Role of pancreatoscopy in management of pancreatic disease: A systematic review

Tarun Kaura, Field F Willingham, Saurabh Chawla

ORCID number: Tarun Kaura (0000-0002-3031-7029); Field F Willingham (0000-0002-7071-3001); Saurabh Chawla (0000-0001-6841-4929).

Author contributions: All authors equally contributed to this paper with conception and design, literature review and analysis, drafting and critical revision and editing, and approval of the final version.

Conflict-of-interest statement: All authors declare no potential conflicts of interest. No financial support.

PRISMA 2009 Checklist statement: The authors have read the PRISMA 2009 Checklist, and the manuscript was prepared and revised according to the PRISMA 2009 Checklist.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

Manuscript source: Invited manuscript

Abstract

BACKGROUND
Per-oral pancreatoscopy (POP) plays a role in the diagnosis and therapy of pancreatic diseases. With recent technological advances, there has been renewed interest in this modality.

AIM
To evaluate the efficacy and safety of POP in management of pancreatic stone disease and pancreatic ductal neoplasia.

METHODS
To determine the safety and efficacy of POP in the management of pancreatic diseases, a systematic search was conducted in MEDLINE, EMBASE and Ovid. Articles in languages other than English and case reports were excluded. All published case series were eligible. Data specific to POP were extracted from studies, which combined cholangiopancreatoscopy. Ten studies were included in the analysis of POP therapy for pancreatic stone disease, and 15 case series satisfied the criteria for inclusion for the role of POP in the management of pancreatic ductal neoplasia. The examined data were subcategorized according to adjunctive modalities, such as direct tissue sampling, cytology, the role of intraoperative POP, intraductal ultrasound (IDUS) and POP combined with image-enhancing technology.

RESULTS
The success rate for complete ductal stone clearance ranged from 37.5%-100%. Factors associated with failure included the presence of strictures, multiple stones
and the inability to visualize the target area. Although direct visualization can identify malignant and premalignant conditions, there is significant overlap with benign diseases. Visually-directed biopsies provide a high degree of accuracy, and represent a unique approach for tissue acquisition in patients with ductal abnormalities. Addition of pancreatic fluid cytology increases diagnostic yield for indeterminate lesions. Protrusions larger than 3 mm noted on IDUS are significantly more likely to be associated with malignancy. The rate of adverse events associated with POP ranged from 0%-35%.

CONCLUSION
Current evidence supports wider adoption of pancreatoscopy, as it is safe and effective. Improved patient selection and utilization of novel technologies may further enhance its role in managing pancreatic disease.

Key words: Pancreatoscopy; Cholangiopancreatoscopy; Chronic pancreatitis; Pancreatic duct stones; Intraductal papillary mucinous neoplasm; Pancreatic cancer; Pancreatic duct stricture

©The Author(s) 2019. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: This updated review focuses on the current evidence regarding the use of per oral pancreatoscopy (POP) in the management of complex pancreatic ductal diseases. Traditionally, treatment of pancreatic stone disease has been performed by endoscopic retrograde cholangiopancreatography; POP may fill a void, offering durable relief while avoiding surgery in certain scenarios. POP also plays a complementary role to endoscopic ultrasonography in the evaluation of pancreatic ductal abnormalities with suspicion of neoplasia. With rapid advancements in imaging technology, POP may play a wider therapeutic role in the treatment of pancreatic ductal neoplasia.

INTRODUCTION
Evaluating the pancreatic duct (PD) is challenging due to its anatomy, which occasionally limits visualization by cross-sectional imaging, relative inaccessibility to available endoscopic devices, and certain unique obstructive disease entities. These may limit diagnostic and therapeutic endeavors under fluoroscopic guidance. Evaluation of these entities has relied heavily on various radiologic modalities including computed tomography (CT) scans, magnetic resonance imagings (MRIs), endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic ultrasonography (EUS)[1]. ERCP-guided brushings of pancreatobiliary strictures for cytological examination has a diagnostic yield ranging from 30%-57%[2-4]. Even with the addition of endobiliary biopsy forceps and endoscopic needle aspiration, the diagnostic yield and negative predictive value remains low[5]. Stone extraction from the PD may be limited by stone impaction at side branch take-offs, or a narrow proximal PD, which may limit balloon extraction. Furthermore, non-endoscopic interventions of the pancreas are associated with significant morbidity and mortality.

For these reasons, direct visualization of the pancreatic ductal system is helpful in evaluating and managing certain pancreatic diseases. Attempts at direct visualization of the PD with per-oral pancreatoscopy (POP) were initially described in the 1970s using a mother-baby system[6]. However, there were drawbacks, including the need for two endoscopists, scope fragility and poor image resolution, which limited its adoption for mainstream use.

The recent development of catheter-based systems, primarily developed for bile duct use (single operator cholangioscopy), has addressed some of these limitations, thus promoting widespread application of this modality for both biliary and pancreatic ductal use. Features, such as four-way tip deflection, dedicated irrigation, accessory channels, and digital image acquisition with significant improvement in
image quality, field-of-view and ability to add image-enhancing technology, have made these systems more user-friendly. They have also resulted in diagnostic and therapeutic advances in the management of complex pancreatic diseases.

We present an updated review of the current literature on POP for the management of pancreatic diseases.

**MATERIALS AND METHODS**

To determine the safety and efficacy of POP in the management of pancreatic diseases, a systematic search was conducted in MEDLINE, EMBASE and Ovid. We used the key words “pancreatoscopy”, “cholangiopancreatoscopy”, “IPMN”, “chronic pancreatitis” and “pancreatic stone disease” to identify relevant articles. Articles in languages other than English and case reports were excluded. All published case series were eligible. Data specific to POP was extracted from studies that combined cholangiopancreatoscopy. The subject population was heterogeneous among the studies reviewed. Ten studies were included in the analysis of POP therapy for pancreatic stone disease (Table 1). Fifteen case series satisfied the inclusion criteria for the role of POP in the management of pancreatic ductal neoplasia (Table 2). The examined data were subcategorized according to the adjunctive modality, such as direct tissue sampling, cytology, role of intraoperative POP, intraductal ultrasound (IDUS) and POP combined with image-enhancing technology.

**RESULTS**

**Endoscopic pancreatic ductal stone therapy**

Chronic pancreatitis is characterized by ongoing inflammation that leads to fibrotic changes in the pancreas, resulting in diminished exocrine and endocrine function. Chronic abdominal pain is the main symptom, which may be severe enough to limit quality of life. Several mechanisms, such as outflow obstruction leading to ductal hypertension from strictures/stones and perineural inflammation, have been implicated in the pain pathogenesis of chronic pancreatitis. Continued ductal obstruction may eventually lead to parenchymal atrophy and loss of exocrine and endocrine function, which may cause other symptoms including anorexia, malabsorption and weight loss. Therefore, relief of pancreatic ductal obstruction is a cornerstone in the management of this disease.

Options for therapy depend on ductal morphology and the presence of PD stones and/or strictures. Pancreatic ductal stones, which can occur in up to 90% of patients, represent a significant target for therapeutic intervention[7]. Stone predominant disease, associated with a uniformly dilated PD, is often seen in patients with idiopathic or genetic etiologies, as compared to the complex ductal morphology with strictures seen in patients with chronic alcoholic pancreatitis[8].

Traditional ERCP techniques using extraction balloons and stone extraction baskets have a limited success rate of around 50%, even in expert hands[9]. The complication rate of pancreatic mechanical lithotripsy is three-fold higher than biliary lithotripsy, including trapped and broken baskets that occur in up to 10%[9]. Extra corporeal shockwave lithotripsy (ESWL) is an important adjunct to managing pancreatic ductal stones, with a success rate of 60% for pain relief[10]. However, the limited availability, cost, need for multiple sessions, along with concomitant ERCP to remove stone fragments and treat downstream strictures, have limited widespread use[11]. Furthermore, ESWL also requires a radiopaque target such as a calcified stone or the tip of a stent, thus limiting applicability with radiolucent stones. The management of radiolucent stones is more demanding, as it may require ultrasound guidance or contrast injection through a nasopancreatic catheter[12]. In addition, ESWL is less effective in patients with dense or multiple stones[13].

POP-guided intraductal lithotripsy has the potential to combine the advantages of endoscopy and ESWL. POP-guided intraductal lithotripsy was initially described by Howell et al[14], and significant advances have been achieved since then. Intraductal lithotripsy under direct visualization can be achieved by either electrohydraulic therapy (EHL) or laser lithotripsy (LL). The EHL probe consists of two coaxially insulated electrodes attached to a generator producing high voltage electrical impulses at a frequency of 1 to 20 Hz, with power settings between 50%-100%[15]. Sparks at this site produce high amplitude hydraulic pressure waves during water immersion, which help in stone fragmentation[16]. Neodymium: yttrium-aluminum-garnet lasers have been used for pancreatobiliary stone fragmentation by transforming optical energy into mechanical energy in the form of shockwaves via
local plasma formation[17].

Pancreatography-guided lithotripsy

Ten published studies were selected for review based on the inclusion criteria. Only two prospective studies with a total of 9/134 patients were identified. There were no prospective randomized studies. Only three published studies had more than ten patients, however, they are all retrospective in nature. A majority of the included patients had chronic pancreatitis due to excessive alcohol use.

Based on the available data, the success rate of POP-guided PD stone therapy ranges between 37.5%-100% (Table 1) as compared to the success rate of ESWL, which ranges between 59%-76%[18]. Only one study retrospectively compared single-operator pancreatoscopy with traditional mother daughter technique. This study showed no significant differences in success rate, although there was a trend towards better success with the catheter-based system, with a complete clearance rate of 68%-73%[19]. Dorsal duct POP-guided endotherapy via minor papilla access was successfully attempted in cases in which the duct immediately upstream of the major papilla was inaccessible[9,19]. This can be performed in patients with pancreatic divisum or acquired obstruction of the ventral duct (pseudo-divisum) from strictures or stones. Brauer et al[20] reported 80% clinical success via minor papilla in five patients with painful pancreatitis.

Most studies included patients who had failed conventional ERCP techniques[12,21,23] or ERCP with ESWL[14,21,23]. Median reported PD stone size ranged from 5 mm[23] to 15 mm[1]. Some studies[14] reported 23 h observation after index POP procedure or pancreatic sphincterotomy. Most studies reported the placement of plastic PD stents for drainage after POP-guided therapy, necessitating multiple procedures. Shin et al[18] placed a self-expanding fully covered metal stent for downstream PD stricture prior to successful POP-guided EHL lithotripsy of a 1.1 cm large PD stone.

Parbhu et al[23] reported a 50% success rate in 20 patients using only balloon or basket sweeps due to better visualization with POP. Complete clearance in a single procedure was reported in 100% patients by Maydeo et al[21] and 61% by Attwell et al[9]. The majority of patients required multiple procedures to achieve clinical success.

Attwell et al[9] attained better technical success of complete clearance in patients who had stones in the head/neck (92%) as compared to the body/tail (67%). The same study demonstrated better success for patients with single stone (87%) vs patients with multiple stones (69%). Factors predicting the failure of therapy include multiple strictures, multiple stones and direct visualization failure.

POP was also reported to have an adjunctive intraoperative role with POP-guided EHL during lateral pancreatojejunostomy, having shown reduced rates of subsequent hospitalization and surgeries[19].

The risk of side effects ranges between 0%-29% (Table 1), without any reported mortalities. Broad-spectrum antibiotic prophylaxis was used before POP[18], although no clear study to date has evaluated its benefit. Side effects include post-procedure pain and pancreatitis, which was mild in most of the patients using the Cotton criteria. A single study reported perforation with guidewire[9], which was managed.

---

Table 1  Per oral pancreatoscopy-guided pancreatic ductal stone therapy

| Year | Ref. | Patients, n | Design | Device | EHL/LL | Success rate | AE % | Follow-up in mo |
|------|------|-------------|--------|--------|--------|--------------|------|-----------------|
| 1999 | Howell et al[14] | 6 | R/M | M-B | EHL | 83 | 0 | 6 |
| 2009 | Fishman et al[9] | 6 | R/M | Spyglass® | EHL | 50 | 0 | NA |
| 2011 | Maydeo et al[21] | 4 | P/S | Spyglass® | LL | 100 | 13.3 | 1 |
| 2013 | Alatawi et al[12] | 5 | P/S | Spyglass® | LL | 80% | 0 | 21 |
| 2014 | Attwell et al[9] | 46 | R/S | Olympus M-B (31) vs Spyglass® (15) | LL/EHL | 68 vs 73 (scope type) | 10 | 18 |
| 2014 | Ito et al[19] | 8 | R/S | Spyglass® | EHL | 37.5 | 25 | NA |
| 2015 | Attwell et al[9] | 28 | R/M | Spyglass® | LL | 79 | 29 | 13 |
| 2016 | Navaneethan et al[22] | 5 | R/M | Spyglass® | LL | 80 | 0 | NA |
| 2017 | Bekkali et al[20] | 6 | R/S | Spyglass® | EHL | 83 | 0 | 30 |
| 2017 | Parbhu et al[23] | 20 | R/M | Spyglass® | EHL/LL | 85 | 7.3 | NA |

1Combined with ESWL.
2Combined study of patients with biliary and pancreatic ductal stones.

EHL: Electro hydraulic lithotripsy; LL: Laser lithotripsy; P: Prospective; R: Retrospective; S: Single-center; M: Multicenter; AE: Adverse events; M-B: Mother baby.

---

[17] Local plasma formation.

[18] Pancreatography-guided lithotripsy.
### Table 2: Role of per oral pancreatoscopy in pancreatic ductal neoplasia

| Year | Ref. | N  | Design | Key findings | Adjunct modalities/success | AE% | Follow up |
|------|------|----|--------|--------------|-----------------------------|-----|-----------|
| 1997 | Uehara et al[42] | 11 | P      | Made early diagnosis of CIS missed by other modalities | Cytology in all (with secretin) | NR  | 34 mo     |
| 1998 | Jung et al[46] | 18 | P      | Visual differentiation - IPMN, Cancer, Chr pancreatitis | Cytology in all | 6   | 2 yr      |
| 1998 | Mukai et al[47] | 25 | R/S    | Papillary lesions > 3 mm, trend towards malignancy | IDUS (> sensitive than POP) for detecting protrusions > 3 mm | 4   | NA        |
| 1998 | Tajiri et al[48] | 52 | P      | Visual intraductal findings to differentiate Chr pancreatitis and neoplasia | 81% success | 3.8 | NA        |
| 2000 | Yamaguchi et al[27] | 41 | R/S    | Villous/vegetative lesions with red marks correlate with atypical adenoma/cancer | 73.2% success | NA  | 38.5 mo   |
| 2002 | Kodama et al[47] | 42 | P      | POP correctly identified all stenosis due to Chr pancreatitis | 75% success | 1.8 | NA        |
| 2002 | Hara et al[33]  | 60 | R/S    | POP + IDUS 88% accuracy in differentiating benign vs malignant POP better for MD type, IDUS better for SB type | IDUS in 40 patients Cytology in 36 patients - Low Sens 13% | 7   | 38.4 mo   |
| 2003 | Yamao et al[44] | 115 | R      | Protrusion, friability 100% spec for malignant stenosis | 83% success (lower for pancreatic tumor > 2 cm) | 12  | 2 yr      |
| 2005 | Yamaguchi et al[43] | 103 | R/S    | Cytology has better diagnostic value when collected by POP vs catheter Better for MD type vs SB type | Cytology in 32 with POP, 71 via catheter | NR  | 18 mo     |
| 2005 | Yasuda et al[44] | 26 | R      | IDUS 100% Sens for lesions > 3 mm, POP Sens 67% No carcinoma in protrusions < 3 mm Biopsy Sens 50% for cancer | IDUS | 0   | NA        |
| 2010 | Miura et al[48] | 21 | R/S    | Protrusions and vascular patterns seen better with NBI as compared to white light | Narrow Band imaging (NBI) Technical success 90% | 0   | 2 yr      |
| 2014 | Arnelo et al[34] | 44 | P/S    | Spyglass Sens 84%, spec 75% Acc for MD type 76% Acc for BD type 78% | Obtained - Brushings in 88% Biopsy in 41% | 17  | 2.3 yr    |
conservatively. There is a risk of ductal wall injury if the high energy produced is directed towards it\(^\text{[26]}\), although none were reported in the evaluated studies. Two studies with more than 25% risk of side effects\(^\text{[9,23]}\) had combined use of ESWL and LL/EHL, likely related to patients having more complex stone disease. In the study by Ito \textit{et al}\(^\text{[23]}\), POP-guided EHL was used as a rescue therapy in patients who failed ESWL.

The overall safety profile is similar as compared to ESWL, which so far has only one reported mortality, along with a few rare complications that include splenic rupture, bowel perforation and liver trauma\(^\text{[18]}\).

Even though there are many published case series evaluating the efficacy of POP-guided therapy for pancreatolithiasis, there is lack of robust randomized prospective data. In addition, most of these studies are from tertiary care centers, and therefore may not be generalizable to the community. PD stone therapy remains challenging, and new prospective data will be needed to better define indications of POP-guided therapy for pancreatic stones. We feel a multidisciplinary consensus meeting between pancreatic endoscopists, pancreatic surgeons and radiologists may help determine the best approach for these patients.

\section*{DISCUSSION}

\textbf{Role of POP in pancreatic ducal neoplasia}

Ohashi \textit{et al}\(^\text{[27]}\) first described mucin-producing tumors of the pancreas (MPTP) in 1982\(^\text{[28]}\). Mucin-producing tumors are comprised of two separate entities: Intraductal papillary mucinous neoplasm (IPMN) and mucinous cystic neoplasm (MCN). IPMN is characterized by papillary proliferation of mucin-producing neoplastic epithelium, which causes cystic dilation of the PD\(^\text{[29]}\). The entity is comprised of a spectrum of epithelial changes ranging from hyperplasia to carcinoma\(^\text{[30]}\). IPMN accounts for up to 7% of clinically-diagnosed pancreatic neoplasms, and up to 50% of incidentally-diagnosed pancreatic cysts\(^\text{[31]}\).

Diagnosis of IPMN has increased in recent decades, mainly due to the widespread use of high-resolution cross-sectional abdominal imaging\(^\text{[32]}\). Since IPMN has malignant potential in 65%-70% of patients\(^\text{[33]}\), the differentiation between benign and malignant tumors is crucial to plan the appropriate therapy, along with timing and extent of surgery if needed.

Various modalities have been employed to assess these lesions. A number of factors, such as main duct diameter, cyst diameter, and the presence or absence of septa and nodules, have been useful in identifying lesions with a higher risk of malignant transformation. However, these features are less prominent in uncharacteristic or early lesions. The multicentric nature of IPMN poses an additional challenge, and may lead to recurrence even after surgical resection with negative margins. Sauvanet \textit{et al}\(^\text{[34]}\) reported the limitation of using frozen sections by the existence of discontinuous ("skip") lesions that range from 6%-19% of IPMN in surgical series, and can lead to reoperation in up to 8% of cases. Direct pancreatoscopy has been shown to be useful in differentiating benign mucin-producing tumors of the pancreas from more dysplastic lesions\(^\text{[35]}\).

\textbf{Role of POP visual impression and POP-guided biopsy}
In 2000, Yamaguchi et al. investigated the efficacy of POP in differentiating between benign and malignant MPTP by comparing findings in 41 patients with surgical pathology, and characterized them according to the shape of the intraductal elevations and the color features on the lesions. They reported a technical success rate of 73.2%, where failure of examination was associated with branched ductal-type lesions. They classified elevated lesions as sessile, semi-pedunculated, villous and vegetative, and color markings were reported as white or red (spotty/linear). Red color markings were noted only over semi-pedunculated or villous-type lesions. The correlation of POP findings with surgical pathology indicated that villous and vegetative tumors were observed only in patients with severely atypical adenoma and adenocarcinoma. Red color markings were also characteristic of this group, with a sensitivity of 87.5% compared with 16.7% for the group, including hyperplasia and mild/moderately atypical adenoma. In this series, 23% of the patients underwent segmental pancreatic resection with favorable outcomes. Panreatoscopy also helped identify synchronous lesions at different sites, which were missed by other modalities in three patients, helping to determine the location of surgical resection.

Similar conclusions were noted in a retrospective study of 60 patients who underwent POP (IDUS performed in 40) by Hara et al. They found protruding lesions by POP in 67% of the patients, with better yield in main ductal-type lesions as compared to branching ductal-types. A fish egg appearance with vascular patterning and villous and vegetative lesions were significantly more likely to be malignant as compared to granular appearance or fish eggs without vascular markings.

Aurino et al. prospectively studied the utility of POP in evaluating IPMN in 44 patients with a technical success rate of 93%. They reported additional diagnostic information provided by POP-affected clinical decision-making in 76% of the patient cohort. With operated cases as a reference, the sensitivity of POP was 84% and specificity was 75% in identifying malignant lesions. A classic fish eye papilla was noted in only 35% of the patients with a final diagnosis of MD-IPMN. POP-guided biopsy was diagnostic in 13 of the 17 patients, with adequate tissue acquisition in four. Nagayoshi et al. evaluated 17 patients with radiological diagnosis of IPMN. They used the Spyglass® optical probe inserted into a regular ERCP catheter to inspect lesions in patients with non-dilated MPD or severe angulation, with success in 4/5 patients. Ten patients with protruding lesions were identified, but biopsies could only be obtained in seven due to insufficient angulation of the probe. Targeted biopsies had a sensitivity of 25% and a specificity of 100%. Yasuda et al. reported that targeted biopsies had 50% sensitivity and 100% specificity for detecting malignant IPMN in 11 patients. Targeted biopsies may be more challenging in pancreatoscopy as compared to cholangioscopy due to smaller MPD diameter, more tortuous course and the inability to adequately visualize side branch lesions. The diagnostic accuracy could also be affected by the quality of images obtained.

Panreatoscopy findings in pancreatic cancer may include findings similar to the above, along with erythema, friability, erosions, infiltrative strictures (with near occlusions of the lumen) with irregular margins, or signs of extrinsic compression with normal mucosa. In a series by Kodama et al., 5/8 cases of pancreatic cancer were seen adequately, and all had stenosis with a ductal cut-off of MPD.

Parbhoo et al. studied the impact of POP in 16 patients who had EUS suggestive of IPMN, but definitive diagnosis could not be achieved. They achieved 100% success in obtaining biopsies with a diagnostic accuracy of 75%. Four patients in this cohort had negative biopsies, but strong visual impression led the authors to recommend surgery, with a postoperative diagnosis of IPMN.

El Hajj et al. investigated the role of POP in 79 patients with suspected pancreatic ductal neoplasia, with a technical success of 97%. In the subset of patients with confirmed neoplasia (n = 33), POP-guided tissue sampling with the index procedure could confirm diagnosis in 88%. The sensitivity, specificity and accuracy of POP was 87%, 86%, 87%, respectively, whereas it was 91%, 95% and 94%, respectively, for POP plus targeted tissue sampling. The diagnostic yield reported here may be higher due to the more extensive methods employed - a minimum of three passes with either POP-directed direct biopsy, POP-assisted fluoroscopic-guided biopsy or POP-guided brushings; a combination of the above was employed in eight patients.

POP-directed tissue acquisition has been shown to be very useful in distinguishing benign from malignant PD strictures. Jung et al. prospectively evaluated 18 patients who had indeterminate ductal abnormalities using POP with brush cytology and biopsy (EUS used in three patients only). They confirmed neoplasia in seven and chronic pancreatitis in eight. Macroscopic features of strictures in chronic pancreatitis include white-gray smooth narrowing without superficial vessels. These visual impressions may be critical in distinguishing various etiologies of unexplained pancreatic ductal abnormalities (Table 3). Other findings may include turbid pancreatic juice, protein plugs, indistinct vascular markings, erythema or rough
surfaces. Similar findings were noted by Yamao et al, where benign stenotic lesions in the PD demonstrated smooth mucosa without protrusions, friability or tumor vessels.

Parbhoo et al were successful in dilating 100% strictures in five patients in their study, and were able to obtain targeted biopsies in 80%. Dorsal ductal pancreatoscopy (DDP) via minor papilla can be considered in patients with true or pseudo-divisum presenting with indeterminate strictures, which may be inaccessible via major papilla. Brauer et al attempted DDP in five patients, with technical success of 80%. One failure reported was the inability to obtain biopsies due to acute angulation. These studies suggest the possible role of POP in patients with indeterminate PD strictures.

**POP with cytology**

Uehara et al reported the early diagnosis of pancreatic carcinoma in situ (CIS) in their study of 72 patients using POP with cytology. Of these, 11 patients had presented with minimal symptoms and abnormal imaging, showing dilated PD without any localizing signs seen by other modalities such as EUS/ERP/CT. A combination of POP with pancreatoscopic cytology was useful in diagnosing and locating CIS, with 100% recurrence-free post-operative survival up to a median of 34 mo. Cytology with POP assistance had a better diagnostic yield compared to catheter-assisted collection (100% vs 60%). Hara et al assessed the value of pancreatic juice cytology in 36 out of 60 patients, with low sensitivity of 13% and accuracy of 44% in identifying malignant lesions. K-Ras point mutations were noted in 31 out of 36 patients with high conversion regardless of histologic grade, which manifests as low specificity. Similar results were elicited from a retrospective study of 103 patients by Yamaguchi, who found a suboptimal impact of pancreatic juice cytology in differentiating between benign and malignant IPMN. The sensitivity was higher for main PD tumors as compared to branch type (57.9% vs 47.4%) with better results when the pancreatic juice was collected by POP as compared to catheter. In this study, there was a small additional benefit of cytology, even when no high-risk lesions were seen on POP, as 4/7 patients with no malignant stigmata on POP exams had positive cytology. Nagayoshi et al also compared regular pancreatic cytology with irrigation cytology, with reported sensitivity and specificity of 67% and 100%, respectively.

The exact cytological discrimination between benign and malignant lesions is difficult, and results from different studies are variable due to diverse reasons that include observational bias and location of tumors. For this reason, the use of pancreatic juice cytology remains controversial, although supplementary benefits with other modalities can be appreciated. EUS-FNA has the advantage of sampling mural nodules and a superior ability to assess branch-type lesions, which is clearly advantageous in certain settings.

**Intraoperative POP**

The specific utility of POP to guide surgical therapy in patients with MPT has been studied prospectively by Kaneko et al in 24 patients. Using surgical pathology as the standard, they reported that the sensitivity, specificity and overall accuracy of intraoperative pancreatoscopies were 100% as compared to 43.8%, 100%, and 60.9% for endoscopic retrograde pancreatoscopy and, 47%, 100%, and 62.5% for endoscopic ultrasonography, respectively. Ten patients were noted to have intraductal MPT that were missed by ERCP and EUS. Five out of these ten patients had multicentric lesions, with three requiring an extension of the planned surgical margin. The overall accuracy to identify lesions was 100% for intraoperative POP vs 60.9% for ERCP and 62.5% for EUS. Similar findings were demonstrated by Navez et al from a retrospective review of 21 patients with suspected IPMN who underwent intraoperative POP, revealing eight occult lesions. Five of these eight patients underwent modified surgery, with 90.5% disease-free survival at a mean of 93 mo. Tyberg et al outlined the role of POP in guiding surgical therapy for lesions in the PD. Out of 13 patients who underwent POP, the initial surgical plan was altered in eight (62%), with an overall correlation of 88% between pancreatoscopy and final surgical histology.

This confirms that intraoperative pancreatoscopy is safe and effective in evaluating main ductal IPMN, with the specific advantage of diagnosing multicentric lesions. These may be missed on ERCP or EUS, thus highlighting its complimentary nature to these modalities. Preoperative thorough direct examination of the PD may be limited due to the acute angle noted at the junction of the duct of Wirsung and Santorini, and intraoperative POP helps in overcoming this problem.

**IDUS with POP**

Mukai et al evaluated mucin-producing tumors in 25 patients with POP and IDUS. They concluded that papillary tumor height of more than 3 mm implied more
Table 3  Per oral pancreatoscopy visual findings for pancreatic ductal abnormalities

|                      | IPMN                                          | Adenocarcinoma                                | Chronic pancreatitis                        |
|----------------------|-----------------------------------------------|-----------------------------------------------|---------------------------------------------|
| Uehara et al[42]     | Papillary projections, irregular/nodular mucoa | Tumor vessels; Erosions                       | Smooth narrowing; White/gray mucoa; Blurred blood vessels |
| Jung et al[39]       | Papillary projections; Villous protrusions    | Protrusions; Tumor vessels; Friability, erosions | Protein plugs/stones; Edema, erythema, scar |
| Tajiri et al[44]     | Papillary projections; Salmon eggs            |                                               |                                             |
| Yamaguchi et al[47]  | (1) Hyperplasia/Mild atypia; sessile or semi pedunculated with white color markings; (2) Severe atypia/adenocarcinoma semi pedunculated or villous or vegetative with red color markings |                                               |                                             |
| Kodama et al[29]     | Papillary projections; Nodular/villous/White/spotty/red | Duct cut off; Friability/erosions             | Stones, proteins plugs; Scar, erythema; Blurred vessels |
| Hara et al[33]       | CIS/Invasive carcinoma; salmon eggs with vascular pattern; Villous/vegetative protrusions |                                               |                                             |
| Yamao et al[41]      | Coarse, granular papillary projections with mucus | Papillary projection with tumor vessels; Protrusion/friability | Coarse erythema                             |
| Miura et al[48]      | (1) High risk - villous/vegetative with tumor vessel; (2) Low risk - sessile / semi pedunculated |                                               |                                             |
| El Hajj et al[38]    | (1) Invasive - villous/vegetative papillary projections; (2) Noninvasive - granular projections with erythema | Protrusion with tumor vessel; Ulceration; Infiltrative stricture | Coarse, blurred vessels, scarring, erythema and edema |

advanced dysplastic lesions. The sensitivity of detecting lesions more than 3 mm was 29% for US, 21% for CT, 86% for EUS, 100% for IDUS and 83% for POP. Adequate examination of papillary lesions using POP was technically successful in 60% of the total patients. The sensitivity for detecting protrusions more than 3 mm was 100% for IDUS and 67% for POP in a study of 26 patients by Yasuda et al[36]. In this study, out of the six patients with adenocarcinoma, none had protrusions less than 3 mm on the resected pathological specimen. The same study demonstrated the suboptimal diagnostic capability of cross-sectional imaging for protruding lesions, with 16% for CT scan and 20% for MRI.

In the study performed by Hara et al[33], 88% of the lesions with villous projections more than 4 mm on IDUS were malignant. The diagnostic accuracy of POP alone in differentiating benign/malignant was 88% and 67% for main duct and branch duct, respectively, as compared to IDUS with an accuracy of 63% and 88%. Their study confirmed that adding IDUS to POP improves the evaluation of branch ductal-type lesions. The combined accuracy rate for different modalities such as CT, EUS, POP and IDUS was 55%, 65%, 75% and 78%, respectively, with the highest rate of 88% for POP plus IDUS combined. Surgical pathology served as the gold standard in this study. Most malignant tumors had POP visual morphology types III, IV or V (as per the Yamaguchi classification). The benefit of using this combined modality was evident in the fact that reduced operations were performed in 33 out of 60 patients, with only one positive resection margin that was due to infiltrative parenchymal changes. Critically, management based on these criteria culminated in an extraordinary 95% 3-year cumulative survival rate and a 93% disease-free survival rate.

IDUS is particularly useful to visualize branches distant from the probe and the parenchyma, and plays a crucial complementary role to POP. IDUS also has better efficacy for early lesions like CIS, due to higher resolution and probe location as compared to EUS.

**POP with image-enhancing technology**

Miura et al[48] assessed POP-guided NBI (narrow band imaging) in 21 patients with IPMN. They used a small diameter videoscope CHF-BP260 (Olympus medical systems) with an outer diameter of 2.9 mm, and achieved technical success of 90%. Vascular patterns and protrusions were detected more clearly in NBI images as compared to examination under white light. Similar findings were observed by Ito et al[49]. NBI identified skip tumor lesions in the tail of the pancreas, which were not
detected by conventional POP.

Other adjuvant imaging modalities utilizing POP are also being evaluated. Meining et al. prospectively studied the role of probe-based confocal laser endomicroscopy (pCLE) in assessing indeterminate pancreatobiliary strictures. The accuracy of the combination of ERCP and pCLE was significantly higher compared with ERCP, with tissue acquisition (90% vs 73%, \( P = 0.001 \)) having higher specificity in the exam when the probe was delivered via cholangiopancreatoscopy as compared to a standard catheter.

The risk of pancreatitis in these series, which ranged between 0%-35%, seemed to be higher in patients without dilated MPD, and also depended on the level of experience of the operator. Arnello et al. recorded one fatal case of post-POP pancreatitis. They postulated that reducing the flow rate could help in minimizing the risk of it, however this needs further evaluation.

The role of POP for intraductal pancreatic neoplasia has evolved over time with the availability of longitudinal data and rapid technological improvements. Prospective multicenter studies of POP with selected adjunct modalities may eventually address the true value of POP in the evaluation and management of pancreatic ductal neoplasia. POP will continue to serve a crucial complementary role for such patients, in addition to cross-sectional imaging and EUS. Appropriate application will likely be restricted to high volume tertiary care centers where multidisciplinary approaches will guide the treatment of such rare diseases.

In conclusion, this review illustrates the crucial role POP may play in the management of pancreatic disease by providing direct macroscopic assessment, targeted tissue acquisition and the opportunity for guided endotherapy. The application of this technology has been largely limited to high volume expert centers due to the procedural complexity, the morbidity of the conditions being treated, technical challenges, and cost. There is significant heterogeneity in the available data, with variable patient follow-up, lack of control arms and retrospective designs. Innovations like larger fields-of-view, higher image resolution, integrated image enhancements, and larger working channels may augment the capability of the procedure. Well-designed and powered prospective trials would refine the role of POP in the management of pancreatic disease.

**ARTICLE HIGHLIGHTS**

**Research background**
Pancreatoscopy has been used for over 30 years in the diagnosis and management of pancreatic diseases; however, its use remains limited to large volume referral centers. Data regarding its efficacy and safety are limited and have been available mainly from single or multicenter retrospective case series. Well-designed large randomized controlled trials are lacking and may be difficult to conduct due to a heterogeneous patient population. With this study, we have compiled a systematic review of available data, thus highlighting the valuable role of per oral pancreatoscopy in managing pancreatic diseases.

**Research motivation**
The main aim of our study was to systematically analyze available data regarding the therapeutic potential of pancreatoscopy in managing difficult pancreatic stone disease and pancreatic ductal neoplasia. It appears to be safe, with rare serious side effects, and serves a crucial complementary role to other pancreatic endoscopic modalities.

**Research objectives**
The main objective of the study was to gather data related to the safety and efficacy of pancreatoscopy. We wanted to identify the success rates and factors associated with treatment failure for pancreatoscopic management of stone disease. We also aimed to analyze the pancreatoscopic visual findings associated with pancreatic ductal neoplasia, and how it can be differentiated from benign pancreatic duct strictures. The diagnostic potential of adjunctive techniques like POP guided/assisted biopsy, pancreatic juice cytology and intraductal ultrasound (IDUS) was evaluated separately.

**Research methods**
This is a systematic review of available studies published in English. We performed an extensive medical database search to identify relevant publications. Case reports and stand-alone abstract publications were excluded from the final analysis. Data regarding safety and efficacy were extracted and presented. Studies addressing the role of POP in management of pancreatic ductal neoplasia with adjunctive modalities were examined separately.

**Research results**
Pancreatocopy is overall safe, with rare reported serious side effects. The success rate ranges between 37.5%-100% for treating pancreatic stone disease. Factors associated with failure include the presence of multiple stones, stones in side branches causing failure of visualization, and the
presence of stricture. Visual impression during pancreatoscopy provides important information in patients with indeterminate pancreatic ductal strictures. The key finding in our study was the association between villous projections with red color markings, which is associated with high-risk advanced neoplastic lesions across multiple studies. Smooth narrowing with the presence of coarse mucosa, protein plugs or stones, and blurred mucosal vessels are seen in patients with strictures caused by chronic pancreatitis. POP-assisted tissue acquisition, as well as adjunctive techniques such as cytology, narrow band imaging and IDUS, greatly enhance the diagnostic potential and help in treatment planning.

Research conclusions
Pancreatoscopy is an overall safe and effective diagnostic and therapeutic modality. It serves as an important bridge for patients with pancreatolithiasis who fail conventional Endoscopic retrograde cholangiopancreatography or ESWL. Patients with multiple stones in body/tail, or those with pancreatic strictures, may have risk of decreased success with POP-guided therapy; the recognition of these factors may help in treatment planning. POP visual impression provides a plethora of information regarding etiology in patients with indeterminate pancreatic ductal strictures, although there is an overlap between benign and malignant conditions. POP-guided tissue acquisition has been shown to greatly enhance the diagnostic yield, but limitations persist due to technical challenges. The addition of newer imaging technology may further augment the potential of POP in managing such scenarios.

Research perspectives
Appropriate future action may involve multicenter prospective studies to identify patient characteristics, which may make them amenable to POP-guided endotherapy for pancreatic diseases. Continued improvement in imaging technology, such as narrow band imaging and probe-based confocal laser endomicroscopy, need to be evaluated extensively before mainstream use is implemented.

REFERENCES

1. Nguyen NQ, BinmoellerKF, Shah JN. Cholangioscopy and pancreatoscopy (with videos). Gastrointest Endosc 2009; 70:1200-1210 [PMID: 19863954 DOI: 10.1016/j.gie.2009.07.010]
2. McGuire DE, Venu RP, BrownRD, Etzkorn KP, Glass WR, Abu-Hammour A. Brush cytology for pancreatic carcinoma: an analysis of factors influencing results. Gastrointest Endosc 1996; 44:300-304 [PMID: 8935230 DOI: 10.1016/S0016-5107(96)70168-2]
3. Kurzawinski TR, Deery A, Dooley JS, Dick R, Holbbs KE, Davidson BR. A prospective study of biliary cytology in 100 patients with bile duct strictures. Hepatology 1993; 18:1399-1403 [PMID: 8244264 DOI: 10.1016/0270-9199(93)90236-K]
4. Stewart CJ, Mills PR, Carter R, O'Donohue J, Fullarton G, Imrie CW, Murray WR. Brush cytology in the assessment of pancreatico-biliary strictures: a review of 406 cases. J Clin Pathol 2001; 54:449-455 [PMID: 11376018 DOI: 10.1136%2Fjcp.54.6.449]
5. Jailwala J, Fogel EL, Sherman S, Gottlieb K, Flueckiger J, Buckstop LG, Lehman GA. Triplet-tissue sampling at ERCP in malignant biliary obstruction. Gastrointest Endosc 2000; 51:383-390 [PMID: 10744806 DOI: 10.1016/S0016-5107(00)70435-4]
6. Kawai K, Nakajima M, Akasaka Y, Shimamoto K, Murakami K. [A new endoscopic method: the peroral choledocho-pancreatoscopy (author's transl)]. Leber Magen Darm 1976; 6: 121-124 [PMID: 699632]
7. Ammann RW, Munch R, Otto R, Buehler H, Freiburghaus AU, Siegenthaler W. Evolution and regression of pancreatic calcification in chronic pancreatitis. A prospective long-term study of 107 patients. Gastroenterology 1988; 95:1018-1028 [PMID: 3410125 DOI: 10.1016/0016-5085(88)90178-3]
8. Khalid A, Whitcomb DC. Conservative treatment of chronic pancreatitis. Eur J Gastroenterol Hepatol 2002; 14: 943-949 [PMID: 12352213 DOI: 10.1080/0959667021000000040]
9. Attwell AR, Patel S, Khalaf EH, Rajmaen IL, Yen R, Shah RJ. ERCP with per-oral pancreatoscopy-guided laser lithotripsy for calcific chronic pancreatitis: a multicenter U.S. experience. Gastrointest Endosc 2015; 82:311-318 [PMID: 25841555 DOI: 10.1016/j.gie.2015.01.020]
10. Thomas M, Howell DA, Carr-Locke DJ, Mel Wilcox C, Chak A, Rajman J, Watkins JL, Schmalz MJ, Geenen JE, Catalan MF. Mechanical lithotripsy of pancreatic and biliary stones: complications and available treatment options collected from expert centers. Am J Gastroenterol 2007; 102:1896-1902 [PMID: 17573790 DOI: 10.1111/j.1572-0241.2007.01350.x]
11. Tandan M, ReddyDN, Talukdar R, Vinod K, Santosh D, Lakhtakia S, Gupta R, Ramchandani MJ, Banerjee R, Saha P, Baradar J, Rao GV. Long-term clinical outcomes of extracorporeal shockwave lithotripsy in painful chronic calcific pancreatitis. Gastrointest Endosc 2013; 78:726-733 [PMID: 23891446 DOI: 10.1016/j.gie.2013.05.012]
12. Alatalwi A, Leblanc S, Vienne A, Pratico CA, Gaudric M, Duchmann JC, Boyer J, Mangialavori L, Chassaide S, Peat P. Pancreatoscopcy-guided intracorporeal laser lithotripsy for difficult intrahepatic duct stones: a case series with prospective follow-up (with video). Gastrointest Endosc 2013; 78:179-183 [PMID: 23540440 DOI: 10.1016/j.gie.2013.02.015]
13. Ohyama H, Mikata R, Ishihara T, Tsuyuguchi T, Sakai Y, Saito J, Hasegawa Y, Yasui S, Ishii K, Itoh S, Nishikawa T, Watanabe Y, Yokosuka O. Efficacy of stone density on noncontrast computed tomography in predicting the outcome of extracorporeal shock wave lithotripsy for patients with pancreatic stones. Pancreas 2013; 44:422-428 [PMID: 25438070 DOI: 10.1097/MPA.00000000000000277]
14. Howell DA, Dy RM, Hanson BL, Nezhad SF, Broaddus SB. Endoscopic treatment of pancreatic duct stones using a 10F pancreatoscope and electrohydraulic lithotripsy. Gastrointest Endosc 1999; 50:829-833 [PMID: 10570346 DOI: 10.1016/S0016-5107(99)00765-9]
15. Shah RJ. Innovations in Intraductal Endoscopy: Cholangioscopy and Pancreatoscopy. Gastrointest Endosc Clin N Am 2015; 25:779-792 [PMID: 26431604 DOI: 10.1016/j.giec.2015.06.012]
16. Sievert CE, Silvis SE. Evaluation of electrohydraulic lithotripsy as a means of gallstone fragmentation in a canine model. Gastrointest Endosc 1987; 33:233-235 [PMID: 3596188 DOI: 10.1016/0016-5107(87)90248-3]
Kaura T et al. Pancreatoscopy for managing pancreatic disease.

17 Hochberger J, Gruber E, Wirtz P, Dürr U, Kolb A, Zanger U, Hahn EG, Eill C. Lithotripsy of gallstones by means of a quality-switched giant-pulse neodymium:yttrium-aluminum-garnet laser. Basic in vitro studies using a highly flexible fiber system. Gastroenterology 1991; 101:1391-1398 [PMID: 1682203 DOI: 10.1016/s0016-5085(91)90093-9]

18 Tandan M, Talukdar R, Reddy DN. Management of Pancreatic Calculi: An Update. Gut Liver 2016; 10:873-880 [PMID: 27784444 DOI: 10.5009/gnl1555]

19 Attwell AR, Brauer BC, Chen YK, Yen RD, Fukami N, Shah RJ. Endoscopic retrograde cholangiopancreatography with per oral pancreatoscopy for calcific chronic pancreatitis using endoscope and catheter-based pancreatoscopes: a 10-year single-center experience. Pancreas 2014; 43:268-274 [PMID: 24515807 DOI: 10.1097/MPA.0b013e3182965d81]

20 Brauer BC, Chen YK, Ringold DA, Shah RJ. Peroral pancreatoscopy via the minor papilla for diagnosis and therapy of pancreatic diseases. Gastrointest Endosc 2013; 78:545-549 [PMID: 23799144 DOI: 10.1016/j.gie.2013.05.003]

21 Maydeo A, Kwek BE, Bhandari S, Bapat M, Dhir V. Single-operator cholangioscopy-guided laser lithotripsy in patients with difficult biliary and pancreatic ductal stones (with videos). Gastroendosc 2011; 74:1308-1314 [PMID: 22136776 DOI: 10.1016/j.gie.2011.08.047]

22 Parbhoo SK, Siddiqui AA, Murphy M, Noor A, Taylor LJ, Mills A, Adler DG. Efficacy, Safety, and Outcomes of Endoscopic Retrograde Cholangiopancreatography With Per-Oral Pancreatoscopy: A Multicenter Experience. J Clin Gastroenterol 2017; 51: e101-e105 [PMID: 28059943 DOI: 10.1097/MCG.0000000000001976]

23 Ito K, Igarashi Y, Okano N, Mimura T, Kishimoto Y, Hara S, Takuma K. Efficacy of combined endoscopic lithotomy and extracorporeal shock wave lithotripsy, and additional electrohydraulic lithotripsy using the SpyGlass direct visualization system or X-ray guided EHL as needed, for pancreatic lithiasis. Biomed Res Int 2014; 2014:732781 [PMID: 24999474 DOI: 10.1155/2014/732781]

24 Shin SK, Cho JH, Kim YS. Peroral pancreatoscopy with electrohydraulic lithotripsy for pancreatic duct stone after placement of fully covered self-expandable metal stent. Endoscopy 2015; 47 Suppl 1 UCTN: E234-E235 [PMID: 26069979 DOI: 10.1055/s-0035-151858]

25 Rios CA, Adams DB. Does intraoperative electrohydraulic lithotripsy improve outcome in the surgical management of chronic pancreatitis? Am Surg 2001; 67:533-537; discussion 537-538 [PMID: 11409800 DOI: 10.1097/0016-5085(2001)067<0533:DIIEHL>2.0.CO;2]

26 Teichman JM, Rao RD, Rogenes VJ, Harris JM. Ureteroscopic management of ureteral calculi: electrohydraulic versus holmium:YAG lithotripsy. J Urol 1997; 158:1357-1361 [PMID: 902119 DOI: 10.1016/s0022-5347(01)64214-9]

27 Yamaguchi T, Hara T, Tsuuyuguuchi T, Ishihara T, Tsuayuichi S, Saitou M, Saisho H. Peroral pancreatoscopy in the diagnosis of mucin-producing tumors of the pancreas. Gastrointest Endosc 2000; 52:67-73 [PMID: 10882965 DOI: 10.1016/s0016-5085(00)80207-2]

28 Cooper CL, O'Toole SA, Kench JG. Classification, morphology and molecular pathology of premalignant lesions of the pancreas. Pathology 2013; 45:286-304 [PMID: 23442735 DOI: 10.1097/PAT.0b013e328352205]

29 Lafermina J, Katabi N, Klimstra D, Correa-Gallcco G, Guajoux S, Kingham TP, Dematteo RP, Fong Y, D'Angelica ML, Jamargin WR, Do RK, Brennan MF, Allen PJ. Malignant progression in IPMN: a cohort analysis of patients initially selected for resection or observation. Ann Surg Oncol 2013; 20:440-447

30 Andrejevic-Blant S, Kosmahl M, Sipos B, Klöppel G. Pancreatic intraductal papillary-mucinous neoplasms: a new and evolving entity. Virchows Arch 2007; 451:863-869 [PMID: 17899180 DOI: 10.1007/s00428-007-0512-6]

31 Del chiaro M, Verbeke C, Salvia R, Klöppel G, Wernser J, McKay C, Friess H, Manfredi R, Van Cutsem E, Löhr M, Segersvärd R. European Study Group on Cystic Tumours of the Pancreas. European experts consensus statement on cystic tumours of the pancreas. Dig Liver Dis 2013; 45:703-711 [PMID: 23415709 DOI: 10.1016/j.dld.2013.01.010]

32 Sauvanet A, Couvelard A, Belghiti J. Role of frozen section assessment for intrahepatic and mucinous tumor of the pancreas. World J Gastroenterol 2010; 2:352-358 [PMID: 21160845 DOI: 10.4240/wjg.v2.i2.352]

33 Hara T, Yamaguchi T, Ishihara T, Tsuyuguchi T, Kondo F, Kato K, Asano T, Saisho H. Diagnosis and patient management of intraductal papillary-mucinous tumor of the pancreas. World J Gastroenterol 2010; 67:352-358 [PMID: 1682203 DOI: 10.1097/MPS.0b013e3181e32702]

34 Arneulo et al. Pancreatoscopy and intraductal papillary-mucinous neoplasms: a new and evolving entity. Virchows Arch 2007; 451:863-869 [PMID: 17899180 DOI: 10.1007/s00428-007-0512-6]

35 Nagayoshi Y, Aso T, Ohotsuka T, Kono H, Ideno N, Igarashi H, Takahata S, Oda Y, Ito T, Tanaka M. Peroral pancreatoscopy using the SpyGlass system for the assessment of intraductal papillary mucinous neoplasm of the pancreas. J Hepatobiliary Pancreat Sci 2014; 21:410-417 [PMID: 24123930 DOI: 10.1002/jbhp.41]

36 Yasuda K, Sakata M, Ueda M, Uno K, Nakajima M. The use of pancreatoscopy in the diagnosis of intraductal papillary mucinous tumor of the pancreas. Clin Gastroenterol Hepatol 2005; 3:553-557 [PMID: 16012998 DOI: 10.1016/s1542-3565(05)00263-6]

37 Kodama T, Koshitani T, Sato H, Imamura Y, Kato K, Abe M, Wakabayashi N, Tatsumi Y, Horii Y, Yamane Y, Yamagishi T. Endoscopic diagnosis of the pancreas for pancreatic diseases. Am J Gastroenterol 2002; 97:617-622 [PMID: 11922556 DOI: 10.1111/j.1572-0241.2002.05539.x]

38 El Hajj II, Brauer BC, Wani S, Fukami N, Attwell AR, Shah RJ. Role of per-oral pancreatoscopy in the evaluation of suspected pancreatic duct neoplasia: a 13-year U.S. single-center experience. Gastroenterology 2017; 85:737-745 [PMID: 27473181 DOI: 10.1016/j.gastro.2016.07.040]

39 Jung M, Zipf A, Schönbrod D, Herrmann G, Caspary WF. Is pancreatoscopy of any benefit in clarifying the diagnosis of pancreatic duct lesions? Endoscopy 1998; 30:271-280 [PMID: 9618767 DOI: 10.1055/s-2000-1001254]

40 Kodama T, Imamura Y, Sato H, Koshitani T, Abe M, Kato K, Uehira H, Horii Y, Yamane Y, Kashima K, Yamagishi H. Feasibility study using a new small electronic pancreatoscope: description of findings in chronic pancreatitis. Endoscopy 2003; 35:305-310 [PMID: 12662477 DOI: 10.1055/s-2003-81348]

41 Yamao K, Ohashi K, Nakamura T, Suzuki T, Sawai K, Hara K, Fukutomi A, Baba T, Okubo K, Tanaka
Kaura T et al. Pancreatoscropy for managing pancreatic disease

K, Moriyama I, Fukuda K, Matsumoto K, Shimizu Y. Efficacy of peroral pancreatoscopy in the diagnosis of pancreatic diseases. Gastrointest Endosc 2003; 57: 205-209 [PMID: 12556785 DOI: 10.1016/j.gie.2003.03.022]

42 Uehara H, Nakaizumi A, Tatsuta M, Ishi H, Kitamura T, Ohigashi H, Hishikawa O, Takenaka A. Diagnosis of carcinoma in situ of the pancreas by peroral pancreatoscopy and pancreatoscopic cytology. Cancer 1997; 79: 454-461 [PMID: 9028354 DOI: 10.1002/(SICI)1097-0142(19970201)79:3<454::AID-CNCR3>3.0.CO;2-I]

43 Yamaguchi T, Shirai Y, Ishihara T, Sudo K, Nakagawa A, Ito H, Miyazaki M, Normura F, Saisho H. Pancreatic juice cytology in the diagnosis of intraductal papillary mucinous neoplasm of the pancreas: significance of sampling by peroral pancreatoscopy. Cancer 2005; 104: 2830-2836 [PMID: 16287152 DOI: 10.1002/cncr.21565]

44 Kaneko T, Nakao A, Nomoto S, Furukawa T, Hirooka Y, Nakashima N, Nagasaka T. Intraoperative pancreatoscopy with the ultrathin pancreatoscope for mucin-producing tumors of the pancreas. Arch Surg 1998; 133: 263-267 [PMID: 9517737 DOI: 10.1001/archsurg.133.3.263]

45 Navez J, Hubert C, Gigot JF, Borbath I, Amet L, Sempoux C, Lannoy V, Deprez P, Jabbour N. Impact of Intraoperative Pancreatoscropy with Intraductal Biopsies on Surgical Management of Intraductal Papillary Mucinous Neoplasm of the Pancreas. J Am Coll Surg 2015; 221: 982-987 [PMID: 26304184 DOI: 10.1016/j.jamcollsurg.2015.07.451]

46 Tyberg A, Rajimain I, Siddiqui A, Armelo U, Adler DG, Xu MM, Nassani N, Sejal DV, Kedia P, Nah Lee Y, Gress FG, Ho S, Gaidhane M, Digital Pancreaticeocholangioscopy for Mapping of Pancreaticiliary Neoplasia: Can We Alter the Surgical Resection Margin? J Clin Gastroenterol 2019; 53: 71-75 [PMID: 29517713 DOI: 10.1097/MCG.0000000000001008]

47 Mukai H, Yasuda K, Nakajima M. Differential diagnosis of mucin-producing tumors of the pancreas by intraductal ultrasonography and peroral pancreatoscopy. Endoscopy 1998; 30 Suppl 1: A99-102 [PMID: 9765097 DOI: 10.1055/s-2007-100146]

48 Miura T, Igarashi Y, Okano N, Kuki K, Okubo Y. Endoscopic diagnosis of intraductal papillary-mucinous neoplasm of the pancreas by means of peroral pancreatoscopy using a small-diameter videoscope and narrow-band imaging. Dig Endosc 2010; 22: 119-123 [PMID: 20447205 DOI: 10.1111/j.1443-1661.2010.00926.x]

49 Itoi T, Sofuni A, Tokawa F, Kurihara T, Tsuchiya T, Ishii K, Tsuji S, Ikeuchi N, Ariyasa Y, Moriyasu F. Initial experience of peroral pancreatoscopy combined with narrow-band imaging in the diagnosis of intraductal papillary mucinous neoplasms of the pancreas (with videos). Gastrointest Endosc 2007; 66: 793-797 [PMID: 17909025 DOI: 10.1016/j.gie.2007.03.109]

50 Meining A, Chen YK, Pleskov D, Stevens P, Shah RJ, Chuttani R, Michalek J, Silivka A. Direct visualization of indeterminate pancreaticobiliary strictures with probe-based confocal laser endomicroscopy: a multicenter experience. Gastrointest Endosc 2011; 74: 961-986 [PMID: 21802675 DOI: 10.1016/j.gie.2011.05.009]

51 Fishman DS, Tarnasky PR, Patel SN, Rajmain I. Management of pancreaticobiliary disease using a new intra-ductal endoscope: the Texas experience. World J Gastroenterol 2009; 15: 1353-1358 [PMID: 19294705 DOI: 10.3748/wjg.15.1353]

52 Navaneethan U, Hasan MK, Konmaraju K, Zha X, Hebert-Magee S, Hawes RH, Vargo JJ, Varadarajulu S, Parsi MA. Digital, single-operator cholangioscopy for the diagnosis and management of pancreaticobiliary disorders: a multicenter clinical experience (with video). Gastrointest Endosc 2016; 84: 649-655 [PMID: 26995690 DOI: 10.1016/j.gie.2016.03.789]

53 Bekkali NL, Murray S, Johnson GJ, Bandula S, Amin Z, Chapman MH, Pereira SP, Webster GJ. Pancreatoscopy-Directed Electrohydraulic Lithotripsy for Pancreatic Ductal Stones in Painful Chronic Pancreatitis Using SpyGlass. Pancreas 2017; 46: 528-530 [PMID: 28196019 DOI: 10.1097/MPA.0000000000001790]

54 Tajiri H, Kobayashi M, Ohtsu A, Ryu M, Yoshida S. Peroral pancreatoscopy for the diagnosis of pancreatic diseases. Pancreas 1998; 16: 408-412 [PMID: 9548687 DOI: 10.1097/00006676-199804000-00032]

P- Reviewer: Sugimoto M, Fujino Y
S- Editor: Dou Y
L- Editor: Filipodia
E- Editor: Tan WW
