

## Endoscopic ultrasound versus computed tomography for preoperative evaluation of primary ampullary tumors

Radiological evaluation of primary ampullary tumors

Yusuf Uzum<sup>1</sup>, Hakan Camyar<sup>2</sup>, Ugur Bayram Korkmaz<sup>1</sup>, Zeynep Zehra Gumus<sup>1</sup>, Emrah Alper<sup>3</sup>

<sup>1</sup>Department of Internal Medicine, Katip Celebi University, Ataturk Training and Research Hospital, Izmir

<sup>2</sup>Department of Gastroenterology, Katip Celebi University, Ataturk Training and Research Hospital, Izmir

<sup>3</sup>Department of Gastroenterology, Koc University Hospital, Istanbul, Turkey

### Abstract

**Aim:** The study aimed to compare the efficacy of endoscopic ultrasound (EUS) and computed tomography (CT) in detecting primary tumor and evaluating preoperative vascular and peripheral invasion in histopathologically proven malignant ampullary tumors.

**Material and Methods:** Fifty-two patients who underwent surgery or endoscopic ampullectomy for the primary ampullary tumors between 2014 and 2016 were evaluated. The demographic data and EUS, CT, pathology results of all patients were recorded. The efficacy of EUS and CT in detecting tumor, peripheral tissue invasion, and vascular tissue invasion was evaluated and compared with pathology results.

**Results:** Forty-nine patients had the Whipple procedure and 3 patients underwent endoscopic ampullectomy. In pathology results, all patients had adenocarcinoma histology, and the mean tumor diameter was 20.12 mm. The rate of peripheral tissue invasion and vascular invasion was 86.5%, 5.8% respectively. Ampullary mass was detected in 41 (78.8%) patients by EUS, in 35 (67.3%) by CT ( $p=0.002$ ). Three patients had a vascular invasion in pathology. The sensitivity and specificity of EUS in detecting vascular invasion were 66% and 100%, respectively. CT failed to demonstrate vascular invasion in these 3 patients.

**Discussion:** The results showed that EUS was superior to CT in detecting a mass, peripheral tissue invasion, and vascular invasion. Although EUS is superior to CT, CT plays an important role in the evaluation of distant metastases, and therefore CT and EUS are two important complementary radiological tests in the evaluation of these patients.

### Keywords

Endoscopic Ultrasound; Ampullary tumors; Preoperative evaluation

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Corresponding Author: Yusuf Uzum, Department of Internal Medicine, Katip Celebi University, Ataturk Training and Research Hospital, Izmir, Turkey.

E-mail: yusufuzum@gmail.com P: +902322444444, +905366658786

Corresponding Author ORCID ID: <https://orcid.org/0000-0001-5027-1827>

**Introduction**

Tumors of the Ampulla of Vater account for only 0.2% of gastrointestinal tract tumors and often manifest with jaundice, abdominal pain, and anemia [1,2]. Patients with tumors of the major ampulla have a better prognosis compared to other periampullary malignancies because symptoms tend to manifest relatively early when the disease is still localized. Thus, accurate preoperative staging of ampullary tumors is critical for surgical planning and predicting the patient’s prognosis.

There are different diagnostic modalities available for delineating stages of the tumor with examination of tumor invasion (T) and nodal involvement (N). These include magnetic resonance imaging (MRI), computed tomography (CT), endoscopic ultrasound (EUS), and transpapillary intraductal ultrasound (IDUS). Although having conflicting results, CT and EUS are the most commonly used methods for staging cancer [3,4]. Nevertheless, there is no consensus on the role of EUS in the locoregional staging of ampullary tumors [5].

CT is commonly performed on patients with symptoms of the biliary tract due to its widespread availability. It is often considered an acceptable imaging test for metastatic spread, tumor, and nodal staging, especially if an EUS expert is not readily available [3].

Some studies have shown that EUS is more effective than CT to demonstrate the ampulla, closely related anatomical structures (lymph nodes, bile duct, pancreatic duct) and the interface between the duodenal wall and pancreas [6-9]. EUS can visualize the local extent of tumors, and the status of regional lymph nodes and the detection of malignant stenosis of the distal bile duct with a sensitivity of up to 96% [10]. EUS can be a technically challenging procedure, and although it is widely available, it is very much operator-dependent [8]. The most effective method to demonstrate the efficacy of CT and EUS is to compare them with histopathological results. These studies have compared the preoperative evaluation of T- and N-staging of CT and EUS with the histopathological staging of the resected specimen, and EUS has been suggested as the best modality of choice in the locoregional stage of the ampullary lesion [5]. The majority of these studies were limited to a small number of ampullary tumors and had different ampullary diseases such as benign ampullary adenoma.

This study aims to investigate the efficacy of EUS and CT in the detection of primary tumor and evaluation of preoperative vascular and peripheral invasion in histopathologically confirmed malignant ampullary tumors.

**Material and Methods**

In this study, we retrospectively evaluated patients who underwent surgery (pancreaticoduodenectomy) or endoscopic ampullectomy for the primary ampullary tumor in our hospital between 2004 and 2016. Patients who had been preoperatively evaluated with both EUS and CT were included in the study. The demographic data (age, gender) and the results of EUS, CT, pathology of all patients were recorded. Peripheral tissue invasion was defined as the direct extension and penetration by the tumor into the duodenum, pancreatic head. Vascular invasion was defined as the direct extension and penetration by cancer into the portal vein (PV), superior mesenteric vein (SMV),

superior mesenteric artery (SMA), and branches. The efficacy of EUS and CT in detecting tumor, peripheral tissue invasion, and vascular invasion were evaluated and compared with the pathology results of patients.

**Statistical analysis**

All analyzes were performed using the Statistical Package for the Social Sciences software version 20.0 (SPSS Inc, USA) program. The normality of the distribution was checked for all continuous variables using the Kolmogorov-Smirnov Test. Categorical variables were shown as frequencies and percentages; numeric variables were described by means and standard deviations or medians and interquartile ranges. The percentage of sensitivity, specificity, and accuracy of invasion detection was calculated for EUS and CT. A p-value less than .05 was accepted as a statistically significant difference.

**Results**

Fifty-two patients diagnosed with primary ampullary tumors were included in the study. The mean age of the patients was 61.9±10.2 years, and two-thirds of the patients were male (59.6%). Forty-nine (94.2%) patients underwent the Whipple procedure, and 3 (5.8%) patients underwent endoscopic ampullectomy.

When the pathology results of the patients were examined, it was seen that half of the cancers were attributable to moderately differentiated adenocarcinoma histology. The mean tumor diameter was 20.12±1.16 mm in the pathology specimens. It was found that 86.5% of the patients had peripheral tissue invasion, and 5.8% had vascular invasion (Table 1).

**Table 1.** Pathology characteristics

Pathology (n, %)	
Well	18 (34.6%)
Intermediate	26 (50.0%)
Poor	8 (15.4%)
Peripheral tissue invasion (n, %)	
Present	45 (86.5%)
Absent	7 (13.5%)
Vascular invasion (n, %)	
Present	3 (5.8%)
Absent	49 (94.2%)
Diameter (mm) (Mean, standard deviation)	20.12 (1,16)

Ampullary mass was detected in 41 (78.8%) patients using EUS, in 35 (67.3%) patients using CT. There was a significant difference between EUS and CT in detecting ampullary mass (p<0.001). The mean diameter of EUS-detected ampullary tumors was 20.5 mm. The mean diameter of CT-detected ampullary tumors was 24 mm (Table 2).

Peripheral tissue invasion was detected in 20 (38.5%) patients by using EUS, in 8 (15.4%) patients by using CT (Table 2). For detection of peripheral tissue invasion, the specificity of EUS and CT was 100%, and sensitivity was 44.44% for EUS and 17.77% for CT (Table 3). There was a significant difference between EUS and CT in detecting peripheral tissue invasion (p=0.002) (Table 2).

**Table 2.** CT and EUS in mass detection, peripheral tissue invasion, vascular invasion and diameter

	EUS (n=52)	CT (n=52)	p-value
Mass detection (n, %)	41 (78.8%)	35 (67.3%)	<0.001
Peripheral tissue invasion (n, %)	20 (38.5%)	8 (15.4%)	0.002
Vascular invasion (n, %)	2 (3.8%)	-	-
Diameter (mm) (median, IQR)	20.5 (15)	24 (10)	<0.001

Three patients had vascular invasion in pathology, and EUS detected 2 of them. CT failed to demonstrate vascular invasion in these three patients. Forty-nine patients had no vascular invasion in pathology. CT and EUS showed no invasion in all of these patients without pathological vascular invasion (Table 3).

**Table 3.** The concurrency in detecting peripheral tissue invasion and vascular invasion between different types of imaging techniques and pathology

	Present	Absent	Sensitivity	Specificity
<b>Pathological invasion</b>				
EUS invasion				
Present	20	0	44.4%	100.0%
Absent	25	7		
CT invasion				
Present	8	0	17.8%	100.0%
Absent	37	7		
<b>Pathological vascular invasion</b>				
EUS invasion				
Present	2	0	100%	98%
Absent	1	49		
CT invasion				
Present	0	0	0%	94%
Absent	3	49		

**Discussion**

In the literature, the number of studies covering only ampullary tumors is limited, and the number of patients with primary ampullary tumors involved in the periampullary tumors studies is low. In our study, CT and EUS were compared with pathology in 52 patients with primary ampullary tumors.

In the literature, primary ampullary cancers are frequently seen in patients with more than 50 years of age, especially between the ages of 60 to 70, and are mostly detected in men. In our study, the mean age of 52 patients was 61.9 years, and 59.6% of the patients were male. However, despite the same anatomical structure and similar risk factors, the reason for the frequent occurrence in men has not been found yet. This may be due to smoking that is more common in men.

In our study, CT was able to identify 67.3% of the tumor mass, and this was consistent with the literature. In a multicenter study by Bakkevold et al., 472 pancreatic and ampullary tumor patients were investigated, and the rate of mass detection of CT was found to be 58% in 30 patients with ampullary carcinoma [11].

In our study, an ampullary mass was detected in 78.8% of

patients with EUS. The rate of detection of mass in EUS was found to be between 74-90% in nine comprehensive studies [2-4,12-17].

In our study, it was determined that the EUS technique was superior to CT in detecting the primary tumor. Maluf-Filho F, et al. reported a total of 61 patients with periampullary tumors, and only 10 of them had an ampullary tumor. In this study, it was shown that EUS was superior to CT in detecting primary tumors, but it was not statistically significant. It was reported that small tumors in the ampullary region could not be seen due to low CT resolution [4]. In another study, when 21 patients with periampullary tumors had been examined, EUS was found to be more sensitive in detecting the tumor compared to CT (100% and 67%, respectively) [18]. In the study by Chien-Hua Chen et al., 41 patients had been diagnosed with an ampullary tumor. In this study, the primary tumor detection rate using EUS was 97.6%, and CT was 28.6%. This difference was found to be statistically significant [9].

Ampullary tumors usually grow into the lumen of the duodenum, and ampullary area in the duodenal lumen contains too much air and luminal content. Ampullary tumors are generally small tumors at the time of diagnosis. The diagnostic effectiveness of CT is low due to the location and size of the mass. The lack of air and content artifact during endosonographic evaluation and the easy identification of diverticula provide high diagnostic efficacy to EUS.

According to the TNM classification of primary ampullary tumors, T1 stage is defined as tumors limited to the ampulla, T2 stage is defined as tumors invading the duodenal invasion, T3 stage is defined as tumors invading the pancreas (less than 2 cm), T4 stage is defined as invading pancreas (more than 2 cm) and adjacent organs. In our study, 7 (13%) patients were T1 stage, 21 (40%) patients were T2 stage, 21 (40%) patients were T3 stage, and 3 (7%) patients were T4 stage in the pathology results.

In our study, peripheral tissue invasion (stage T2 and T3) and vascular invasion (stage T4) were found in 45 patients according to the pathology results. EUS was found to be superior to CT in determining the peripheral tissue invasion. The sensitivity for demonstrating peripheral tissue invasion was also superior to the CT. As in our study, Everson et al. also looked at peripheral tissue invasion in ampullary tumors. The sensitivity of EUS and CT was found to be 85% and 35%, respectively [3].

In the study by Artifon et al., the sensitivity of CT in T2 and T3 stages with ampullary cancer has been found to be 35% and 75%, respectively [3]. In a study of 41 patients with ampullary cancer, the rate of CT detection of peripheral tissue invasion was 26.1% [9]. In our research, it was determined as 17.7%.

In our study, the rate of detection of peripheral tissue invasion by EUS was 44.4%. According to the pathology results, EUS was compatible with pathology in 6 (85%) of 7 T1 tumor patients, in 6 (28%) of 21 T2 tumor patients, in 11 (52%) of 21 T3 tumor patients and 2 (66.6%) of 3 T4 tumor patients. According to these results, the compatibility of EUS with the pathology result is higher in tumors that are in the very early stage (stage T1) and in later stages (stage from T2 to T4).

In the study by Ito et al., endoscopic ultrasonography determined 45% of patients with duodenal wall invasion [20]. In

our research, pathology results of patients in whom EUS could not detect duodenal invasion were examined, and it was seen that most of them were microscopic invasions.

Primary ampullary tumors can invade the surrounding vascular structures SMV, SMA, PV. However, the frequent growth of these tumors to the intraluminal area and being away from large vascular structures leads to a low risk of vascular invasion in the early stages.

In the preoperative evaluation of 52 patients with EUS and CT, CT showed no vascular invasion in any patients, whereas EUS revealed that two patients had vascular invasion. Although EUS detected vascular invasion in 2 patients, these two patients were operated on because of the negative CT results. According to the pathology result, the vascular invasion was seen in 3 patients, and EUS was able to show vascular invasion preoperatively in 2 of them. The rate of detection of EUS in patients with vascular invasion in the histopathological examination was found to be 66.6%. In the literature, we could not find a study investigating the efficacy of EUS in detecting vascular invasions of primary ampullary tumors. Both EUS and CT had high specificity in the preoperative evaluation of vascular invasion.

In the study of Rösch T. et al., 46 patients with pancreatic cancer and 14 patients with ampullary tumors were examined. The rate of CT to detect invasion of vascular structures, such as SMV and PV, was found to be 75% [17]. However, in this study, pancreatic and ampullary tumors were evaluated together for vascular invasion, and no separate subgroup analysis of primary ampullary tumors was performed.

There are few studies in the literature on the sensitivity of vascular invasion of EUS in periampullary tumors. In the study by Rösch T. et al. with 75 patients with periampullary tumors, the sensitivity and specificity of the EUS procedure for demonstrating vascular invasion were 43% and 91%, respectively [21]. In another study, the sensitivity and specificity of EUS detecting vascular invasion in 37 patients with periampullary tumors were 20% and 100%, respectively [22]. In our study, the sensitivity of EUS in demonstrating vascular invasion was found to be compatible with the literature.

There are some limitations to our study. It was not considered to what extent the use of invasive interventions such as Percutaneous Transhepatic Cholangiography (PTC) and endoscopic retrograde cholangiopancreatography (ERCP) for bile duct drainage affects efficacy before radiological and endoscopic examinations such as EUS and CT. In our clinical experience, we think that previous invasive procedures might decrease the effectiveness of CT and EUS in tumor evaluation. Although the EUS was made by a single operator, the CT was evaluated by different radiologists. Due to the small number of patients with vascular invasion in pathology, the statistical analysis of the comparison of CT and EUS in terms of vascular invasion was not sufficient.

In conclusion, radiological and endoscopic examinations are essential in the early diagnosis, staging, and treatment of ampullary tumors. In our study, we aimed to compare CT and EUS in terms of their contribution to early diagnosis and staging of ampullary tumors. The results showed that EUS was superior in detecting mass, peripheral tissue invasion, and vascular invasion than CT. In the literature, it has been reported that EUS

should be the first choice in patients in whom ampullary tumors cannot be detected by CT and in patients with insufficient information for vascular and peripheral tissue invasion by CT. Our results also support this approach. Moreover, the results support the realization of EUS in patients who are considered to have ampullary tumors due to their current superiority, regardless of CT.

EUS appears to be superior to CT, but EUS is an operator-dependent procedure and can only work well in experienced hands. CT and EUS are two important complementary examinations in the evaluation of these patients.

#### Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

#### Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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#### Conflict of interest

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