

# Diagnosis of Ampullary Cancer

Kei Ito Naotaka Fujita Yutaka Noda Go Kobayashi Jun Horaguchi

Department of Gastroenterology, Sendai City Medical Center, Sendai, Japan

## Key Words

Ampullary cancer · Endoscopic papillectomy ·  
Pancreaticoduodenectomy · Ultrasonography

## Abstract

Endoscopic papillectomy has been reported to be the treatment of choice in patients with ampullary adenoma. For ampullary cancer, pancreaticoduodenectomy is the standard treatment. Since neither lymphatic permeation, vascular invasion, nor lymph node metastasis is observed in patients with ampullary cancer limited to the mucosa, endoscopic resection of such tumors can be justified if no ductal infiltration into the bile or pancreatic duct is documented. For its application, accurate preoperative staging is mandatory. Transpapillary intraductal ultrasonography can provide useful information for making therapeutic decisions, especially in the selection of patients for endoscopic papillectomy.

Copyright © 2010 S. Karger AG, Basel

## Introduction

The widespread use of esophagogastroduodenoscopy and extracorporeal ultrasonography (US) has contributed to the detection of ampullary neoplasms. Histologically, ampullary neoplasms include adenomas, adenocarcinomas, and adenosquamous, small-cell, adenoendocrine, and undifferentiated carcinomas. Resection is recommended for ampullary adenoma because of the risk of progression to adenocarcinoma. Endoscopic papillectomy for ampullary adenoma has been reported since the early 1980s [1, 2]. For ampullary cancer, pancreaticodu-

denectomy has been considered to be the standard treatment. However, some reports have suggested endoscopic treatment as an alternative to surgery for selected patients with ampullary cancer. Therefore, accurate preoperative staging is mandatory for making therapeutic decisions. The diagnosis of ampullary cancer and the clinical significance of endoscopic procedures are discussed in this article.

## Diagnosis of Ampullary Cancer

The ampulla of Vater is a vital structure traversed by important ducts and surrounded by the pancreas and the duodenum. Accurate preoperative staging of ampullary cancer is challenging. Nowadays, numerous modalities such as extracorporeal US, computed tomography (CT), magnetic resonance cholangiopancreatography, esophagogastroduodenoscopy, biopsy, endoscopic US (EUS), endoscopic retrograde cholangiopancreatography (ERCP), intraductal US, and angiography are available for diagnosing ampullary neoplasms. Appropriate and efficient selection of such modalities is necessary for lessening procedure-related complications as well as the burden on the patients.

Endoscopic findings are important for the diagnosis of ampullary neoplasms. The typical endoscopic finding of ampullary adenoma is a discolored lobular/pine cone-like tumor. A reddish nodular tumor associated with erosion and easy bleeding indicates malignancy. Ulceration or fold convergency of the neighboring duodenum suggests tumor invasion into the duodenal wall or pancreatic parenchyma. It is not always possible to distinguish

**Table 1.** Diagnostic accuracy of EUS for tumor staging in ampullary cancer

First author	T <sub>1</sub>	T <sub>2</sub>	T <sub>3</sub> –T <sub>4</sub>	Overall accuracy
Yasuda [6] (1988)	75% (3/4)	67% (2/3)	100% (4/4)	82% (9/11)
Mitake [7] (1990)	100% (5/5)	67% (10/15)	75% (6/8)	75% (21/28)
Tio [8] (1996)	60% (3/5)	92% (12/13)	92% (13/14)	88% (28/32)
Itoh [9] (1997)	100% (20/20)		75% (9/12)	90% (29/32)
Kubo [10] (1999)	67% (6/9)	71% (10/14)	83% (10/12)	74% (26/35)
Cannon [11] (1999)	100% (16/16)	53% (8/15)	78% (15/19)	78% (39/50)
Menzel [12] (1999)	–	–	–	62% (5/8)
Chen [13] (2001)	67% (2/3)	88% (7/8)	67% (6/9)	75% (15/20)
Skordilis [14] (2002)	–	83% (5/6)	90% (10/11)	88% (15/17)
Ito [15] (2007)	62% (13/21)	45% (5/11)	88% (7/8)	63% (25/40)
Artifon [16] (2009)	0% (0/2)	85% (11/13)	75% (9/12)	74% (20/27)

adenoma from carcinoma with duodenoscopy only, and histological evaluation by forceps biopsy is mandatory for the establishment of a definitive diagnosis. Since ampullary cancer usually derives from the ampullary portion of the bile duct (BD)/pancreatic duct (PD) or the common channel, a forceps biopsy specimen should be obtained from the BD/PD orifice. The diagnostic accuracy of forceps biopsy in ampullary neoplasms reportedly ranges from 47 to 95%.

Uchiyama et al. [3] employed magnifying endoscopy with narrow band imaging, which can provide endoscopic images of microvessels and the surface structure of tumors, in 14 patients with suspected ampullary neoplasms. Endoscopic findings were classified as I, oval-shaped villi; II, pine cone/leaf-shaped villi, and III, irregular/non-structured villi. Tortuous, dilated, and network-like vessels were defined as abnormal vessels. Type II/III and type I were seen in patients with adenoma/adenocarcinoma and in those with non-neoplastic tumors, respectively. Abnormal vessels were observed only in patients with adenocarcinoma. Further studies are necessary for the establishment of diagnostic criteria with this new technique.

Tumor staging with EUS and/or intraductal US is performed in patients with suspected ampullary cancer. CT/MRI is recommended for the detection of distant metastases. EUS is performed in an outpatient setting with a low frequency of procedure-related complications. Transpapillary intraductal US can be performed in a single session with cholangiopancreatography, biopsy, and biliary stent placement. On the other hand, percutaneous transhepatic intraductal US has several disadvantages, such as a prolonged admission period for maturation of

the fistula, risk of tumor dissemination into the abdominal cavity and/or the sinus tract, and inability of pancreatography.

### Clinical Significance of Tumor Staging for Ampullary Cancer

Surgical resection has long been the standard treatment for ampullary cancer. However, since the introduction of endoscopic papillectomy for ampullary adenoma in 1983 by Suzuki et al. [1], and a subsequent report by Binmoeller et al. [2], many cases treated by endoscopic resection have been reported. Since neither lymphatic permeation, vascular invasion, nor lymph node metastasis is observed in patients with ampullary cancer limited to the mucosa, local resection of such tumor can be justified if neither ductal infiltration into the BD nor into the PD is observed [4, 5]. Due to its less invasiveness compared with surgical resection that has high morbidity, endoscopic papillectomy is likely to be recognized as a treatment of choice for selected cases of ampullary cancer. Accurate preoperative tumor staging has a greater significance than before for determining an appropriate treatment.

### EUS and Intraductal US for Ampullary Cancer

The utility of EUS for ampullary neoplasms has been reported (table 1) [6–16]. Artifon et al. [16] reported a comparative study of EUS versus CT for staging of ampullary cancer. In 27 patients with ampullary cancer who

**Table 2.** Diagnostic accuracy of intraductal US for tumor staging in ampullary cancer

First author	T <sub>1</sub>	T <sub>2</sub>	T <sub>3</sub> –T <sub>4</sub>	Overall accuracy
Itoh [9] (1997)	100% (6/6)	93% (13/14)	75% (9/12)	88% (28/32)
Menzel [12] (1999)	80% (4/5)	100% (7/7)	100% (3/3)	93% (14/15)
Ito [15] (2007)	96% (18/21)	64% (7/11)	75% (6/8)	78% (31/40)

underwent EUS, CT, and surgical resection, EUS was more sensitive and specific than CT for tumor and nodal staging. The diagnostic accuracy of EUS in tumor staging is reportedly 0–100% in T<sub>1</sub>, 45–100% in T<sub>2</sub>, and 75–100% in T<sub>3</sub>–T<sub>4</sub>. Overall accuracy in tumor staging by EUS ranges from 62 and 90%.

Only three studies describing the efficacy of both EUS and intraductal US for ampullary neoplasms have been reported according to the MEDLINE database (table 2) [9, 12, 15]. Intraductal US has a high resolution due to the use of high-frequency US (20–30 MHz) compared with that of EUS (5–10 MHz). An intraductal US probe can be passed through the biopsy channel of an endoscope directly into the BD.

Itoh et al. [9] reported the diagnostic accuracy of intraductal US and EUS in a prospective study including 32 patients with ampullary cancer who had undergone surgical resection. Intraductal US was performed percutaneously in 24 patients and transpapillarily in the other 8 patients. The staging accuracy of intraductal US following the TNM classification [17] was 88%. Although they concluded that intraductal US was superior to EUS with regard to depiction of the sphincter of Oddi and detailed staging, the accuracy of EUS in tumor staging according to the TNM classification was higher (90%) than that of intraductal US. Menzel et al. [12] reported a prospective study involving 27 consecutive patients with ampullary neoplasms (12 adenomas and 15 adenocarcinomas). Local surgical resection was performed in 8 patients (7 adenomas and 1 carcinoma), whereas the remaining 19 patients underwent pancreaticoduodenectomy. Transpapillary intraductal US was performed in only 15 patients in their study. They concluded that intraductal US was significantly superior to EUS in terms of tumor visualization and staging (staging accuracy: 93 vs. 62%).

In our study [15], intraductal US was performed transpapillarily in 40 patients with ampullary neoplasms before surgery (n = 30) or endoscopic papillectomy (n = 10). Thirty-three patients had adenocarcinomas (pT<sub>1</sub>, 14; pT<sub>2</sub>, 11, and pT<sub>3</sub>–pT<sub>4</sub>, 8) and 7 had adenomas. Tumor depiction

by EUS and intraductal US was achieved in 95 and 100% of the patients, respectively. The diagnostic accuracy of EUS and that of intraductal US in tumor staging were 62 and 86% in adenomas and pT<sub>1</sub>, 45 and 64% in pT<sub>2</sub>, and 88 and 75% in pT<sub>3</sub>–pT<sub>4</sub>. The overall accuracy of EUS and that of intraductal US in tumor staging were 63 and 78% (p = 0.14). In 10 patients who underwent endoscopic papillectomy, the accuracy of EUS and that of intraductal US in tumor staging were 80 and 100%. Ductal infiltration into the BD and the PD was correctly assessed in 88 and 90%, respectively, by EUS and in 90% in both by intraductal US. Both EUS and intraductal US correctly diagnosed ductal infiltration in all papillectomized patients. Consequently, intraductal US was superior to EUS in terms of tumor staging for ampullary neoplasms, especially for patients suitable for application of endoscopic papillectomy. Duodenal involvement could not be estimated by EUS in 15% of the patients because the muscularis propria of the duodenal wall was not clearly visualized. Therefore, the diagnostic accuracy of EUS in tumor staging was lower than that of other studies. Recently, an electronic radial echoendoscope has become commercially available. This newly developed scope is expected to improve the staging accuracy of EUS for ampullary neoplasms with regard to visualization of the structure of the duodenal wall. On the other hand, intraductal US was able to demonstrate the muscularis propria of the duodenal wall in all patients. The sphincter of Oddi was difficult to depict with EUS and intraductal US in our study, probably due to the low density of its muscle fibers. Evaluation of tumor invasion of the sphincter of Oddi remains challenging because discrimination of the tumor from the sphincter of Oddi is difficult by these modalities. In order to determine the stage of ampullary cancer more precisely, further improvement in the hardware for stable visualization of the sphincter of Oddi is required.

In conclusion, intraductal US provides useful information for making therapeutic decisions, especially in cases suitable for endoscopic papillectomy.

## References

- 1 Suzuki K, Kantou U, Murakami Y: Two cases with ampullary cancer who underwent endoscopic excision (in Japanese with English abstract). *Prog Dig Endosc* 1983;23:236–239.
- 2 Binmoeller KF, Boaventura S, Ramsperger K, Soehendra N: Endoscopic snare excision of benign adenomas of the papilla of Vater. *Gastrointest Endosc* 1993;39:127–131.
- 3 Uchiyama Y, Imazu H, Kakutani H, Hino S, Sumiyama K, Kuramochi A, Tsukinaga S, Matsunaga K, Nakayoshi T, Goda K, Saito S, Kaise M, Kawamura M, Omar S, Tajiri H: New approach to diagnosing ampullary tumors by magnifying endoscopy combined with a narrow-band imaging system. *J Gastroenterol* 2006;41:483–490.
- 4 Ito K, Fujita N, Noda Y, Kobayashi G, Kimura K, Horaguchi J, Sugawara T, Takasawa O: Modes of spread in early ampullary cancer in terms of establishing proper indications for endoscopic papillectomy. *Dig Endosc* 2004;16:224–228.
- 5 Ito K, Fujita N, Noda Y, Kobayashi G, Kimura K, Horaguchi J, Takasawa O: Case of early ampullary cancer treated by endoscopic papillectomy. *Dig Endosc* 2004;16:157–161.
- 6 Yasuda K, Mukai H, Cho E, Nakajima M, Kawai K: The use of endoscopic ultrasonography in the diagnosis and staging of carcinoma of the papilla of Vater. *Endoscopy* 1988;20:218–222.
- 7 Mitake M, Nakazawa S, Tsukamoto Y, Naitoh Y, Kimoto E, Hayashi Y: Endoscopic ultrasonography in the diagnosis of depth invasion and lymph node metastasis of carcinoma of the papilla of Vater. *J Ultrasound Med* 1990;9:645–650.
- 8 Tio TL, Sie LH, Kallimanis G, Luiken GJ, Kimmings AN, Huibregtse K, Tytgat GN: Staging of ampullary and pancreatic carcinoma: comparison between endosonography and surgery. *Gastrointest Endosc* 1996;44:706–713.
- 9 Itoh A, Goto H, Naitoh Y, Hirooka Y, Furukawa T, Hayakawa T: Intraductal ultrasonography in diagnosing tumor extension of cancer of the papilla of Vater. *Gastrointest Endosc* 1997;45:251–260.
- 10 Kubo H, Chijiwa Y, Akahoshi K, Hamada S, Matsui N, Nawata H: Pre-operative staging of ampullary tumours by endoscopic ultrasound. *Br J Radiol* 1999;72:443–447.
- 11 Cannon ME, Carpenter SL, Elta GH, Nostrom TT, Kochman ML, Ginsberg GG, Stotland B, Rosato EF, Morris JB, Eckhauser F, Scheiman JM: EUS compared with CT, magnetic resonance imaging, and angiography and the influence of biliary stenting on staging accuracy of ampullectomy neoplasms. *Gastrointest Endosc* 1999;50:27–33.
- 12 Menzel J, Hoepffner N, Sulkowski U, Reimer P, Heinecke A, Poremba C, Domschke W: Polypoid tumors of the major duodenal papilla: preoperative staging with intraductal US, EUS, and CT – a prospective, histopathologically controlled study. *Gastrointest Endosc* 1999;49:349–357.
- 13 Chen CH, Tseng LJ, Yang CC, Yeh YH, Mo LR: The accuracy of endoscopic ultrasound, endoscopic retrograde cholangiopancreatography, computed tomography, and transabdominal ultrasound in the detection and staging of primary ampullary tumors. *Hepatogastroenterology* 2001;48:1750–1753.
- 14 Skordilis P, Mouzas IA, Dimoulios PD, Alexandrakis G, Moschandrea J, Kouroumalis E: Is endosonography an effective method for detection and local staging of the ampullary carcinoma? A prospective study. *BMC Surg* 2002;2:1.
- 15 Ito K, Fujita N, Noda Y, Kobayashi G, Horaguchi J, Takasawa O: Preoperative evaluation of ampullary neoplasm with EUS and transpapillary intraductal US – a prospective and histopathologically controlled study. *Gastrointest Endosc* 2007;60:740–747.
- 16 Artifon ELA, Couto D Jr, Sakai P, Silveria EB: Prospective evaluation of EUS versus CT scan for staging of ampullary cancer. *Gastrointest Endosc* 2009;70:290–296.
- 17 Hamilton SR, Aaltonen LA (eds): *World Health Organization Classification of Tumours. Pathology and Genetics of Tumours of the Digestive System*. Lyon, IARC Press, 2000.