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## Introduction

Adenomas of the ampulla of Vater are rare with prevalence of 0.04–0.12% at autopsy [1–4]. Nonetheless, these lesions are encountered not infrequently by endoscopists, likely owing to the small size at which they may result in symptoms of biliary obstruction as well as the increased use of endoscopy. The potential early onset of symptoms, in addition to increasing experience with therapeutic ERCP, likely contributes to the early detection, treatment, and excellent survival associated with these lesions.

Ampullary adenomas are most commonly small, sessile polypoid lesions. Pathologically they are generally villous and tubulovillous adenomas. They are often sporadic, though they also occur in association with genetic polyposis syndromes such as familial adenomatous polyposis (FAP), which confer a 300-fold increased risk of developing an ampullary adenoma [5, 6]. Nearly

90% of FAP patients develop ampullary adenomas in their lifetime with about 4% progressing to malignancy [7]. This contrasts with sporadic ampullary adenomas which have a reported incidence of malignant transformation ranging from 25 to 85%. Therefore, these lesions require resection or surveillance [8, 9]. Resection has historically been limited to pancreaticoduodenectomy (PD) and transduodenal excision (TDE); however, in 1993 the first report of endoscopic resection with curative intent, also known as endoscopic ampullectomy (or papillectomy), was published [10]. Since that time, with growing interest in minimally invasive techniques aimed at lowering the morbidity and mortality associated with such procedures, investigations into choosing optimal candidates for and techniques of endoscopic ampullectomy have ensued. Additionally, more optimal application of new and existing technologies, including endoscopic ultrasound (EUS), may aid in the selection of patients who will most likely benefit from therapeutic endoscopic ampullectomy.

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## Indications for Ampullectomy

There exist no clear and widely accepted guidelines regarding selection of patients for surveillance versus resection of ampullary adenomas [11]. There are however known differences in risk of transformation to carcinoma depending on patient characteristics, with the main differentiating factor being the presence or absence of a hereditary polyposis syndrome. Classification and plan of care differ for patients with ampullary

adenomas in the setting of FAP compared to those with sporadic ampullary adenomas.

## Case 1

A 22-year-old male with history of FAP undergoes a screening upper endoscopy during which numerous polyps are discovered throughout the stomach. At the ampulla, a smooth, 5-mm polypoid lesion is noted and biopsy results are consistent with an adenoma. What is the next step?

## FAP-Associated Adenomas

Patients with FAP are often discovered to have multiple upper gastrointestinal adenomas, making resection of only an ampullary lesion unattractive if the goal of resection is total prevention of carcinoma. The risk of histologic progression of upper intestinal adenomas in FAP has been demonstrated to be low (on the order of 11% in one large study), making surveillance with biopsies of an ampullary lesion a reasonable approach in most of this patient population [7, 12]. Microscopic adenomatous changes within an endoscopically normal-appearing ampulla are common, occurring in up to 27% of patients; therefore, biopsies should be obtained of the ampulla regardless of endoscopic appearance in FAP patients [13]. The patient may be informed of the possibility of missing progression with endoscopic forceps biopsy surveillance, though studies aimed at evaluating this risk have not focused on the FAP patient population [14, 15].

After colon cancer, ampullary carcinoma is the most prevalent malignancy and leading cause of mortality in FAP patients, affect-

ing about 5–6% of patients [16]. Spigelman et al developed a severity classification system for FAP patients with duodenal polyps, which includes ampullary lesions (Table 18.1) [17]. Using this model, points are accumulated according to number, size, pathology, and degree of dysplasia of polyps to obtain a stage classification from 0 to IV. Stage I indicates mild disease, and stages III–IV indicate severe polyposis. Most patients (80%) have stage I–III disease with 10–20% harboring stage IV disease. Over time, more patients develop advanced stage IV disease with up to 43% at age 60 and 52% by age 70 [18, 19]. Stage IV disease is also associated with higher probability (up to 36% at 10 years) of developing cancer compared to less than 1% for stages I–III; therefore, stage IV patients warrant surgical referral, as they may be candidates for pancreaticoduodenectomy [19, 20]. However, a recent study demonstrated that endoscopic management of stage IV FAP patients may be feasible. Patients with stage IV FAP underwent endoscopic treatment with removal of all duodenal polyps >1 cm including ampullary adenomas and control of smaller polyps with intensive ongoing endoscopic surveillance. All these patients achieved Spigelman downstaging with no invasive duodenal cancer diagnosed at mean 9-year follow-up, and 8.5% required surgery for advanced neoplasia [21]. Therefore, endoscopic management of even stage IV disease by removing >1 cm lesions with close surveillance may be successful with potentially decreased mortality from ampullary and duodenal cancers. In addition, if histologic progression is identified on biopsy surveillance, or symptoms of biliary obstruction occur with ampullary lesions, evaluation for excision of the lesion should be pursued.

**Table 18.1** Spigelman classification of duodenal polyps in familial adenomatous polyposis

Score (points)	1	2	3
<i>No. of polyps</i>	1–4	5–20	>20
<i>Size (mm)</i>	1–4	5–10	>10
<i>Histology</i>	Tubular	Tubulovillous	Villous
<i>Dysplasia</i>	Mild	Moderate	Severe

Stage 0: 0 point, Stage I: 1–4 points, Stage II: 5–6 points, Stage III: 7–8 points, Stage IV: 9–12 points

## Case 1 Continued

The patient is classified as stage II by the Spigelman classification with 5 total points. Therefore, after discussion with his gastroenterologist, he elects to continue with routine surveillance of the ampullary lesion given his relatively low risk of malignant transformation.

## Sporadic Adenomas

Sporadic adenomas are most frequently discovered in patients over the age of 40, and most commonly in the seventh decade of life, during evaluation for signs or symptoms of biliary obstruction. Painless jaundice is by far the most common presenting symptom found in 50–75% of these patients [22, 23]. Other symptoms include biliary colic, weight loss, and vague abdominal pain with reports of acute pancreatitis. In general, unlike FAP-associated adenomas, sporadic adenomas of the ampulla require resection especially when symptoms are present or histology is consistent with high-grade dysplasia.

## Case 2

A 72-year-old female with severe aortic stenosis, diabetes, and prior myocardial infarction presents with new-onset painless jaundice and mild transaminitis on comprehensive metabolic profile. Right upper quadrant ultrasound reveals dilation of the common bile duct, which is confirmed on contrast-enhanced CT of the abdomen. No pancreatic mass or other signs of metastatic disease are noted on CT. What is the next step?

## What Diagnostic Tools are Available?

The diagnosis and workup of an ampullary adenoma relies on endoscopic, radiographic, and histologic evaluation. Many non-adenomatous lesions including Brunner's gland tumors, inflammatory polyps, carcinoid tumors, and

**Table 18.2** Histopathologic lesions of the ampulla of Vater [35]

Benign	Malignant
<i>Tubulovillous adenoma</i> (40%)	<i>Adenocarcinoma</i>
<i>Villous adenoma</i> (30%)	<i>Neuroendocrine tumor</i>
<i>Tubular adenoma</i> (10%)	<i>Cystadenoma</i>
<i>Adenomyoma</i>	<i>Signet ring cell carcinoma</i>
<i>Carcinoid</i>	<i>Lymphoma</i>
<i>Hemangioma</i>	
<i>Leiomyoma</i>	
<i>Lipoma</i>	
<i>Lymphangioma</i>	
<i>Neurofibroma</i>	
<i>Hamartoma</i>	
<i>Fibroma</i>	
<i>Granular cell tumor</i>	

hamartomas may cause lesions of the ampulla (Table 18.2). The goal of this evaluation is to rule out cancer, which would require surgical intervention, and to diagnose adenomas, which may be amenable to endoscopic resection.

## Endoscopy: How Accurate is Ampullary Biopsy?

Endoscopy provides useful information from both endoscopic visualization of the ampullary lesion and histology from forceps biopsy. It is important to recognize foci of cancer may still exist within an otherwise benign-appearing adenoma, and furthermore, false-negative biopsy results may occur in 17–40% [24–28]. Accuracy of forceps biopsy of ampullary lesions may improve by performing biopsies after sphincterotomy. An old study reported that the false-negative rate dropped to 0% by waiting to take biopsies at least 10 days after sphincterotomy [29] while another report confirmed improved accuracy when biopsies were taken immediately after sphincterotomy [30]. However, a prospective study of ampullary biopsy before and after sphincterotomy found sensitivity of forceps biopsy for malignancy improved insignificantly

**Table 18.3** TNM staging of ampullary carcinoma

<i>Primary Tumor (T)</i>	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor limited to ampulla of Vater or sphincter of Oddi
T2	Tumor invades duodenal wall
T3	Tumor invades pancreas
T4	Tumor invades peripancreatic soft tissues or other adjacent organs or structures other than pancreas
<i>Regional lymph nodes (N)</i>	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis
<i>Distant metastasis (M)</i>	
M0	No distant metastasis
M1	Distant metastasis

from 21% to only 37% following sphincterotomy [31]. In addition, this practice is likely not feasible unless the patient has had prior sphincterotomy or is having an ERCP for other indications necessitating a sphincterotomy at the time an ampullary lesion is discovered. Care should be taken to avoid the pancreatic orifice during biopsy as pancreatitis has been reported following ampullary biopsies [32].

Despite the problem of biopsy sampling error, recently confirmed by a large series where 53% of invasive cancers were missed by biopsy, only 5% of these invasive cancers were deemed endoscopically resectable. The following endoscopic findings are believed to indicate potential malignancy and therefore unsuitable for endoscopic ampullectomy: friability, ulceration, more than 50% lateral extension, obvious duodenal infiltration with induration and firmness, and intraductal extension more than 1 cm from the papilla [10, 33]. There are growing reports of adjunctive endoscopic technologies in the evaluation of ampullary lesions including narrow band imaging and magnification endoscopy [34]. Given the inaccuracy of endoscopic biopsy for diagnosing invasive malignancy in ampullary adenomas, further evaluation may be needed. This could ultimately entail endoscopic resection of the ampulla to obtain a definitive diagnosis in addition to providing potentially curative therapy.

## Radiology

Transabdominal ultrasound is commonly used as a first-line examination in patients with jaundice and may demonstrate ductal dilatation proximal to the ampullary adenoma. Pancreatic protocol multidetector row CT of the abdomen with contrast is often used to rule out a pancreatic mass and metastatic disease in patients with painless jaundice and should be performed for this indication prior to ERCP and ampullectomy. Spiral CT is likely the best modality for the evaluation of vascular invasion though its role in evaluating the presence of carcinoma in ampullary lesions is limited [35]. Magnetic resonance cholangiopancreatography (MRCP) provides non-invasive imaging of pancreatic and biliary ductal anatomy, which may not be necessary in all patients, but is useful in high-risk populations. Finally, percutaneous transhepatic cholangiography (PTC) may be used to evaluate the biliary tree in the case of a failed or difficult ERCP although this is rarely necessary.

## EUS: When is EUS Indicated?

EUS offers several advantages in the workup of ampullary adenomas to evaluate for the presence of invasive cancer. Ultrasonographic architecture and three-dimensional reconstruction of the lesion may be used to detect invasive carcinoma which is not evident on forceps biopsy or other imaging techniques [36, 37]. Ampullary carcinomas are staged using the TNM staging similar to other cancers (Table 18.3). As with other cancers, M staging is best performed with radiologic imaging, typically CT or MRI. EUS and IDUS are the modalities of choice for local T staging of ampullary carcinoma (Table 18.4). Overall accuracy of EUS T staging is estimated at 78–84% with greatest accuracy for T2 and T3 stages (T1 60%, T2 92%, T3 92%, T4 50%) [35]. Overstaging can occur from peritumoral inflammation or concomitant pancreatitis [38]. EUS accuracy for N staging ranges from 50 to 100%. Intraductal ultrasound has the highest accuracy (70–100%) of all modalities for T staging [39]. A recent study comparing IDUS and EUS for T staging demonstrated similar overall accuracy

**Table 18.4** T and N staging accuracy of CT, MRI, EUS, and IDUS [35, 39, 75]

	CT	MRI	EUS	IDUS
<i>T</i> staging accuracy (%)	5–24	46	75–84	78–100
<i>N</i> staging accuracy (%)	33–59	77	50–100	67–93

CT computed tomography, MRI magnetic resonance imaging, EUS endoscopic ultrasound, IDUS intraductal ultrasound

(78 versus 63%,  $p=0.1$ ) although there was a trend toward increased accuracy with IDUS for T1 and T2 (T1: 86 versus 62%, T2: 64 versus 45%, T3-4: 75 versus 88%) [40]. While EUS is performed before ERCP and ampullectomy, IDUS is more invasive and occurs only during ERCP after achieving bile duct cannulation by passing a 20- to 30-MHz probe over a guide-wire into the bile duct and slowly withdrawing through the ampulla. A recent retrospective study reported that EUS and ERCP had comparable accuracy (91% and 84%) for determining intraductal extension of ampullary lesions. In addition, there was no difference in accuracy between radial and linear echoendoscopes [41]. Most experts agree that EUS is indicated for lesions >3 cm, displaying potentially malignant endoscopic features, or demonstrating high-grade dysplasia or carcinoma in situ on histology [42]. Others also advocate EUS for lesions >2 cm in size [35, 43]. Small benign-appearing lesions, especially those less than 1 cm, are unlikely to harbor malignancy, and EUS evaluation is generally unnecessary prior to proceeding to endoscopic snare resection [43].

The technique of EUS imaging of the ampulla uses water or saline to fill the duodenum. Once in the second portion of the duodenum, the echoendoscope is rotated counterclockwise maintaining apposition to the duodenal wall until the ampulla is visualized by EUS. Alternatively, the ampulla can be located endoscopically followed by EUS imaging of this region. It is important to assess the lesion for tissue invasion, ductal infiltration, and evidence of local lymphadenopathy. The choice of a radial or linear echoendoscope is personal preference although the ability to perform fine-needle aspiration (FNA) favors the linear scope. EUS-FNA should be performed on lymph nodes as well as ampullary masses using a 22-

25-gauge needle as 19-gauge needles are typically difficult to use in the duodenum.

### What are Indications for Endoscopic Versus Surgical Resection?

If EUS identifies invasive carcinoma, regardless of tumor staging, pancreaticoduodenectomy is the treatment of choice when the goal is curative therapy. Studies have demonstrated high recurrence rates for these lesions with transduodenal resection [14, 44]. Lesions with high-grade dysplasia, carcinoma in situ, and/or ductal invasion less than 1 cm may still be considered for endoscopic resection [39, 45, 46]. Generally endoscopic resection is reserved for ampullary masses smaller than 4–5 cm. Multivariate analysis of factors associated with malignancy identified only a negative saline lift sign as predictive of malignancy (odds ratio 28.4,  $p=0.015$ ) while size  $\geq 2$  cm trended toward significance ( $p=0.059$ ) [47].

Surgical excision is currently recommended for the following:

- Larger lesions (>4–5 cm)
- Lesions with carcinoma (histologic or suspicious on endoscopic evaluation)
- Lymph node involvement or significant ductal invasion (>1 cm)
- Lack of access to experienced interventional endoscopist
- Patient preference

### Case 2 Continued

The patient proceeds to EUS, which reveals a 2.5-cm ampullary mass with endoscopically benign features. There is minimal ductal invasion and

no vascular invasion on EUS. Endosonographic images also reveal no submucosal invasion or signs of local metastatic disease. Biopsy results are consistent with tubular adenoma. Given her comorbid conditions and lesion characteristics, the patient elects for endoscopic ampullectomy over surgical resection.

## Techniques of Ampullectomy

For benign and pre-malignant lesions, debate continues not only regarding endoscopic versus surgical resection, but also between the two most common surgical approaches to ampullectomy. Endoscopic ampullectomy for benign ampullary lesions has demonstrated equivalent efficacy and mortality with decreased morbidity compared to surgical ampullectomy [48].

## Surgical Approach to Benign Adenoma

Two procedures, pancreaticoduodenectomy and transduodenal resection, may be considered. For benign adenomas, transduodenal resection is preferred given the reduced morbidity and mortality associated with the procedure although it comes with a higher recurrence rate. Using a midline or subcostal laparotomy, the mass is identified and lateral duodenectomy is performed. Circumferential ampullary resection is undertaken using needle-tip electrocautery. Morbidity and potential mortality associated with surgery may be undesirable or unacceptable for some patients with comorbid conditions.

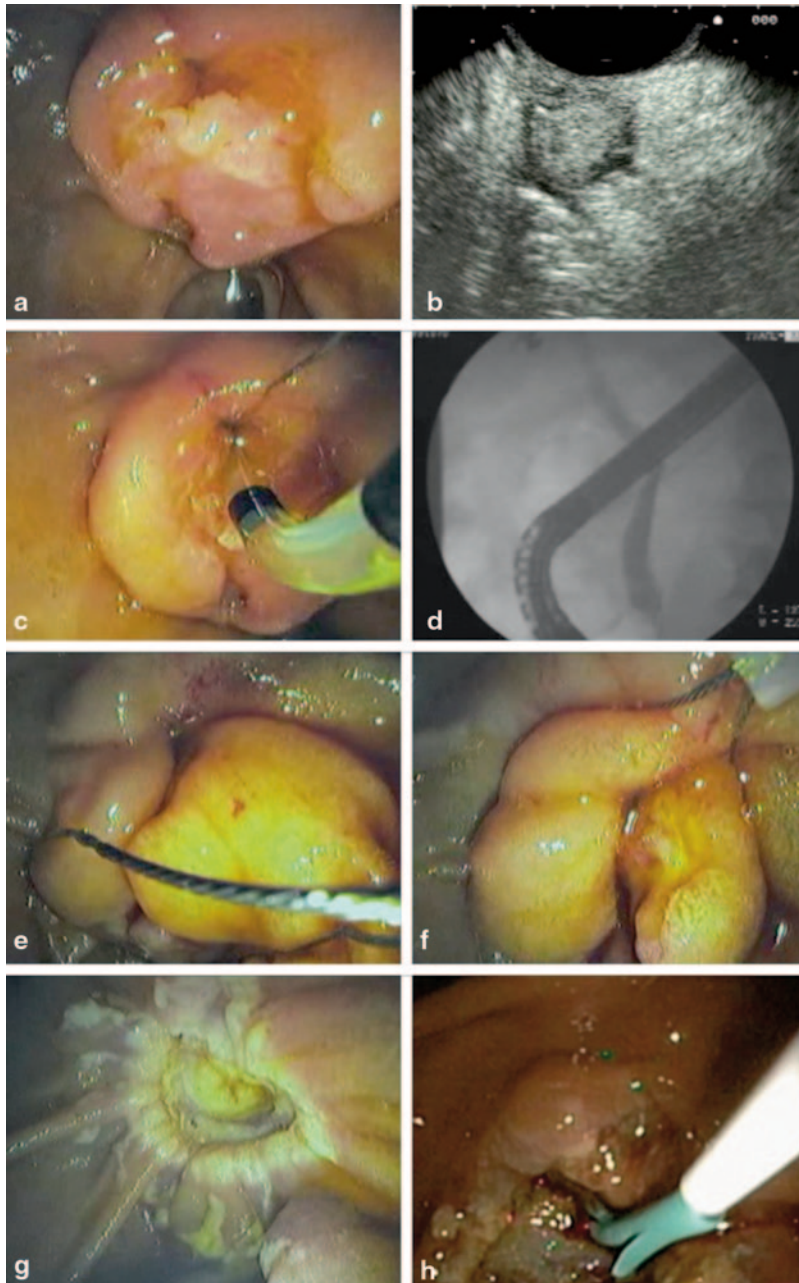
## Endoscopic Ampullectomy/ Papillectomy

Endoscopic ampullectomy (EA) may be considered in patients meeting the previously described indications for endoscopic resection and for non-surgical candidates. The technique varies greatly across centers. Regardless, the procedure requires proficiency with a side-viewing therapeutic duodenoscope, which is used to visualize the

lesion and allows use of thermal ablation probes. Many institutions perform the procedure under conscious sedation, though general anesthesia may also be employed.

After inspection, a double-lumen sphincterotome and hydrophilic guidewire are used for biliary and pancreatic duct cannulation (Fig. 18.1 and Video 18.1). Contrast should be injected into both ducts to assess for intraductal extension of the ampullary adenoma. Generally, biductal sphincterotomy is performed to allow for decompression and stenting post-ampullectomy although there is a concern for potential increased risk of complications of bleeding and perforation and interference with pathologic evaluation of the resected specimen from cautery [49, 50]. Furthermore, with larger lesions it may be difficult to identify appropriate landmarks to perform sphincterotomy safely. Post-resection sphincterotomies may be done as well. Some centers place wires into the ducts and proceed with ampullectomy with wires in place. Next, submucosal injection of epinephrine diluted in saline 1:20,000 may be used to facilitate lifting the tumor from the muscularis propria. This also may provide evidence of unidentified carcinomatous invasion if lift is not accomplished (absence of the “positive lift sign”) [51]. The risk of bleeding and deeper penetration of tissue burning is also mitigated by the submucosal lift technique [52]. Nevertheless, this step may make snare placement and resection more challenging and distort the ampullary anatomy, and the author usually avoids submucosal injection.

Ampullectomy is then performed, preferably en bloc, using a monopolar polypectomy snare (as in colon mucosal polypectomy) with electrocautery at 40–60 W using blended current, though currently there are neither guidelines regarding power output nor mode of current. The snare may be groomed prior to insertion to generate a slight curve at the tip of the snare to aid in en bloc resection. Typically the tip of the snare is anchored immediately above the lesion and opened to unfold around the lesion in a cephalad to caudal direction. Lesions greater than 2 cm may require piecemeal resection.



**Fig. 18.1** Procedural steps of endoscopic ampullectomy. **a** Lesion is identified and margins examined. **b** EUS performed for staging prior to resection without evidence of invasion or extension into the bile duct. **(c)** Pancreatic duct sphincterotomy is performed. **d** Cholangiogram con-

firms no evidence of ductal invasion. **e** Snare is deployed around the ampullary lesion. **f** Snare is firmly closed around the lesion for en-bloc resection. **g** Ampullary site is examined for residual abnormal tissue. **h** Prophylactic pancreatic duct stent is placed

Immediately after resection, the specimen(s) should be retrieved to avoid loss distally, and snare or Roth net (US Endoscopy, Mentor, OH)

retrieval is preferred over aspiration given the importance of maintaining specimen architecture for histologic evaluation. Administering

**Table 18.5** Procedural steps of endoscopic ampullectomy. (Adapted from [35])

<i>Inspection</i>	Evaluate for firmness, ulceration, induration, friability, size
<i>Cannulation</i>	Achieve with double lumen sphincterotome and hydrophilic guidewire. Assess for intraductal invasion or stricture. Inject dilute epinephrine solution for flat lesions
<i>Sphincterotomy</i>	Routine pancreatic sphincterotomy recommended. Biliary sphincterotomy performed routinely or in absence of free bile flow
<i>Resection</i>	Polypectomy snare used to grasp adenoma at the base. Apply 45–60 W blended current to cut/cauterize
<i>Ablation</i>	Monotherapy for flat or small lesions. Adjunctive therapy for residual tissue post-ampullectomy
<i>Stenting</i>	3- or 5-Fr stent placed in PD, may be placed prior to ampullectomy for small lesions. Biliary stenting for poorly draining bile duct after sphincterotomy
<i>Observation</i>	Observe site for evidence of bleeding. If present, inject 1:20,000 epinephrine
<i>Prophylaxis</i>	Rectal indomethacin immediately post-procedure to prevent pancreatitis

intravenous glucagon is helpful to diminish peristalsis and thereby aid in tissue retrieval. Ablative therapy may be used as primary therapy for recurrent small flat lesions not amenable to snare resection, or adjuvant treatment for residual abnormal tissue in the resection bed. Various forms of ablative therapies have been suggested including monopolar or bipolar electrocautery, Nd:YAG laser photoablation, and argon plasma coagulation, with data lacking to guide the use of one approach over the other. A retrospective series of 103 patients with ampullary adenomas (both sporadic and FAP) reported that performing ablative therapy after resection did not affect long-term success of ampullectomy (81% with ablation versus 78% without ablation) although there was a trend toward decreased recurrence with ablation (3 versus 14%,  $p=0.2$ ) [53].

After ampullectomy is performed, a short 3-Fr or 5-Fr pancreatic duct (PD) stent must be placed to reduce the risk of post-ampullectomy pancreatitis [54]. If pre-resection sphincterotomy was not performed, techniques to help identify the pancreatic orifice, in addition to careful inspection, include injecting dilute methylene blue mixed with contrast into the pancreatic duct before resection which will stain the pancreatic orifice blue and using intravenous secretin to promote flow of clear pancreatic juice. A 3-Fr pancreatic stent will typically fall out, and this should be confirmed with an abdominal X-ray. With 5-Fr stent placement, repeat duodenoscopy 2–3 weeks post-ampullectomy will

allow for stent retrieval as well as excision or fulguration of any remaining abnormal tissue. Common bile duct (CBD) stenting may also be performed, though there are no data to suggest it is necessary to prevent post-ampullectomy cholangitis. In cases with smaller lesions, the PD stent may be placed prior to ampullectomy to avoid the difficulty of cannulating post-ampullectomy. This may also protect the orifice from electrocautery damage during snare resection and fulguration of any residual tissue [55]. Table 18.5 reviews the steps in performing endoscopic ampullectomy.

Complications of the procedure may occur in up to 15–28% of cases. Post-ampullectomy pancreatitis (5–33%) is generally mild and resolves with conservative management. Ampullectomy bleeding (2–13%) may be controlled with conservative measures and endoscopic hemostasis. Papillary stenosis (0–8%) may be treated with sphincterotomy, stenting and/or balloon dilation. Perforation (0–4%) and cholangitis (0–4%) are both infrequently encountered and mortality is exceedingly uncommon [6, 10, 29, 33, 53, 55–64].

### Prophylactic Interventions

Prophylactic placement of PD and CBD stents is discussed above. Whether routine use of prophylactic antibiotics is necessary remains unanswered, but is not currently recommended [65]. There is strong evidence to support the utility of



routine prophylactic rectal indomethacin in the prevention of post-ERCP, and by corollary, post-ampullectomy pancreatitis [66].

## Endoscopic Palliation

In patients who are not surgical or endoscopic ampullectomy candidates, endoscopic biliary drainage with palliative intent is very appropriate. Ampullectomy or transpapillary stent placement may be employed for decompression of the biliary or pancreatic ducts in cases of obstruction from an ampullary mass [67].

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## Case 2 Continued

Three months after ampullectomy, the patient returns for surveillance duodenoscopy, which reveals no residual adenoma or recurrence of her previously resected lesion. She is scheduled for another EGD in 6 months to survey for recurrence at the site of prior ampullectomy.

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## Surveillance

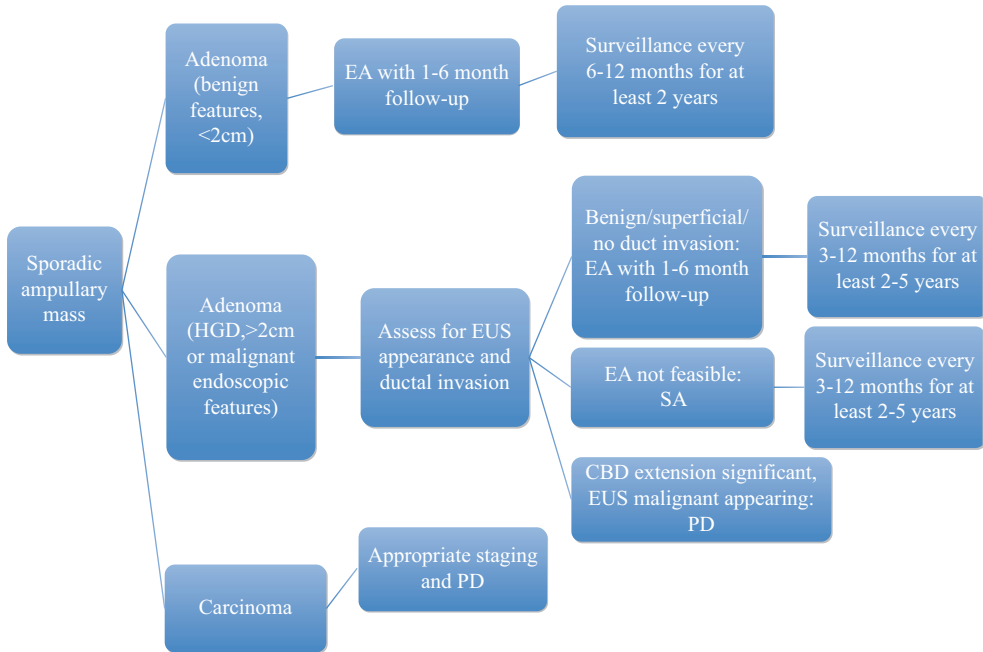
Unlike patients who undergo colectomy for colon cancer, patients do not require endoscopic surveillance following pancreaticoduodenectomy for an ampullary lesion, unless they have a polyposis syndrome. There are no guidelines on the interval and duration of endoscopic surveillance following endoscopic or transduodenal ampullectomy. An initial examination with an experienced interventional endoscopist, side-viewing duodenoscope, and biopsies at 1–6 months with repeat examination every 3–12 months for at least 2 years is recommended [11]. ERCP is not necessary in the absence of symptoms. In patients with lesions  $\geq 2$  cm, intraductal involvement, or high-grade dysplasia on post-resection histology, surveillance intervals should be on the more frequent end of these ranges. Technical factors with an individual case may also dictate surveillance intervals; for example, in lesions with incomplete or piecemeal resection, more frequent examina-

tions may be required in order to prevent or detect recurrence. FAP patients should then continue with routine upper endoscopy surveillance of duodenal polyps in the upper gastrointestinal tract, which is based on the Spigelman classification (stage 0/I: every 5 years; stage II: every 3 years; stage III: every 1–2 years.) [20]. The endpoint for surveillance in patients with sporadic ampullary adenomas is unclear with experts recommending at least 2-year follow-up [68]. Very long-term follow-up studies of endoscopic ampullectomy patients are lacking, and surveillance guidelines may change when these data become available.

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## Recurrence

Mean endoscopic success rate with complete excision of the ampullary lesion from a review of 967 patients was 82% [64]. In patients who have undergone surgical transduodenal ampullectomy, recurrence has been reported to occur in 0–50% of patients [27, 69–73]. Reported recurrence rates following endoscopic ampullectomy for sporadic lesions are lower, ranging from 0 to 33% [33, 74]. In a recent study of FAP patients, recurrence rates after endoscopic ampullectomy are higher at 58.3% over mean 7-year follow-up [13]. The only factor predictive of recurrence was lesion size  $> 1$  cm (77 versus 36% in smaller lesions,  $p=0.002$ ). Only 3 patients (12%) required Whipple surgery during follow-up although these were not performed due to ampullary adenoma recurrence. In a retrospective analysis of endoscopic ampullectomy, predictors of successful endoscopic ampullectomy and lower recurrence included age over 48, male sex, lesion size less than 24 mm, and absence of familial polyposis syndrome [6]. A more recent study of 182 patients following endoscopic ampullectomy noted the following factors associated with recurrence: jaundice at the time of presentation, ampullary adenocarcinoma, intraductal involvement noted on ERCP, and piecemeal resection [75, 76]. With recurrent adenomas, the treatment algorithm is the same as the initial therapeutic approach. Recurrent tumor should be removed and ablated every 2–3 months until biopsy specimens return with no residual adenoma [53].



**Fig. 18.2** Suggested management algorithm of a sporadic ampullary mass. *PD* pancreaticoduodenectomy, *SA* surgical ampullectomy, *EA* endoscopic ampullectomy, *HGD* high-grade dysplasia

## Key Points

- Ampullary adenomas are often asymptomatic and most frequently present with painless jaundice, and 70% are tubulovillous or villous adenomas
- Ampullary adenomas may occur sporadically or in the setting of polyposis syndromes like FAP, and the risk of progression to carcinoma is present in both, which mandates at a minimum ongoing biopsy surveillance. Sporadic adenomas should be resected (Fig. 18.2).
- EUS enables pre-therapy staging to guide the ideal choice of therapy (pancreaticoduodenectomy, transduodenal ampullectomy, or endoscopic ampullectomy) prior to resection in many patients.
- Malignant ampullary lesions should be referred for surgical resection, preferably pancreaticoduodenectomy.
- Endoscopic ampullectomy may be preferred for benign lesions less than 4–5 cm with no malignant endoscopic or EUS features given

the equivalent risk of recurrence and favorable morbidity compared to surgery.

- Surveillance of all patients post-ampullectomy should continue at 3–12 month intervals for at least 2–5 years after resection.
- Recurrent adenomas should be evaluated and treated in the same way as a primary lesion.

## Video Caption

Video 18.1 Endoscopic ampullectomy

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