Tumors of the papilla and ampulla of Vater are rare neoplasms which are usually detected at an early stage due to their symptoms. The accurate preoperative histological diagnosis and staging of ampullary tumors is often difficult and inconclusive, leading to controversy over the adequate treatment of these lesions. Three procedures are currently being used to treat such tumors. Pancreatoduodenectomy (PD) is a procedure with low morbidity and mortality at experienced centers, and is considered the treatment of choice for invasive carcinoma and large benign ampullary lesions with suspicion of malignancy. Transduodenal local excision (TDE) of ampullary tumors is a relatively simple procedure with operative morbidity and mortality rates comparable to PD. TDE is challenged at endoscopic centers by endoscopic snare excision (ESE). Due to technical advances, the safety and outcomes of ESE for ampullary tumors have improved in recent years. ESE and TDE represent adequate methods for treatment of benign tumors and also for small malignant tumors detected at an early stage if the diagnosis and stage have been accurately established preoperatively. Due to the safety of PD and the technical advances of ESE, TDE is reserved for selected patients. Randomized controlled studies are needed to establish the correct indications for PD, TDE, and ESE.

Key words Tumor of papilla of Vater · Ampullectomy · Transduodenal local excision · Pancreatoduodenectomy · Endoscopic snare excision

Introduction

The ampulla of Vater, which is a flask-like dilatation of a tubular structure, was first described in 1720 by the German anatomist Abrahamus Vater. Since then, it has become well known that this anatomic entity, consisting of three epithelia (the bile duct, the pancreatic duct, and the duodenal mucosa), is extremely complex. In 70% of individuals the ampulla of Vater is formed by the union of the terminal segments of the pancreatic and common bile ducts (type I). In another 20%, the ampulla is missing and the biliopancreatic junction is close to the papilla of Vater, an opening through a small mucosal elevation to the posteromedial duodenal wall (type II). In type III, the ampulla is the termination of the common bile duct only, as the pancreatic duct enters the duodenum separately next to the ampulla. And in type IV the biliopancreatic junction is distant from the papilla.

Tumors of the ampulla of Vater are called ampullomas or ampullary tumors. Benign neoplasms in this area include lipomas, hamartomas, lymphangiomas, hemangiomas, leiomyoblastomas, and neurogenic tumors such as neurofibromas. Villous and tubulovillous adenomas, however, remain the most common benign tumors. In terms of histopathological classification, 40% are tubulovillous adenomas, 30% villous adenomas, 10% tubular adenomas, and 20% non-epithelial lesions, such as adenomyosis and — rarely — endocrine adenoma. Almost all primary papillary cancers are adenocarcinomas, which account for up to a third of all operable pancreatoduodenal tumors, though sarcomas, lymphomas, carcinoids, and islet-cell cancers also have been reported. All these neoplastic lesions, due to their particular location, could have serious consequences, including biliary obstruction, cholangitis, and acute attacks of pancreatitis and bleeding, all of which might require surgical intervention.
While some reports point to low rates of recurrence of benign adenomas after local resection, others cite high recurrence rates. Endoscopic snare excision (ESE) of the papilla has recently become technically feasible and is considered an alternative in patients with high comorbidity and poor physical health status.

Inability to preoperatively exclude adenocarcinoma of the ampulla of Vater with imaging methods and sometimes with endoscopic biopsies is still a problem. Moreover, the possibility of invasive carcinoma within the adenoma is not excluded by negative biopsy; thus, endoscopic biopsies might produce false-negative results prior to surgery.

Therefore, the management of papillary tumors still remains controversial and interdisciplinary because of the complex anatomy of the ampullary region and the difficulty of accurately diagnosing and staging the tumor through imaging and endoscopy preoperatively.

**Staging of tumors of the papilla of Vater**

Tumors of the ampulla of Vater include tumors arising in the ampulla (intraampullary type), tumors arising on the ampulla (periampullary type), and tumors arising at the junction of the mucosa of the ampulla and that of the papilla or tumors involving both the intraampullary and periampullary regions of the duodenum (mixed type). Intraampullary tumors are mucinous neoplasms composed of gastrointestinal, biliary, and pancreatic ductal epithelium. Periampullary tumors contain predominantly gastrointestinal epithelium. Generally, the tumor might present as an intraluminal polypoid mass, or as a mass behind the opening of the papilla with normal-appearing mucosa, or even as an irregular mucosal ulceration along the duodenal wall. The preoperative classification of an ampullary tumor as adenoma or carcinoma, and differentiation from adenocarcinoma of pancreatic origin, as well as the accurate estimation of the tumor size, represent major problems in the treatment of these lesions.

Conventional imaging techniques such as transabdominal ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI) are considerably less sensitive than when used for other diseases, in both the diagnosis and staging of ampullary tumors, and should not be relied upon for initial diagnosis. These procedures cannot detect small tumors, but indicate the presence of a tumor by indirect signs, such as dilatation of the common bile and main pancreatic ducts. However, CT and/or MRI are the best methods for evaluating the liver for distant metastases or the presence of malignant lymph nodes, and remain the imaging methods of choice for the detection of visceral spread, although this is rare at the time of diagnosis of ampullary adenocarcinoma. Despite this, chronic pancreatitis associated with an ampullary lesion may be interpreted as a pancreatic cancer on CT and MRI.

Endoscopic ultrasonography (EUS) has become an important modality in assessing ampullary tumors, because it can clearly delineate the layered structures of the duodenal wall in the ampullary region and can accurately diagnose the presence and extent of tumor invasion into the duodenum, the head of the pancreas, or the bile duct. EUS has been demonstrated to have 74%–83% accuracy in staging the extent of ampullary tumors. Those incorrectly assessed were more commonly overstaged rather than understaged due to peripapillary edema associated with biliary stents or pancreatitis. On the other hand, reports have shown that EUS cannot reliably differentiate adenoma from pT1 carcinoma and has limited value in determining the presence of lymph node or distant metastasis. In addition, the extent of microscopic tumor infiltration is substantially influenced by peripapillary inflammation when endoscopic manipulations such as sphincterotomy have been performed prior to EUS. Moreover, this technique is less widely available than CT or MRI. Intraductal high-frequency ultrasound (IDUS) gives complementary information in diagnosing tumor extension and demonstrates whether infiltration of Oddi’s muscle layer exists, but has low sensitivity in the detection of lymph node metastasis.

Endoscopic retrograde cholangiopancreatography (ERCP), with multiple forceps biopsies or cytologic brushings of the periampullary region and ducts, has emerged as a widely accepted and essential technique for clarifying the diagnosis of ampullary tumors. However, while the region of the ampulla is easily accessible for biopsy, endoscopic histological examination is thought to miss the diagnosis in up to 60% of cases and cannot be relied upon to provide accurate local staging. Some reports indicate the value of immunohistochemical staining for the p53 protein in endoscopic biopsies of the ampulla. In their study, Younes et al. found that, of nine initial biopsies negative for carcinoma, seven were positive for p53, and of these, six (86%) were found to be carcinomas upon resection. In addition, intraoperative frozen sections differentiate correctly between malignant and benign lesions of the papilla with up to 97% sensitivity and 100% specificity.

**Treatment of tumors of the papilla of Vater**

Given these observations and the fact that these lesions can have serious consequences, a controversy exists over how to treat them. Because of the malignant po-