers in Texas, authors reported(23) that SpyGlass POCS modified a preoperative diagnosis of a malignant biliary stricture in 69% (20/29) cases, prevented unnecessary surgery in 7% (2/29) cases, and changed diagnosis from malignant to benign in 45% of patients with strictures. A case series of five patients(46) with symptomatic portal biliopathy suggested utility of POCS for determining patient management. POCS also has potential utility in determining treatment of post liver transplantation anastomotic strictures(47-53).

Recommendation Grade: B. Quality of evidence: 2++.

Complications: Overall complications were explicitly reported in three prospective studies(12,13,21) at levels of 7.6% (17/226), 5.7% (2/35), and 8.4% (3/36), and in four retrospective series(15,26,32,33) at 2.0% (2/97), 8.9% (16/179), 6.7% (2/30), and 13.3% (2/15). Thus the weighted mean overall complication rate was 7.1% (44/618).

The most common complication was cholangitis, explicitly reported(12,13,21,26,32,33) in 5.7% (2/35), 5.6% (2/36), 5.0% (9/179), 2.0% (2/97), 0% (0/30), and 6.7% (1/15) of cases respectively, amounting to a mean incidence of cholangitis of 4.1% (16/392). One review(54) reported that cholangitis, pancreatitis and perforation rates were higher in POCS than in ERCP alone.

Recommendation Grade: B. Quality of evidence: 2++.

Consensus statement 3

Table 5 provides a capsule summary of the third consensus statement, namely that POCS and POCS-guided lithotripsy is recommended for treatment of difficult CBD stones when standard techniques fail.
Table 6 Consensus statement 4

In patients with main duct IPMN POPS may be used to assess the extent of tumor to assist surgical resection

**Recommendation Grade C**

**Quality of evidence: 2+**

**Technical success:** Technical success for POPS in patients with IPMN is reported between 73% and 92% when defined as ability to reach and examine the targeted lesion.

**Diagnostic accuracy:** Diagnostic measures of POPS with or without POPS-guided biopsy for malignancy in IPMN are rarely reported in detail, and range from 50% to 68% sensitivity and from 87% to 100% specificity. Diagnostic accuracy seems better in main duct IPMN than in side branch IPMN.

**POPS findings in IPMN:** The most commonly reported POPS findings associated with malignancy in IPMN are villous patterns and vascular images. Granular mucus and fish-like patterns without vascularity were not associated with malignancy.

**POPS and IDUS:** Some studies document enhanced diagnostic accuracy when POPS is combined with endosonographic measures, particularly IDUS.

**Pre-operative and intra-operative POPS:** The role of POPS to pre-operatively provide diagnostic information on malignancy and to pre-operatively and/or intra-operatively document the location and extent of dysplastic IPMN is generally reported.

**Technical success:** Technical success for POCS and POCS-guided lithotripsy for the treatment of difficult CBD stones is defined as stone fragmentation and removal. POCS and POCS-guided lithotripsy for the treatment of difficult CBD stones when standard techniques fail, including ERCP stone extraction and mechanical lithotripsy, ranges from 71%-100%[4,7,22,35-58]. Explicitly reported technical success levels for POCS and POCS-guided lithotripsy were 83.3%, 100%, 71.2%, 83.3%, 96.4%, 92.3%, 100%, 79.2%, 81%, 100%, 95%, 100%, 88.9%, 97% in prospective studies and case series[15,23,70] and 90.2%, 90%, 73% in retrospective studies[15,23,70]. Intra-hepatic stones appear to be managed mostly transhepatically and are not discussed in this paper.

**Recommendation Grade: A. Quality of evidence: 1+.**

**Direct visualization advantage:** One of the key therapeutic benefits of POCS is the capacity to directly visualize and treat large intraductal stones not removed at ERCP[6-21]. Studies have shown that nearly all bile duct stones which failed conventional endoscopic removal (5%-10% of patients) could be removed non-surgically using POCS and POCS-guided lithotripsy[21,27]

POCS has proven to be valuable in complicated choledocholithiasis, especially in guiding the positioning of an electrohydraulic lithotripsy (EHL) probe or laser fiber on the surface of stone[21,23,65]. The direct visualization helped prevent injury during ERCP from an EHL probe positioning under fluoroscopy.

**Recommendation Grade: B. Quality of evidence: 2++.**

**Residual stone detection:** An additional advantage of POCS is successful identification of stones missed on ERCP[58]. Stones can be clearly differentiated from filling defects because of soft-tissue masses and more readily discerned than during ERCP when associated with other biliary abnormalities such as strictures[21]. In a prospective study, of 66 patients who underwent POCS-directed EHL or laser lithotripsy, 11% had 1 or more stones identified only by POCS but not by ERCP[21]. Other prospective studies identified additional stones via cholangioscopy not seen at ERCP in 18% (9/49), 28% (9/32) patients[62,64]. Retrospective reviews of patients with altered GI anatomy[71,72] reported 21% (4/19) patients in whose bile duct stones appeared to be completely removed by cholangiography and POCS detected residual stones.

**Recommendation Grade: B. Quality of evidence: 2++.**

**Complications:** Overall complications have a low incidence[73] and were explicitly reported in 7 prospective studies[17,21,23,61,64,69] at levels of 13.3% (8/60), 5.7% (2/35), 6.1% (4/66), 8.4% (3/36), 5.3% (4/75), 3.8% (2/53), 4.3% (3/69). In a retrospective study[33], the complication rate was reported at 9% (16/179). Several studies and a comprehensive review reported no complications in patients that underwent POCS and POCS-guided lithotripsy for the treatment of difficult CBD stones[27,59,62]. Thus the weighted mean overall complication rate was 7.7% (39/504). The most common complication is cholangitis, explicitly reported[17,21,23,61,64] in 5.0% (3/60), 5.7% (2/35), 3.0% (2/66), 5.6% (2/36), 1.9% (1/53) of cases or procedures respectively, amounting to a mean incidence of cholangitis of 4.0% (10/250). Cholangitis was often mild and could be treated with oral antibiotics[64] but severe and fatal cases were reported[15].

**Recommendation Grade: A. Quality of evidence: 1+.**

**Consensus statement 4**

Table 6 provides a capsule summary of the fourth consensus statement, namely that in patients with main duct IPMN POPS may be used to assess the extent of tumor to assist surgical resection.

**Technical success:** Technical success is typically defined as the ability to reach the IPMN lesions and examine them under POPS, which requires clearing the view of mucus. It is explicitly reported in three publications[74-76] as 73% in 41 patients, 82% in 11...
Intra-operatively guide surgery in pre-operative settings of the IPMN lesion and extent of dysplasia can help.

Pre-operative and intra-operative POPS: ERCP and EUS and IDUS for examination of pancreatic duct IPMN. ERCP and EUS also point to the value of POPS in combination with IDUS. An additional series of 6 patients reached 50% (3/6) of cases. Studies focused on identifying POPS findings that seem associated with malignancy in IPMN generally point to villous or papillary tumors and proliferation of blood vessels to be correlated with malignancy. Conversely, granular mucosa with fish-egg-like patterns without vascular images seem associated with benign IPMN lesions.

POPS findings in IPMN: Studies focused on identifying POPS findings that seem associated with malignancy in IPMN generally point to villous or papillary tumors and proliferation of blood vessels to be correlated with malignancy. Conversely, granular mucosa with fish-egg-like patterns without vascular images seem associated with benign IPMN lesions.

POPS and IDUS: One careful study in 60 patients undergoing pre-operative POPS, 40 of 60 patients also underwent intraductal ultrasonography (IDUS). For POPS sensitivity and specificity were 65% and 88% respectively. Using IDUS findings of protrusions of 1 mm or more, sensitivity and specificity were 68% and 89% respectively. For POPS and IDUS combined in 40 patients, sensitivity and specificity were 91% and 82% respectively. Authors concluded POPS and IDUS combined provides improved differential diagnosis between malignant and benign IPMN. Another series also point to the value of POPS in combination with ERCP and EUS and IDUS for examination of pancreatic duct IPMN.

POPS-guided EHL or laser lithotripsy: EHL was reported for 17 cases, with stone clearance reported in 71% (12/17). Laser lithotripsy was reported for 9 cases, with stone clearance reported in 100% (9/9). Stone clearance was reported in 70% (32/46) with EHL or laser lithotripsy in 39 of those cases. POPS-guided EHL vs ESWL: POPS-guided EHL compared to ESWL for treatment of pancreatic duct stones is reported as difficult and as being only rarely indicated.

POPS: Peroral pancreatoscopy; EHL: Electrohydraulic lithotripsy; ESWL: Extracorporeal shock-wave lithotripsy.

Diagnostic accuracy: Study reports and one comprehensive review of POPS for assessment of presence or absence of malignancy in IPMN ranges in sensitivity from 50% to 68%, and in specificity from 75% to 100%. In the three study reports, 60 patients in one study underwent POPS without biopsy and a combined 23 patients underwent POPS with POPS-guided biopsy. Diagnostic accuracy of POPS for malignancy in patients with main duct IPMN seems better than for patients with side branch IPMN.

Recommendation Grade: C. Quality of evidence: 2+. Patients and 92% in 13 patients.

Consensus statement 5

Table 7 Consensus statement 5

In difficult pancreatic ductal stones, POPS-guided lithotripsy may be useful in fragmentation and extraction of stones.

Recommendation Grade: C. Quality of evidence: 2-.

POPS-guided EHL or LL: EHL guided by POPS was reported successful in two publications with successful pancreatic stone clearance in 50% (3/6) and 100% (1/1) of cases. Stones were mostly in the head of the pancreas. There were no serious adverse events. Laser lithotripsy (LL) by POPS was reported in two publications with successful pancreatic stone clearance in 100% (9/9) of cases. There were no complications in the patients with pancreatic duct stones. All four reports used the SpyGlass system. Stones were described as difficult to remove as stones were impacted, cast-like, or located above a distal PD stricture. A new prospective study reported stone clearance was reported in 70% (32/46) with EHL or laser lithotripsy in 39 of those cases; mechanical lithotripsy was used in the remaining 7 cases. Per oral pancreatoscopy related complications were found in 10%. Dilation of the stricture and biliary and pancreatic sphincterotomy are common in POPS-guided EHL. Several qualitative reports support that POPS may be helpful for identification of pancreatic duct stones missed in prior imaging studies, and also that intended POPS-guided EHL can sometimes be avoided after careful assessment of the pancreatic duct stones under POPS.

Recommendation Grade: C. Quality of evidence: 2+.

POPS-guided EHL vs extracorporeal shock-wave lithotripsy: A comprehensive review of various techniques used to perform POPS specifically comments on the use of extracorporeal shock-wave lithotripsy (ESWL) and POPS-guided EHL in combination. A small series of 6 patients reached 50% stone clearance and symptom improvement. A single case report identified the value of intraductal EHL for non-calciﬁed pancreatic stones. Where possible, ESWL alone is reported as easier than POPS-guided.

POPS-guided EHL or laser lithotripsy: EHL was reported for 17 cases, with stone clearance reported in 71% (12/17). Laser lithotripsy was reported for 9 cases, with stone clearance reported in 100% (9/9). Stone clearance was reported in 70% (32/46) with EHL or laser lithotripsy in 39 of those cases. POPS-guided EHL vs ESWL: POPS-guided EHL compared to ESWL for treatment of pancreatic duct stones is reported as difficult and as being only rarely indicated.

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Table 7 Consensus statement 5

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POPS-guided EHL or laser lithotripsy: EHL was reported for 17 cases, with stone clearance reported in 71% (12/17). Laser lithotripsy was reported for 9 cases, with stone clearance reported in 100% (9/9). Stone clearance was reported in 70% (32/46) with EHL or laser lithotripsy in 39 of those cases. POPS-guided EHL vs ESWL: POPS-guided EHL compared to ESWL for treatment of pancreatic duct stones is reported as difficult and as being only rarely indicated.

POPS: Peroral pancreatoscopy; EHL: Electrohydraulic lithotripsy; ESWL: Extracorporeal shock-wave lithotripsy.

Diagnostic accuracy: Study reports and one comprehensive review of POPS for assessment of presence or absence of malignancy in IPMN ranges in sensitivity from 50% to 68%, and in specificity from 75% to 100%. In the three study reports, 60 patients in one study underwent POPS without biopsy and a combined 23 patients underwent POPS with POPS-guided biopsy. Diagnostic accuracy of POPS for malignancy in patients with main duct IPMN seems better than for patients with side branch IPMN.

Recommendation Grade: C. Quality of evidence: 2+.

POPS findings in IPMN: Studies focused on identifying POPS findings that seem associated with malignancy in IPMN generally point to villous or papillary tumors and proliferation of blood vessels to be correlated with malignancy. Conversely, granular mucosa with fish-egg-like patterns without vascular images seem associated with benign IPMN lesions.

Recommendation Grade: C. Quality of evidence: 2+.

POPS and IDUS: One careful study in 60 patients undergoing pre-operative POPS, 40 of 60 patients also underwent intraductal ultrasonography (IDUS). For POPS sensitivity and specificity were 65% and 88% respectively. Using IDUS findings of protrusions of 1 mm or more, sensitivity and specificity were 68% and 89% respectively. For POPS and IDUS combined in 40 patients, sensitivity and specificity were 91% and 82% respectively. Authors concluded POPS and IDUS combined provides improved differential diagnosis between malignant and benign IPMN. Another series also point to the value of POPS in combination with ERCP and EUS and IDUS for examination of pancreatic duct IPMN.

Recommendation Grade: D. Quality of evidence: 3.

Pre-operative and intra-operative POPS: Location of the IPMN lesion and extent of dysplasia can help guide surgery in pre-operative settings or even intra-operatively to better determine the resection line in the pancreas.

Recommendation Grade: D. Quality of evidence: 3.

Consensus statement 5

Table 7 provides a capsule summary of the fifth consensus statement, namely that in difficult pancreatic ductal stones, POPS-guided lithotripsy may be useful in fragmentation and extraction of stones.
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Table 8  Consensus statement 6

| Additional indications for POCPS include selective guidewire placement, unexplained hemobilia, assessing intraductal biliary ablation therapy, and extraction of migrated stents |
| Recommendation Grade C |
| Quality of evidence: 2+ |

The primary indications of peroral cholangiopancreatoscopy are indeterminate stricture, indeterminate filling defect and stones, but the application of the technology is vast and is forever expanding. While not many cases are performed and documented, the indications extend to selective guidewire placement, unexplained hemobilia, assessment of intraductal biliary ablation therapy as well as the extraction of migrated stents. These additional indications have been reported in clinical studies as well as comprehensive reviews of POCPS.

POCPS: Peroral cholangiopancreatoscopy.

EHL, but an ERCP is typically still needed to clear distal pancreatic duct stones or stone fragments. 


**Consensus statement 6**

Table 8 provides a capsule summary of the sixth consensus statement, indicating that additional indications for POCPS include selective guidewire placement, unexplained hemobilia, assessing.

**Selective guidewire placement:** Peroral cholangioscopy has successfully been used in a number of studies[4,6,9,11] for selective guidewire placement, including access to disease segments in complicated bile duct strictures or openings of cystic ducts that are difficult to access by conventional ERCP. SpyGlass was successfully used to enter the cystic duct for guidewire placement and gallbladder stenting in a patient with pre-transplant cirrhosis and symptomatic cholelithiasis who had previously failed multiple attempts to cannulate the cystic duct for gallbladder stenting at ERCP[12].

An overview[16] of the SpyGlass system for cholangiopancreatoscopy in 2009 focused on indications, clinical applications and studies to date and attempted to clarify the role of this important technology which allows for direct visualization of the bile and pancreatic ducts, tissue acquisition and access for therapeutic interventions, including stone removal. A notable therapeutic indication is the facilitation of selective guidewire access to the gallbladder or intrahepatic ducts.

Other comprehensive reviews[4,6,9,11,58] of peroral cholangioscopy authors have noted that cholangioscopy also facilitates selective guidewire placement into complicated bile duct strictures, intrahepatic ducts and the gallbladder or opening of a cystic duct that is difficult to access by conventional ERCP.

Recommendation Grade: C. Quality of evidence: 2+.

**Unexplained hemobilia:** POCs for the assessment of unexplained hemobilia is a rare but useful method. In a comprehensive review[27] of intraductal biliary and pancreatic endoscopy, authors note that a diagnostic indication of cholangioscopy is the evaluation of hemobilia of unknown etiology. Other comprehensive reviews[2,6] of applications of POCS, indicated the procedure can be used for both the localization and treatment of hemobilia. In a retrospective review of 61 patients, hemobilia was indicated in 4 cases and the site of bleeding was identifies in all cases[52].

Recommendation Grade: C. Quality of evidence: 2+.

**Assessment of intraductal biliary ablation therapy:** Cholangiopancreatoscopy has been further developed for further applications such as tumor ablation, according to a comprehensive review conducted in 2009[6] and a review of SpyGlass[22] specifically.


**Extraction of migrated stents:** Proximal (upstream) migration of pancreatic duct stents is a recognized complication that occurs in up to 5.2% of patients[51]. A case review[91] of a single patient demonstrates that with POPS, they were able to visualize the distal end of a migrated stent; the 4-way deflection of the cholangioscope allowed for maneuverability to successfully cannulate the stent with a guidewire and then remove it.

In a prospective observational clinical feasibility study of 35 patients[12] the indication for POCs was gallbladder stent placement in 1 patient (3%). In another study of 22 patients[52], 25 cholangioscopy attempts were made and 22 were successful (88%; 19 patients). A biopsy forceps under cholangioscopic visualization was used to release a dislodged fully covered self-expanding metal stent in the CBD. Authors felt that cholangioscopy is useful in improving diagnostic validity and offering new therapeutic interventions. The stent was then removed using a duodenoscope.

In a prospective study of 12 patients[24] at University of Chicago, 18 cholangioscopies with the mother-baby endoscope were performed and a fragmented stent was the indication in one patient. Authors concluded that direct visualization of the biliary tree with the ability to sample or treat lesions significantly aided in the care of all patients in whom the baby endoscope was successfully passed by providing the correct diagnosis
and, when appropriate, by allowing definitive treatment of lesions.

A comprehensive review[30] of peroral cholangioscopy indicated that there are both diagnostic and therapeutic applications. Authors note that a primary therapeutic indication is endoscopic extraction, including stone removal but that another indication is removal of proximally migrating stents that cannot be removed by conventional ERCP.

Recommendation Grade: C. Quality of evidence: 2+.

DISCUSSION

A workgroup of experts in the field of POCPS established six consensus statements regarding the utility of POCPS, with associated recommendation grades A (1), B (2), or C (3). Overall, the consensus points to POCPS as an important tool in association with ERCP, particularly for diagnosis of indeterminate biliary strictures and for intra-ductal lithotripsy when other lithotripsy techniques have failed. It also states that POCPS may be useful for pre-operative assessment of the extent of main duct tumors in IPMN, for fragmentation and extraction of difficult pancreatic stones, and for unusual indications including selective guidewire placement, unexplained hemobilia, assessing intraductal biliary ablation therapy, and extraction of migrated stents.

The six consensus statements are as follows: (1) POCPS is now an important additional tool during ERCP. Recommendation grade B; (2) In patients with indeterminate biliary strictures, POC and POCs-guided targeted biopsy are useful for establishing a definitive diagnosis. Recommendation grade B; (3) POCs and POCs-guided lithotripsy are recommended for treatment of difficult CBD stones when standard techniques fail. Recommendation grade A; (4) In patients with main duct IPMN POPS may be used to assess extent of tumor to assist surgical resection. Recommendation grade C; (5) In difficult pancreatic ductal stones, POPS-guided lithotripsy may be useful in fragmentation and extraction of stones. Recommendation grade C; and (6) Additional indications for POCPS include selective guidewire placement, unexplained hemobilia, assessing intraductal biliary ablation therapy, and extracting migrated stents. Recommendation grade C.

COMMENTS

Background
Per-oral cholangiopancreatocscopy (POCPS) is not a new imaging modality to assist the gastroenterological endoscopist in diagnosis and treatment of pancreatobiliary diseases. However, recent technological advances have made this modality more broadly used. Given the relatively high incidence of pancreatobiliary ductal disorders in Asia, consensus statements from users in the region seem relevant.

Research frontiers
Constant technological improvements are ongoing and are anticipated to make POCPS an increasingly adopted modality in the management of patients with pancreatobiliary disease.

Innovations and breakthroughs
Recent advancements include the addition of narrow band imaging, single operator cholangiopancreatoscopes, and ultra-thin gastrosopes.

Applications
This paper provides a concise review of available evidence of the clinical utility of POCPS in a wide range of indications.

Terminology
In this paper cholangiopancreatoscopy was abbreviated to “POCP” which is not necessarily universally adopted terminology.

Peer-review
The paper includes a commendable and extensive review of the literature. It is well-written but do have some suggestions to hopefully enhance its strength.

REFERENCES

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