Expert consensus on endoscopic papillectomy using a Delphi process

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Background and Aims: Consensus regarding an optimal algorithm for endoscopic treatment of papillary adenomas has not been established. We aimed to assess the existing degree of consensus among international experts and develop further concordance by means of a Delphi process.

Methods: Fifty-two international experts in the field of endoscopic papillectomy were invited to participate. Data were collected between August and December 2019 using an online survey platform. Three rounds were conducted. Consensus was defined as ≥70% agreement.

Results: Sixteen experts (31%) completed the full process, and consensus was achieved on 47 of the final 79 statements (59%). Diagnostic workup should include at least an upper endoscopy using a duodenoscope (100%) and biopsy sampling (94%). There should be selected use of additional abdominal imaging (75%-81%). Patients with (suspected) papillary malignancy or over 1 cm intraductal extension should be referred for surgical resection (76%). To prevent pancreatitis, rectal nonsteroidal anti-inflammatory drugs should be administered before resection (82%) and a pancreatic stent should be placed (100%). A biliary stent is indicated in case of ongoing bleeding from the papillary region (76%) or concerns for a (micro)perforation after resection (88%). Follow-up should be started 3 to 6 months after initial papillectomy and repeated every 6 to 12 months for at least 5 years (75%).

Conclusions: This is the first step in developing an international consensus–based algorithm for endoscopic management of papillary adenomas. Surprisingly, in many areas consensus could not be achieved. These aspects should be the focus of future studies. (Gastrointest Endosc 2021;94:760-73.)

(footnotes appear on last page of article)

The first endoscopic papillectomy (EP) for papillary adenoma (n = 2) was described in 1983, and the first substantial cohort (n = 25) was published 10 years later.[1,2] A number of predominantly retrospective case and cohort studies have been published subsequently.[3-7] Despite the lack of randomized controlled trials and prospective series, EP for papillary adenoma is considered a relatively safe, minimally invasive treatment for lesions without significant intraductal extension or invasive disease.[5] It has proven difficult to generate high-level scientific knowledge on the best treatment algorithm primarily because of low incidence and therefore difficult to conduct large prospective or randomized controlled studies. Subsequently, a consensus for EP practices has not been established. In 2015 the Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy attempted to develop an evidence-based guideline on the role of endoscopy in papillary and duodenal adenomas.[8] However, based on the current literature only limited recommendations regarding the optimal diagnostic workup, treatment, and follow-up protocol could be made. Unsurprisingly, at present there remains a wide variety in daily practice, mostly based on individual preferences.[9,10]

The aim of this study was to assess the level of consensus among international experts and to obtain further consensus by using a Delphi process. The Delphi

method was developed by the Rand Corporation in the 1950s and was originally used in forecasting.[11] Since then, the Delphi method is considered to be a reliable instrument to develop clinical consensus guidelines. This iterative structured process is widely used to achieve expert consensus for subjects where no definitive evidence is available and where expert opinion is important.[12-14] The process consists of a series of questionnaires (usually 3), and after each round the responses are summarized and anonymously redistributed for discussion in the next round(s).[15] Accordingly, the ultimate goal is to conduct a proposal for a more standardized treatment protocol on the performance of EP.

METHODS

Systematic literature search

A systematic search of literature was performed in PubMed and EMBASE databases on December 18, 2020. The search strategy can be found in Supplementary Figure 1 (available online at www.giejournal.org).

Expert panel selection

Researchers were identified through authorship of relevant articles. Senior authors of original articles published in the last 15 years with a cohort of at least 20 patients were selected. Thus, 38 authors were invited. Furthermore, 14 longstanding and internationally recognized experts in the field of EP who did not appear in the search were selected to include broad clinical experience that might not be found in published literature. After the first round, only respondents who performed at least 30 EPs in their career were asked to join the consecutive rounds.

Conduct of surveys

Three rounds were conducted. The first survey was based on systematic literature and personal experience in daily practice of the senior authors (M.J. Bourke and R. P. Voermans). The survey consisted of 54 multiple-choice questions divided over 6 different sections: background of the respondent, diagnostic workup, lesion assessment and staging, technical aspects, adverse events and their management, and follow-up. After each question there was an option to add other answer options or to share general comments on the question. The questions of which the answers reached consensus were transformed into statements and presented again to respondents in the next round. Questions without consensus were extracted, modified based on the comments of the respondents, and proposed again in the consecutive round(s). After each round responses were summarized and anonymously redistributed for discussion in the next round(s) to provide respondents the opportunity to review and possibly change their answers based on group consensus.

Consensus development process

Data were collected between August and December 2019 using an online survey platform. The invited experts were given at least 2 weeks to complete the survey(s), with reminder e-mails sent twice during each completion period. Participants' names and contact details were recorded to acknowledge their participation in the eventual article and to be able to ask them to participate in possible follow-up studies. However, participants were unaware of the names of other participants, and results were anonymized.

Statistical analysis and grading of statements

Respondents were able to show their level of agreement with the proposed statements by scoring on a 5-point Likert-scale (1 = completely disagree, 2 = disagree, 3 = neutral, 4 = agree, 5 = completely agree) and could comment on their reason to agree or disagree.[16] Consensus was defined as at least 70% agreement between the respondents (either (dis)agree or completely (dis)agree). Questions in which participants were asked to rank the answer possibilities were analyzed using median and interquartile range (IQR) in which an IQR $\leq$1 was considered consensus.[17,18] Strength of the consensus statements was based on the level of evidence of the supporting literature according to the definitions of the Oxford Centre for Evidence-Based Medicine.[19]

RESULTS

Systematic review

After removing duplicates, 827 records were identified. Based on title and abstract screening, 627 records were excluded. Only an abstract was available for 92 records, resulting in 108 full-text articles that were screened for eligibility. The inclusion and exclusion process is summarized in Supplementary Figure 1. The relevant results are described and discussed together with the results of the Delphi process below.

Participants

Fifty-two experts were invited. Twenty-eight (53.8% response rate) completed the first round, 17 (32.7% response rate) completed the second round, and 16 joined round 3 (30.7% response rate). Three participants of round 1 were not asked to join consecutive rounds because they had performed fewer than 30 EPs in their career. The 16 final participants included gastroenterologists from 10 different countries and 3 continents (Asia, North America, and Europe). Most participants (15 [94%]) primarily worked in a university hospital setting. All participants performed at least 30 EPs, and 11 (69%) had at least 20 years of experience. A summary of the study process is depicted in Figure 1.

Recommendation statements

In the last round, a final 79 statements were proposed to the participants; the most important consensus statements are summarized in Table 1. Figure 2 depicts a consensus-based flowchart summarizing these statements. All statements that reached consensus are shown in Table 2. A selection of statements that did not reach consensus in the final round is shown in Table 3. The results of all 3 rounds are provided in Supplementary Tables 1-3 (available online at www.giejournal.org).

Diagnostic workup. The standard diagnostic workup of a patient with a papillary lesion should include a gastroduodenoscopy with a side-viewing instrument (100%) and biopsy sampling (94%) before resection. Additional abdominal imaging should only be performed for specific indications (75%-81%). Magnetic resonance imaging (MRI)/magnetic resonance cholangiopancreatography (MRCP) or endoscopic ultrasound (EUS) can be used to rule out intraductal extension and should at least be performed in case of cholestatic laboratory features (81%) and/or lesion size >2 cm (75%) (Table 1). Figure 3 shows intraductal extension on MRI/MRCP and EUS. No consensus was reached that intraductal extension should be ruled out standardly in every patient before resection (53%) (Supplementary Table 2). MRI/MRCP or computed tomography (CT) should be performed in case of significant weight loss and/or endoscopic signs of malignancy. In case of jaundice a CT should be performed as well (Table 1).

The only existing international guideline in EP from 2015 states that endoscopic retrograde cholangiopancreatography (ERCP) should be performed in every patient at the time of resection to assess for evidence of intraductal extension.[8] However, this was shown not to be common practice, with only 25% of respondents considering endoscopic cholangiography as part of the standard diagnostic workup (Supplementary Table 1). Our study does agree with the previous guideline statement that biopsy sampling should be performed in every patient before resection (94%). Nevertheless, the accuracy of biopsy sampling in papillary lesions is questionable; according to pathology studies preresection biopsy sampling accurately diagnosed 70% of papillary malignancies[20-22] compared with at least 80% in the colon.[23] Biopsy sampling is also important when the diagnosis of adenoma is considered in a larger than normal papilla.

Lesion assessment. Because the accuracy of biopsy sampling in papillary lesions is questionable, careful endoscopic assessment is considered most important. However, final pathology may differ from the initial endoscopic diagnosis. Limited data of patients suspected to have a benign adenoma based on endoscopic appearance indicate that final pathology shows another diagnosis (such as normal mucosa, gastric heterotopia, adenomyomatosis, hamartoma, neuroendocrine tumor, or adenocarcinoma) in 10% to 20%.[6,24,25] Furthermore, a recent series of patients who underwent EP showed that in only half of the lesions in which the resection specimen showed adenocarcinoma, malignancy was already suspected based on the endoscopic appearance, further questioning the accuracy of endoscopic assessment.[26]

Advanced imaging techniques such as narrow-band imaging and chromoendoscopy have proven to be a valuable addition to white-light imaging in the diagnosis of colorectal lesions.[27] However, the possible benefit of narrow-band imaging in the assessment of papillary lesions is only described in a small case series.[28] Accordingly, there is consensus that these techniques are not helpful in distinguishing between benign and malignant papillary lesions at this moment (71%) (Table 2).

Despite the current lack of a predefined classification system to determine whether a papillary lesion is most likely benign or malignant (89%) (Table 2), consensus exists that features such as ulceration (median, 4; IQR, 1) and immobility (median, 4; IQR, 1) should be considered features of a potential malignant lesion, regardless of biopsy sample results (Supplementary Table 2). When ulceration is present, this lesion can even be defined as most likely malignant based on this sole feature, regardless of biopsy sample results (94%) (Table 1). In case the biopsy sample shows high-grade dysplasia, firm consistency is considered an important characteristic as well (median, 4; IQR, 1). Features such as smooth or irregular surface, tumor size >4 cm, spontaneous bleeding, and excessive friability are, as sole criteria, of less importance when assessing a papillary lesion (Supplementary Table 2).

Patient selection. Although certain features would define a lesion as most likely malignant, none of the mentioned characteristics should be considered as an independent reason to refer for surgical management (Supplementary Table 2).

Considering the risk of incomplete endoscopic resection, consensus exists that patients should be referred for surgical management when ingrowth in the pancreatic duct (PD) or common bile duct (CBD) of >1 cm is present (76%) (Table 1). Jaundice (86%), ingrowth in the PD (79%) or CBD ≤1 cm (86%), and classification as an umbilicated lesion (a sign of central retraction) (82%) are not considered independent reasons to refer the patient for surgical management (Table 2). Nonetheless, no consensus exists on which additional techniques should be used to endoscopically resect ingrowth in the CBD or PD ≤1 cm (Supplementary Table 2-3). Furthermore, no agreement exists that intraductal extension should be ruled out routinely before resection (53%) (Supplementary Table 2).

Moreover, in case a patient is unfit for surgery, endoscopic resection can, if technically feasible, still be considered in case of adenocarcinoma (75%) or ingrowth in the CBD >1 cm (81%) (Table 2). Additionally, intraductal radiofrequency ablation (RFA) has been successfully described in small studies.[29-31] Accordingly, experts agree that EP with the additional use of RFA can be considered

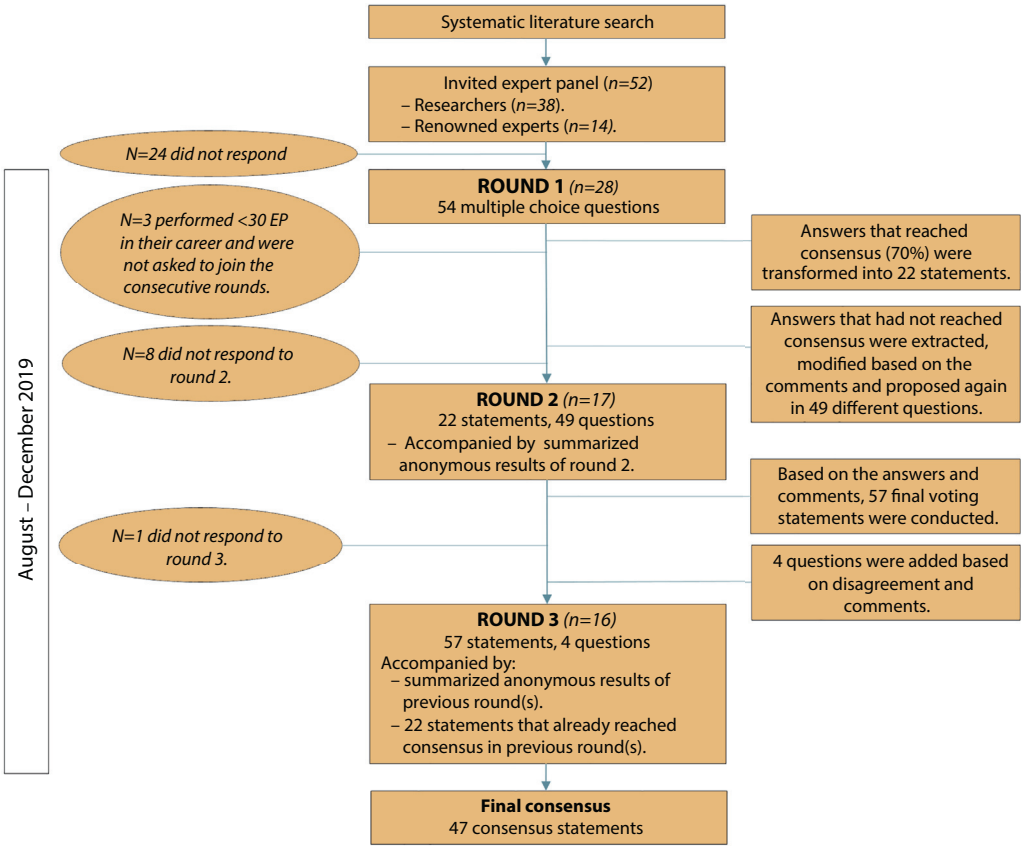

Figure 1. Flowchart study process. *EP*; Endoscopic papillectomy.

in a patient who is not a surgical candidate when ingrowth in the CBD >1 cm is present (75%) (Table 1). However, no consensus exists whether to consider endoscopic resection in combination with RFA when surgery is still an option (44%) (Supplementary Table 3).

Technical aspects. Resection should be performed at the plane of the duodenal wall (94%) with fractionated current (short, regular pulses of cutting current integrated in background of coagulation current), regardless of the size of the lesion (94%) (Table 2). A systematic review comparing fractionated and cutting current showed no difference in adverse events. This result was confirmed by a small randomized controlled pilot study that showed no difference in terms of safety and efficacy. Although the use of fractionated current might prevent immediate bleeding in larger adenomas, it may cause crush artefacts.[32,33]

Pancreatic and biliary sphincterotomy should, if indicated, only be performed after resection (100%) (Table 2). Indications for biliary sphincterotomy are concomitant bile duct stones or suboptimal drainage (81%) (Table 1). No consensus exists on indications for pancreatic sphincterotomy (38%-44%) (Table 3).

Submucosal injection should in general only be performed in case of a laterally spreading lesion (88%) (Table 1). This statement is confirmed by a small randomized controlled trial that could not show advantages in the use of submucosal injection and concluded that resection without lifting would be simpler and therefore primarily the recommended technique.[34,35]

The effect of preventive PD stent placement on postpapillectomy pancreatitis (PPP) has been claimed by 1 small randomized controlled trial. However, this difference was only significant in the per-protocol analysis but not in the intention-to-treat analysis.[36] Nevertheless, more recently 2 systematic reviews and meta-analyses of available literature supported the preventive effect of PD stent placement as well.[37,38] Accordingly, experts agree on the routine use of a PD stent to prevent PPP (100%) (Table 1). Different methods of PD stent placement have been studied; for example cannulating the PD before resection and performing resection with the guidewire in situ has been suggested. Because this method could potentially hamper complete en-bloc resection, consensus was achieved that the PD should be cannulated after resection (100%) (Table 2).[39-42] However, it remains unclear if injecting the PD before resection would be helpful in finding the PD after resection (44%) (Table 3).[43,44] Moreover, there was no consensus regarding the use of a PD stent with or without an internal flap (46% vs 54%) (Supplementary Tables 1-2).

TABLE 1. Important consensus statements

Statement	Agreement	Grading*
Diagnostic workup		
1. Gastroduodenoscopy with side-viewing instrument should always be performed before resection.	100%	D
2. Biopsy sampling should always be performed before resection.	94%	D
3. Either MRI/MRCP or EUS should be performed in case of a lesion larger than 2 cm and/or in case of cholestatic laboratory features.	75%	D
4. Either MRI/MRCP or CT should be performed in case of significant weight loss and/or in case of endoscopic signs of malignancy.	81%	D
5. CT should be performed in case of jaundice.	75%	D
Lesion assessment and staging		
6. When a lesion shows ulceration, this lesion should be defined as most likely malignant.	94%	D
7. Patient should be referred for surgical management in the following cases, considering patient is suitable for surgery:		
a. Ingrowth in the PD >1 cm.	76%	D
b. Ingrowth in the CBD >1 cm.	81%	D
8. If there is ingrowth in the CBD >1 cm, endoscopic papillectomy with radiofrequency ablation can be considered in a patient who is not a surgical candidate because of age and/or comorbidity, considering the lesion seems favorable for endoscopic resection.	75%	C
Technical aspects		
9. Submucosal injection should only be performed in case of a laterally spreading lesion.	88%	C
10. PD stent should be routinely placed to prevent postintervention pancreatitis.	100%	B
11. CBD stent should only be placed on indication, namely	82%	D
a. If there are concerns for a perforation in the papillary region after resection, a fully covered self-expanding metal stent should be placed in the CBD.	88%	D
b. In case of bleeding from the papillary region during the procedure.	76%	D
12. Biliary sphincterotomy should be performed in case of concomitant bile duct stones and in case drainage is deemed suboptimal.	81%	D
Adverse events and management		
13. Rectal nonsteroidal anti-inflammatory drugs should be given before resection.	82%	B
Follow-up		
14. In case initial pathology shows low-grade dysplasia, first follow-up (after removal of possible placed stents) should be performed within 6 months.	81%	D
15. In case initial pathology shows high-grade dysplasia, first follow-up (after removal of possible placed stents) should be performed within 3 months.	94%	D
16. Follow-up should be performed for at least 5 years.	75%	D

CBD, Common bile duct; *CT*, computed tomography; *EUS*, endoscopic ultrasound; *MRCP*, magnetic resonance cholangiopancreatography; *MRI*, magnetic resonance imaging; *PD*, pancreatic duct.
*Grading: A, level 1a-1b evidence; B, level 2a-3b evidence; C, level 4 evidence; D, level 5 evidence.

No consensus exists that pancreas divisum should be routinely excluded before resection (65%) (Supplementary Table 2). In the final round only 63% agreed that either EUS or MRI/MRCP should be performed in every patient before resection (Table 3).

A CBD stent should only be placed on indication (82%) (Table 1). No consensus was reached on the standard placement of a stent inside the CBD (18%) (Supplementary Table 1) to, for example, prevent postintervention cholangitis, which has been described in 0% to 7% of cases.[3,5,26] Possible indications to place a CBD stent are concerns for a (micro)perforation (88%) or ongoing bleeding from the papillary region during the procedure (76%). In case of concerns for a (micro) perforation, a fully covered self-expanding metal stent (FCSEMS) is preferred over a plastic stent (88%) (Table 1). FCSEMSs could also be useful in case of bleeding from the biliary region by tamponading the bleeding vessel.[45] Remarkably, no consensus was reached that a FCSEMS was preferred in case of bleeding as well, probably because the statement did not incorporate bleeding from the papillary region (63%) (Table 3). In case of residual tissue, stent placement could also facilitate the direct inspection of the distal CBD in the first follow-up procedure

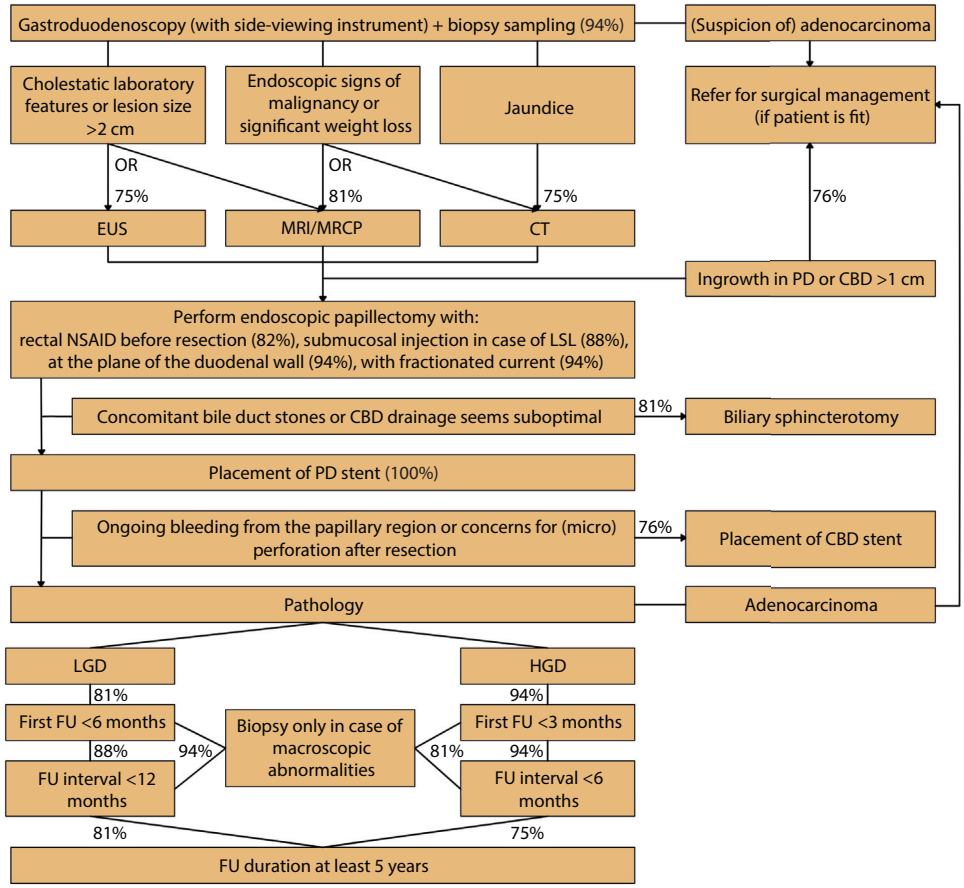

Figure 2. Consensus-based flowchart. Percentages indicate degree of agreement. *CBD*, Common bile duct; *CT*, computed tomography; *EUS*, endoscopic ultrasound; *FU*, follow-up; *HGD*, high-grade dysplasia; *LGD*, low-grade dysplasia; *LSL*, laterally spreading lesion; *MRCP*, magnetic resonance cholangiopancreatography; *MRI*, magnetic resonance imaging, *NSAID*, nonsteroidal anti-inflammatory drug; *PD*, pancreatic duct.

to exclude and treat possible intraductal extension.[4] Nonetheless, no consensus was achieved on the treatment of residual adenomatous tissue and the use of FCSEMSs in this manner (31%) (Table 3).

Snare tip soft coagulation of the resection margins after endoscopic mucosal resection (EMR) of adenomas in the colon results in a 4-fold reduction in recurrence at first follow-up.[46] Recent (preliminary) data show similar results after EMR of duodenal adenomas, suggesting that snare tip soft coagulation could also prevent recurrence after EP.[47] However, considering the potential risk of perforation and/or pancreatitis this technique is, reasonably, not part of current practice at the moment (56%), and further prospective study is required to evaluate its potential utility (Table 3).

Prophylactic clip closure of the mucosal defect to prevent bleeding has been successfully described after endoscopic resection of large colon polyps.[48] Also, a recent small prospective study examined the preventive closure of the frenulum after EP, which led to a decrease in delayed bleeding without a shown increase in pancreatitis or perforation rates and without lengthening procedure time.[49] However, data are limited, and there is no agreement whether standard clip closure of the mucosal defect after resection should be performed (38%) (Table 3).

The use of antispasmodic drugs such as glucagon and scopolaminebutyl can be helpful in reducing the risk of losing the specimen distally into the small bowel; however, no consensus exists whether to administer these drugs routinely before resection (56%) (Table 3). Probably because, in case of an adequate complete prone position of the patient, the risk of losing a specimen is considered low because it will generally migrate proximally with gravity toward the duodenal bulb. Figures 4 and 5 show the removal of a conventional and an extensive laterally spreading papillary adenoma, respectively, including placement of a PD and CBD stent, en-bloc removal of the adenoma at the plane of the duodenal wall, and clipping of the frenulum.

Adverse events and management. In addition to the placement of a PD stent after resection, rectal nonsteroidal anti-inflammatory drugs should be given before resection to further aid in the prevention of PPP (82%) (Table 1). This consensus statement is supported by studies regarding pancreatitis prevention in conventional ERCP practice that showed a significant

TABLE 2. Final consensus statements

Statement	Agreement	Grading*
Diagnostic workup		
1. Gastroduodenoscopy with side-viewing instrument should always be performed before resection.	100%	D
2. Advanced imaging techniques (such as narrow-band imaging or chromoendoscopy) are *not* helpful to distinguish between benign and malignant lesions.	71%	D
3. Biopsy sampling should always be performed before resection.	94%	D
4. Either MRI/MRCP or EUS should be performed in case of cholestatic laboratory features with or without jaundice.	81%	D
5. Either CT, MRI/MRCP, or EUS should be performed in case of cholestatic laboratory features with or without jaundice.	75%	D
6. CT should be performed in case of jaundice.	75%	D
7. Either MRI/MRCP or EUS should be performed in case of a lesion larger than 2 cm.	75%	D
8. Either MRI/MRCP or CT should be performed in case of significant weight loss.	81%	D
9. Either MRI/MRCP or CT should be performed in case of endoscopic signs of malignancy.	81%	D
Lesion assessment and staging		
10. No predefined classification system to determine if a papillary adenoma is most likely benign or malignant exists.	89%	D
11. When a lesion shows ulceration, this lesion should be defined as most likely malignant.	94%	D
12. The following characteristics are *not* a sole reason to define the lesion as most likely malignant:		
a. Smooth surface	96%	D
b. Spontaneous bleeding	86%	D
c. Lesion size >4 cm	86%	D
13. Patient should be referred for surgical management in case of ingrowth in the PD >1 cm, considering patient is suitable for surgery.	76%	D
14. Patient should be referred for surgical management in case of ingrowth in the CBD >1 cm, considering patient is suitable for surgery.	81%	D
15. The following situations are *not* a sole reason to refer for surgical management:		
a. Jaundice	86%	D
b. Ingrowth in the PD ≤1 cm	79%	D
c. Ingrowth in the CBD ≤1 cm	86%	D
d. An umbilicated lesion	82%	D
16. If biopsy sample shows LGD and ulceration is present, the lesion could still be resected endoscopically; there is no need to refer the patient for surgical management based on this sole characteristic, considering the lesion seems favorable for endoscopic resection.	88%	D
17. If there is ingrowth in the CBD >1 cm, endoscopic resection can still be considered if the patient is not a surgical candidate because of age and/or comorbidity, considering the lesion seems favorable for endoscopic resection.	81%	D
18. If there is ingrowth in the CBD >1 cm, EP with radiofrequency ablation can be considered in a patient that is not a surgical candidate because of age and/or comorbidity, considering the lesion seems favorable for endoscopic resection.	75%	C
19. If biopsy sample shows adenocarcinoma in situ or well-differentiated adenocarcinoma, endoscopic resection can still be considered if the patient is not a surgical candidate because of age and/or comorbidity, considering the lesion seems favorable for endoscopic resection.	75%	D
Technical aspects		
20. Submucosal injection should only be performed in case of a laterally spreading lesion.	88%	C
21. Resection of the lesion should be performed at the plane of the duodenal wall.	94%	D
22. EP should be performed with fractionated current.	94%	D
23. If pancreatic sphincterotomy is indicated, then it should be performed after resection.	88%	D
24. Biliary sphincterotomy should be performed in case of concomitant bile duct stones and in case drainage is deemed suboptimal.	81%	D

(*continued on the next page*)

TABLE 2. Continued

Statement	Agreement	Grading*
25. If biliary sphincterotomy is indicated, then it should be performed after resection.	100%	D
26. PD stent should be routinely placed to prevent postintervention pancreatitis.	100%	B
27. PD should be cannulated after resection.	100%	D
28. CBD stent should only be placed on indication, namely	82%	D
a. If there are concerns for microperforations in the papillary region after resection.	88%	D
b. In case of bleeding from the papillary region during the procedure.	76%	D
29. In case there are concerns for microperforations in the papillary region a fully covered self-expanding metal stent should be placed in the CBD.	88%	D
Adverse events and management		
30. Rectal nonsteroidal anti-inflammatory drugs should be given before resection.	82%	B
Follow-up		
31. In case initial pathology shows LGD		
a. First follow-up (after removal of possible placed stents) should be performed within 6 months.	81%	D
b. At first follow-up, biopsy specimens should only be taken when macroscopic abnormalities are present.	94%	D
c. Follow-up interval should be 12 months or less.	88%	D
d. At further follow-up, biopsy specimens should only be taken when macroscopic abnormalities are present.	94%	D
e. Follow-up should be performed for at least 5 years.	81%	D
32. In case initial pathology shows HGD		
a. First follow-up (after removal of possible placed stents) should be performed within 3 months.	94%	D
b. At first follow-up, biopsy specimens should only be taken when macroscopic abnormalities are present.	81%	D
c. Follow-up interval should be 6 months or less.	94%	D
d. At further follow-up, biopsy specimens should only be taken when macroscopic abnormalities are present.	81%	D
e. Follow-up should be performed for at least 5 years.	75%	D

CBD, Common bile duct; *CT*, computed tomography; *EUS*, endoscopic ultrasound; *EP*, endoscopic papillectomy; *HGD*, high-grade dysplasia; *LGD*, low-grade dysplasia; *MRCP*, magnetic resonance cholangiopancreatography; *MRI*, magnetic resonance imaging; *PD*, pancreatic duct.
*Grading: A, level 1a-1b evidence; B, level 2a-3b evidence; C, level 4 evidence; D, level 5 evidence.

reduction in incidence when using nonsteroidal anti-inflammatory drug suppositories.[50-52] In addition, studies suggest that preventive vigorous pre- and perprocedural hydration reduces the pancreatitis rate even further.[53-55] This outcome still needs to be confirmed by an adequately powered randomized controlled trial of which the results have not yet been published.[56] Accordingly, no consensus could be reached that vigorous hydration should be considered in, for example, cases without any major cardiac comorbidity (63%) (Table 3).

Consensus could not be achieved on whether patients should be treated with a proton pump inhibitor (PPI) to decrease the risk of delayed bleeding after performing an EP (69%) (Table 3). Although the effect of acid suppression by a PPI in the treatment of upper GI tract bleeding caused by (artificial) ulcers is evident, the benefit of PPI use in the prevention of delayed bleeding after EP or, for example, sphincterotomy is not established and questionable given the relatively high pH in the duodenum.[57,58]

Considering bleeding, different methods were proposed to stop the bleeding such as the use of FCSEMSs, Hemospray (Cook Medical, Bloomington, Ind, USA), epinephrine injection, clips, or coagulation. No consensus could be achieved on the best treatment method in case of bleeding during the procedure (Supplementary Tables 2-3). Furthermore, no consensus seems to exist as to whether to perform reintervention (38%) or initially treat a patient conservatively (63%) in case of delayed bleeding when the patient is hemodynamically stable after resuscitation (Table 3).

Follow-up. Biopsy sampling during follow-up only needs to be performed when macroscopic abnormalities are present (81%). The first follow-up should be performed within 3 months (94%) with an interval to the second follow-up of 6 months or less (94%) in case of high-grade dysplasia compared with, respectively, 6 (81%) and 12 months (88%) in case of low-grade dysplasia. In both cases follow-up should be continued for at least 5 years (75%-81%) (Table 2); however, 31-38% of experts would

TABLE 3. Selection of final round statements that did not reach consensus

Statement	Agreement
Diagnostic workup	
1. Either MRI/MRCP or EUS should be performed in every patient before resection.	63%
2. An endoscopic cholangiogram either before or during EP should only be performed if other performed tests are found inconclusive and there is still doubt about the presence of intraductal extension.	44%
Technical aspects	
3. STSC of the margins should *not* be performed after EP.	56%
4. STSC can be performed for the margins of the laterally spreading component but not the papillary margins.	50%
5. Pancreatic sphincterotomy after resection should only be performed in case of	
a. Extension in the pancreatic duct.	38%
b. Extension in the pancreatic duct or if drainage is deemed suboptimal.	44%
6. It can be helpful to inject the PD before resection to make it easier to find the PD after resection in case of extension in the pancreatic duct.	44%
7. In case there is bleeding during the procedure, an FCSEMS instead of a plastic stent should be placed in the CBD.	63%
8. In case there are concerns for residual adenomatous tissue in the distal part of the CBD, an FCSEMS should be placed in the CBD.	31%
9. Standard clip closure of the mucosal defect after resection should *not* be performed.	38%
10. Glucagon or scopulaminebutyl should be provided routinely before resection to reduce the risk of losing the specimen in the GI tract.	56%
Adverse events and management	
11. Vigorous hydration should be considered in patients without any cardiac comorbidity to further decrease the risk of postintervention pancreatitis.	63%
12. Every patient should be treated with PPI after performing an EP.	69%
13. Patients treated with PPI after resection should be treated for at least 2 weeks.	69%
14. If a bleeding occurs after EP and patient is hemodynamically stable after resuscitation with <1.2 mmol/L drop in hemoglobin	
a. Reintervention should be performed within 12 hours.	38%
b. Conservative treatment (continue or start PPI) is initially indicated.	63%
Follow-up	
15. Every patient should be admitted for observation after EP for	
a. At least 24 hours.	69%
b. At least 48 hours.	44%

CBD, Common bile duct; *EP*, endoscopic papillectomy; *EUS*, endoscopic ultrasound; *FCSEMS*, fully covered self-expanding metal stent; *MRCP*, magnetic resonance cholangiopancreatography; *MRI*, magnetic resonance imaging; *PD*, pancreatic duct; *PPI*, proton pump inhibitor; *STSC*, snare tip soft coagulation.

perform lifelong follow-up, as long as the patient is fit (Supplementary Table 3). Recent data on long-term follow-up after EP show that recurrence has been found even 5 years after the index procedure, confirming the need for consideration of longer follow-up.[7,26]

Finally, there was consensus that patients should be admitted for observation after the procedure (82%) (Supplementary Table 2). However, participants could not agree on the length of necessary observation, 69% would observe at least 24 hours, and 44% at least 48 hours (Table 3).

DISCUSSION

EP is established as the preferred method to manage benign papillary adenomas.[5,59] EP is minimally invasive, and modeling using well-validated scoring systems has shown it is safer and less expensive than surgical management.[60] Moreover, in case of unsuspected cancer in the papillectomy specimen, it does not preclude or compromise subsequent surgery in a surgically fit patient. Although generally considered safe, EP is not without risks, with serious adverse events occurring in 15-35% of patients and recurrence in up to 20% during surveillance.[3-7,26] It is therefore incumbent on those managing these patients to further refine and optimize the EP procedure to mitigate against these adverse events. However, high-level scientific knowledge to guide this process is largely absent because papillary adenomas are uncommon, and thus large prospective multicenter or randomized controlled studies have not been executed. Therefore, unsurprisingly, an evidence-based consensus for EP has not been established. We sought to address this deficiency by using a Delphi process among international experts.

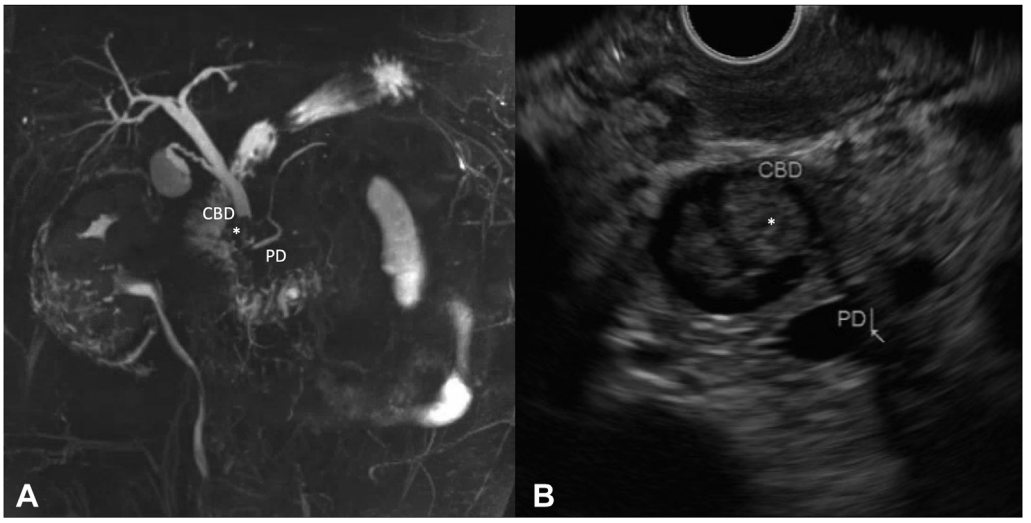

Figure 3. A, MRCP showing ingrowth (*) in the distal common bile duct (CBD) of approximately 15 mm. **B,** EUS showing ingrowth (*) in the distal CBD of approximately 12.5 mm and dilatation of both CBD (14.4 mm) and pancreatic duct (PD) (5.5 mm).

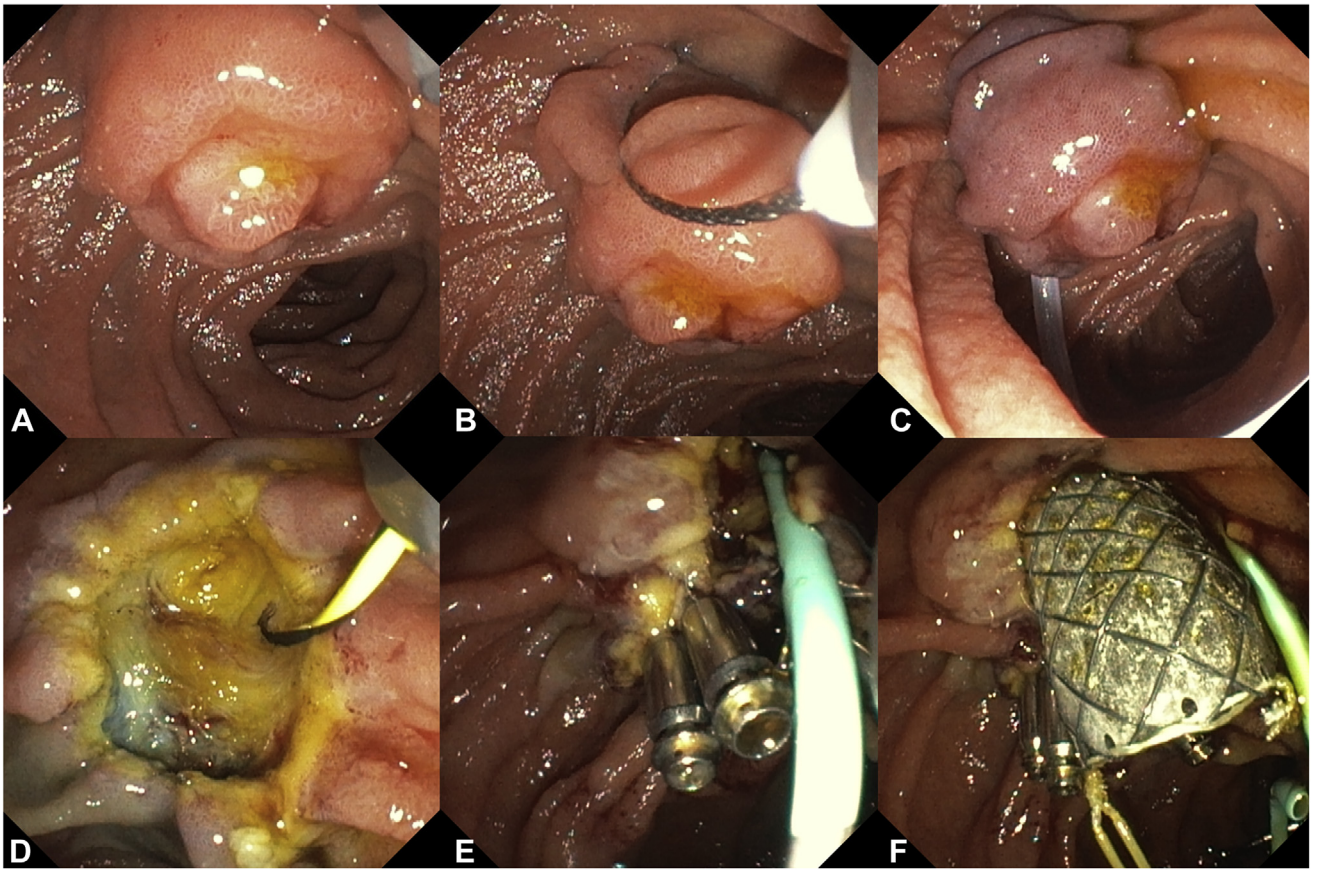

Figure 4. A-C, Conventional en-bloc papillectomy at the level of the duodenal wall for 15 mm papillary adenoma. **D-F,** Exposure of biliary and pancreatic orifices with a 5F pancreatic stent and fully covered metal biliary stent. Clip closure of the frenulum for the prophylaxis of post-papillectomy bleeding.

Sixteen international experts joined the final round, and consensus was reached on 47 of the final 79 proposed statements. It was necessary to propose a large number of statements to fully evaluate this complex multifaceted procedure. Based on the consensus achieved, insight was given in the main characteristics that should be taken

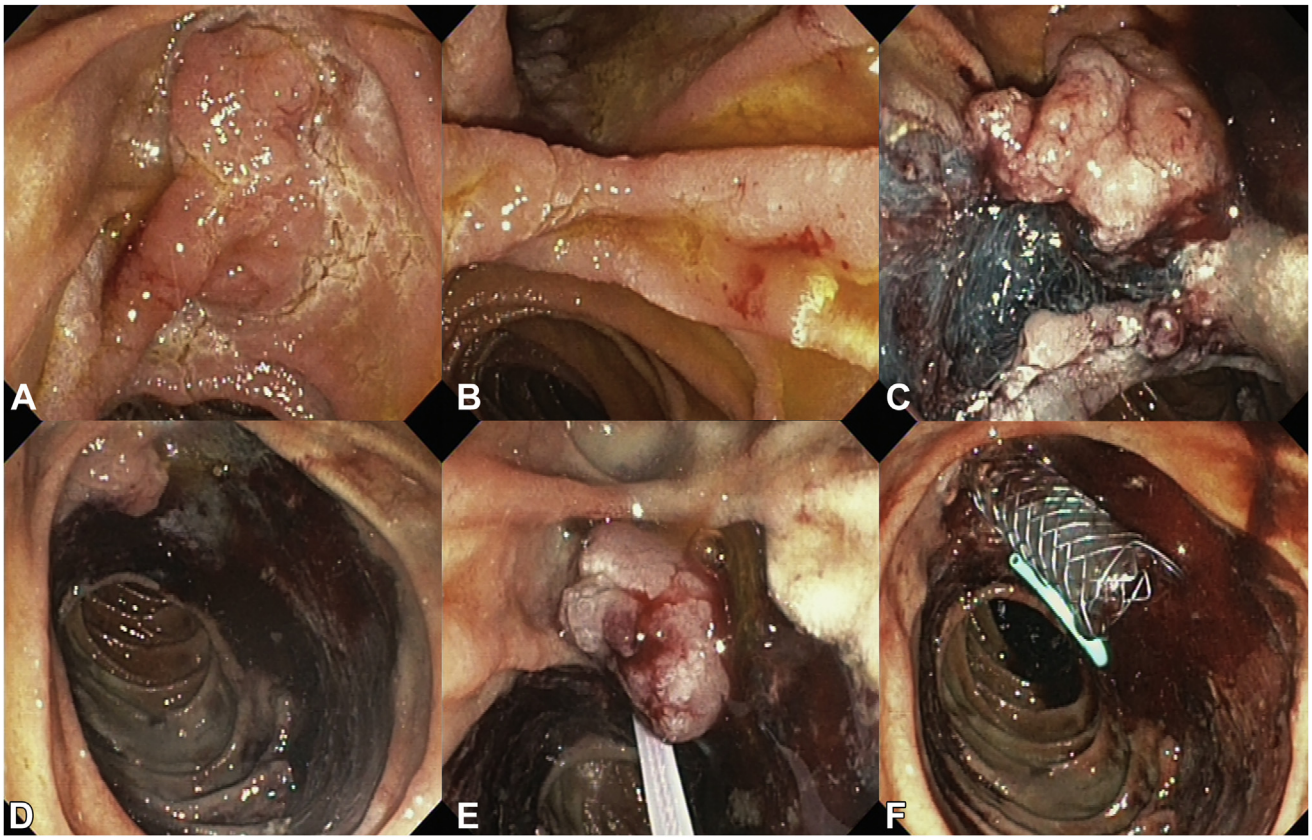

Figure 5. **A** and **B,** Extensive laterally spreading papillary adenoma involving greater than two-thirds of the duodenal circumference. **C** and **D,** Piecemeal EMR of the laterally spreading components resulting in 90% circumferential mucosal defect. **E** and **F,** En-bloc papillectomy followed by a 5F pancreatic stent and fully covered metal biliary stent.

into account when classifying a papillary lesion and reasons to refer a patient for surgical management. Furthermore, a consensus-based algorithm regarding diagnostic workup, technical aspects, and follow-up is proposed and is depicted in Figure 2.

As stated, biopsy sampling is only accurate in 70% of the papillary malignancies, and therefore endoscopic assessment can be considered most important.[20-22] To improve this classification, it would be helpful to have a predefined scoring system to better assess these lesions. This does not currently exist, and although we were able to identify important characteristics deemed to be associated with malignancy, further study is needed to propose a useful scoring system to improve the assessment of papillary lesions. Also, advanced imaging techniques such as narrow-band imaging or chromoendoscopy could be further assessed to determine their possible additional value to the classification of papillary lesions.

Besides the need for studies regarding optimal diagnosis, a lack of consensus on different technical aspects of the procedure warrants future prospective studies. For example, the benefit of FCSEMS placement after resection in case of bleeding from the papillary region or when residual tissue is present, RFA in case of ingrowth in the CBD, and the use of snare tip soft coagulation of the margins of the laterally spreading segment need to be further evaluated to determine their utility in daily practice. Furthermore, preventive measures such as vigorous hydration to prevent PPP and PPI to prevent delayed bleeding after resection are not part of the proposed consensus algorithm because, due to the paucity of data, no consensus could be reached on the benefit of these methods, showing the need for future well-targeted studies.

This study is not free of limitations. According to the low patient numbers in the literature and the absence of systematic prospective studies, high-level scientific enquiry to inform evidence-based consensus is lacking. Consequently and unsurprisingly, because of the lack of consensus on certain critical steps in the process, it is impossible to propose a complete algorithm for EP. In addition, note should be taken that the proposed protocol in this study mainly focuses on patients with sporadic papillary adenoma and is not directly translatable to patients with a genetic predisposition as in familial adenomatous polyposis syndrome. Although the resection technique and the prevention and treatment of adverse events can be considered the same, the diagnostic and follow-up protocol contain important differences. Final limitations are inherent to the study design; the expert panel,

although reliant on published literature, was partly composed on personal expert knowledge, which makes the study eligible for personal bias. Because an adequate sample of possible participants was not available, test–retest reliability could not be performed, and, most importantly, when consensus was reached, this does not certainly mean that the correct answer has been found.[15]

However, given the lack of large prospective, randomized studies, this Delphi consensus provides the best available evidence regarding the management of these relatively uncommon lesions. The invited expert panel can be considered an adequate reflection of the experience in EP because researchers and renowned experts (therefore, wide clinical and scientific experience) were included. Furthermore, the size of the panel can be considered reliable for content validation because 5 to 10 experts are considered sufficient.[61] By using a Delphi process, consensus could be achieved in a group of geographically spread experts, obviating the need for direct confrontation, leaving room for individual thought.[11] The use of anonymous group feedback gave participants the opportunity to change their opinion based on group consensus. Moreover, consensus statements were supported by available literature after systematic review of the literature. Accordingly, this study provides a unique agreement and the best available, evidence-based guideline for the endoscopic management of papillary adenomas.

In conclusion, this Delphi study provides the current highest level of evidence regarding the different aspects of the performance of EP. Although there are surprisingly many areas in which no consensus exists and scientific data are lacking, this study led to the first consensus-based management algorithm for papillary adenomas. Therefore, this study can be considered a vital step around which future studies can be designed to ultimately generate a more robust evidence-based consensus guideline for EP. Furthermore, important insights were observed in areas in which a high variety in daily practice still exists, and, accordingly, future studies could be targeted.

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REFERENCES

1. Suzuki K, Kantou U, Murakami Y. Two cases with ampullary cancer who underwent endoscopic resection. Prog Dig Endosc 1983:236-9.
2. Binmoeller KF, Boaventura S, Ramsperger K, et al. Endoscopic snare excision of benign adenomas of the papilla of Vater. Gastrointest Endosc 1993;39:127-31.
3. van der Wiel SE, Poley JW, Koch AD, et al. Endoscopic resection of advanced ampullary adenomas: a single-center 14-year retrospective cohort study. Surg Endosc 2019;33:1180-8.
4. Klein A, Qi Z, Bahin FF, et al. Outcomes after endoscopic resection of large laterally spreading lesions of the papilla and conventional ampullary adenomas are equivalent. Endoscopy 2018;50:972-83.
5. Ridtitid W, Tan D, Schmidt SE, et al. Endoscopic papillectomy: risk factors for incomplete resection and recurrence during long-term follow-up. Gastrointest Endosc 2014;79:289-96.
6. Napoleon B, Gincul R, Ponchon T, et al. Endoscopic papillectomy for early ampullary tumors: long-term results from a large multicenter prospective study. Endoscopy 2014;46:127-34.
7. Sahar N, Krishnamoorthi R, Kozarek RA, et al. Long-term outcomes of endoscopic papillectomy for ampullary adenomas. Dig Dis Sci 2020;65:260-8.
8. Chathadi KV, Khashab MA, Acosta RD, et al; ASGE Standards of Practice Committee. The role of endoscopy in ampullary and duodenal adenomas. Gastrointest Endosc 2015;82:773-81.
9. El Hajj I, Cote GA. Endoscopic diagnosis and management of ampullary lesions. Gastrointest Endosc Clin North Am 2013;23:95-109.
10. Bassan M, Bourke M. Endoscopic ampullectomy: a practical guide. J Interv Gastroenterol 2012;2:23-30.
11. Dalkey NC; The Rand Corporation. The Delphi method: an experimental study of group opinion. Santa Monica, CA: Rand Corporation; 1969.
12. Bennett C, Vakil N, Bergman J, et al. Consensus statements for management of Barrett's dysplasia and early-stage esophageal adenocarcinoma, based on a Delphi process. Gastroenterology 2012;143:336-46.
13. Powell C. The Delphi technique: myths and realities. J Adv Nurs 2003;41:376-82.
14. Goggins M, Overbeek KA, Brand R, et al. Management of patients with increased risk for familial pancreatic cancer: updated recommendations from the International Cancer of the Pancreas Screening (CAPS) Consortium. Gut 2020;69:7-17.
15. Hasson F, Keeney S, McKenna H. Research guidelines for the Delphi survey technique. J Adv Nurs 2000;32:1008-15.
16. Likert R. Technique for the measurement of attitudes. Arch Psychol 1932:1932-53.
17. Sumsion T. The Delphi technique: an adaptive research tool. Br J Occup Ther 1998;61:153-6.
18. von der Gracht HA. Consensus measurement in Delphi studies. Review and implications for future quality assurance. Technol Forecast Soc Change 2012;79:1525-36.
19. Centre for Evidence Based Medicine. Oxford Centre for Evidence-based Medicine—levels of evidence. Oxford, UK: Centre for Evidence-Based Medicine; 2009.
20. Yamaguchi K, Enjoji M, Kitamura K. Endoscopic biopsy has limited accuracy in diagnosis of ampullary tumors. Gastrointest Endosc 1990;36:588-92.
21. Bellizzi AM, Kahaleh M, Stelow EB. The assessment of specimens procured by endoscopic ampullectomy. Am J Clin Pathol 2009;132:506-13.
22. Elek G, Gyori S, Toth B, et al. Histological evaluation of preoperative biopsies from ampulla vateri. Pathol Oncol Res 2003;9:32-41.
23. Petrelli NJ, Létourneau R, Weber T, et al. Accuracy of biopsy and cytology for the preoperative diagnosis of colorectal adenocarcinoma. Surg Oncol Clin North Am 1999;71:46-9.
24. Ahn DW, Ryu JK, Kim J, et al. Endoscopic papillectomy for benign ampullary neoplasms: how can treatment outcome be predicted? Gut Liver 2013;7:239-45.
25. Cheng CL, Sherman S, Fogel EL, et al. Endoscopic snare papillectomy for tumors of the duodenal papillae. Gastrointest Endosc 2004;60:757-64.
26. Fritzsche JA, Klein A, Beekman MJ, et al. Endoscopic papillectomy; a retrospective international multicenter cohort study with long-term follow-up. Surg Endosc. Epub 2020 Nov 6.

27. Bisschops R, East JE, Hassan C, et al. Advanced imaging for detection and differentiation of colorectal neoplasia: European Society of Gastrointestinal Endoscopy (ESGE) guideline—update 2019. Endoscopy 2019;51:1155-79.
28. Uchiyama Y, Imazu H, Kakutani H, et al. New approach to diagnosing ampullary tumors by magnifying endoscopy combined with a narrow-band imaging system. J Gastroenterol 2006;41:483-90.
29. Camus M, Napoleon B, Vienne A, et al. Efficacy and safety of endobiliary radiofrequency ablation for the eradication of residual neoplasia after endoscopic papillectomy: a multicenter prospective study. Gastrointest Endosc 2018;88:511-8.
30. Rustagi T, Irani S, Reddy ND, et al. Endoscopic radiofrequency ablation for intraductal extension of ampullary neoplasms [abstract]. Gastrointest Endosc 2016;83:AB298.
31. Choi YH, Yoon SB, Chang JH, et al. The safety of radiofrequency ablation using a novel temperature-controlled probe for the treatment of residual intraductal lesions after endoscopic papillectomy. Gut Liver 2021;15:307-14.
32. Iwasaki E, Minami K, Itoi T, et al. Impact of electrical pulse cut mode during endoscopic papillectomy: pilot randomized clinical trial. Dig Endosc 2020;32:127-35.
33. Minami K, Iwasaki E, Fukuhara S, et al. Electric endocut and autocut resection for endoscopic papillectomy: a systematic review. Intern Med 2019;58:2767-72.
34. Hyun JJ, Lee TH, Park JS, et al. A prospective multicenter study of submucosal injection to improve endoscopic snare papillectomy for ampullary adenoma. Gastrointest Endosc 2017;85:746-55.
35. Chung KH, Lee SH, Choi JH, et al. Effect of submucosal injection in endoscopic papillectomy of ampullary tumor: propensity-score matching analysis. United Eur Gastroenterol J 2018;6:576-85.
36. Harewood GC, Pochron NL, Gostout CJ. Prospective, randomized, controlled trial of prophylactic pancreatic stent placement for endoscopic snare excision of the duodenal ampulla. Gastrointest Endosc 2005;62:367-70.
37. Wang Y, Qi M, Hao Y, et al. The efficacy of prophylactic pancreatic stents against complications of post-endoscopic papillectomy or endoscopic ampullectomy: a systematic review and meta-analysis. Therap Adv Gastroenterol 2019;12:1756284819855342.
38. Spadaccini M, Fugazza A, Frazzoni L, et al. Endoscopic papillectomy for neoplastic ampullary lesions: A systematic review with pooled analysis. United Eur Gastroenterol J 2020;8:44-51.
39. Lee TY, Cheon YK, Shim CS, et al. Endoscopic wire-guided papillectomy versus conventional papillectomy for ampullary tumors: a prospective comparative pilot study. J Gastroenterol Hepatol 2016;31:897-902.
40. Kim SH, Moon JH, Choi HJ, et al. Usefulness of pancreatic duct wire-guided endoscopic papillectomy for ampullary adenoma for preventing post-procedure pancreatitis. Endoscopy 2013;45:838-41.
41. Kobayashi M, Ryozawa S, Iwano H, et al. The usefulness of wire-guided endoscopic snare papillectomy for tumors of the major duodenal papilla. PLoS One 2019;14:e0211019.
42. Moon JH, Cha SW, Cho YD, et al. Wire-guided endoscopic snare papillectomy for tumors of the major duodenal papilla. Gastrointest Endosc 2005;61:461-6.
43. Poincloux L, Scanzi J, Goutte M, et al. Pancreatic intubation facilitated by methylene blue injection decreases the risk for postpapillectomy acute pancreatitis. Eur J Gastroenterol Hepatol 2014;26:990-5.
44. Nakahara K, Okuse C, Suetani K, et al. A novel endoscopic papillectomy after a pancreatic stent placement above the pancreatic duct orifice: inside pancreatic stenting papillectomy. J Clin Gastroenterol 2014;48:796-800.
45. Donatelli G, Dumont JL, Derhy S, et al. New indications for fully covered lumen-apposing metal stents: biliary stenting to treat post-sphincterotomy bleeding or ampullary stenosis. Endoscopy 2018;50:E36-7.
46. Klein A, Tate DJ, Jayasekeran V, et al. Thermal ablation of mucosal defect margins reduces adenoma recurrence after colonic endoscopic mucosal resection. Gastroenterology 2019;156:604-13.
47. Sidhu M, Fritzsche JA, Klein A, Shahidi N, et al. Outcomes of thermal ablation of the defect margin after duodenal endoscopic mucosal resection (with videos). Gastrointest Endosc 2020;93:1373-80.
48. Pohl H, Grimm IS, Moyer MT, et al. Clip closure prevents bleeding after endoscopic resection of large colon polyps in a randomized trial. Gastroenterology 2019;157:977-84.
49. Kagawa K, Kubota K, Kurita Y, et al. Effect of preventive closure of the frenulum after endoscopic papillectomy: A prospective pilot study. J Gastroenterol Hepatol 2020;35:374-9.
50. Elmunzer BJ, Scheiman JM, Lehman GA, et al. A randomized trial of rectal indomethacin to prevent post-ERCP pancreatitis. N Engl J Med 2012;366:1414-22.
51. Elmunzer BJ, Waljee AK, Elta GH, et al. A meta-analysis of rectal NSAIDs in the prevention of post-ERCP pancreatitis. Gut 2008;57:1262-7.
52. Khoshbaten M, Khorram H, Madad L, et al. Role of diclofenac in reducing post-endoscopic retrograde cholangiopancreatography pancreatitis. J Gastroenterol Hepatol 2008;23(7 Pt 2):e11-6.
53. Buxbaum J, Yan A, Yeh K, et al. Aggressive hydration with lactated Ringer's solution reduces pancreatitis after endoscopic retrograde cholangiopancreatography. Clin Gastroenterol Hepatol 2014;12:303-7.
54. Shaygan-nejad A, Masjedizadeh A, Ghavidel A, et al. Aggressive hydration with lactated Ringer's solution as the prophylactic intervention for postendoscopic retrograde cholangiopancreatography pancreatitis: a randomized controlled double-blind clinical trial. J Res Med Sci 2015;20:838-42.
55. Choi JH, Kim HJ, Lee BU, et al. Vigorous periprocedural hydration with lactated Ringer's solution reduces the risk of pancreatitis after retrograde cholangiopancreatography in hospitalized patients. Clin Gastroenterol Hepatol 2017;15:86-92.
56. Smeets XJNM, da Costa DW, Fockens P; Dutch Pancreatitis Study Group. Fluid hydration to prevent post-ERCP pancreatitis in average- to high-risk patients receiving prophylactic rectal NSAIDs (FLUYT trial): study protocol for a randomized controlled trial. Trials 2018;19:207.
57. Sachar H, Vaidya K, Laine L. Intermittent vs continuous proton pump inhibitor therapy for high-risk bleeding ulcers: a systematic review and meta-analysis. JAMA Intern Med 2014;174:1755-62.
58. Leung WK, But DYK, Wong S-Y, et al. Prevention of post-sphincterotomy bleeding by proton pump inhibitor: a randomized controlled trial. J Dig Dis 2018;19:369-76.
59. Klein A, Tutticci N, Bourke MJ. Endoscopic resection of advanced and laterally spreading duodenal papillary tumors. Dig Endosc 2016;28:121-30.
60. Klein A, Ahlenstiel G, Tate DJ, et al. Endoscopic resection of large duodenal and papillary lateral spreading lesions is clinically and economically advantageous compared with surgery. Endoscopy 2017;49:659-67.
61. Lynn MR. Determination and quantification of content validity. Nurs Res 1986;35:382-5.

Abbreviations: CBD, common bile duct; CT, computed tomography; EP, endoscopic papillectomy; EMR, endoscopic mucosal resection; ERCP, endoscopic retrograde cholangiopancreatograpy; EUS, endoscopic ultrasound; FCSEMS, fully covered self-expanding metal stent; IQR, interquartile range; MRCP, magnetic resonance cholangiopancreatography; MRI, magnetic resonance imaging; PD, pancreatic duct; PPP, postpapillectomy pancreatitis; PPI, proton pump inhibitor; RFA, radiofrequency ablation.

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APPENDIX

EMBASE (OVID)

Database(s): Embase Classic+Embase 1947 to 2020 December 17

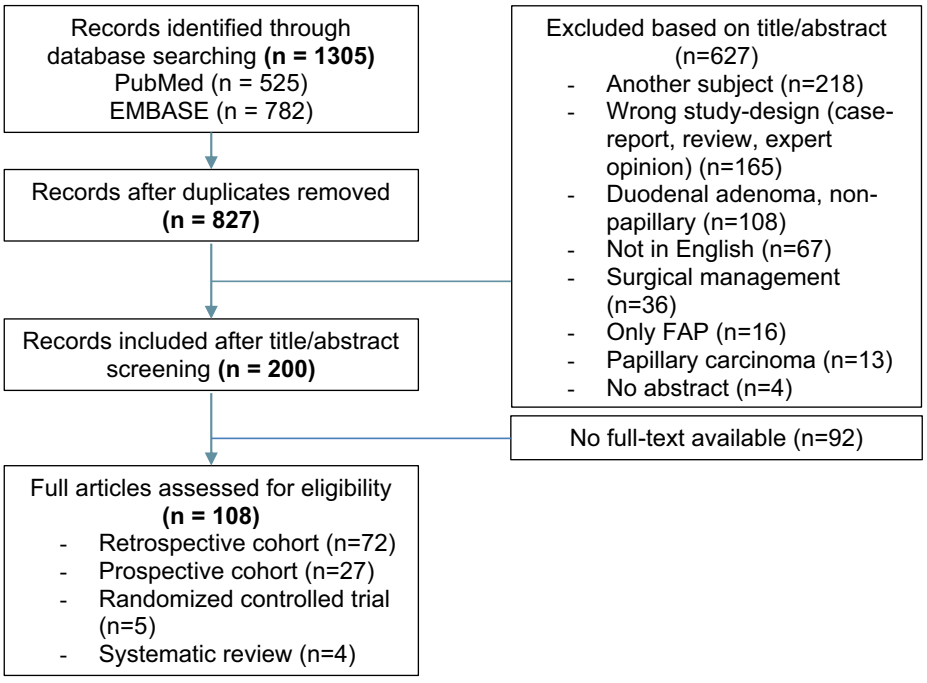
#	Searches	Results
1	(endoscopic ampullectom* or papillectom*).ti,ab,kw.	692
2	((endoscopic resect* or endoscopic excision*) and (papilla* or ampulla*)).ti,ab,kw.	573
3	1 or 2	1114
4	limit 3 to (conference abstract status and yr="1883 - 2014")	194
5	3 or 4	920
6	limit 5 to English language	**782**

PubMed

Search performed on 2020 December 18

#	Searches	Results
1	(endoscopic resect*[tiab] OR endoscopic excision*[tiab]) AND (papilla*[tiab] OR ampulla*[tiab])	262
2	(endoscopic ampullectom*[tiab] OR papillectom*[tiab])	326
3	1 OR 2	**525**

Flowchart in- and exclusion



Supplementary Figure 1. Literature search.

SUPPLEMENTARY TABLE 1. Survey round 1

Question	Agreement
Expertise	
1. In which country do you work?	
a. United States of America	29%
b. Japan	14%
c. France	11%
d. Korea	11%
e. Germany	7%
f. Italy	7%
g. Netherlands	7%
h. Belgium	4%
i. Finland	4%
j. Switzerland	4%
k. United Kingdom	4%
2. In which type of practice do you primarily work?	
a. Academic practice	86%
b. Private practice	11%
c. Nonacademic practice	7%
d. Other	4%
3. How many years have you been in practice?	
a. <5 years	0%
b. 5-10 years	7%
c. 10-20 years	25%
d. >20 years	68%
4. Do you perform colonoscopies every week?	
a. Yes	82%
b. No	18%
5. How many colonoscopies do you perform every week? (n = 23)	
a. <5 per week	30%
b. 5-10 per week	35%
c. 10-20 per week	22%
d. >20 per week	13%
6. Do you perform basic polypectomy?	
a. Yes	93%
b. No	7%
7. Do you perform colonic EMR?	
a. Yes	82%
b. No	18%
8. How many ERCPs do you perform yearly?	
a. <100 per year	4%
b. 100-200 per year	21%
c. 200-400 per year	36%
d. >400 per year	39%

(*continued on the next page*)

SUPPLEMENTARY TABLE 1. Continued

Question	Agreement
9. How many endoscopic papillectomies are performed yearly in your center?	
a. <5 per year	4%
b. 5-10 per year	18%
c. 10-20 per year	36%
d. >20 per year	43%
10. How many endoscopic papillectomies did you perform in your career?	
a. <5 in total	0%
b. 5-10 in total	4%
c. 10-30 in total	7%
d. >30 in total	89%
11. Do you perform EUS?	
a. Yes	79%
b. No	21%
12. How many EUS do you perform yearly? (n = 21)	
a. <50 per year	5%
b. 50-100 per year	5%
c. 100-200 per year	9%
d. >200 per year	82%
Diagnostic workup	
1. Do you get patients referred to perform an endoscopic papillectomy?	
a. Yes	100%
b. No	0%
2. Which diagnostic modalities are usually already performed by the referring physician?	
a. CT	50%
b. EUS	29%
c. MRCP	29%
d. Cholangiography	7%
e. None of the above	25%
f. Other	
i. Gastroduodenoscopy	29%
3. What are possible reasons to perform a CT before resection?	
a. Part of the standard diagnostic workup	43%
b. Jaundice	64%
c. Cholestatic laboratory features, without clinical signs of jaundice	43%
d. Significant weight loss	57%
e. Double duct sign on other imaging	61%
f. Age older than 50	11%
g. Large (>2 cm) adenoma	36%
h. Endoscopic features of possible malignancy	79%
i. Other	7%
4. What are possible reasons to perform an MRCP before resection?	
a. Part of the standard diagnostic workup	46%
b. Jaundice	71%
c. Cholestatic laboratory features, without clinical signs of jaundice	68%
d. Significant weight loss	36%

(*continued on the next page*)

SUPPLEMENTARY TABLE 1. Continued

Question	Agreement
e. Double duct sign on other imaging	57%
f. Age older than 50	7%
g. Large (>2 cm) adenoma	43%
h. Endoscopic features of possible malignancy	54%
i. Other	11%
5. What are possible reasons to perform an EUS before resection?	
a. Part of the standard diagnostic workup	50%
b. Jaundice	61%
c. Cholestatic laboratory features, without clinical signs of jaundice	57%
d. Significant weight loss	39%
e. Double duct sign on other imaging	61%
f. Age older than 50	11%
g. Large (>2 cm) adenoma	54%
h. Endoscopic features of possible malignancy	75%
i. Other	14%
6. What are possible reasons to perform a cholangiography before resection?	
a. Part of the standard diagnostic workup	25%
b. Jaundice	54%
c. Cholestatic laboratory features, without clinical signs of jaundice	29%
d. Significant weight loss	14%
e. Double duct sign on other imaging	50%
f. Age older than 50	4%
g. Large (>2 cm) adenoma	14%
h. Endoscopic features of possible malignancy	50%
i. Other	21%
7. Do you routinely perform biopsy sampling before resection?	
a. Yes	75%
b. No	25%
Lesion assessment and staging	
1. Do you use any kind of predefined classification system to determine if a lesion of the ampulla of Vater is most likely benign or malignant?	
a. Yes	11%
b. No	89%
2. Which of the following characteristics on endoscopic imaging do you normally take into account to determine if the lesion is benign or malignant?	
a. Presence of ulceration	100%
b. Aspect of the surface (granular vs smooth)	43%
c. Friability	61%
d. Firmness/rigidity	82%
e. Mobility	61%
f. Spontaneous bleeding	54%
g. Tumor size	57%
h. Umbilicated lesion	46%
i. Other	0%

(*continued on the next page*)

SUPPLEMENTARY TABLE 1. Continued

Question	Agreement
3. Is there a specific tumor size that would raise your suspicion of the lesion being malignant?	
a. Tumor size does not raise the suspicion of being malignant	54%
b. >1 cm	0%
c. >2 cm	18%
d. >3 cm	21%
e. >4 cm	7%
4. Do you believe any of the characteristics mentioned below is specific enough by itself to define a lesion as most likely malignant? If yes, which?	
a. Ulceration	79%
b. Smooth surface	4%
c. Excessive friability	18%
d. Firm consistency	32%
e. Immobility	36%
f. Spontaneous bleeding	14%
g. Tumor size >4 cm	14%
h. No, only a combination of the characteristics makes it possible to define a lesion as most likely malignant	21%
i. Other	4%
5. What are possible reasons to refer the patient for surgical management instead of performing endoscopic papillectomy?	
a. Jaundice (without evident signs of malignancy based on endoscopic imaging)	14%
b. Ingrowth CBD $\leq$1 cm	14%
c. Ingrowth PD $\leq$1 cm	21%
d. Ingrowth CBD >1 cm	75%
e. Ingrowth PD >1 cm	86%
f. Tumor size >4 cm	18%
g. Other	18%
6. Do you use any advanced imaging techniques to distinguish adenomatous from nonadenomatous tissue?	
a. Yes, always	29%
b. Yes, sometimes	36%
c. No, never	36%
7. Do you look for signs of central retraction, also called an umbilicated lesion?	
a. Yes, this raises the suspicion of malignancy and patient should be referred for surgical management	18%
b. Yes, but the lesion could still be removed endoscopically if there are no further signs of malignancy	75%
c. No	7%
8. Considering a fit, 70-year-old patient without any significant comorbidities, how would you treat the lesion if biopsy before resection shows only adenomatous tissue with low-grade dysplasia but endoscopic imaging shows possible signs of malignancy?	
a. Endoscopically resect the lesion based on the biopsy sample result, disregarding the endoscopic imaging. Only refer the patient for surgery if the resected specimen shows malignancy.	82%
b. Refer the patient for surgical management.	18%
9. When there is ingrowth in the CBD of more than 1 cm, would you consider endoscopic papillectomy in combination with RFA?	
a. Yes	50%
b. No, I would refer the patient for surgical treatment	50%
Technical aspects	
1. Where do you perform the resection of the lesion?	
a. At the plane of the duodenal wall	100%
b. Just above the plane of the duodenal wall	0%

(*continued on the next page*)

SUPPLEMENTARY TABLE 1. Continued

Question	Agreement
2. What type of electrosurgical current do you use most often while performing endoscopic papillectomy?	
a. Pure coagulation current	0%
b. Pure cutting current	14%
c. Fractionated current (short regular pulses of cutting current integrated in background of coagulation current)	79%
d. Other	7%
3. Do you standard use submucosal injection before endoscopic papillectomy?	
a. Yes	4%
b. No, only in case of lateral spreading	79%
c. No	18%
4. Do you routinely perform pancreatic sphincterotomy?	
a. Yes, always	14%
b. Yes, sometimes	36%
c. No, never	50%
5. When you perform pancreatic sphincterotomy do you in general perform it before or after resection? (n = 14)	
a. Before resection	0%
b. After resection	100%
6. Do you routinely place a stent in the PD to prevent postintervention pancreatitis?	
a. Yes	89%
b. Only if PD drainage is deemed suboptimal or if the PD is difficult to cannulate after the procedure	11%
c. No	0%
7. Do you cannulate the PD before or after resection?	
a. Cannulate before resection and perform the resection with guidewire inside the PD.	7%
b. Inject the PD before resection and cannulate it after resection.	43%
c. Cannulate after resection.	50%
8. What kind of PD stent do you use in general?	
a. Stent with an internal flap	46%
b. Stent without an internal flap	54%
9. Do you routinely perform biliary sphincterotomy?	
a. Yes, always	32%
b. Only in case of concomitant bile duct stones	57%
c. No, never	11%
10. When you perform biliary sphincterotomy do you in general perform it before or after resection? (n = 25)	
a. Before resection	4%
b. After resection	96%
11. Do you place a stent in the common bile duct after resection as standard practice?	
a. Yes	18%
b. No, only on indication	71%
c. No, never	11%
12. What are the indications to place a stent in the CBD after resection? (n = 20)	
a. Bleeding during the procedure	80%
b. Residual adenomatous tissue	70%
c. Concerns for microperforations after resection	80%

(*continued on the next page*)

SUPPLEMENTARY TABLE 1. Continued

Question	Agreement
d. Advanced resection	25%
e. Multiple submucosal injections	5%
f. Extensive piecemeal resection	20%
g. Other	30%
13. What type of biliary stent do you prefer if the bile duct is 8 mm in diameter? (n = 25)	
a. Plastic	72%
b. FCSEMS	28%
14. What adjunct modality do you use most commonly to remove small (<1 cm) residual tissue during index procedure after papillectomy?	
a. Cold forceps biopsy	32%
b. Argon plasma coagulation	43%
c. Monopolar/multipolar coagulation probe	4%
d. Snare tip soft coagulation	36%
e. Other	18%
15. Do you use snare tip soft coagulation of the margins after resection?	
a. Yes	0%
b. Yes, but only in case of lateral spread	25%
c. No	75%
16. Would you perform RFA when EUS shows ingrowth in the CBD of <1 cm?	
a. Yes	50%
b. No	50%
Complications and management	
1. Do you standard give rectal indomethacin/diclofenac suppository before resection to prevent postintervention pancreatitis?	
a. Yes	75%
b. No	25%
2. Do you use vigorous hydration to prevent postintervention pancreatitis?	
a. Yes	54%
b. No	46%
3. Do you routinely start patients on PPI after performing an endoscopic papillectomy?	
a. Yes	50%
b. No, only on indication	32%
c. No, never	18%
4. What are the indications to start patients on PPI after performing an endoscopic papillectomy?	
a. Excessive friability of tissue during the procedure	11%
b. Use of antithrombotic medication	33%
c. Advanced resection	67%
d. Multiple submucosal injections	0%
e. Extensive piecemeal resection	67%
f. Other	11%
5. For how long will you normally treat patients with PPI after performing an endoscopic papillectomy?	
a. 24 hours	9%
b. Between 24 hours and 2 weeks	39%
c. Between 2 weeks and 1 month	52%
d. More than 1 month	0%

(*continued on the next page*)

SUPPLEMENTARY TABLE 1. Continued

Question	Agreement
6. If bleeding occurs after endoscopic papillectomy and the patient is hemodynamic stable after resuscitation with <2 g/dL drop in hemoglobin, how would you manage it initially?	
a. Continue PPI, but no endoscopic intervention because patient is stable.	25%
b. Endoscopic reintervention to treat bleeding.	64%
c. Other	11%
Follow-up	
1. After which period would you perform the first endoscopic follow-up?	
a. 3 months	54%
b. 3-6 months	4%
c. 6 months	18%
d. 12 months	4%
e. Other	21%
2. Which follow-up interval do you use if no residual adenomatous tissue is seen at first follow-up endoscopy?	
a. 6 months	46%
b. 12 months	39%
c. >12 months	4%
d. Other	11%
3. Until when would you perform endoscopic follow-up?	
a. Up to 2 years after endoscopic papillectomy	11%
b. Up to 3 years after endoscopic papillectomy	14%
c. Up to 5 years after endoscopic papillectomy	32%
d. Up to 10 years after endoscopic papillectomy	7%
e. Lifelong, as long as patient is fit	32%
f. Other	4%
4. Do you take biopsy samples during follow-up as standard practice?	
a. Yes	36%
b. No, only when macroscopic abnormalities are present	64%
c. No, never	0%

CBD, Common bile duct; *CT*, computed tomography; *EMR*, endoscopic mucosal resection; *ERCP*, endoscopic retrograde cholangiopancreatography; *EUS*, endoscopic ultrasound; *FCSEMS,* fully covered self-expanding metal stent; *MRCP*, magnetic resonance cholangiopancreatography; *MRI*, magnetic resonance imaging; *PD,* pancreatic duct; *PPI,* proton pump inhibitor; *RFA,* radiofrequency ablation.

SUPPLEMENTARY TABLE 2. Survey round 2

Question	Agreement
Diagnostic workup	
Please fill out the order in which you believe the different diagnostic modalities should be performed for different indications (1 = first choice, 2 = only if test(s) of first choice are inconclusive, 3 = only if test(s) of second choice are inconclusive, 4 = only if test(s) of third choice are inconclusive, 5 = only if all earlier performed test(s) are inconclusive, 6 = never)	
1. In every patient	
a. CT	3 (IQR 4)
b. MRCP	2 (IQR 2)
c. EUS	2 (IQR 1)
d. Endoscopic cholangiography	4 (IQR 2)
e. Biopsy sampling	1 (IQR 0)
2. In case of jaundice	
a. CT	2 (IQR 2)
b. MRCP	2 (IQR 1)
c. EUS	2 (IQR 1)
d. Endoscopic cholangiography	3 (IQR 3)
e. Biopsy sampling	1 (IQR 0)
3. In case of cholestatic laboratory features without clinical signs of jaundice	
a. CT	2 (IQR 1)
b. MRCP	1 (IQR 1)
c. EUS	2 (IQR 1)
d. Endoscopic cholangiography	3 (IQR 2)
e. Biopsy sampling	1 (IQR 1)
4. In case of significant weight loss	
a. CT	1 (IQR 1)
b. MRCP	2 (IQR 2)
c. EUS	2 (IQR 2)
d. Endoscopic cholangiography	4 (IQR 2)
e. Biopsy sampling	1 (IQR 1)
5. In case of double duct sign on other imaging	
a. CT	2 (IQR 1)
b. MRCP	2 (IQR 1)
c. EUS	1 (IQR 1)
d. Endoscopic cholangiography	3 (IQR 2)
e. Biopsy sampling	1 (IQR 0)
6. In case patient is older than 50 years	
a. CT	2 (IQR 2)
b. MRCP	2 (IQR 2)
c. EUS	2 (IQR 1)
d. Endoscopic cholangiography	4 (IQR 2)
e. Biopsy sampling	1 (IQR 0)
7. In case of large (>2 cm) adenoma	
a. CT	2 (IQR 2)
b. MRCP	2 (IQR 1)
c. EUS	1 (IQR 1)
d. Endoscopic cholangiography	4 (IQR 2)
e. Biopsy sampling	1 (IQR 0)

(*continued on the next page*)

SUPPLEMENTARY TABLE 2. Continued

Question	Agreement
8. In case of endoscopic signs of malignancy	
a. CT	1 (IQR 1)
b. MRCP	2 (IQR 1)
c. EUS	2 (IQR 1)
d. Endoscopic cholangiography	3 (IQR 2)
e. Biopsy sampling	1 (IQR 0)
9. Do you believe pancreas divisum should be ruled out in every patient before resection?	
a. Yes	65%
b. No	35%
10. Could you please fill out in which order the following diagnostic modalities should be performed to rule out pancreas divisum before resection? (1 = first choice, 2 = only if first choice is inconclusive, 3 = only if earlier performed test(s) are found inconclusive, 4 = never)	
a. MRCP	2 (IQR 0)
b. EUS	2 (IQR 0)
c. Endoscopic cholangiography	3 (IQR 1)
11. Do you believe local extension should be ruled out in every patient before resection?	
a. Yes	53%
b. Yes, except for small (<2 cm) adenoma or in case of familial adenomatous polyposis	29%
c. No	18%
12. Could you please fill out in which order the following diagnostic modalities should be performed to rule out local extension before resection? (1 = first choice, 2 = only if first choice is inconclusive, 3 = only if earlier performed test(s) are found inconclusive, 4 = never)	
a. MRCP	2 (IQR 1)
b. EUS	1 (IQR 0)
c. Endoscopic cholangiography	2 (IQR 1)
Lesion assessment and staging	
1. When a lesion shows ulceration, this lesion should be defined as most likely malignant.	94%
2. The following characteristics are *not* a reason to define the lesion as most likely malignant	
a. Smooth surface	71%
b. Spontaneous bleeding	53%
c. Lesion size >4 cm	35%
3. You should refer a patient for surgical management in case of	
a. Ingrowth in the PD >1 cm	76%
b. Ingrowth in the CBD >1 cm	47%
4. The following situations are *not* a reason to refer the patient for surgical management	
a. Jaundice	41%
b. Ingrowth in the PD ≤1 cm	41%
c. Ingrowth in the CBD ≤1 cm	65%
d. An umbilicated lesion	53%
5. When a lesion shows ulceration, do you believe this patient should be referred for surgical management? (n = 16)	
a. Yes, regardless of possible biopsy sampling results	38%
b. Only when biopsy specimen shows HGD	63%

(*continued on the next page*)

SUPPLEMENTARY TABLE 2. Continued

Question	Agreement
6. If a patient is not a surgical candidate because of age and/or comorbidity, in which of the following situations would you still resect the lesion endoscopically?	
a. There is ingrowth of >1 cm in the CBD	59%
b. There is ingrowth of >1 cm in the PD	35%
c. The lesion shows ulceration	35%
d. Biopsy sample shows adenocarcinoma	47%
e. In none of the above described situations	29%
f. Other	0%
7. When there is ingrowth in the CBD of >1 cm, would you consider endoscopic papillectomy with RFA?	
a. In a fit 60-year-old patient	47%
b. In a patient who is not a surgical candidate because of age and/or comorbidity	76%
8. Do you believe any advanced imaging techniques (such as narrow-band imaging or chromoendoscopy) would be helpful to distinguish between benign and malignant lesions?	
a. Yes	29%
b. No	71%
9. If the biopsy sample shows LGD, which of the following characteristics would make you to refer the patient for surgical management? (0 = would not take this into account, 5 = would refer patient for surgical treatment based on the sole characteristic)	
a. Ulceration	4 (IQR 1)
b. Smooth or irregular surface	2 (IQR 2)
c. Excessive friability	1 (IQR 3)
d. Firm consistency	3 (IQR 2)
e. Immobility	4 (IQR 1)
f. Spontaneous bleeding	2 (IQR 3)
g. Tumor size >4 cm	2 (IQR 2)
10. If the biopsy sample shows HGD, which of the following characteristics would make you to refer the patient for surgical management?	
a. Ulceration	4 (IQR 1)
b. Smooth or irregular surface	3 (IQR 3)
c. Excessive friability	4 (IQR 3)
d. Firm consistency	4 (IQR 1)
e. Immobility	4 (IQR 0)
f. Spontaneous bleeding	4 (IQR 2)
g. Tumor size >4 cm	3 (IQR 2)
Technical aspects	
1. Resection of the lesion should be performed at the plane of the duodenal wall.	94%
2. Endoscopic papillectomy should be performed with fractionated current.	94%
3. Submucosal injection should only be performed in case of a laterally spreading lesion.	88%
4. If pancreatic sphincterotomy is performed, then it should be performed after resection.	88%
5. PD stent should be placed routinely to prevent postintervention pancreatitis.	100%
6. PD should be cannulated after resection.	100%
7. If biliary sphincterotomy is performed, it should be performed after resection.	100%
8. A CBD stent should only be placed on indication.	82%
9. A CBD stent should be placed in the following cases:	
a. In case of bleeding during the procedure.	76%
b. If there are any concerns for microperforations.	88%
c. In case of residual adenomatous tissue.	59%

(*continued on the next page*)

SUPPLEMENTARY TABLE 2. Continued

Question	Agreement
10. STSC of the margins after endoscopic papillectomy should *not* be performed.	65%
11. When do you believe a pancreatic sphincterotomy should be performed?	
a. Never	29%
b. In case of intrapancreatic duct extent	59%
c. In case of pancreas divisum instead of PD stent	6%
d. Other	12%
12. Do you believe it is better to inject the PD before resection to make it easier to find the PD after resection?	
a. Yes	41%
b. No	59%
13. Which kind of PD stent would you choose in the following situations?	
a. Always with an internal flap	47%
b. Always without an internal flap	35%
c. Without an internal flap, but in case of large (>2 cm) lesions	0%
d. Without an internal flap, but in case of perforation	18%
e. Without an internal flap, but after coagulation or RFA	18%
f. Other	0%
14. When would you perform biliary sphincterotomy?	
a. Always	18%
b. In case of bile duct stones	76%
c. In case of drainage is deemed suboptimal	53%
d. Other	6%
15. Which stent do you prefer in a bile duct with diameter ≤8 mm in the following cases	
a. Bleeding during the procedure	
i. Plastic	41%
ii. FCSEMS	59%
iii. No stent	0%
b. Concerns for microperforations after resection	
i. Plastic	35%
ii. FCSEMS	65%
iii. No stent	0%
c. Residual tissue	
i. Plastic	29%
ii. FCSEMS	71%
iii. No stent	0%
16. Which stent do you prefer in a bile duct with diameter >8 mm in the following cases	
a. Bleeding during the procedure	
i. Plastic	24%
ii. FCSEMS	65%
iii. No stent	12%
b. Concerns for microperforations after resection	
i. Plastic	18%
ii. FCSEMS	71%
iii. No stent	12%

(*continued on the next page*)

SUPPLEMENTARY TABLE 2. Continued

Question	Agreement
c. Residual tissue	
i. Plastic	41%
ii. FCSEMS	35%
iii. No stent	24%
17. What adjunct modalities would you consider to remove small (<1 cm) residual tissue during index procedure after papillectomy?	
a. Cold forceps biopsy sampling	65%
b. APC	53%
c. Monopolar/multipolar coagulation probe	12%
d. STSC	18%
e. Hot snare	41%
f. Cold snare	53%
g. Other	6%
18. How would you resect the lesion when EUS shows ingrowth in the CBD of <1 cm?	
a. Snare resection in combination with RFA	24%
b. Snare resection in combination with APC	35%
c. Resect intraductal residue in second procedure	47%
d. Resect intraductal residue in second procedure after placement of FCSEMS during first procedure	18%
e. Other	6%
19. Do you standardly use clips to close the defect after resection?	
a. Yes	41%
b. No	59%
20. Do you standardly give buscopan or glucagon before resection to reduce the risk of loss of specimen further in the GI tract?	
a. Yes	59%
b. No	41%
21. Would you use a different current to resect the lesion based on the size of the lesion?	
a. Large (>2 cm) lesion	
i. Pure coagulation current	0%
ii. Pure cutting current	6%
iii. Fractionated current	94%
b. Small (<2 cm) lesion	
i. Pure coagulation current	6%
ii. Pure cutting current	24%
iii. Fractionated current	71%
Complications and management	
1. Rectal indomethacin or diclofenac should be given before resection.	82%
2. If bleeding occurs during intervention, which modalities to stop the bleeding would you consider?	
a. FCSEMS	71%
b. Coagulation grasper	65%
c. Goldprobe	12%
d. Hemospray	41%
e. STSC	24%
f. APC	12%
g. Other	35%

(*continued on the next page*)

SUPPLEMENTARY TABLE 2. Continued

Question	Agreement
3. When would you start patients on PPI after performing an endoscopic papillectomy?	
a. Always	65%
b. Extensive friability of the tissue during the procedure	6%
c. Use of antithrombotic medication	0%
d. Advanced resection of large lesion	24%
e. Multiple submucosal injections	6%
f. Extensive piecemeal resection	18%
g. Never	12%
4. How long do you believe patients should be treated with PPI after resection?	
a. 24 hours	6%
b. 48 hours	0%
c. 1 week	24%
d. 2 weeks	18%
e. 3 weeks	0%
f. 1 month	47%
5. If a bleeding occurs after endoscopic papillectomy and the patient is hemodynamic stable after resuscitation with <2-g/dL drop in hemoglobin, how would you manage it initially?	
a. Expectative (continue or start PPI), no endoscopic intervention because patient is stable	41%
b. Endoscopic reintervention to treat bleeding within working hours	47%
c. Endoscopic reintervention to treat bleeding as an emergency procedure	12%
Follow-up	
1. Do you standardly admit patients for observation after endoscopic papillectomy? If yes, how long, if no complications occur?	
a. 6 hours	0%
b. 24 hours	29%
c. 48 hours	35%
d. Other	
i. No	18%
ii. >48 hours	18%
2. After which period should first follow-up be performed after presumed complete removal (excluding the removal of possible placed stents within 1-3 months)?	
a. In case initial pathology shows LGD	
i. 3 months	35%
ii. 3-6 months	29%
iii. 6 months	24%
iv. 6-12 months	12%
v. >12 months	0%
b. In case initial pathology shows HGD	
i. 3 months	76%
ii. 3-6 months	24%
iii. 6 months	0%
iv. 6-12 months	0%
v. >12 months	0%

(*continued on the next page*)

SUPPLEMENTARY TABLE 2. Continued

Question	Agreement
3. What should be the follow-up interval if no residual tissue is seen at first follow-up?	
a. In case initial pathology shows LGD	
i. 6 months	35%
ii. 12 months	53%
iii. >12 months	12%
b. In case initial pathology shows HGD	
i. 6 months	65%
ii. 12 months	35%
iii. >12 months	0%
4. Until when should endoscopic follow-up be performed?	
a. In case initial pathology shows LGD	
i. Up to 2 years	12%
ii. Up to 3 years	12%
iii. Up to 5 years	41%
iv. Up to 10 years	12%
v. Lifelong, as long as patient is fit	24%
b. In case initial pathology shows HGD	
i. Up to 2 years	12%
ii. Up to 3 years	0%
iii. Up to 5 years	47%
iv. Up to 10 years	6%
v. Lifelong, as long as patient is fit	35%
5. Should biopsy samples be taken routinely at first follow-up?	
a. In case initial pathology shows LGD	
i. Yes	29%
ii. No, only when macroscopic abnormalities are present	71%
b. In case initial pathology shows HGD	
i. Yes	35%
ii. No, only when macroscopic abnormalities are present	65%
6. Should biopsy samples be taken routinely at further follow-up?	
a. In case initial pathology shows LGD	
i. Yes	18%
ii. No, only when macroscopic abnormalities are present	82%
b. In case initial pathology shows HGD	
i. Yes	35%
ii. No, only when macroscopic abnormalities are present	65%

CBD, Common bile duct; *CT*, computed tomography; *EUS*, endoscopic ultrasound; *FCSEMS,* fully covered self-expanding metal stent; *IQR*, interquartile range; *HGD*, high-grade dysplasia; *LGD*, low-grade dysplasia; *MRCP*, magnetic resonance cholangiopancreatography; *MRI*, magnetic resonance imaging; *STSC*, snare tip soft coagulation; *APC*, argon plasma coagulation; *PD,* pancreatic duct; *PPI,* proton pump inhibitor; *RFA,* radiofrequency ablation.

SUPPLEMENTARY TABLE 3. Survey round 3

Question	Agreement
Diagnostic workup statements	
1. Gastroduodenoscopy (with side-viewing instrument) should always be performed before resection.	100%
2. Biopsy sampling should always be performed before resection.	94%
3. Either MRI/MRCP or EUS should be performed in every patient before resection.	63%
4. Either MRI/MRCP or EUS should be performed in case of cholestatic laboratory features with or without jaundice.	81%
5. Either CT, MRI/MRCP or EUS should be performed in case of cholestatic laboratory features with or without jaundice.	75%
6. CT should be performed in case of jaundice.	75%
7. Either MRI/MRCP or EUS should be performed in case of a lesion larger than 2 cm.	75%
8. Either MRI/MRCP or CT should be performed in case of significant weight loss.	81%
9. Either EUS, MRI/MRCP, or CT should be performed in case of significant weight loss.	63%
10. Either MRI/MRCP or CT should be performed in case of endoscopic signs of malignancy.	81%
11. Either CT or EUS should be performed in case of endoscopic signs of malignancy.	69%
12. Either MRI/MRCP, EUS, or CT should be performed in case of endoscopic signs of malignancy.	81%
13. An endoscopic cholangiogram either before or during endoscopic papillectomy should only be performed if other performed tests are found inconclusive and there is still doubt about the presence of intraductal extension.	44%
Lesion assessment and staging	
1. Patient should be referred for surgical management in case of ingrowth in the CBD of more than 1 cm, considering patient is suitable for surgery.	81%
2. If biopsy sample shows LGD and ulceration is present, the lesion could still be resected endoscopically; there is no need to refer the patient for surgical management based on this sole characteristic, considering the lesion seems favorable for endoscopic resection.	88%
3. If biopsy sample shows HGD and ulceration is present, the lesion could still be resected endoscopically; there is no need to refer the patient for surgical management based on this sole characteristic, considering the lesion seems favorable for endoscopic resection.	63%
4. If there is ingrowth in the CBD of more than 1 cm, endoscopic resection can still be considered if the patient is not a surgical candidate because of age and/or comorbidity, considering the lesion seems favorable for endoscopic resection.	81%
5. If biopsy sample shows adenocarcinoma in situ or well-differentiated adenocarcinoma, endoscopic resection can still be considered if the patient is not a surgical candidate because of age and/or comorbidity, considering the lesion seems favorable for endoscopic resection.	75%
6. If there is ingrowth in the CBD of more than 1 cm, endoscopic papillectomy with RFA should *not* be performed in a fit 60-year-old patient.	44%
7. If there is ingrowth in the CBD of more than 1 cm, endoscopic papillectomy with RFA can be considered in a patient that is not a surgical candidate because of age and/or comorbidity, considering the lesion seems favorable for endoscopic resection.	75%
Technical aspects	
1. Snare tip soft coagulation of the margins should *not* be performed after endoscopic papillectomy.	56%
2. Snare tip soft coagulation can be performed for the margins of the laterally spreading component, but not the papillary margins.	50%
3. Pancreatic sphincterotomy after resection should only be performed in case of extension in the pancreatic duct.	38%
4. Pancreatic sphincterotomy after resection should be performed in case of extension in the pancreatic duct or if drainage is deemed suboptimal.	44%
5. It can be helpful to inject the PD before resection to make it easier to find the PD after resection in case of extension in the pancreatic duct.	44%
6. Biliary sphincterotomy should be performed only in case of concomitant bile duct stones.	44%
7. Biliary sphincterotomy should be performed in case of concomitant bile duct stones and in case drainage is deemed suboptimal.	81%
8. In case there is bleeding during the procedure, an FCSEMS instead of a plastic stent should be placed in the CBD.	63%
9. In case there are concerns for microperforations in the papillary region, an FCSEMS should be placed in the CBD.	88%

(*continued on the next page*)

SUPPLEMENTARY TABLE 3. Continued

Question	Agreement
10. In case there are concerns for residual adenomatous tissue in the distal part of the CBD, an FCSEMS should be placed in the CBD.	31%
11. In case there are concerns for residual adenomatous tissue in the distal part of the CBD, either a plastic stent or FCSEMS should be placed in the CBD.	44%
12. Please rank the following items in which order you would consider them if there is ingrowth in the CBD of <1 cm, which seems accessible from the duodenum. (1 = first choice, 5 = never)	
a. Snare resection in combination with RFA	2 (IQR 1.5)
b. Snare resection in combination with APC	3 (IQR 3.25)
c. Resect intraductal residue in second procedure after placement of FCSEMS during first procedure	3 (IQR 1.25)
d. Resect with snare inside duct	2.5 (IQR 2.25)
13. Standard clip closure of the mucosal defect after resection should *not* be performed.	38%
14. Glucagon or buscopan should be provided routinely before resection to reduce the risk of losing the specimen into the GI tract.	56%
Adverse events and management	
1. Vigorous hydration should be considered in patients without any cardiologic comorbidity to further decrease the risk of postintervention pancreatitis.	63%
Please rank the following methods in which order you would consider them to use in case of intraprocedural bleeding in the following hypothetical situations (1 = first choice, 6 = never)	
2. In case of bleeding from the papillectomy site (not from lateral spreading component) considering the PD is already protected by a stent.	
a. FCSEMS	3.5 (IQR 1.5)
b. Hemospray	5 (IQR 2)
c. Epinephrine	2 (IQR 1.25)
d. Clips	3 (IQR 1)
e. Coagulation probe (or other instrument used to coagulate)	2 (IQR 1)
3. In case of bleeding from the papillectomy site (not from lateral spreading component) however the PD is not yet protected by a stent.	
a. FCSEMS	4 (IQR 2.25)
b. Hemospray	4 (IQR 3)
c. Epinephrine	1 (IQR 1)
d. Clips	3 (IQR 3.25)
e. Coagulation probe (or other instrument used to coagulate)	2 (IQR 2)
4. In case of bleeding from the lateral spreading component.	
a. FCSEMS	5.5 (IQR 1)
b. Hemospray	4 (IQR 2)
c. Epinephrine	2 (IQR 2)
d. Clips	2.5 (IQR 2)
e. Coagulation probe (or other instrument used to coagulate)	2 (IQR 1)
5. Every patient should be treated with PPI after performing an endoscopic papillectomy.	69%
6. Patients treated with PPI after resection should be treated for at least 2 weeks.	69%
7. Patients treated with PPI after resection should be treated for at least 1 month.	56%
8. If a bleeding occurs after endoscopic papillectomy and the patient is hemodynamic stable after resuscitation with <2-g/dL drop in hemoglobin, reintervention should be performed within 12 hours.	38%
9. If a bleeding occurs after endoscopic papillectomy and the patient is hemodynamic stable after resuscitation with <2-g/dL drop in hemoglobin, conservative treatment (continue or start PPI) is initially indicated.	63%

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SUPPLEMENTARY TABLE 3. Continued

Question	Agreement
Follow-up	
1. Every patient should be admitted for at least 24 hours for observation after endoscopic papillectomy.	69%
2. Every patient should be admitted for at least 48 hours for observation after endoscopic papillectomy.	44%
3. In case initial pathology shows LGD	
a. First follow-up (after removal of possible placed stents) should be performed within 6 months.	81%
b. First follow-up (after removal of possible placed stents) should be performed within 3 months.	56%
c. At first follow-up biopsy samples should only be taken when macroscopic abnormalities are present.	94%
d. Follow-up interval should be 12 months or less.	88%
e. Follow-up interval should be 6 months or less.	38%
f. At further follow-up biopsy samples should only be taken when macroscopic abnormalities are present.	94%
g. Follow-up should be performed for at least 5 years.	81%
h. Follow-up should be performed lifelong, as long as patient is fit.	31%
4. In case initial pathology shows HGD	
a. First follow-up (after removal of possible placed stents) should be performed within 6 months.	31%
b. First follow-up (after removal of possible placed stents) should be performed within 3 months.	94%
c. At first follow-up biopsy samples should only be taken when macroscopic abnormalities are present.	81%
d. Follow-up interval should be 12 months or less.	25%
e. Follow-up interval should be 6 months or less.	94%
f. At further follow-up biopsy samples should only be taken when macroscopic abnormalities are present.	81%
g. Follow-up should be performed for at least 5 years.	75%
h. Follow-up should be performed lifelong, as long as patient is fit.	38%

CBD, Common bile duct; *CT*, computed tomography; *EUS*, endoscopic ultrasound; *MRCP*, magnetic resonance cholangiopancreatography; *MRI*, magnetic resonance imaging; *FCSEMS,* fully covered self-expanding metal stent; *HGD*, high-grade dysplasia; *LGD*, low-grade dysplasia; *STSC*, snare tip soft coagulation; *APC*, argon plasma coagulation; *PD,* pancreatic duct; *PPI*, proton pump inhibitor; *RFA,* radiofrequency ablation.