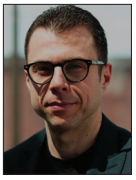
ADVANCES IN ENDOSCOPY

Current Developments in Diagnostic and Therapeutic Endoscopy

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Ampullary Adenoma: How Far Can Endoscopic Papillectomy Go?



Fateh Bazerbachi, MD
Director, Interventional Endoscopy, St Cloud Hospital, St Cloud, Minnesota
Adjunct Associate Professor of Medicine
Division of Gastroenterology, Hepatology and Nutrition
University of Minnesota, Minneapolis, Minnesota

G&H What is the current role of endoscopic papillectomy in the management of ampullary adenomas?

FB First, a note on terminology. In the duodenum, the ampulla is the flask-like swelling within the duodenal wall where the bile and pancreatic ducts meet. The papilla is the nipple-like mucosal mound that we see and resect endoscopically. Papillectomy is therefore the preferred term for the endoscopic procedure, and ampullectomy properly describes the surgical operation. For an adenoma confined to the papilla, without meaningful extension into the ducts, papillectomy is the established first-line treatment, and the major societies agree. Surgery remains an option, but at substantially higher morbidity and cost. Two caveats apply. First, papillectomy is as much a diagnostic procedure as a therapeutic one. Forceps biopsies underestimate these lesions often enough that the resected specimen is frequently our first reliable look at the histology. In our Japanese multicenter study, about 1 in 5 lesions contained carcinoma on final pathology. Second, papillectomy is a program, not a procedure. The program includes staging, resection, expert pathology, surveillance, retreatment, and surgical backup. A patient who cannot commit to all of that, or cannot tolerate its adverse events, is a weak candidate. A center that cannot deliver every part of it should not offer the procedure, however skilled its endoscopists.

G&H What evaluation should be performed before endoscopic resection is considered?

FB The evaluation is multipronged, and it starts with a careful endoscopic examination. A forward-viewing gastroscope fitted with a distal cap can give an adequate view of a small papilla, but a side-viewing duodenoscope remains preferred. The latter is essential for larger lesions, particularly those with a lateral spread, both for a complete examination and targeted biopsies away from the pancreatic orifice. American guidance recommends at least 6 biopsies, especially from ulcerated or indurated areas, because a meaningful fraction of these lesions already harbor malignancy. Even so, endoscopists are not good at recognizing dysplastic tissue at the papilla by eye. One study put the accuracy of endoscopic appearance at about two-thirds. In another, endoscopists reviewing images missed roughly 1 in 3 adenomas, and an artificial intelligence (AI) assistant improved that only modestly.

The next step is transmural evaluation of the duodenal wall and ampullary complex. Most guidance relies on endoscopic ultrasound (EUS) to gauge intraductal extension. EUS can also identify pancreas divisum, which informs resection planning. Magnetic resonance cholangiopancreatography is a useful adjunct. No single test is a gold standard for ductal extension; histology is. When compared with surgical pathology, EUS and endoscopic retrograde cholangiopancreatography (ERCP) perform similarly; each misses roughly 1 case in 5. I therefore use them as complementary tests: EUS beforehand, ideally before any papillary instrumentation or stenting, and the cholangiogram/pancreatogram at the time of resection.

Jaundice, weight loss, or a dilated duct should make you think twice before resecting because they raise suspicion for invasive cancer. An adenoma is soft and pliable and rarely causes fixed obstruction. Cancer is firm and fixed, and it does. Still, the absence of jaundice does not exclude cancer. I have seen several invasive carcinomas that caused only mild, intermittent elevations in liver tests. I suspect the tumor grows and then necroses around the biliary orifice, so the obstruction builds and relieves itself in cycles. Occasionally an endoscopist must perform

urgent ERCP on a patient with an ampullary neoplasm. If that endoscopist will not be the one resecting the lesion, the rule is restraint. Obtain a good-quality EUS first because a stent can degrade later staging. Avoid sphincterotomy and place a plastic stent. Leave the decision about sphincterotomy to whoever will resect the lesion because cautery artifact can compromise both the en bloc resection and the pathologist's ability to read the specimen.

G&H Which endoscopic resection techniques are currently used for ampullary adenomas?

FB The core technique is en bloc snare resection of the papilla with a duodenoscope. Unlike in mucosal resection elsewhere in the gut, a lifting agent is not injected beneath the papilla itself, as it is tethered to the sphincter and ducts, so no meaningful lift is achieved, and injecting there may lead to incomplete resection. Injection is useful for a laterally spreading component on the duodenal wall.

Underwater papillectomy is an interesting development. Water floats the papilla into the lumen, which is what injection tries and fails to do. Early data from a small retrospective series suggest higher rates of en bloc resection with clean margins, without an increase in adverse events. After the papilla and any lateral component are removed, the margins are treated with thermal ablation, and any intraductal extension is addressed.

For very large lesions, papillary endoscopic submucosal dissection (ESD) is emerging, and the early data are interesting. But papillary and duodenal ESD are about as demanding as endoscopy gets, and I see them as a vocation. With the tools we have today, they should remain with a handful of people who dedicate their careers to them, rather than being spread broadly or democratized.

G&H What makes endoscopic resection of ampullary adenomas particularly challenging?

FB The anatomy itself is unforgiving. The bile duct, the pancreatic duct, and the surrounding duodenal wall each bring their own technical challenges and their own adverse events. A laterally spreading component must be resected from the duodenum. Its muscularis propria is among the thinnest in the gastrointestinal tract, Brunner's glands can blunt the submucosal lift, and the blood supply is abundant. The scope is also hard to hold steady beyond the superior duodenal angle. Closure is harder too. It depends on gathering redundant, pliable tissue, and the thin duodenal wall, fixed in the retroperitoneum, offers little. Intraductal extension adds another layer, and the challenges compound quickly. All of that comes before any intraprocedural adverse event. A brisk bleed fills the narrow duodenal lumen within seconds, and unlike in the colon, repositioning the patient rarely exposes the vessel. Then there is the diagnosis. As I noted, neither the endoscopic appearance nor the biopsy reliably excludes cancer beforehand. Even an en bloc resection does not guarantee a readable specimen because thermal artifact often obscures the margins. In our study, about 90% of lesions were removed en bloc. Yet only about 60% of those specimens were confirmed R0, and only about half of all resections overall. Removing a lesion in one piece does not mean it was completely removed.

G&H How is the approach tailored to the characteristics of the lesion?

FB A small lesion confined to the papilla is removed by en bloc snare resection. When there is a laterally spreading component, that portion is removed by endoscopic mucosal resection (EMR), piecemeal if necessary, but the papilla itself should still be captured in one piece. Large lesions removed piecemeal, and those with positive margins, need close follow-up every few months, with thermal ablation as needed, until biopsies confirm the adenoma is gone. Cryoballoon ablation of residual tissue through a duodenoscope has also been reported. Short ductal extension can be treated in expert hands. Finally, familial adenomatous polyposis (FAP) changes the calculus entirely, and papillary lesions in that setting belong within multidisciplinary programs dedicated to FAP.

G&H How does intraductal extension affect the approach, and how much intraductal disease can reasonably be treated endoscopically?

FB The real question is how much ductal extension is too much. I frame it as three questions: Can I resect it? Can my pathologist read it? If so, will it stay gone? Our data are sobering. Ductal extension was uncommon, but when present, only about 1 in 5 resections was R0. And even when the margins were clean, bile duct involvement raised the risk of recurrence roughly fivefold. A negative margin does not mean a clean duct. The reason is anatomic. R0 is conventionally defined by two margins: the mucosal edge around the lesion and the deep base beneath it. But the bile and pancreatic ducts run through the middle of the papilla, and the snare cuts straight across them. Their cut ends form a third margin, one that conventional definition of R0 does not capture. It is also the hardest part of the specimen to read: the ducts are tiny, they collapse, and intense cautery can obliterate them. If adenoma has crept up the ductal lining, the edges and base can be perfectly clean while adenoma remains in the duct stump. There it sits above the scar, where surveillance biopsies cannot reach it, and it declares itself later as recurrence. That may

explain why, in our study, bile duct involvement predicted recurrence even after an apparently R0 resection. It is also why assessing ductal extension before resection matters so much for predicting outcome.

But where do we draw the line? European guidance allows up to 2 cm of intraductal extension in expert centers. American guidance, and most Japanese practice, set the limit at about 1 cm in surgically fit patients. Between 1 and 2 cm, I reserve papillectomy for patients who are not surgical candidates. Beyond 2 cm in a fit patient, surgery is the answer; in an unfit patient, ablation aims at control, not cure. But in truth, all of these thresholds rest on a measurement we cannot make reliably. As I noted, EUS and ERCP each miss a meaningful share of ductal extension, and neither gives a precise length. My hope is that technology, including AI, will give us more objective measurements, so that this decision no longer depends on an endoscopist's gestalt, divined from experience.

G&H What are the associated major adverse events, and which strategies are most effective for preventing them?

FB Papillectomy is not a benign procedure. The most recent pooled analysis, of nearly 5000 lesions, puts the overall adverse event rate at about 30%, mostly bleeding and pancreatitis. Our own multicenter data came in at about 1 in 3. The comparison I find most sobering is that papillectomy carries roughly the pancreatitis risk of a high-risk ERCP plus the bleeding risk of a duodenal EMR. In effect, the endoscopist is performing two high-risk procedures at once. For pancreatitis, prevention rests on a prophylactic pancreatic stent, together with rectal NSAIDs and aggressive hydration with lactated Ringer's solution.

Bleeding is harder. Some endoscopists place a fully covered metal stent across the papilla to tamponade bleeding, borrowing from its use after sphincterotomy. But no data show that it prevents bleeding after papillectomy, and because the resection defect is wider than a sphincterotomy, the bleeding area may not be tamponaded by the stent. When there is a laterally spreading component, closing the defect matters more. Through-the-scope clips are the usual tool, and a growing panoply of options now includes endoscopic hand suturing with a through-the-scope needle holder. Hemostatic agents can treat active oozing, but they have not been shown to prevent bleeding when applied prophylactically. The evidence for biliary stents to prevent cholangitis or stricture is similarly thin.

Practice also differs around the world. In Japan, patients are admitted for days; in the West, they are usually observed overnight. Overnight observation catches pancreatitis, but delayed bleeding often appears days later. The length of observation should therefore be tailored to the patient's comorbidities, the technique and extent of the resection, and where the patient lives. Patients who live far away, or in rural areas with limited access to care, should be counseled about the window for delayed bleeding so they can plan accordingly. They should also know where to go if it happens. When feasible, they should be transferred to a facility with interventional endoscopy, preferably the one where the procedure was performed.

G&H How common is recurrence, and what factors predict risk of recurrence?

FB Recurrence is not the rule, but it is common. The most recent pooled analysis puts it at about 15%, although that figure blends very different follow-up periods. In our study, about 1 in 5 patients had recurred by 3 years. Most recurrences appeared within the first year, and almost all were local. Reassuringly, most were retreated endoscopically, successfully in about three-quarters, and only a minority required surgery. Margin status was the dominant predictor. Indeterminate or positive margins carried a two- to threefold higher risk of recurrence. Those recurrences came early, within the first few months, which suggests residual disease rather than new growth. But even R0 was not always curative. About 1 in 10 patients with R0 resections recurred by 3 years, typically later, at a median of more than a year. Piecemeal resection and carcinoma on final pathology also predicted recurrence.

Interestingly, recurrence was higher in the later years of the study. That was a period in which the share of procedures performed by less experienced operators rose from about a quarter to nearly half. This suggests the learning curve matters, and it supports concentrating this procedure in experienced hands.

G&H Which patients should be referred for surgery rather than endoscopic papillectomy?

FB Some cases clearly require surgery: metastatic disease, invasive cancer beyond the mucosa, and significant ductal extension in a surgically fit patient. Then there is a gray zone. It includes very large lesions, beyond 4 to 5 cm; lesions sitting in a diverticulum; and unfavorable features such as ulceration, friability, firmness, or cholestatic liver tests suggesting early obstruction. In these cases, surgery should be considered even when the biopsies are benign. Early cancer is harder. American guidance advises surgical consultation even for intramucosal carcinoma found on biopsy because sphincter involvement is difficult to judge, and lymphatic and vascular spread has been reported even at that early stage. Our Japanese pathway was more permissive. Very early cancers confined to the ampulla were observed after a clean resection, and anything deeper, or

with uncertain margins, went to surgery. Part of that gap is nomenclature: Japanese pathologists call some lesions carcinoma that Western pathologists would call high-grade dysplasia.

In my view, these lines are not fixed. They mark the current reach of our tools more than the nature of the disease. Arthur C. Clarke observed that the only way to discover the limits of the possible is to venture a little past them, and endoscopy, for better or worse, has a habit of doing exactly that. Lesions in diverticula, giant laterally spreading tumors, and short-segment ductal extension were all once contraindications. With better resection techniques, tools, and adjunctive therapies, they are increasingly treated in expert hands. But technical success and long-term benefit do not always march together. Each extension of the frontier has to be earned by long-term outcomes, not by technical bravado.

G&H What surveillance is recommended, and how long should it continue?

FB American and European guidance agree on the schedule: a first examination at about 3 months with a side-viewing duodenoscope, then at 6 and 12 months, and then yearly for at least 5 years. The scar is biopsied every time, even when it looks normal. That differs from colonic practice, where a scar that looks normal on careful optical evaluation may not be sampled. After piecemeal resection of a large lesion, or after positive margins, follow-up is closer, every few months. Any residual tissue is resected or ablated, and this is repeated until biopsies confirm the adenoma is gone. As for duration, most recurrences appear in the first two years, so that is where surveillance should be most intense, but recurrence does not stop at that boundary. In our study, recurrence after clean resections was still slowly rising at 5 years. Of the 3 metastatic recurrences, 2 followed R0 resections; the numbers are small but sobering. I am cautious about de-escalating too early, while weighing the patient's comorbidities, life expectancy, and willingness to continue. Beyond 5 years, guidance leaves surveillance to individual judgment. It suggests continuing for higher-risk features: piecemeal resection, uncertain or positive margins, ductal involvement, or high-grade dysplasia. I generally follow that, although evidence for any particular interval at that stage is limited. In FAP, surveillance is lifelong regardless, guided by the overall duodenal disease burden.

G&H What are the most important unanswered questions that future research should focus on?

FB This may sound controversial, but in my view the most fundamental question is when we should resect at all. In FAP, long-term follow-up suggests that most ampullary adenomas do not progress meaningfully over many years and that cancer is uncommon. Resection also does not stop new lesions from forming because the whole duodenal field is at risk, and recurrence is high. For small sporadic lesions with low-grade dysplasia, natural-history data are scarce. Yet we offer a procedure with roughly a 1-in-3 complication rate and a 1-in-5 recurrence rate to prevent a cancer whose probability we cannot reliably estimate. We need natural-history cohorts, biomarkers, and validated risk tools to tell us which lesions can safely be watched.

A second priority is to revisit the definition of R0 for the ampullary complex so that it accounts for ductal involvement. We also need to standardize how these specimens are handled, sectioned, and reported. A Canadian-led international Delphi consensus recently set pathology reporting standards for ESD specimens. A similar effort for papillectomy specimens is overdue.

Third is staging. Histology is the true reference standard, but we still do not know which preoperative test, or which combination of EUS, cholangiography, and intraductal imaging, best approximates it.

Fourth, and closely related, is how we define cure. When can we say an ampullary adenoma has truly been eradicated? Should surveillance include ERCP with sampling of the distal bile duct, whether by biopsy, brushings, or bile analysis? Should that be reserved for high-risk cases, such as high-grade dysplasia, where adenoma left behind in the duct carries the greatest consequence? Do those cases warrant prophylactic ablation of the distal duct to treat microscopic extension we cannot see? And can AI help us stratify risk and predict which patient needs which approach?

Finally, training and centralization are key. Papillectomy is complex before, during, and after the procedure, and much remains unknown. It demands both biliary and luminal resection skills, which few operators master together. It also demands an institution that can support the patient long after the procedure itself. That means managing delayed complications, providing years of surveillance, and offering retreatment, or surgery when the limits of a minimally invasive approach have been reached.

Disclosures

Dr Bazerbachi has no relevant conflicts of interest to disclose.

Suggested Reading

Barakat M, Maranki J, Irani S, Chahal P. AGA clinical practice update on management of ampullary neoplasms: expert review [published online September 9, 2026]. *Clin Gastroenterol Hepatol.* doi:10.1016/j.cgh.2026.07.013.

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