GUIDELINE

The role of endoscopy in ampullary and duodenal adenomas

This is one of a series of statements discussing the use of gastrointestinal endoscopy in common clinical situations. The Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy prepared this text. In preparing this guideline, MEDLINE and PubMed databases were used to search publications through the last 15 years related to ampullary and duodenal adenomas by using the keyword(s) "ampullary adenoma" and each of the following: "ampullectomy," "duodenal adenoma," and "familial adenomatous polyposis." The search was supplemented by accessing the "related articles" feature of PubMed with articles identified on MEDLINE and PubMed as the references. Pertinent studies published in English were reviewed. Studies or reports that described fewer than 10 patients were excluded from analysis if multiple series with greater than 10 patients addressing the same issue were available. Recommendations were made on the basis of the reviewed studies and were graded as to the strength of the supporting evidence (Table 1).

Guidelines for appropriate use of endoscopy are based on a critical review of the available data and expert consensus. Further controlled clinical studies may be needed to clarify aspects of this statement, and revision may be necessary as new data appear. Clinical consideration may justify a course of action at variance to these recommendations.

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.1 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.1

Ampullary adenomas have historically been treated surgically. Surgical options include pancreaticoduodenectomy (Whipple's procedure) or transduodenal ampullectomy (which can occasionally leave behind residual adenomatous tissue).2-4 Surgical management often allows complete removal but carries morbidity, including anastomotic dehiscence and fistulae in 9% and 14% of patients, respectively, and mortality rates ranging from 1% to 9%,1,5-7 although complication rates tend to be related to surgical case volume.

Endoscopic approaches for the evaluation and treatment of ampullary adenomas now represent a viable alternative to surgical therapy.

Evaluation of ampullary lesions before endoscopic therapy

Ampullary adenomas cannot always be distinguished from ampullary carcinomas or nonadenomatous polyps (carcinoid tumors, gangliocytic parangangiomas, etc) on the basis of endoscopic appearance alone. Suspicious ampullary lesions should be biopsied before endoscopic resection is attempted. Brush cytology may offer additional information to biopsy for the detection of malignancy in selected cases.8

There is no consensus on which ampullary adenomas should be kept under surveillance and which lesions should be removed endoscopically or surgically. An incidental, small ampullary adenoma may not require further evaluation or therapy, depending on the clinical context. Lesions with high-grade dysplasia often warrant therapy because they may harbor malignancy missed on biopsy and to prevent progression to malignancy.9 Several authors have advocated that endoscopic resection should only be performed in patients without evidence of invasive cancer.10-12 Although endoscopic removal of ampullary adenocarcinoma has been described, it cannot be endorsed for routine management.13,14 The finding of high-grade dysplasia is not a contraindication to endoscopic removal, but it should prompt removal of the lesion by either endoscopic or surgical means rather than management by surveillance on the basis of health status.15

There are no definitive guidelines as to the size or diameter above which endoscopic removal of ampullary adenomas should not be attempted. Many authors recommend that lesions ≥4 to 5 cm not be treated endoscopically, although there are reports of successful endoscopic resection of ampullary lesions of greater size.10-12,16 The size of the lesion, however, can affect the endoscopic approach to resection, as discussed below.

Endoscopic features such as firmness, ulceration, nonlifting with attempted submucosal injection to create a submucosal fluid cushion, and friability suggest possible malignancy and such lesions should be considered for
surgical resection even in the absence of malignancy on biopsy specimens.12

Role of endoscopic retrograde cholangiopancreatography and endoscopic ultrasound. ERCP and EUS provide useful information in the assessment of ampullary adenomas. EUS and intraductal US (IDUS) have emerged as useful techniques to assess the depth of involvement in patients with ampullary neoplasms. These modalities allow the assessment and extent of intraductal extension and extension beyond the muscularis propria and can allow evaluation of periampullary lymph nodes in those patients suspected of having cancer. EUS or IDUS examination should be considered 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. Several authors have used evidence of intraductal extension as a criterion for surgical referral.24-26 Other investigators have shown that less than 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.27,28

Endoscopic resection techniques

Techniques of endoscopic removal of ampullary adenomas remain unstandardized, likely because of the

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relatively small number of formal investigations into this practice. Importantly, 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 resections 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 two are often used interchangeably in the literature.29

Submucosal injection. Several authors have advocated the use of submucosal injection immediately before endoscopic papillectomy in a manner similar to that used before performing endoscopic mucosal resection for colorectal polyps. The failure of a lesion to manifest a “lift sign” is associated with malignancy and is considered a contraindication to attempts at complete endoscopic resection (although further endoscopic therapy could be performed as a form of palliation in a poor operative candidate).27 Fluids injected into the submucosa have included saline solution, epinephrine, methylene blue, and viscous materials such as hydroxypropyl methylcellulose.27,30-35 Volumes of injected fluid are not standardized and vary widely. Some authors have not used submucosal injection, and there are insufficient data to conclude that this is a necessary step in the procedure.23-25

Endoscopic resection
Endoscopic papillectomy is performed by use of 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.24,30,32 There is no evidence documenting the utility of one type of snare over another. Snare position during papillectomy is also not standardized, with investigators describing successful papillectomy with snares oriented in both a cephalad to caudal orientation and a caudal to cephalad orientation; the majority of published series have not specifically commented on the orientation of the snare during the procedure.23,24,27,36

If the lesion can be completely ensnared, en bloc resection with electrocautery can be performed. En bloc resection has the advantages of potentially shortening the procedure time, requiring less electrocautery, and providing a complete tissue sample for pathologic evaluation. Piecemeal resection (with electrocautery) is often performed for lesions larger than 2 cm or in cases where an attempt at en bloc resection has left visible neoplastic tissue in place. Piecemeal resection may produce electrocautery-related injury to tissue fragments sent for pathologic analysis. Piecemeal snare resection may require repeated submucosal injections over time to achieve sustained elevation of the adenomatous tissue. Larger lesions may require multiple endoscopic procedures to be completely removed. Most published series reported using a combination of en bloc and piecemeal resection techniques as the types of lesions treated were of mixed size and architecture.10,25,33,37-39

Electrocautery settings. There is no consensus as to which type of current should be used during endoscopic papillectomy. Both pure cutting current and blended current have been used and neither has been proven to be superior over the other at this time. Power settings are also not standardized.10,24,26,30,38,40

Pancreatic or biliary stenting. Given the potential for significant tissue injury to the pancreatic and biliary orifices during endoscopic removal of ampullary adenomas, pancreatic or biliary sphincterotomies are frequently performed during the procedure. Pancreatic or biliary sphincterotomy may assist in providing pancreaticobiliary drainage after papillectomy, simplify attempts to access the common bile duct and pancreatic duct for stent placement, and assist in postprocedure surveillance. There is no consensus as to whether these maneuvers should be performed at all, much less before or after the papillectomy.23,26,27,30,38,41

Pancreatic or biliary stenting. Endoscopic papillectomy is associated with an increased risk for postprocedural pancreatitis. Several studies have shown that placement of a prophylactic pancreatic duct stent reduces the risk of post-ERCP pancreatitis.42 It has been implied then that placement of a pancreatic stent during endoscopic papillectomy may also minimize the risk of stenosis of the pancreatic duct orifice and may also allow safer use of adjunctive coagulative therapies, but this theory is unproven.12,16,25,30,40 Other authors have suggested that pancreatic duct stents should only be used if pancreatic duct drainage is deemed suboptimal or if the pancreatic duct is difficult to cannulate after the procedure.10,26,27 If a pancreatic duct stent is placed before papillectomy is performed, it may prevent en bloc removal of the lesion, although en bloc resection may make subsequent pancreatic duct stent placement difficult.

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 postprocedure pancreatitis in the stent group.41 On the basis of these data, prophylactic pancreatic duct stenting during papillectomy is recommended to reduce the risk of postprocedural pancreatitis.

Prophylactic biliary stenting to reduce the risk of postprocedural cholangitis has not been widely performed and cannot be uniformly recommended at this time unless there is concern for inadequate biliary drainage after the papillectomy.10,12,30

Ablative therapies. Although they are not routinely used as primary therapy for ampullary adenomas, ablative therapies (argon plasma coagulation, laser therapy, monopolar or bipolar electrocoagulation) are useful to
destroy residual or recurrent adenomatous tissue not removed during attempts at primary snare resection. Argon plasma coagulation is the most frequently used modality, given its widespread availability and superficial depth of tissue destruction. \(10,12,24,25,27,30,33,37,39\) Unfortunately, tissue treated in this manner is not available for pathologic analysis and any suspicious area should be biopsied before ablation.

**Postprocedure evaluation.** Endoscopic removal of ampullary adenomas is considered a “high-risk” procedure for complications. A period of postprocedure inpatient observation should be considered for the detection and treatment of any immediate or early delayed complications, especially after extensive removal and treatment of large lesions, in patients with comorbid medical illnesses, those who do not have ready access to medical care, and those without support measures.

**Results of endoscopic therapy**

**Clinical success.** Data on the clinical success of endoscopic papillectomy are largely based on retrospective, heterogeneous case series. Successful papillectomy rates range from 46% to 92%, although multiple procedures were often required to completely remove all adenomatous tissue. \(10,12,16,24,25,30,37\) Larger lesions are more likely to be incompletely excised at the initial endoscopic procedure.

**Complications.** Early complications after endoscopic papillectomy are similar in nature to other complications of ERCP and include pancreatitis, perforation, bleeding, sedation complications, and cholangitis. Late complications include the development of pancreatic or biliary stenosis. Reported complication rates derived from data from large, tertiary care referral centers and experienced therapeutic endoscopists are as follows: pancreatitis 8% to 15%, perforation 0% to 4%, bleeding 2% to 13%, cholangitis 0% to 2%, and papillary stenosis 0% to 8%. \(10,12,16,24,25,30,37\)

Death after papillectomy is rare but has been reported. \(27\)

**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. Reported surveillance intervals have varied but, in general, have included an initial surveillance examination 1 to 6 months after the index procedure followed by repeat examinations with a duodenoscope every 3 to 12 months thereafter for a period of at least 2 years with periodic examinations thereafter. \(10,16,25,30,32,35,37,39\) Lesions found to contain areas of high-grade dysplasia may need to be followed more closely. Endpoints for surveillance have not been established. One reasonable approach for sporadic (non-FAP) ampullary polyps is to adopt a surveillance policy similar to that of patients with flat colonic polyps. \(45,46\)

**Role of papillectomy in FAP**

The precise role of endoscopic papillectomy in patients with FAP remains unclear because the natural history of the disease and overall outcome in these patients is dependent on the entire duodenal carcinogenic risk rather than that of the ampullary lesion alone. \(1\) Natural history studies in patients with FAP suggest slow histologic progression of proximal lesions over time and a relatively low risk for development of cancer. \(15\) Of note, patients who have undergone protocolecotony are still at high risk for development of ampullary lesions and should undergo periodic surveillance for duodenal and ampullary adenoma and carcinoma. \(26\)

**NONAMPULLARY DUODENAL ADENOMAS**

Adenomas 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 and have the potential to undergo malignant transformation to duodenal cancer. Management of patients with FAP, Peutz-Jeghers syndrome, and other related conditions is discussed in another guideline. \(1\) The remainder of this guideline will focus on the management of sporadic duodenal adenomas.

**Evaluation of nonampullary duodenal lesions before endoscopic therapy**

The endoscopic appearance of duodenal adenomas may be indistinguishable from nonadenomatous polyps such as Brunner’s gland tumors, inflammatory polyps, carcinoid tumors, and hamartomas. Suspicious lesions should be biopsied before attempted endoscopic resection. Before endoscopic resection of a duodenal polyp, it is important to ensure that the polyp does not involve the ampulla because the pancreaticobiliary systems need to be addressed as discussed above. Examination with a side-viewing endoscope or EUS can be helpful in making this distinction.

**Role of EUS.** The precise role of EUS in the management of duodenal adenomas is unclear. EUS can establish the relationship of the lesion to the pancreaticobiliary tree when this is uncertain after forward and side-viewing examinations and can obviate the need for ERCP. EUS can also allow determination of endoscopic resectability when biopsy specimens have shown high-grade dysplasia and endoscopic findings are suspicious for malignancy, and it may be useful for evaluation of polyps larger than 2 cm. \(45,46\)
Endoscopic resection techniques

Techniques of endoscopic removal of duodenal adenomas are not standardized, although the general approach is similar to that of colonic polyps, particularly those of the right colon because of the thinness of the duodenal wall. A submucosal injection to create a submucosal fluid cushion may be useful for removal of flat polyps. The lack of lifting during injection suggests underlying malignancy, as previously mentioned. Endoscopic mucosal resection techniques have also been described in the removal of duodenal lesions. Adjuvant ablative therapies such as the use of argon plasma coagulation or electrocoagulation may be used to destroy residual or recurrent adenomatous tissue not removed during attempts at primary snare resection. Small or flat lesions may sometimes be completely removed with ablative methods alone such as argon plasma coagulation, neodymium:yttrium-aluminum-garnet laser, or electrocautery.

Results of endoscopic resection for sporadic duodenal adenoma

Data on the clinical success of resection of duodenal adenoma in patients with sporadic polyps are based on a few small case series. In one series of 21 patients with lesions of a median size of 27.5 mm (range 8-50 mm), the success rate for endoscopic removal after a 3-month interval was 55%. After a median follow-up period of 71 months, local recurrences developed in 25%, which were re-treated endoscopically. No patients had carcinoma during the follow-up period.

Generally, larger lesions are more difficult to remove, and lesions with greater than 33% circumferential involvement of the lumen should be considered for surgical resection. Complications after endoscopic resection of duodenal adenomas are similar in nature to complications of colonoscopic polypectomy and include perforation, bleeding, and complications related to sedation.

Surveillance for residual or recurrent neoplastic tissue

It is recommended that all patients who have undergone endoscopic resection of duodenal adenomas be considered for surveillance endoscopy for the detection and treatment of recurrence. On the basis of limited data, formal recommendations cannot be given regarding surveillance intervals and should be applied on an individual basis on the adequacy of resection, degree of dysplasia, and underlying comorbid medical illnesses. End points 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 neoplasia are at higher risk for the development of colorectal neoplasia. Until more definitive data are available, it is reasonable to offer screening colonoscopy to all patients who have duodenal or ampullary adenomas.

SUMMARY

- Ampullary and duodenal adenomas have the potential for malignant transformation and require appropriate diagnostic evaluation. (1C)
- Both ERCP and EUS are important tools in the evaluation and staging of ampullary adenomas and can assist in selecting candidates for endoscopic or surgical therapy. (1C)
- Techniques of endoscopic removal of ampullary neoplasms are not standardized and should be performed by experienced endoscopists. (2C)
- Patients undergoing endoscopic removal of ampullary and duodenal neoplasms should undergo postsurgical surveillance to ensure complete tissue removal and lack of disease recurrence. (2C)
- Endoscopy is useful for evaluation and resection of sporadic duodenal adenomas using techniques similar to those used during polypectomy. (2C)
- Patients with sporadic ampullary or duodenal adenomas are at increased risk for colon polyps and should be offered screening colonoscopy. (2C)

REFERENCES