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Invited Review

Endoscopic treatment of ampullary neoplasms

I. Scotiniotis

SUMMARY

The past decade has witnessed the acceptance of endoscopic ampulletomy as an effective technique in the management of non-invasive ampullary neoplasms. The ideal lesion should be smaller than 3cm and not extend into the biliary or pancreatic ducts. Endoscopic ultrasonography is helpful in excluding invasion prior to resection. Snare resection can be combined with thermal techniques of fulguration to improve success rates. Pancreatic stent placement has led to lower rates of post-ampullectomy pancreatitis, the major complication of the procedure. Performed in endoscopic centers of expertise, endoscopic ampullectomy constitutes a less morbid alternative to traditional surgical approaches toward ampullary neoplasms.

The ampulla of Vater is the commonest site of neoplasia in the small bowel. Still, ampullary neoplasms are rare overall, accounting for about 1% of all GI tract tumors. Many histologic types of ampullary neoplasms have been described, but adenomas/adenocarcinomas form the overwhelming majority. Their importance has been recognized for many years in patients with Familial Adenomatous Polyposis (FAP), who display a 124-fold increased risk of developing ampullary carcinoma compared to the general population. Duodenal neoplasia develops in 40-100% of FAP patients, with the ampulla of Vater a prominent site of involvement. This supports the practice of regular endoscopic surveillance of the duodenum, and especially the ampullary region, in FAP patients. In light of the low incidence of FAP in the general population, however, about 75% of ampullary neoplasms still occur sporadically. Sporadic neoplasms are usually diagnosed in patients in their seventies, compared to several decades earlier in FAP patients. Presenting symptoms are usually non-specific, and may reflect ampullary (biliary or pancreatic) obstruction. Cholestasis, with or without overt jaundice, is present in 50-75% of cases, and up to 25% of those patients have associated common bile duct stones secondary to impaired bile flow. Less commonly, patients, may present with acute pancreatitis, chronic blood loss with iron deficiency anemia, or overt upper GI bleeding. In today's era of widely available endoscopy, a significant proportion of ampullary neoplasms are found incidentally in patients undergoing upper endoscopy for unrelated reasons. A side-viewing duodenoscope should always be used to evaluate the ampulla when a lesion is suspected, and biopsies should be taken.

The adenoma-carcinoma sequence is as applicable to ampullary neoplasms as it is for other GI malignancies. The finding of ampullary dysplasia, especially high-grade, carries a defined risk of harboring or developing cancer, and necessitates a therapeutic approach for all patients with a reasonable life expectancy.

Surgical approaches

If frank carcinoma is present, the only truly curative procedure is Whipple pancreaticoduodenectomy. Early surgical series established that endoscopic biopsies cannot reliably exclude the presence of foci of invasive carcinoma within ampullary adenomas; such foci were found in 30% of surgical specimens. This supported an aggressive surgical approach toward ampullary adenomas, and Whipple pancreaticoduodenectomy was considered the mainstay in the management of these lesions for many decades. Problems with this approach included the high mortality (3-5% even in specialized centers) and morbidity, especially in FAP patients, where the procedure cannot be considered curative in light of the presence of satellite neoplastic lesions along the remainder of the duodenum.

Gastroenterology Department, "Hygeia" Hospital

Author for correspondence:

Ilias Scotiniotis, MD, Hygeia Hospital, Erythrou Stavrou 4, Marousi, Tel.: +2106827940, Fax: +2106867036, e-mail: scotiniotis@yahoo.com

Local surgical excision (surgical ampullectomy), initially described in 1899 for the management of ampullary lesions, experienced a period of resurgence in the second half of the last century, as a procedure with significantly lower morbidity and mortality. Surgical ampullectomy involves post-excisional reimplantation of the biliary and pancreatic ducts into the duodenal wall, a considerable technical challenge. Furthermore, it is associated with recurrence rates as high as 20-30%.

Endoscopic Ampullectomy

Originally conceived as an alternative for poor surgical candidates, endoscopic ampullectomy gained momentum as confidence in endoscopic technique grew in the past two decades. The first extensive series was published in 1993,[1] and significant experience has accured since then. Performed in centers with significant expertise in interventional endoscopy, it is now considered a preferred method of resection of non-invasive ampullary neoplasms. To that end, all effort must be made to carefully select patients so that those with invasive foci of carcinoma, for whom the procedure cannot be considered curative, are excluded. Inadequate detection of invasive carcinoma from superficial biopsies from the ampulla have led some experts to advocate performing a sphincterotomy in order to improve the histologic yield from deeper biopsies. The presence of high-grade dysplasia (or *carcinoma in situ*) should not be a contraindication to endoscopic ampullectomy. On the other hand, endoscopic signs of invasion, such as a lesion that feels rigid on probing, that is ulcerated, or that displays a 'bulging' submucosal effect, should be considered. Careful cholangiography and pancreatography are used to exclude intraductal extension of the neoplasm. Endoscopic ultrasonography (EUS) has enhanced our ability to detect invasive disease of the ampulla, with the largest series reporting a sensitivity of 91% and a specificity of 75% in the detection of invasion of the duodenal wall.[2]

Technique

In deciding how to best remove a non-invasive ampullary neoplasm, the endoscopist must clearly note the margins of the lesion. These can be enhanced by performing chromoendoscopy (spraying methylene blue or indigo carmine dye on the lesion). A standard snare of the type used in colonoscopic polypectomy is then used to resect the lesion. *En bloc* resection (in a single piece) is the preferred method, since it ensures complete removal and allows the best histopathologic assessment of the lesion. Immediate retrieval of the entire resected specimen is crucial, as air insufflation and peristalsis in the duodenum may rapidly move the specimen downstream and cause it to be lost.

If residual adenomatous tissue remains after snare excision, this can be fulgurated during the same session using thermal techniques, such as Argon Plasma Coagulation or the Nd:YAG laser. The post-ampullectomy placement of a temporary plastic stent into the pancreatic duct has become common practice in order to protect the orifice from thermal injury by the snare and reduce the risk of pancreatitis. Temporary stenting of the bile duct has a less established role and is performed at the discretion of the endoscopist.

Outcomes

Following the initial publication in 1993, several series have reported on long-term outcomes of ampullectomy. Pooling the results from the largest reports, which involve about 270 patients, has shown success rates of 74-88%.[3-6] Success is defined as complete resection of the lesion, including successful endoscopic retreatment of the area if recurrence is noted. Unsuccessful cases have consisted mainly of those with invasive disease in the ampullectomy specimen (0-13% of cases in these series), or those lesions that could not be completely treated, regardless of the number of sessions. The likelihood of success is higher if the lesion is smaller than 3cm, if adjunctive thermal ablation is performed, and if the lesion is not associated with FAP (as expected, the epithelium of FAP patients is predisposed to recurrent neoplasia). Overall, 13-20% of patients undergoing ampullectomy have subsequently required surgery for a variety of reasons. Of course, ultimate assessment of the success of endoscopic ampullectomy will require extensive long-term follow-up, which is not available for a large number of these recently published series.

Complications

The observed incidence of post-ampullectomy pancreatitis has averaged 9.2% in the above-mentioned series. The subsequent adoption of pancreatic stent placement has been associated with reduced rates of pancreatitis, similar to the observation in high-risk sphincterotomy patients. A single death has occurred due to severe pancreatitis in a patient in whom pancreatic stent placement was not undertaken. The strength of the non-randomized evidence in favor of pancreatic stent placement makes it unlikely that a prospective study of no stent versus stent placement following ampullectomy will ever be undertaken.

Bleeding immediately following resection is usually

minor and easily controlled endoscopically. Delayed bleeding rates have averaged 4.9% in these series, and can be more severe, although usually managed endoscopically as well. A single mild perforation has also been reported, which was managed conservatively. Papillary stenosis may rarely occur as the ampullectomy site heals, and can result in the distant development of acute pancreatitis. However, this rare complication may also be prevented by pancreatic stent placement, and can easily be managed with sphincterotomy.

Surveillance

Endoscopy must be repeated 2-4 weeks following ampullectomy in order to remove the pancreatic duct stent and assess the orifice for residual adenoma, which can be resected or fulgurated. It is reasonable to obtain biopsies from the resection site to document histology at that time.

Even complete resection of a lesion does not obviate the need for endoscopic surveillance. Recurrence is seen in about 10% of cases of sporadic adenomas, and occurs within the first 2 years following ampullectomy. A 6-month interval for surveillance for the first 2 years is therefore reasonable for sporadic adenomas, after which time surveillance may be discontinued. FAP patients, on the other hand, continue to carry a lifelong risk of recurrence, and should therefore be examined on a 3-year interval indefinitely after the first 2 years.

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