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Endoscopic papillectomy: Indications, techniques, and results

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Abstract

Endoscopic papillectomy (EP) is currently accepted as a viable alternative therapy to surgery in sporadic ampullary adenoma and has been reported to have high success and low recurrence rates. At present, the indications for EP are not yet fully established. The accepted criteria for EP include size (up to 5 cm), no evidence of intraductal growth, and no evidence of malignancy on endoscopic findings (ulceration, friability, and spontaneous bleeding). Endoscopic ultrasound (EUS) is the imaging modality of choice for local T staging in ampullary neoplasms. Data reported in the literature have revealed that linear EUS is superior to helical computed tomography in the preoperative assessment of tumor size, detection of regional nodal metastases and detection of major vascular invasion. Endoscopic ampullectomy is performed using a standard duodenoscope in a similar manner to snare polypectomy of a mucosal lesion. There is no standardization of the equipment or technique and broad EP methods are described. Endoscopic ampullectomy is considered a "high-risk" procedure due to complications. Complications of endoscopic papillectomy can be classified as early (pancreatitis, bleeding, perforation, and cholangitis) and late (papillary stenosis) complications. The appropriate use of stenting after ampullectomy may prevent post-procedural pancreatitis and papillary stenosis. Tumor recurrence of benign lesions occurs in up to 20% of patients and depends on tumor size, final histology, presence of intraductal tumor, coexisting familial adenomatous polyposis (FAP), and the expertise of the endoscopist. Recurrent lesions are usually benign and most can be retreated endoscopically.

Key words: Endoscopic papillectomy; Papillary neoplasms; Major duodenal papilla; Endoscopic retrograde cholangiopancreatography; Endoscopic sphincterotomy

Core tip: Endoscopic papillectomy is a relatively safe and effective therapy and should be established as a first-line therapy for adenomas of the major duodenal papilla. Accurate staging of the tumor is important in the selection of patients. Performed by experienced endoscopists leads to successful tumor eradication in over 85% of patients with ampullary adenomas.

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INTRODUCTION

Endoscopic papillectomy (EP) was first reported by Suzuki *et al*[1]. Endoscopic papillectomy is currently accepted as a viable alternative therapy to surgery in sporadic ampullary adenoma and has been reported to have high success and low recurrence rates.

In the present report, several issues relating to EP

were assessed: indications, optimal papillectomy technique, complications, and results.

DEFINITION

The term "endoscopic papillectomy" refers to resection of the mucosa and submucosa of the duodenal wall, in the area of the anatomical attachments of the ampulla of Vater, including the tissue around the bile duct and the pancreatic-duct orifices.

Endoscopic papillectomy differs from surgical "ampullectomy" which consists of resection of the ampulla of Vater, *via* a duodenotomy, including resection of pancreatic-head tissue, followed by separate reinsertion of the common bile duct and main pancreatic duct into the duodenal wall.

INDICATIONS

The most critical point in EP is assessment of the indication. At present, the indications for EP are not yet fully established. These could be dictated by the collection of features that can predict complete removal of a lesion, while minimizing procedure-related morbidities.

The accepted criteria for EP include size (up to 5 cm), no evidence of intraductal growth, and no evidence of malignancy on endoscopic findings (ulceration, friability, and spontaneous bleeding)[2-9].

The indications for EP are evolving[10-16]. The application of piecemeal resection when appropriate, resulted in a gradual increase in the size of the tumor resected[17]. Intraductal extension less than 1 cm does not seem to be an absolute contraindication for EP, because the tumor can be exposed to the luminal side with balloon sweeping and, thus, resected completely[18-20]. Cancer in adenoma without invasion of the muscularis propria of the duodenum, pancreas, or extension along the bile or pancreatic duct is also a possible indication for this treatment[21-25].

It is important to note that, on some occasions, EP may be indicated as a total biopsy[26].

PRE-OPERATIVE ASSESSMENT

A common pre-operative problem is achieving a reliable distinction between benign and malignant papillary tumors.

On the basis of endoscopic appearance alone, ampullary adenomas cannot always be distinguished from ampullary carcinomas or non-adenomatous polyps (carcinoid tumors, gangliocytic paragangliomas, *etc.*)[27-29]. Ulceration, friability, and spontaneous bleeding are generally related to malignant lesions. The increased application of magnifying endoscopy and narrow-band imaging can assist in selecting candidates for endoscopic therapy[30,31].

A definitive tissue diagnosis is a prerequisite for appropriate management, but malignancy may be missed in up to 30% of tumors in the major duodenal papilla when forceps biopsy specimens are obtained[32-34]. Moreover, the coexistence of carcinoma within adenoma cannot be excluded by pre-procedural biopsy. Some authors advocate deeper biopsy after sphincterotomy for accurate diagnosis of endoscopic biopsy[35]. A prospective study, however, reported that sensitivity was found to be 21% before and 37% after sphincterotomy, concluding that endoscopic forceps biopsies do not allow for reliable preoperative diagnosis of ampullary tumors[36]. Thus, in some cases, endoscopic papillectomy can be recommended as a diagnostic tool prior to surgery, due to the high false-negative rate of biopsy[26].

STAGING

Endoscopic ultrasound (EUS) is the imaging modality of choice for local T staging. Data reported in the literature have revealed that linear EUS is superior to helical Computed tomography (CT) in the preoperative assessment of tumor size, detection of regional nodal metastases and detection of major vascular invasion in patients with periampullary malignancies[37-43].

Many experts agree that lesions less than 1 cm in diameter without suspicious signs of malignancy (ulceration, induration, bleeding and or biopsies showing high-grade dysplasia or carcinoma), do not require EUS, but this needs further prospective study and validation[9]. Intraductal ultrasound (IDUS) using a 20 MHz frequency probe may be more accurate in visualizing the mucosal layers compared with standard echoendoscopes[44-47].

EUS/IDUS are able to accurately detect involvement of the bile and pancreatic ducts. Tumor extension into either ductal system can also be assessed by endoscopic retrograde cholangiopancreatography (ERCP). This should be performed before ampullectomy if EUS is not available or the findings on EUS are equivocal. Although the presence of intraductal extension of tumor generally indicates the need for surgery, it has been shown that tumor extension of ± 1 cm into the common bile duct or pancreatic duct can be further resected and ablated endoscopically[18-20].

CT scan, magnetic resonance imaging (MRI), and positron emission tomographic scans are highly sensitive for the detection of distant metastases. In the assessment of nodal involvement, MRI has been found to be superior to both CT and endoscopic ultrasound[38].

TECHNIQUE

Endoscopic ampullectomy is performed using a standard duodenoscope in a similar manner to snare polypectomy of a mucosal lesion. There is no standardization of the equipment or technique and broad EP methods are described. There are also no guidelines regarding the power output and the mode of electrosurgical current (cutting or coagulation), the use of adjunctive interventions, such as submucosal injection, post-ampullectomy ablative therapy, and prophylactic stent placement. The need for prophylactic antibiotics prior to ampullectomy has not

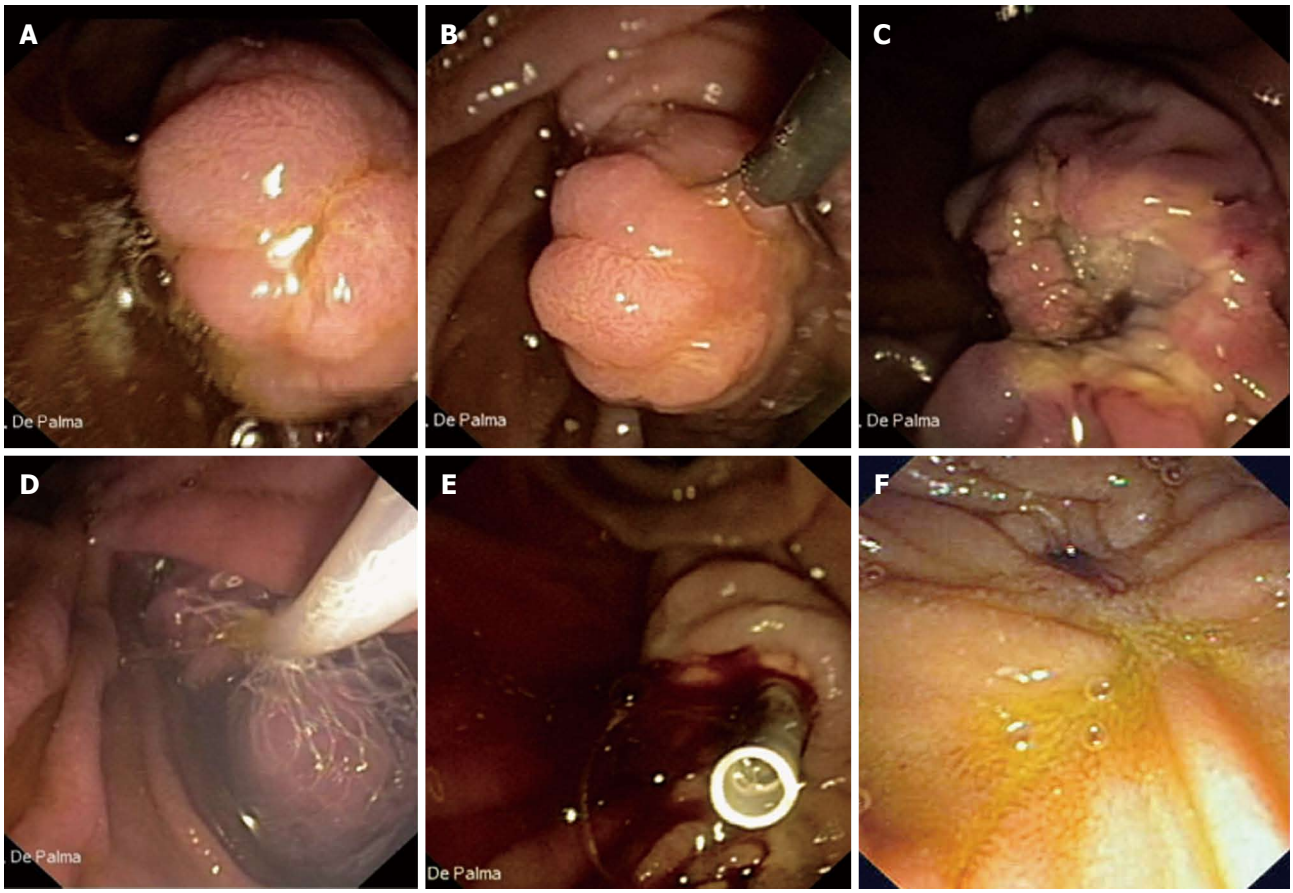

Figure 1 Aggressive efforts to retrieve all resected tissue in all patients for histopathologic evaluation are mandatory. A: Endoscopic view of a 3 cm neoplastic lesion of the major papilla; B: The lesion is entirely entrapped by the endoscopic snare; C: The lesion is completely resected (*en-bloc* resection); D: The resected specimen is retrieved by a Roth Net® device (US Endoscopy, Mentor, OH, United States); E: A plastic stent is implanted into the main pancreatic duct to prevent post-papillectomy pancreatitis; F: Duodenal view 6 mo after papillectomy. No evidence of recurrent disease is observed.

been established[48].

The procedure starts with cannulation of both the bile duct and pancreatic duct, and the ducts are partially filled with contrast to ensure easy recannulation after the major papilla is resected. To preserve access to the pancreatic duct, some experts have included methylene blue in the contrast injected into the pancreatic duct to assist in identifying the pancreatic orifice.

Once delineation of the biliary and pancreatic ducts has been made a standard polypectomy snare and blended electrosurgical current (50-60 J) are generally used. The papillary tumor is snared at the base, and constant tension is applied to the snare loop during electrosurgery until the lesion is transected. Aggressive efforts to retrieve all resected tissue in all patients for histopathologic evaluation are mandatory (Figure 1).

Balloon-catheter-assisted papillectomy has also been advocated to facilitate *en bloc* resection mainly of flat papillary tumors[18,19].

For lesions which are not resectable "*en bloc*", piecemeal polypectomy is recommended. However, *en bloc* resection is fundamental in the treatment of neoplastic lesions, because this allows more precise histopathologic evaluation of the resection specimen[19,49].

Submucosal injection of dilute epinephrine is suggested as a means of lifting the tumor from the wall; this may also decrease the risk of bleeding. It is uncertain, however, whether epinephrine injection reduces the risk of bleeding and perforation[11,20,50].

If residual neoplastic tissue remains after snare excision this should be destroyed. Argon plasma coagulation is the most frequently used modality due to the non-contact approach that limits the depth of tissue injury[9,48,50,51].

Many authorities suggest that placement of a pancreatic stent reduces the risk of papillectomy-related pancreatitis, minimizes the risk of stenosis of the pancreatic duct orifice and allows safer use of adjunctive coagulative therapies, however, this theory is unproven. Others advocate pancreatic stent placement only if the pancreatic duct does not drain after papillectomy[52-55]. The only prospective, randomized, controlled trial to evaluate the role of prophylactic pancreatic duct stenting for the reduction of post-ERCP pancreatitis after endoscopic papillectomy showed a statistically significant decrease in the rate of post-procedure pancreatitis in the stent group[56]. There are no data on the length of the duct to be stented. Most pancreatic stents will spontaneously migrate out of the pancreatic duct within 2 wk of insertion. This is confirmed by an abdominal X-ray at 2 wk. A stent that remains *in situ* is removed endoscopically.

Table 1 Outcomes after endoscopic papillectomy

Ref.	Patients	Successful resection	Complications	Mortality	Recurrence	Need for surgery
Binmoeller *et al*[2]	25	23	5	0	6	3
Vogt *et al*[72]	18	12	4	0	6	NA
Zádorová *et al*[5]	16	13	4	0	3	1
Desilets *et al*[50]	13	12	1	0	0	1
Norton *et al*[51]	26	12	5	0	2	1
Bohnacker *et al*[20]	87	74	29	0	15	17
Catalano *et al*[7]	103	83	10	0	10	16
Cheng *et al*[8]	55	39	12	0	9	4
Han *et al*[10]	33	20	11	0	2	2

NA: Not available.

Prophylactic biliary stenting to reduce the risk of post-procedural cholangitis has not been widely performed and cannot be uniformly recommended at this time unless there is concern about inadequate biliary drainage after a papillectomy[2,8,50,57].

COMPLICATIONS

Endoscopic ampullectomy is considered a "high-risk" procedure due to complications. Complications of endoscopic papillectomy can be classified as early (pancreatitis, bleeding, perforation, and cholangitis) and late (papillary stenosis) complications.

The overall rate of complications after ampullectomy reported from large, tertiary care referral centers varies between 8% and 35%, with the most common complications being pancreatitis (5%-15%) and bleeding (2%-16%)[14,17,51,58-61]. Most bleeding episodes can be controlled by conservative management and endoscopic hemostasis. Most post-procedural pancreatitis episodes are mild and resolve with conservative management only. Late complications include the development of pancreatic or biliary stenosis (0%-8%) and can be treated with sphincterotomy, stents, and balloon dilation. The appropriate use of stenting after ampullectomy may prevent post-procedural pancreatitis and papillary stenosis[52-57]. As evidenced by a recent randomized trial, prophylactic rectal indomethacin significantly reduces the incidence and severity of post-ERCP pancreatitis providing an incremental benefit over temporary pancreatic stents[62].

Mortality after endoscopic ampullectomy is rare, but has been reported to be 0.4% (range 0%-7%) on average[63].

OUTCOMES

The results of endoscopic treatment of ampulla tumors reported in the literature are shown in Table 1. Outcome data of endoscopic ampullectomy are based on retrospective, heterogeneous case series. Because there is no consensus on the definition of "success" after endoscopic papillectomy, it is difficult to compare the outcome of the reported studies. Conventionally, "success" may be defined as complete resection of the tumor with endoscopic papillectomy (as the absence of endoscopically visible and histologically proven residual adenoma during a follow-up period of 3 to 6 mo).

Recurrence of benign lesions occurs in up to 20% of patients and depends on tumor size, final histology, presence of intraductal tumor, coexisting FAP, and the expertise of the endoscopist[14,63-71]. Recurrent lesions are usually benign and most can be retreated endoscopically.

CONCLUSION

Endoscopic papillectomy is a relatively safe and effective therapy and should be established as a first-line therapy for adenomas of the major duodenal papilla. Accurate staging of ampullary tumors is important in the selection of appropriate candidates for endoscopic or surgical therapy. Compared with surgery, endoscopic ampullectomy is associated with lower morbidity and mortality, and appears to be a preferred treatment modality for small benign ampullary tumors that have no intraductal extension. Endoscopic ampullectomy performed by experienced endoscopists leads to successful tumor eradication in over 85% of patients with ampullary adenomas.

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