

The role of endoscopy in ampullary and duodenal adenomas

Prepared by: ASGE STANDARDS OF PRACTICE COMMITTEE

Krishnavel V. Chathadi, MD, Mouen A. Khashab, MD, Ruben D. Acosta, MD, Vinay Chandrasekhara, MD, Mohamad A. Eloubeidi, MD, MHS, FASGE, Ashley L. Faulx, MD, FASGE, Lisa Fonkalsrud, BSN, RN, CGRN, Jenifer R. Lightdale, MD, MPH, FASGE, John R. Saltzman, MD, FASGE, Aasma Shaukat, MD, MPH, FASGE, Amy Wang, MD, Brooks D. Cash, MD, FASGE, Previous Committee Chair, John M. DeWitt, MD, FASGE, Chair

This document was reviewed and approved by the Governing Board of the American Society for Gastrointestinal Endoscopy.

This is one of a series of statements discussing the use of GI endoscopy in common clinical situations. The Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy (ASGE) prepared this text. In preparing this guideline, a search of the medical literature was performed by using PubMed from January 1980 through December 2013 by using the keyword(s) "ampulla AND adenoma," "ampullary adenoma," "duodenal adenoma," "papilla AND adenoma," "gastrointestinal endoscopy," "endoscopy," "endoscopic procedures," and "procedures." The search was supplemented by accessing the "related articles" feature of PubMed, with articles identified on PubMed as the references. Pertinent studies published in English were reviewed. Additional references were obtained from the bibliographies of the identified articles and from recommendations of expert consultants. When little or no data existed from well-designed prospective trials, emphasis was given to results from large series and reports from recognized experts. Guidelines for appropriate use of endoscopy were based on a critical review of the available data and expert consensus at the time the guidelines were drafted. Further controlled clinical studies may be needed to clarify aspects of this guideline. This guideline may be revised as necessary to account for changes in technology, new data, or other aspects of clinical practice. The recommendations were based on reviewed studies and were graded on the strength of the supporting evidence by using the GRADE criteria¹ (Table 1).

This guideline is intended to be an educational device to provide information that may assist endoscopists in providing care to patients. This guideline is not a rule and should not be construed as establishing a legal standard of care or as encouraging, advocating, requiring, or discouraging any particular treatment. Clinical

decisions in any particular case involve a complex analysis of the patient's condition and available courses of action. Therefore, clinical considerations may lead an endoscopist to take a course of action that varies from these guidelines.

AMPULLARY ADENOMAS

Adenomas of the major duodenal papilla, also known as *ampullary adenomas*, can occur sporadically or in the context of genetic syndromes such as familial adenomatous polyposis (FAP). These lesions have the potential to undergo malignant transformation to ampullary cancer, and their clinical significance extends beyond the need to treat any associated symptoms. Endoscopic screening and surveillance of high-risk patients, such as those with FAP, also has led to increasing recognition of ampullary adenomas.²⁻⁶ Ampullary adenomas have historically been treated surgically. Surgical options have traditionally included pancreaticoduodenectomy (the Whipple procedure) or transduodenal ampullectomy (which can occasionally leave behind residual adenomatous tissue).⁷⁻⁹ Although surgical management often allows complete removal, it is associated with morbidity, including postoperative anastomotic dehiscence and fistulae in up to 9% and 14% of patients, respectively, and mortality rates ranging from 1% to 9%.¹⁰⁻¹² Endoscopic approaches to the evaluation and treatment of ampullary adenomas have developed considerably in recent years, and these techniques now represent a viable alternative to surgical therapy in select cases.^{13,14} The management of ampullary adenomas in the setting of FAP has been addressed in a previous American Society for Gastrointestinal Endoscopy (ASGE) guideline.¹⁵

Evaluation of ampullary lesions before endoscopic therapy

A side-viewing duodenoscope is generally required for optimal visualization of the papilla; however, adenomatous change of the papilla may not be apparent by visual

TABLE 1. GRADE system for the quality of evidence for guidelines

Quality of evidence	Definition	Symbol
High	Further research is very unlikely to change our confidence in the estimate of effect.	⊕⊕⊕⊕
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.	⊕⊕⊕○
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.	⊕⊕○○
Very low	Any estimate of effect is very uncertain.	⊕○○○

GRADE, Grading of Recommendations Assessment, Development and Evaluation.
Adapted from Guyatt et al.¹

inspection alone. Furthermore, ampullary adenomas may not be distinguishable from ampullary carcinomas or non-adenomatous polyps such as carcinoid tumors or gangliocytic paragangliomas.^{16,17} Therefore, biopsy specimens from suspicious ampullary lesions are recommended and should be obtained before proceeding with attempted endoscopic resection to both confirm the diagnosis and exclude a focus of cancer. Pancreatitis has been reported after biopsies of the papilla, and, therefore, care should be taken to obtain tissue away from the pancreatic duct orifice.¹⁸

Diagnostic (adenoma and carcinoma diagnosis) rates for ampullary biopsies of 45% to 80% have been reported, with false-negative results in 16% to 60% of patients with carcinoma.^{9,19-26} The rate of false-negative biopsies may be minimized by sampling within 10 days after sphincterotomy^{27,28} or obtaining at least 6 biopsy specimens.²⁹ Biopsy of flat lesions that involve more than 1 fold can result in submucosal fibrosis, potentially impeding subsequent endoscopic resection. Orienting the forceps parallel to the folds while taking the tissue gently from between the folds may decrease the risk of subsequent fibrosis.¹³

Brush cytology may aid detection of ampullary malignancy in selected cases.³⁰⁻³⁴ Other techniques such as polymerase chain reaction analysis of DNA for *K-ras* gene mutations,³⁵⁻³⁷ immunohistochemical staining (for the p53 tumor suppressor gene and other panels composed of CK7, CK20, CDX2, MUC1, and MUC2),³⁸⁻⁴² microRNA expression,⁴³ and assessment of aneuploidy by flow cytometry have been suggested for use in clinical practice but currently remain investigational.

There is no consensus on which ampullary adenomas should undergo surveillance or resection with endoscopy or surgery. Lesions with high-grade dysplasia usually warrant therapy to prevent progression to malignancy and also to exclude malignancy missed on biopsy.^{44,45} Several authors have advocated that endoscopic resection should be performed only in patients without evidence of invasive cancer.⁴⁶⁻⁵¹ Although endoscopic removal of ampullary adenocarcinoma has been described, this cannot be endorsed for routine management.^{52,53}

There are no definitive guidelines regarding the size or diameter above which endoscopic removal of ampullary

adenomas should not be attempted. Many authors recommend that lesions ≥ 4 cm not be treated endoscopically, although there are reports of successful endoscopic resection of ampullary lesions of greater size.⁴⁵⁻⁴⁸ The size of the lesion, however, can affect the endoscopic approach to resection, as discussed later.

Endoscopic features such as firmness, ulceration, nonlifting of the periampullary component with submucosal injection, and friability suggest possible malignancy, and such lesions should be considered for surgical excision even in the absence of malignancy on biopsy specimens.⁴⁸ Failure to obtain an adequate lift to achieve a cleavage plane for resection was the strongest predictor of malignancy in one study.⁵⁴

Imaging: role of ERCP and EUS

ERCP, EUS, and intraductal US can provide useful information in the assessment of ampullary adenomas. They permit assessment of the degree (if any) of intraductal extension of the adenoma. EUS and intraductal US also may identify malignancy and permit evaluation of its extension beyond the muscularis propria, thus allowing triage of patients to endoscopic or surgical therapy. EUS has been shown to be superior to CT, magnetic resonance imaging, or transabdominal US for tumor staging.^{55-62,66} Magnetic resonance imaging has been found to be superior to EUS for nodal staging for these patients, whereas CT scans and positron emission tomography scans can detect small metastases not seen on EUS or intraductal US.^{59,60} One prospective study comparing EUS, intraductal US, and CT scans found that tumor visualization was superior with intraductal US (100%) compared with EUS (59%) and CT (30%).⁶³ The overall accuracy of intraductal US for tumor diagnosis was superior to that of EUS (88.9% vs 56.3%; $P = .05$). However, another study found that intraductal US may overestimate tumor staging for ampullary neoplasms.⁶⁴

It is uncertain whether all patients with ampullary adenomas should undergo EUS before therapy. Some experts propose that lesions < 1 cm in diameter or those that do not have obvious signs of malignancy (ulceration, induration, bleeding) do not require US evaluation before endoscopic removal.⁶⁵ If available, EUS examination should be

considered for larger lesions or those with features concerning for malignancy before endoscopic or surgical resection is performed.

ERCP with both biliary and pancreatic duct evaluation should be performed at the time of endoscopic resection to assess for evidence of extension into either ductal system. Ductography is particularly important if EUS was not performed or did not evaluate for any ductal extension of the neoplasm. Both modalities perform similarly in evaluating intraductal extension of ampullary adenomas.⁶⁶ Several authors have used evidence of intraductal extension as a criterion for surgical referral.⁶⁷⁻⁶⁹ Other investigators have shown that <1 cm of extension into the common bile duct or pancreatic duct does not preclude endoscopic therapy because tissue invading to this level may be endoscopically exposed and ablated.^{54,70} Balloon dilation or balloon catheters may facilitate endoscopic resection of intraductal extension of ampullary adenomas by exposing or inverting involved tissue.^{71,72}

Addition of chromoendoscopy agents may aid in enhancing endoscopic visualization of adenoma margins. Chromoendoscopy with nonabsorptive dye such as indigo carmine also can be used to avoid incomplete resection, especially when the margins of a flat lesion are difficult to discern.^{13,73}

Endoscopic resection techniques

Techniques of endoscopic removal of ampullary adenomas remain nonstandardized likely because of the small number of formal investigations of this practice. The term *ampullectomy* refers to removal of the entire ampulla of Vater and is a surgical term for procedures that require surgical reimplantation of the distal common bile duct and pancreatic duct within the duodenal wall. Technically, when endoscopic resection of lesions at the major papilla are performed, only tissue from the papilla can be removed endoscopically, and thus the term *papillectomy* is more appropriate than the term *ampullectomy*, although the 2 often are used interchangeably in the literature.⁷⁴

Submucosal injection

Several authors have used submucosal injection immediately before endoscopic papillectomy in a manner similar to that used before performing EMR. The failure of a lesion to manifest a lift sign is associated with malignancy and is considered a contraindication to attempted complete endoscopic resection (although further endoscopic therapy could be performed as a form of palliation in a poor operative candidate).⁵⁴ Fluids injected into the submucosa have included saline solution, epinephrine, and viscous materials such as hydroxypropyl methylcellulose.^{48,54,75-77} Volumes of injected fluid are not standardized and vary widely among published studies. It is important to note that ampullary lesions are tethered down by the biliary and pancreatic ducts and may not lift with submucosal

injection. In addition, the surrounding normal mucosa that does lift may “mushroom” around the ampullary adenoma. This mushroom may partially depress the central aspect of the tumor, which may preclude adequate snare placement and complete excision.²⁵ Some authors have not used submucosal injection, and currently there are insufficient data to conclude that this is a mandatory step in the procedure.^{65,67,68} Recently, a novel technique of “underwater” EMR without submucosal injection has been reported for the resection of ampullary adenomas and sporadic laterally spreading–non ampullary duodenal adenomas, wherein water submersion floats the adenoma for ensnarement.^{78,79}

Endoscopic resection

Endoscopic papillectomy generally is performed with a duodenoscope and endoscopic snares and electrocautery. In most reports, standard “braided” polypectomy snares have been used, although fine-wire snares, specifically designed for ampullary resection, are available.^{48,67,75} There is no evidence of superiority of one type of snare over another. Snare position during papillectomy is also nonstandardized; investigators have described snare placement oriented in both a cephalad to caudal or caudal to cephalad orientation. However, the majority of published series have not specifically commented on the orientation of the snare during papillectomy.^{54,65,67,80} Use of a larger-channel therapeutic duodenoscope allows easier passage of snares and thermal ablation probes and also facilitates aspiration of insufflated air and argon gas when instruments are present in the channel.

If the lesion can be ensnared completely, en bloc resection with electrocautery should be performed. En bloc resection has the advantages of potentially shortening the procedure time, requiring less cautery, and providing a complete tissue sample for pathology evaluation. This method also minimizes the likelihood of encountering subsequent residual neoplasia within submucosal fibrosis (which may prove difficult to treat) at follow-up procedures.¹³ However, a pancreatic stent (to ensure duct drainage) is not placed before en bloc resection because the snare would have to transect the stent for resection of the papilla. It then can be difficult to identify the main pancreatic duct orifice for stent placement after resection. Pancreatic duct identification after resection may be facilitated by injecting methylene blue into the pancreatic duct before en bloc resection.⁸¹ Recent publications have described a modified specimen retrieval technique to permit easier pancreatic stent placement before papillectomy. This technique uses standard snare papillectomy over an insulated wire or stent placed in the pancreatic duct. Retrieval of the specimen is facilitated by perpendicular needle-knife incision of the snared specimen to release it from the wire or stent.^{82,83}

Piecemeal resection with electrocautery often is performed for lesions >2 cm or for cases in which visible

neoplastic tissue remains after attempted en bloc resection. Piecemeal resection may produce electrocautery-related injury to tissue fragments sent for pathology analysis and may require repeated submucosal injections to achieve sustained elevation of adenomatous tissue. Larger lesions may require multiple endoscopic procedures to be removed completely. Most published series report using a combination of en bloc and piecemeal resection techniques because the types of lesions treated were of variable size and morphology.^{27,46,68,77,84,85} Use of a balloon-tipped catheter to expose adenomas extending intraductally, permitting complete endoscopic resection, has been described.^{71,72}

Regardless of the endoscopic technique used, resected specimens should be retrieved immediately to decrease the likelihood of specimen migration in the distal small bowel from peristalsis and air insufflation. Some experts use glucagon to reduce peristalsis during the procedure. Care should be taken not to aspirate the specimen through the accessory channel into a trap because this can lead to fragmentation.

Electrocautery settings

There is no consensus on which type of current should be used during endoscopic papillectomy. Both pure cutting current and blended current have been used, and neither can be advocated over the other at this time. Power settings are also nonstandardized.^{46,67-69,85,86}

Pancreatic and/or biliary sphincterotomy

Given the potential for significant tissue injury to the pancreatic and biliary orifices during endoscopic removal of ampullary adenomas, pancreatic and/or biliary sphincterotomies often are performed during papillectomy. These may assist in providing pancreaticobiliary drainage after papillectomy and facilitate attempts to access the common bile duct and pancreatic duct for stent placement, and they may ease postprocedure surveillance. There is no consensus as to whether these maneuvers should be performed.^{54,65,69,75,85,87}

Pancreatic and/or biliary stenting

Endoscopic papillectomy is associated with an increased risk of postprocedural pancreatitis. Several studies have shown that placement of a prophylactic pancreatic duct stent reduces the risk of post-ERCP pancreatitis.⁸⁸ It also has been implied that placement of a pancreatic stent during endoscopic papillectomy may minimize the risk of stenosis of the pancreatic duct orifice and may allow safer use of adjunctive coagulative therapies.^{45,48,68,75,86} A recent retrospective study of 82 patients, however, suggested that routine pancreatic duct stenting may not be necessary.⁸⁹ Others have suggested that pancreatic duct stents should be used only if pancreatic duct drainage is deemed suboptimal or if the pancreatic duct is difficult to cannulate after the procedure.^{46,54,69} Pancreatic

duct stent placement typically is performed after papillectomy and may be facilitated by wire-guided papillectomy.⁸³

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 postprocedural pancreatitis in the stent group, although only 19 patients were enrolled in the trial.⁸⁷ On the basis of this and nonrandomized data,^{88,90} prophylactic pancreatic duct stenting during papillectomy is recommended to reduce the risk of postprocedural pancreatitis. Recently, both temporary pancreatic duct stenting and rectal indomethacin were shown to lower the risk and severity of post-ERCP pancreatitis in high-risk populations, such as those undergoing endoscopic papillectomy.⁹¹ Although rectal indomethacin alone appeared to be more effective for preventing post-ERCP pancreatitis than pancreatic stent placement alone or the combination of indomethacin and pancreatic stent placement, a randomized, controlled trial is necessary to confirm these findings.⁹² Placement of a prophylactic biliary stent to reduce the risk of postprocedural cholangitis has not been widely performed and cannot be uniformly recommended at this time unless there is perceived inadequate biliary drainage after the papillectomy.^{46,48,75} Some experts also perform biliary stent placement when there is concern for microperforation after resection.

Ablative therapies

Although they are not routinely used as primary therapy for ampullary adenomas, endoscopic ablative therapies (argon plasma coagulation, laser therapy, photodynamic therapy, monopolar or bipolar electrocoagulation) can be used to destroy residual or recurrent superficial adenomatous tissue not removed during previous attempted snare resection. Argon plasma coagulation (setting of 50-60 W) is the most frequently used modality, given its widespread availability and superficial depth of tissue destruction.^{25,27,46,48,54,67,68,75,77,84} Pancreatic duct stents usually are placed before ablating tissue around the pancreatic duct orifice. Unfortunately, tissue treated with ablative therapy is not available for pathology analysis, and biopsy specimens should be obtained from any suspicious area before ablation.

Postprocedure evaluation

Endoscopic removal of ampullary adenomas is considered a high-risk procedure for adverse events. Postprocedural hospitalization should be considered for the detection and treatment of any immediate adverse events, especially after extensive removal and treatment of large lesions in patients with comorbidities or those without ready access to medical care.

Results of endoscopic therapy

Clinical success. Data on the clinical success of endoscopic papillectomy is based largely on retrospective, heterogeneous case series. Successful papillectomy rates range from 46% to 92%, whereas recurrence rates have been reported as high as 33%. Multiple procedures may be required to completely remove all adenomatous tissue. Larger lesions are more likely to be incompletely excised at the initial endoscopic procedure.^{45,46,48,67,68,74,75,84} Predictors of long-term success (defined as absence of recurrence) on multivariate analysis include patient age >48 years, lesion size ≤24 mm, male sex, and absence of polyposis syndrome (eg, FAP).²⁵ Absence of dilated ducts may predict clinical success,⁹³ whereas intraductal adenoma growth may be associated with lower cure rates and greater need for surgery for incomplete adenoma removal.⁷⁰

Adverse events

Early adverse events after endoscopic papillectomy are similar to those of other ERCP procedures and include pancreatitis, perforation, bleeding, sedation adverse events, and cholangitis. Underlying malignancy and lateral extension have been reported as possible risk factors for bleeding and perforation, respectively.⁹³ In almost all cases, pancreatitis was mild to moderate.⁹³ Carbon dioxide insufflation is advantageous in the event of a duodenal perforation and may decrease the risk of tension pneumoperitoneum.¹³ Late adverse events include the development of pancreatic or biliary stenosis.^{45,46,48,67,68,75,84} Death after papillectomy is rare but has been reported.⁵⁴ Although not directly compared, the adverse event rate for local surgical excision appears to be higher (29%) than adverse event rates for endoscopy.¹⁴ Adverse events after surgical excision include gastric outlet obstruction, pancreatitis, cholangitis, and common bile duct stricture.²²

Surveillance for residual or recurrent neoplastic tissue

It is recommended that all patients who have undergone endoscopic papillectomy undergo surveillance endoscopy for the detection of recurrent neoplastic tissue. Recurrent or residual neoplastic tissue often grows across the postresection scar. Some experts advocate endoscopy with photographic documentation and biopsy of the scar. Varied posttreatment surveillance intervals have been suggested and are typically performed 1 to 6 months after the index procedure followed thereafter with examinations every 3 to 12 months for at least 2 years.^{27,45,46,48,68,75,77,84} Some authors recommend a postresection surveillance strategy for sporadic (non-FAP) ampullary polyps similar to that used for patients with colon polyps treated with piecemeal resection. This strategy incorporates the degree of dysplasia, estimate of resection completeness, and evidence of intraductal involvement into decisions

on surveillance intervals.⁹⁴ Endpoints for surveillance in these patients have not been established.

NONAMPULLARY DUODENAL POLYPS

Polyps of the duodenum that do not involve the major duodenal papilla can occur sporadically or in the context of genetic syndromes such as FAP or Peutz-Jeghers syndrome. Adenomas in these patients also have the potential to undergo malignant transformation into duodenal cancer.

Evaluation of sporadic nonampullary duodenal lesions before endoscopic therapy

The endoscopic appearance of duodenal adenomas may be indistinguishable from nonadenomatous polyps such as inflammatory polyps. Biopsy specimens from suspicious lesions should be obtained and interpreted before attempted endoscopic resection. Before endoscopic resection of a duodenal polyp, it is important to ensure that the polyp does not involve the major papilla. If it does, then the pancreaticobiliary ducts need to be addressed as discussed earlier. Examination with a side-viewing endoscope or EUS can be helpful in making this distinction. The position of the lesion relative to the major papilla should be carefully described and photographically documented when possible before and after intervention. Dorsal pancreatic duct stenting has been reported in patients with pancreas divisum undergoing endoscopic resection of minor papilla adenomas.⁹⁵

Role of EUS

The precise role of EUS in the management of duodenal adenomas is unclear. EUS may obviate the need for ERCP should significant intraductal extension or metastases be noted. The utility of EUS in small adenomas is likely small but may impact management of polyps >2 cm.^{96,97}

Endoscopic resection techniques

The number of large, prospective trials comparing techniques of endoscopic resection of sporadic duodenal adenomas is limited.⁹⁸⁻¹⁰⁰ Although the techniques of endoscopic removal of duodenal adenomas are not standardized, the general approach is similar to that of colon polyps, particularly those of the right side of the colon because of the thinness of the duodenal wall. A submucosal injection to create a fluid cushion may be useful for removal of flat polyps. The lack of lifting during injection suggests underlying malignancy or previous endoscopic manipulation of the lesion with biopsies or attempts at removal or ablation. EMR techniques also have been described in the removal of duodenal lesions.⁹⁶ A cap-assisted “suck and cut” technique has been described for the resection of duodenal adenomas, but data regarding its safety in the duodenum are limited.^{13,96,101} In contrast to other sites of resection,

minimizing suction is important if this technique is used in the duodenum to lower the risk of perforation. Endoscopic submucosal dissection of duodenal adenomas, especially beyond the duodenal bulb, is not recommended because of the high risk of perforation with this technique in the duodenum compared with other luminal sites.¹³ Two studies from centers in Japan and Korea with high volumes of endoscopic submucosal dissection reported duodenal perforation rates as high as 23% and 35%, respectively.^{102,103} Interestingly, the same Japanese group also reported no perforations for EMR of duodenal lesions.¹⁰⁴ Iatrogenic perforations at the time of resection are not as easily recognized in the duodenum compared with resections in the stomach and colon. This delay in diagnosis increases the risk for subsequent surgery and morbidity.¹³ Cold snare polypectomy of duodenal adenomas >1 cm has been described to avoid adverse events related to electrocautery.¹⁰⁵ Band and slough technique for therapy of duodenal adenomas without endoscopic resection also has been reported in a small case series, but a major limitation of this technique is the lack of tissue retrieval.¹⁰⁶

Adjuvant ablative therapies such as argon plasma coagulation or electrocoagulation may be used to destroy superficial, residual or recurrent adenomatous tissue not removed during attempts at primary snare resection.¹⁰⁷

Results of endoscopic resection for sporadic duodenal adenomas

Data on the clinical success of resection of sporadic duodenal adenomas have been based on a few, small case series. In 1 series of 21 patients with lesions measuring a median size of 27.5 mm (range 8-50 mm), the success rate for endoscopic removal after a 3-month interval was 55%.¹⁰⁷ After a median follow-up of 71 months, local recurrences developed in 25% of patients, who received additional endoscopic treatment. No patients developed carcinoma during the follow-up period. In another series of 23 patients with lesions of a median size of 27.6 mm (range 15-60 mm), EMR was performed successfully in 18 patients during a single session.¹⁰⁰ Two patients required 2 sessions and 1 patient required 3 sessions for complete resection. The median follow-up was 13 months (range 4-44 months). During follow-up, 5 patients had minor residual adenomas that were treated successfully with snare resection and/or argon plasma coagulation.

Generally, larger lesions are more difficult to remove, and lesions with >33% circumferential involvement of the lumen should be considered for surgical resection.¹⁰⁸ Although successful endoscopic resection of giant (>3 cm) hemicircumferential laterally spreading tumors (mean size 40.5 mm, range 30-80 mm) has been reported, it is associated with a significantly higher adverse event rate—primarily bleeding—when compared with resection of lesions <3 cm (26.3% vs 3.2%).⁹⁸ Other adverse events after endoscopic resection of duodenal adenomas

include perforation and adverse events related to sedation. The risk of adverse events is higher compared with the resection of similar-sized lesions in the colon.^{13,96,98,109,110}

Postprocedural care and surveillance for residual or recurrent neoplastic tissue

Postprocedural care protocols vary. One of the groups with extensive experience with resection of sporadic duodenal adenomas observed patients for 4 hours before discharge.⁹⁸ Patients were given a clear liquid diet after discharge on the day of the procedure and resumed a normal diet the next day. Antiplatelet agents were held for 7 days. Twice-daily proton pump inhibitor therapy was given for 2 weeks after the procedure. It is recommended that all patients who have undergone endoscopic resection of duodenal adenomas be considered for surveillance endoscopy to detect and treat recurrences.^{97,107} On the basis of limited data, recommendations cannot be provided regarding surveillance intervals and should be applied on an individual basis in the context of adequacy of resection, degree of dysplasia, and underlying comorbid medical illnesses. Endpoints for surveillance have not been established.

Impact of duodenal and ampullary adenomas on colorectal cancer screening

Published data suggest that patients with sporadic ampullary or duodenal adenomas are at higher risk for the development of colorectal neoplasia.¹¹¹⁻¹¹³ Until more definitive data are available, screening colonoscopy should be offered to patients who have duodenal or ampullary adenomas.

RECOMMENDATIONS

1. We recommend that biopsy specimens be obtained and evaluated from ampullary lesions suspicious for neoplasia before attempted endoscopic resection. ⊕⊕⊕○
2. We recommend EUS for large ampullary lesions or duodenal polyps with features concerning for malignancy before endoscopic or surgical resection. ⊕⊕⊕○
3. We suggest ERCP with both biliary and pancreatic duct evaluation at the time of endoscopic papillectomy to assess for evidence of extension into either ductal system. ⊕⊕○○
4. We recommend prophylactic pancreatic duct stent placement and rectal indomethacin during papillectomy to reduce the risk of postprocedural pancreatitis. ⊕⊕⊕○
5. We recommend that patients undergoing endoscopic removal of ampullary and duodenal neoplasms be included in an endoscopic surveillance program to ensure complete tissue removal and assess for disease recurrence. ⊕⊕⊕○

6. We suggest that patients with sporadic ampullary or duodenal adenomas be offered screening colonoscopy.

⊕⊕○○

DISCLOSURE

M. Khasbab is a consultant to and member of the Medical Advisory Board for Boston Scientific and a consultant to Olympus and receives research support from Cook Medical. K. Chathadi is a consultant to Boston Scientific. All other authors disclosed no financial relationships relevant to this publication.

Abbreviations: ASGE, American Society for Gastrointestinal Endoscopy; FAP, familial adenomatous polyposis.

REFERENCES

- Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction—GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol* 2011;64:383-94.
- Offerhaus GJ, Giardiello FM, Krush AJ, et al. The risk of upper gastrointestinal cancer in familial adenomatous polyposis. *Gastroenterology* 1992;102:1980-2.
- Galandiuk S, Hermann RE, Jagelman DG, et al. Villous tumors of the duodenum. *Ann Surg* 1988;207:234-9.
- van Stolk R, Sivak MV Jr, Petrini JL, et al. Endoscopic management of upper gastrointestinal polyps and periampullary lesions in familial adenomatous polyposis and Gardner's syndrome. *Endoscopy* 1987;(19 suppl 1):19-22.
- Stolte M, Pscherer C. Adenoma-carcinoma sequence in the papilla of Vater. *Scan J Gastroenterol* 1996;31:376-82.
- Lindor NM, Greene MH. The concise handbook of family cancer syndromes. Mayo Familial Cancer Program. *J Natl Cancer Institute* 1998;15(90):1039-71.
- Di Giorgio A, Alfieri S, Rotondi F, et al. Pancreatoduodenectomy for tumors of Vater's ampulla: report on 94 consecutive patients. *World J Surg* 2005;29:513-8.
- Bohra AK, McKie L, Diamond T. Transduodenal excision of ampullary tumours. *Ulster Med J* 2002;71:121-7.
- Posner S, Colletti L, Knol J, et al. Safety and long-term efficacy of transduodenal excision for tumors of the ampulla of Vater. *Surgery* 2000;128:694-701.
- Cahen DL, Fockens P, de Wit LT, et al. Local resection or pancreaticoduodenectomy for villous adenoma of the ampulla of Vater diagnosed before operation. *Brit J Surg* 1997;84:948-51.
- Jordan PH Jr, Ayala G, Rosenberg WR, et al. Treatment of ampullary villous adenomas that may harbor carcinoma. *J Gastrointest Surg* 2002;6:770-5.
- Tran TC, Vitale GC. Ampullary tumors: endoscopic versus operative management. *Surg Innov* 2004;11:255-63.
- Bourke MJ. Endoscopic resection in the duodenum: current limitations and future directions. *Endoscopy* 2013;45:127-32.
- Ceppa EP, Burbridge RA, Rialon KL, et al. Endoscopic versus surgical ampullectomy: an algorithm to treat disease of the ampulla of Vater. *Ann Surg* 2013;257:315-22.
- ASGE Standards of Practice Committee; Hirota WK, Zuckerman MJ, Adler DG, et al. ASGE guideline: the role of endoscopy in the surveillance of premalignant conditions of the upper GI tract. *Gastrointest Endosc* 2006;63:570-80.
- Church JM, McGannon E, Hull-Boiner S, et al. Gastroduodenal polyps in patients with familial adenomatous polyposis. *Dis Colon Rectum* 1992;35:1170-3.
- Burke CA, Beck GJ, Church JM, et al. The natural history of untreated duodenal and ampullary adenomas in patients with familial adenomatous polyposis followed in an endoscopic surveillance program. *Gastrointest Endosc* 1999;49(3 Pt 1):358-64.
- Gincul R, Ciocirlan M, Dumortier J, et al. Severe acute pancreatitis following endoscopic biopsy of the minor duodenal papilla. *Endoscopy* 2009;(41 suppl 2):E195-6.
- Yamaguchi K, Enjoji M. Adenoma of the ampulla of Vater: putative precancerous lesion. *Gut* 1991;32:1558-61.
- Ryan DP, Schapiro RH, Warshaw AL. Villous tumors of the duodenum. *Ann Surg* 1986;203:301-6.
- Yamaguchi K, Enjoji M. Carcinoma of the ampulla of Vater. A clinicopathologic study and pathologic staging of 109 cases of carcinoma and 5 cases of adenoma. *Cancer* 1987;59:506-15.
- Clary BM, Tyler DS, Dematos P, et al. Local ampullary resection with careful intraoperative frozen section evaluation for presumed benign ampullary neoplasms. *Surgery* 2000;127:628-33.
- Yamaguchi K, Enjoji M, Kitamura K. Endoscopic biopsy has limited accuracy in diagnosis of ampullary tumors. *Gastrointest Endosc* 1990;36:588-92.
- Lee SY, Jang KT, Lee KT, et al. Can endoscopic resection be applied for early stage ampulla of Vater cancer? *Gastrointest Endosc* 2006;63:783-8.
- Martin JA, Haber GB. Ampullary adenoma: clinical manifestations, diagnosis, and treatment. *Gastrointest Endosc Clin N Am* 2003;13:649-69.
- Elek G, Gyori S, Toth B, et al. Histological evaluation of preoperative biopsies from ampulla vateri. *Path Oncol Res* 2003;9:32-41.
- Ponchon T, Berger F, Chavaillon A, et al. Contribution of endoscopy to diagnosis and treatment of tumors of the ampulla of Vater. *Cancer* 1989;64:161-7.
- Bourgeois N, Dunham F, Verhest A, et al. Endoscopic biopsies of the papilla of Vater at the time of endoscopic sphincterotomy: difficulties in interpretation. *Gastrointest Endosc* 1984;30:163-6.
- Shemesh E, Nass S, Czerniak A. Endoscopic sphincterotomy and endoscopic fulguration in the management of adenoma of the papilla of Vater. *Surg Gynecol Obstet* 1989;169:445-8.
- Bardales RH, Stanley MW, Simpson DD, et al. Diagnostic value of brush cytology in the diagnosis of duodenal, biliary, and ampullary neoplasms. *Am J Clin Pathol* 1998;109:540-8.
- Elek G, Gyokeres T, Schafer E, et al. Early diagnosis of pancreaticobiliary duct malignancies by brush cytology and biopsy. *Pathol Oncol Res* 2005;11:145-55.
- Mohammad Alizadeh AH, Mousavi M, Salehi B, et al. Biliary brush cytology in the assessment of biliary strictures at a tertiary center in Iran. *Asian Pac J Cancer Prev* 2011;12:2793-6.
- Navaneethan U, Singh T, Gutierrez NG, et al. Predictors for detection of cancer in patients with indeterminate biliary stricture and atypical cells on endoscopic retrograde brush cytology. *J Digest Dis* 2014;15:268-75.
- Stewart CJ, Mills PR, Carter R, et al. Brush cytology in the assessment of pancreatico-biliary strictures: a review of 406 cases. *J Clin Pathol* 2001;54:449-55.
- Howe JR, Klimstra DS, Cordon-Cardo C, et al. K-ras mutation in adenomas and carcinomas of the ampulla of Vater. *Clin Cancer Res* 1997;3:129-33.
- Chung CH, Wilentz RE, Polak MM, et al. Clinical significance of K-ras oncogene activation in ampullary neoplasms. *J Clin Pathol* 1996;49:460-4.
- Relias V, Saif MW. Biological identification of ampullary adenocarcinomas. *J Pancreas* 2014;15:306-7.
- Park SH, Kim YI, Park YH, et al. Clinicopathologic correlation of p53 protein overexpression in adenoma and carcinoma of the ampulla of Vater. *World J Surg* 2000;24:54-9.
- Sato T, Konishi K, Kimura H, et al. Adenoma and tiny carcinoma in adenoma of the papilla of Vater—p53 and PCNA. *Hepato-gastroenterology* 1999;46:1959-62.

40. Takashima M, Ueki T, Nagai E, et al. Carcinoma of the ampulla of Vater associated with or without adenoma: a clinicopathologic analysis of 198 cases with reference to p53 and Ki-67 immunohistochemical expressions. *Mod Pathol* 2000;13:1300-7.
41. Younes M, Riley S, Genta RM, et al. p53 protein accumulation in tumors of the ampulla of Vater. *Cancer* 1995;76:1150-4.
42. Ang DC, Shia J, Tang LH, et al. The utility of immunohistochemistry in subtyping adenocarcinoma of the ampulla of vater. *Am J Surg Pathol* 2014;38:1371-9.
43. Schultz NA, Werner J, Willenbrock H, et al. MicroRNA expression profiles associated with pancreatic adenocarcinoma and ampullary adenocarcinoma. *Mod Pathol* 2012;25:1609-22.
44. Meneghetti AT, Safadi B, Stewart L, et al. Local resection of ampullary tumors. *J Gastrointest Surg* 2005;9:1300-6.
45. Zadorova Z, Dvofak M, Hajer J. Endoscopic therapy of benign tumors of the papilla of Vater. *Endoscopy* 2001;33:345-7.
46. 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.
47. Beger HG, Staib L, Schoenberg MH. Ampullectomy for adenoma of the papilla and ampulla of Vater. *Langenbeck's Arch Surg/Deutsche Gesellschaft fur Chirurgie* 1998;383:190-3.
48. Cheng CL, Sherman S, Fogel EL, et al. Endoscopic snare papillectomy for tumors of the duodenal papillae. *Gastrointest Endosc* 2004;60:757-64.
49. De Palma GD, Luglio G, Maione F, et al. Endoscopic snare papillectomy: a single institutional experience of a standardized technique. A retrospective cohort study. *Internat J Surg (London, England)* 2014;13C:180-3.
50. Boix J, Lorenzo-Zuniga V, Moreno de Vega V, et al. Endoscopic resection of ampullary tumors: 12-year review of 21 cases. *Surg Endosc* 2009;23:45-9.
51. Kim JH, Kim JH, Han JH, et al. Is endoscopic papillectomy safe for ampullary adenomas with high-grade dysplasia? *Ann Surg Oncol* 2009;16:2547-54.
52. Jung S, Kim MH, Seo DW, et al. Endoscopic snare papillectomy of adenocarcinoma of the major duodenal papilla. *Gastrointest Endosc* 2001;54:622.
53. Neves P, Leitao M, Portela F, et al. Endoscopic resection of ampullary carcinoma. *Endoscopy* 2006;38:101.
54. Kahaleh M, Shami VM, Brock A, et al. Factors predictive of malignancy and endoscopic resectability in ampullary neoplasia. *Am J Gastroenterol* 2004;99:2335-9.
55. Chen CH, Yang CC, Yeh YH, et al. Reappraisal of endosonography of ampullary tumors: correlation with transabdominal sonography, CT, and MRI. *J Clin Ultrasound* 2009;37:18-25.
56. Rivadeneira DE, Pochapin M, Grobmyer SR, et al. Comparison of linear array endoscopic ultrasound and helical computed tomography for the staging of periampullary malignancies. *Ann Surg Oncol* 2003;10:890-7.
57. Itoh A, Goto H, Naitoh Y, et al. Intraductal ultrasonography in diagnosing tumor extension of cancer of the papilla of Vater. *Gastrointest Endosc* 1997;45:251-60.
58. Chen CH, Tseng LJ, Yang CC, et al. Preoperative evaluation of periampullary tumors by endoscopic sonography, transabdominal sonography, and computed tomography. *J Clin Ultrasound* 2001;29:313-21.
59. Cannon ME, Carpenter SL, Elta GH, et al. EUS compared with CT, magnetic resonance imaging, and angiography and the influence of biliary stenting on staging accuracy of ampullary neoplasms. *Gastrointest Endosc* 1999;50:27-33.
60. Schwarz M, Pauls S, Sokiranski R, et al. Is a preoperative multidagnostic approach to predict surgical resectability of periampullary tumors still effective? *Am J Surg* 2001;182:243-9.
61. Chen CH, Tseng LJ, Yang CC, et al. The accuracy of endoscopic ultrasound, endoscopic retrograde cholangiopancreatography, computed tomography, and transabdominal ultrasound in the detection and staging of primary ampullary tumors. *Hepatogastroenterology* 2001;48:1750-3.
62. Okano N, Igarashi Y, Hara S, et al. Endosonographic preoperative evaluation for tumors of the ampulla of Vater using endoscopic ultrasonography and intraductal ultrasonography. *Clin Endosc* 2014;47:174-7.
63. Menzel J, Hoepffner N, Sulkowski U, et al. Polypoid tumors of the major duodenal papilla: preoperative staging with intraductal US, EUS, and CT—a prospective, histopathologically controlled study. *Gastrointest Endosc* 1999;49(3 Pt 1):349-57.
64. Ito K, Fujita N, Noda Y, et al. Preoperative evaluation of ampullary neoplasm with EUS and transpapillary intraductal US: a prospective and histopathologically controlled study. *Gastrointest Endosc* 2007;66:740-7.
65. Baillie J. Endoscopic ampullectomy. *Am J Gastroenterol* 2005;100:2379-81.
66. Riditid W, Schmidt SE, Al-Haddad MA, et al. Performance characteristics of EUS for locoregional evaluation of ampullary lesions. *Gastrointest Endosc* 2015;81:380-8.
67. Norton ID, Gostout CJ, Baron TH, et al. Safety and outcome of endoscopic snare excision of the major duodenal papilla. *Gastrointest Endosc* 2002;56:239-43.
68. Catalano MF, Linder JD, Chak A, et al. Endoscopic management of adenoma of the major duodenal papilla. *Gastrointest Endosc* 2004;59:225-32.
69. Norton ID, Geller A, Petersen BT, et al. Endoscopic surveillance and ablative therapy for periampullary adenomas. *Am J Gastroenterol* 2001;96:101-6.
70. Bohnacker S, Seitz U, Nguyen D, et al. Endoscopic resection of benign tumors of the duodenal papilla without and with intraductal growth. *Gastrointest Endosc* 2005;62:551-60.
71. Dzeletovic I, Topazian MD, Baron TH. Endoscopic balloon dilation to facilitate treatment of intraductal extension of ampullary adenomas (with video). *Gastrointest Endosc* 2012;76:1266-9.
72. Kim JH, Moon JH, Choi HJ, et al. Endoscopic snare papillectomy by using a balloon catheter for an unexposed ampullary adenoma with intraductal extension (with videos). *Gastrointest Endosc* 2009;69:1404-6.
73. Dekker E, Boparai KS, Poley JW, et al. High resolution endoscopy and the additional value of chromoendoscopy in the evaluation of duodenal adenomatosis in patients with familial adenomatous polyposis. *Endoscopy* 2009;41:666-9.
74. Han J, Kim MH. Endoscopic papillectomy for adenomas of the major duodenal papilla (with video). *Gastrointest Endosc* 2006;63:292-301.
75. Desilets DJ, Dy RM, Ku PM, et al. Endoscopic management of tumors of the major duodenal papilla: refined techniques to improve outcome and avoid complications. *Gastrointest Endosc* 2001;54:202-8.
76. Park SW, Song SY, Chung JB, et al. Endoscopic snare resection for tumors of the ampulla of Vater. *Yonsei Med J* 2000;41:213-8.
77. Charton JP, Deinert K, Schumacher B, et al. Endoscopic resection for neoplastic diseases of the papilla of Vater. *J Hepato-Biliary-Pancreat Surg* 2004;11:245-51.
78. Binmoeller KF, Shah JN, Bhat YM, et al. "Underwater" EMR of sporadic laterally spreading nonampullary duodenal adenomas (with video). *Gastrointest Endosc* 2013;78:496-502 e1.
79. Binmoeller KF, Kato M, Shah JN, et al. "Underwater" ampullectomy for benign adenomas: prospective study of a novel technique [abstract]. *Gastrointest Endosc* 2013;77:AB387.
80. Hirooka Y, Itoh A, Goto H. EUS/IDUS and endoscopic papillectomy. *Dig Endosc* 2004;16(suppl):S176-7.
81. Poincloux L, Scanzì 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.
82. Hwang JC, Kim JH, Lim SG, et al. Endoscopic resection of ampullary adenoma after a new insulated plastic pancreatic stent placement: a pilot study. *J Gastroenterol Hepatol* 2010;25:1381-5.

83. 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.
84. Vogt M, Jakobs R, Benz C, et al. Endoscopic therapy of adenomas of the papilla of Vater. A retrospective analysis with long-term follow-up. *Dig Liver Dis* 2000;32:339-45.
85. Saurin JC, Chavaillon A, Napoleon B, et al. Long-term follow-up of patients with endoscopic treatment of sporadic adenomas of the papilla of Vater. *Endoscopy* 2003;35:402-6.
86. Aiura K, Imaeda H, Kitajima M, et al. Balloon-catheter-assisted endoscopic snare papillectomy for benign tumors of the major duodenal papilla. *Gastrointest Endosc* 2003;57:743-7.
87. 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.
88. Singh P, Das A, Isenberg G, et al. Does prophylactic pancreatic stent placement reduce the risk of post-ERCP acute pancreatitis? A meta-analysis of controlled trials. *Gastrointest Endosc* 2004;60:544-50.
89. Chang WI, Min YW, Yun HS, et al. Prophylactic pancreatic stent placement for endoscopic duodenal ampullectomy: a single-center retrospective study. *Gut Liver* 2014;8:306-12.
90. Yamao T, Isomoto H, Kohno S, et al. Endoscopic snare papillectomy with biliary and pancreatic stent placement for tumors of the major duodenal papilla. *Surg Endosc* 2010;24:119-24.
91. Elmunzer BJ, Scheiman JM, Lehman GA, et al. A randomized trial of rectal indomethacin to prevent post-ERCP pancreatitis. *New Engl J Med* 2012;366:1414-22.
92. Elmunzer BJ, Higgins PD, Saini SD, et al. Does rectal indomethacin eliminate the need for prophylactic pancreatic stent placement in patients undergoing high-risk ERCP? Post hoc efficacy and cost-benefit analyses using prospective clinical trial data. *Am J Gastroenterol* 2013;108:410-5.
93. Irani S, Arai A, Ayub K, et al. Papillectomy for ampullary neoplasm: results of a single referral center over a 10-year period. *Gastrointest Endosc* 2009;70:923-32.
94. Lieberman DA, Rex DK, Winawer SJ, et al. Guidelines for colonoscopy surveillance after screening and polypectomy: a consensus update by the US Multi-Society Task Force on Colorectal Cancer. *Gastroenterology* 2012;143:844-57.
95. Trevino JM, Wilcox CM, Varadarajulu S. Endoscopic resection of minor papilla adenomas (with video). *Gastrointest Endosc* 2008;68:383-6.
96. Ahmad NA, Kochman ML, Long WB, et al. Efficacy, safety, and clinical outcomes of endoscopic mucosal resection: a study of 101 cases. *Gastrointest Endosc* 2002;55:390-6.
97. Perez A, Saltzman JR, Carr-Locke DL, et al. Benign nonampullary duodenal neoplasms. *J Gastrointest Surg* 2003;7:536-41.
98. Fanning SB, Bourke MJ, Williams SJ, et al. Giant laterally spreading tumors of the duodenum: endoscopic resection outcomes, limitations, and caveats. *Gastrointest Endosc* 2012;75:805-12.
99. Abbasi R, Rigaux J, Al-Kawas FH. Nonampullary duodenal polyps: characteristics and endoscopic management. *Gastrointest Endosc* 2010;71:754-9.
100. Alexander S, Bourke MJ, Williams SJ, et al. EMR of large, sessile, sporadic nonampullary duodenal adenomas: technical aspects and long-term outcome (with videos). *Gastrointest Endosc* 2009;69:66-73.
101. Conio M, De Ceglie A, Filiberti R, et al. Cap-assisted EMR of large, sporadic, nonampullary duodenal polyps. *Gastrointest Endosc* 2012;76:1160-9.
102. Matsumoto S, Miyatani H, Yoshida Y. Endoscopic submucosal dissection for duodenal tumors: a single-center experience. *Endoscopy* 2013;45:136-7.
103. Jung JH, Choi KD, Ahn JY, et al. Endoscopic submucosal dissection for sessile, nonampullary duodenal adenomas. *Endoscopy* 2013;45:133-5.
104. Maruoka D, Arai M, Kishimoto T, et al. Clinical outcomes of endoscopic resection for nonampullary duodenal high-grade dysplasia and intramucosal carcinoma. *Endoscopy* 2013;45:138-41.
105. Choksi N, Elmunzer J, Stidham R, et al. Cold-snare piecemeal resection of colonic and duodenal polyps ≥ 1 cm. *Endosc Internat Open* 2015; [http://dx.doi.org/10.1055/s-0034-1392214\(03:E1-E6\)](http://dx.doi.org/10.1055/s-0034-1392214(03:E1-E6)).
106. Koritala T, Zolotarevsky E, Bartley AN, et al. Efficacy and safety of the band and slough technique for endoscopic therapy of nonampullary duodenal adenomas: a case series. *Gastrointest Endosc* 2015;81:985-8.
107. Apel D, Jakobs R, Spiethoff A, et al. Follow-up after endoscopic snare resection of duodenal adenomas. *Endoscopy* 2005;37:444-8.
108. Standards of Practice Committee; Adler DG, Qureshi W, Davila R, et al. The role of endoscopy in ampullary and duodenal adenomas. *Gastrointest Endosc* 2006;64:849-54.
109. Lepilliez V, Chemaly M, Ponchon T, et al. Endoscopic resection of sporadic duodenal adenomas: an efficient technique with a substantial risk of delayed bleeding. *Endoscopy* 2008;40:806-10.
110. Kedia P, Brensinger C, Ginsberg G. Endoscopic predictors of successful endoluminal eradication in sporadic duodenal adenomas and its acute complications. *Gastrointest Endosc* 2010;72:1297-301.
111. Apel D, Jakobs R, Weickert U, et al. High frequency of colorectal adenoma in patients with duodenal adenoma but without familial adenomatous polyposis. *Gastrointest Endosc* 2004;60:397-9.
112. Schneider AR, Seifert H, Trojan J, et al. Frequency of colorectal polyps in patients with sporadic adenomas or adenocarcinomas of the papilla of Vater—an age-matched, controlled study [In German with English abstract]. *Zeitschrift fur Gastroenterologie* 2005;43:1123-7.
113. Murray MA, Zimmerman MJ, Ee HC. Sporadic duodenal adenoma is associated with colorectal neoplasia. *Gut* 2004;53:261-5.