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Endoscopic Ultrasonography in Diagnosis and Staging of Pancreatic Cancer

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The accuracy of endoscopic ultrasonography (EUS) for diagnosis of pancreatic cancers was evaluated in consecutive 232 patients with possible pancreatic cancer, and that for assessment of their locoregional spread was evaluated in 28 patients with pancreatic cancer subjected to pancreatectomy, in comparison with the accuracies of transabdominal ultrasonography (US) and computed tomography (CT). EUS was found to be significantly more accurate than US or CT and was especially useful for detecting small pancreatic cancers of less than 2 cm in diameter. With EUS, pancreatic cancers could be detected as a hypoechoic mass with a relatively unclear margin and irregular internal echoes. EUS was also more sensitive than CT and US for detecting venous and gastric invasions: it was more useful for detecting direct invasion of pancreatic cancers when the tumors were less than 3 cm in diameter. These findings indicate that EUS is an accurate method for diagnosis of pancreatic cancer and assessment of their locoregional spread and is particularly useful for detecting small tumors.

KEY WORDS: endoscopic ultrasonography; pancreatic cancer; early diagnosis; locoregional spread assessment.

The early diagnosis of pancreatic cancers is still difficult, although several imaging techniques are available. Transabdominal ultrasonography (US) has been widely regarded as the best screening procedure for diagnosing pancreatic cancer (1–3). However, diagnosis of masses of less than 3 cm in size or lesions that do not distort the local anatomy by ultrasound is difficult (4). To overcome these problems in US, a new approach, endoscopic ultrasonography (EUS), has been developed for intraluminal ultrasonographic scanning under endoscopic guidance (5, 6). Now, EUS is being considered as the most accurate single test for imaging pancreatic cancer (7–9). In the present study, we examined the clinical value of EUS for diagnosis and staging of pancreatic cancers.

MATERIALS AND METHODS

Patients. From February 1989 to February 1993, 232 patients (140 males and 92 females, mean age 57.7 years) with suspected and/or confirmed pancreatic cancer were evaluated by EUS at our institution. Consecutive cases of possible pancreatic cancer were included in this study. Forty-nine patients eventually were found to have pancreatic cancer, and 21 patients were found to have nonresectable pancreatic cancer. Twenty-eight patients (15 males and 13 females, mean age 62.2 years) with pancreatic cancer were subjected to pancreatectomy. Histological examinations of specimens obtained at pancreatectomy showed that eight of 28 pancreatic cancers were less than 2 cm, eight were 2–3 cm, and 12 were more than 3 cm in longest dimension. Seventeen tumors were located in the head of the pancreas, and 11 in the body and/or tail of the pancreas. The final diagnosis was established by histologic and/or cytologic examinations in all cases of pancreatic cancer. Another 183 patients were observed until June 1994, but no pancreatic cancer was found.

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Methods. The 232 patients in this series were evaluated prospectively by US, CT, and EUS within four weeks, and 28 patients who were subjected to pancreatectomy were evaluated prospectively by US, CT, and EUS within two weeks before operation. All patients were studied by these three diagnostic modalities, but examinations by US, CT, and EUS were performed at random.

EUS was carried out with an Olympus GF-UM3 or JF-UM3 apparatus. The ultrasonic endoscope is a forward–oblique-viewing system. It contains a 7.5-MHz sector transducer at the tip, which is rotated by a motor. The monitor unit (EUM 3) provides a 360-degree sector scan display. The video recording was analyzed at the end of the examination.

EUS examination was performed on patients in the left lateral decubitus, the prone, and/or the supine position according to Yasuda's method (10) as described previously. Briefly, the pancreatic head, the portal vein, and the confluens are visualized from the duodenal second portion and bulb, whereas the pancreatic body and tail, the splenic vessels, and the celiac trunk are visualized from the gastric body. A fluid interface to the gastroduodenal wall was established by either filling the balloon around the tip of the instrument and/or filling the stomach with water. The pancreatograms were analyzed with respect to the location, border, and internal echo characteristics of the pancreatic mass, and duct or cystic formation in the tumor. The EUS criteria used to diagnose vascular involvement were as follows (9): (1) a tumor in the vessel lumen, (2) nonvisualization of a major portal vessel (portal vein, superior mesenteric vein, or splenic vein), and (3) encasement indicated by an abnormal contour of the vessel, with loss of the hyperechoic vascular–parenchymal sonographic interface. The criterion for diagnosing gastric invasion was direct tumor growth beyond the anterior pancreatic capsule into the outer layer or entire gastric wall.

All patients also underwent transabdominal ultrasonography (11) and CT scanning with oral and/or intravenous contrast for diagnosis and staging.

Statistical Analyses. Results were analyzed by the chi-square test, Fisher's exact probability test, or McNemar test (12). Values of $P < 0.05$ were considered significant between two groups. A correction was made for multiple comparisons. According to the Bonferroni inequality, values of $P < 0.05/3 = 0.017$ were considered significant among three groups (13).

RESULTS

Diagnosis of Pancreatic Cancers. The EUS examination lasted 20–40 min, and no severe complications developed during or after the examination period. Table 1 summarizes the diagnostic accuracies of EUS, US, and CT for diagnosis of pancreatic cancers. The sensitivity and predictive value of negative results by EUS were significantly better than those by CT, and overall accuracy was significantly better than that by US and CT. The sensitivity of EUS, US, and CT for diagnosis of pancreatic cancers is summarized in Table 2. We failed to detect pancreatic tumor in 3 cases by EUS, 11 cases by US and 17 cases by CT. Diagnosis by EUS results was significantly more sensitive than those by CT. In particular, results by EUS were significantly better than those by CT in diagnosis of pancreatic cancers less than 3 cm in diameter and also better (not significant) in cancers less than 2 cm in diameter.

TABLE 1. DIAGNOSTIC ACCURACIES OF PANCREATIC CANCERS BY ENDOSCOPIC ULTRASONOGRAPHY (EUS), TRANSABDOMINAL ULTRASONOGRAPHY (US), AND COMPUTED TOMOGRAPHY (CT)

	EUS	*US*	*CT*
Sensitivity	94% (46/49)*	78% (38/49)	65% (32/49)
Specificity	97% (177/183)	91% (167/183)	94% (172/183)
Predictive value of positive results	84% (46/52)	70% (38/54)	74% (32/43)
Predictive value of negative results	98% (177/180)†	94% (167/178)	91% (172/189)
Overall accuracy	96% (223/232)†,‡	88% (205/232)	88% (204/232)

* Significantly different from the value for CT at $P = 0.0004$.
† Significantly different from the value for CT at $P = 0.002$.
‡ Significantly different from the value for US at $P = 0.003$.

Table 3 summarizes the features of pancreatic cancers detected by EUS. In general, pancreatic cancer could be detected as a hypoechoic tumor with a relatively unclear margin and irregular internal echoes. Tumors less than 2 cm were usually observed as hypoechoic, but sometimes as isoechoic tumors without any duct or cyst formation.

Figure 1 shows an endoscopic ultrasonogram of a patient with pancreatic cancer. An indistinctly defined pancreatic mass of 2 cm in diameter with relatively

TABLE 2. DIAGNOSTIC SENSITIVITIES OF PANCREATIC CANCERS BY ENDOSCOPIC ULTRASONOGRAPHY (EUS), TRANSABDOMINAL ULTRASONOGRAPHY (US), AND COMPUTED TOMOGRAPHY (CT) IN RELATION TO RESECTABILITY AND TUMOR SIZE

	Patients examined (N)	*Patients (N and %) correctly diagnosed by*		
		EUS	*US*	*CT*
Resectable cases, tumor size				
≤2 cm	8	7 (88)	5 (63)	3 (38)
2–3 cm	8	8 (100)	6 (75)	4 (50)
≤3 cm	16	15 (94)*	11 (69)	7 (44)
>3 cm	12	12 (100)	10 (83)	10 (83)
Subtotal	28	27 (96)†	21 (75)	17 (61)
Nonresectable cases	21	19 (90)	17 (81)	15 (71)
Total	49	46 (94)‡	38 (78)	32 (65)

* Significantly different from the value for CT at $P = 0.003$.
† Significantly different from the value for CT at $P = 0.002$.
‡ Significantly different from the value for CT at $P = 0.0004$.

TABLE 3. ULTRASONOGRAPHIC FINDINGS IN PANCREATIC CANCERS BY ENDOSCOPIC ULTRASONOGRAPHY (EUS)

Findings	*Patients (N and %)*			
	Size of tumor			
	≤2 cm	*2–3 cm*	*>3 cm*	*Total*
Echo level				
Hypoechoic	5 (71)	8 (100)	11 (92)	24 (89)
Mixed	0 (0)	0 (0)	1 (8)	1 (4)
Isoechoic	2 (29)	0 (0)	0 (0)	2 (7)
Internal echoes				
Regular	4 (57)	3 (37)	4 (33)	11 (41)
Irregular	3 (43)	5 (63)	8 (67)	16 (59)
Border of tumor				
Clear	3 (43)	1 (13)	5 (42)	9 (33)
Unclear	4 (57)	7 (87)	7 (58)	18 (67)
Duct or cyst formation in the tumor				
Present	0 (0)	2 (25)	5 (42)	7 (26)
Absent	7 (100)	6 (75)	7 (58)	20 (74)
Total	7*	8	12	27†

* One case with tumor size less than 2 cm was not detected by EUS.
† The pancreatic tumor in one case among total 28 cases was not detected by EUS.

TABLE 4. DIAGNOSTIC ACCURACY OF DIRECT INVASIONS OF PANCREATIC CANCERS BY ENDOSCOPIC ULTRASONOGRAPHY (EUS)*

Histological diagnosis	*Sizes of tumors*		*Total*
	≤3 cm	*>3 cm*	
Portal vein invasion (%)			
PV (+)	67 (2/3)	75 (3/4)	71 (5/7)
PV (−)	100 (9/9)	0 (0/1)	90 (9/10)
Total	92 (11/12)	60 (3/5)	82 (14/17)
Splenic vein invasion			
SV (+)	(0/0)	60 (3/5)	60 (3/5)
SV (−)	100 (4/4)	50 (1/2)	83 (5/6)
Total	100 (4/4)	57 (4/7)	73 (8/11)
Total vascular invasion	94 (15/16)	58 (7/12)	79 (22/28)
Gastric invasion			
G (+)	(0/0)	100 (3/3)	100 (3/3)
G (−)	100 (4/4)	75 (3/4)	88 (7/8)
Total	100 (4/4)	86 (6/7)	91 (10/11)

* Portal vein invasion was evaluated only for cancers of the pancreas head, and splenic vein invasion and gastric invasion were evaluated only for cancers of the pancreas body and/or tail.

irregular internal echoes was found between the body and tail of the pancreas. The patient underwent pancreatectomy, and histological examination revealed that the tumor was a well-differentiated tubular adenocarcinoma.

Diagnosis of Venous and Gastric Invasions. The diagnostic accuracies of venous (portal vein and splenic vein) and gastric invasion by EUS are summarized in Table 4. The overall accuracies of detection of portal and splenic vein invasion by EUS were 82% and 73%, respectively. In general, the diagnostic rate of portal and splenic vein involvement were better for pancreatic cancers less than 3 cm in diameter than for those more than 3 cm in diameter: the diagnostic rates for portal and splenic vein involvement were 92% and 100%, respectively, for tumors less than 3 cm in diameter, but only 60% and 57%, respectively, for tumors over 3 cm in diameter.

Figure 2 shows a pancreatic cancer directly invading the portal vein. The portal vein shows encasement indicated by an abnormal contour of the vessel, with loss of the hyperechoic vascular–parenchymal sonographic interface. Histological examination of specimens obtained by pancreatectomy confirmed portal vein invasion.

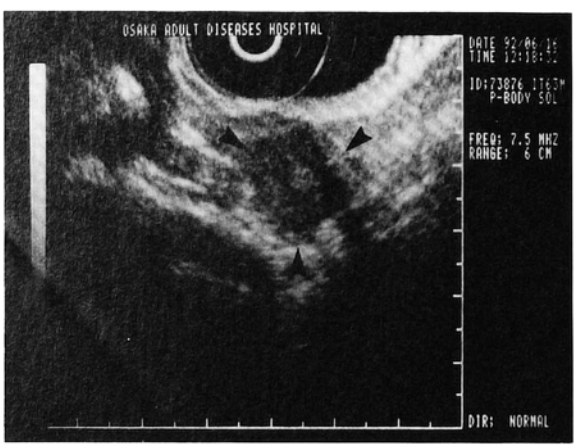

Fig 1. An endoscopic sonogram of a patient with pancreatic cancer. An indistinctly defined pancreatic mass of 2 cm in diameter with relatively irregular internal echoes was found between the body and tail of the pancreas.

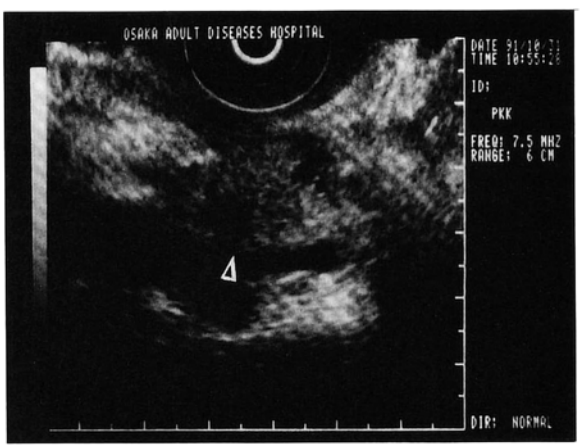

Fig 2. An endoscopic sonogram of a patient with pancreatic cancer directly invading the portal vein. The portal vein shows encasement indicated by an abnormal contour of the vessel, with loss of the hyperechoic vascular–parenchymal sonographic interface.

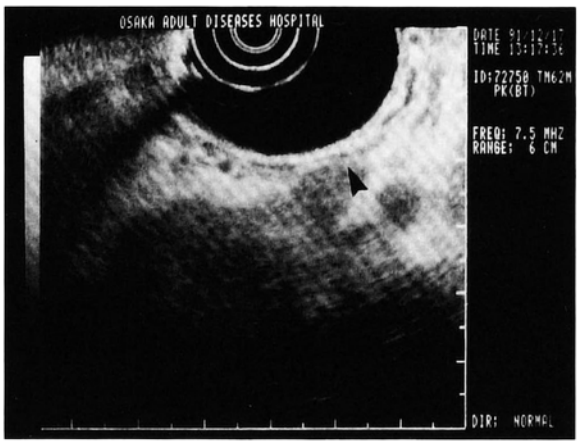

Fig 3. An endoscopic sonogram of a patient with pancreatic cancer directly invading the gastric wall. The tumor extended to the middle layer of the gastric wall.

We have never experienced any cancers of the pancreas head that invaded to gastric wall, so we excluded 17 patients with cancer of the pancreas head for evaluation of detection rate of gastric invasion, and we evaluated the detection rate of gastric invasion only for the 11 patients with cancer of the pancreas body and/or tail. Table 4 also shows that the overall accuracy of EUS for detecting gastric invasion was 91%. The detection rates of tumors less than 3 cm and over 3 cm in diameter were both good. Figure 3 shows an endoscopic sonogram of a patient with pancreatic cancer directly invading the gastric wall. The tumor extended to the middle layer of the gastric wall. Histological examination showed that the pancreatic tumors had invaded the muscle layer of the gastric wall.

The accuracies of EUS, US, and CT for detecting venous and gastric invasions are summarized in Table 5. The results of EUS were significantly more effective than those of the group joined together with US and CT.

TABLE 5. DIAGNOSTIC ACCURACIES OF DIRECT INVASIONS OF PANCREATIC CANCERS BY ENDOSCOPIC ULTRASONOGRAPHY (EUS), TRANSABDOMINAL ULTRASONOGRAPHY (US), AND COMPUTED TOMOGRAPHY (CT)*

Direct invasion of pancreatic cancer	*No. of tumors examined (N)*	*Tumors (N and %) correctly diagnosed by*		
		EUS	*US*	*CT*
Portal vein invasions	17	14 (82)†	8 (47)	7 (41)
Splenic vein invasions	11	8 (73)	7 (64)	6 (55)
Total vascular invasions	28	22 (79)†	15 (54)	13 (48)
Gastric invasions	11	10 (91)‡	6 (55)	5 (45)

* Portal vein invasion was evaluated only for cancers of the pancreas head, and splenic vein invasion and gastric invasion were evaluated only for cancers of the pancreas body and/or tail.
† Significantly different from the value for the group joined together with US and CT at $P = 0.02$.
‡ Significantly different from the value for the group joined together with US and CT at $P = 0.03$.

DISCUSSION

The accuracy of EUS for detecting pancreatic cancers has been reported to be high (7, 14–16) and to be superior to US and CT (7, 15): this is especially true for smaller lesions (7, 15). Recently, Palazzo et al (9) compared the accuracies of EUS, US, and CT for detecting pancreatic cancers and found that detection by EUS was significantly more (91%) than that by CT (66%) or US (64%). They also reported that all cancers of less than 25 mm in diameter were imaged by EUS, but only one by US or CT. In the present study, we also found that EUS was superior to CT and US for diagnosis of pancreatic cancer and that EUS was useful for detecting small pancreatic cancers less than 2 cm in diameter. These findings indicate that EUS is the best method available for early diagnosis of pancreatic cancer.

Diagnosis of the stage of pancreatic cancer is very useful in assessing the prognosis of cancer patients, selecting a suitable treatment schedule, and evaluating the efficacy of the treatment used. EUS was shown to be highly accurate for detection of portal venous involvement and prediction of the T and N stages (17, 18). Palazzo et al (9) reported that EUS was significantly more sensitive (100%) than CT (71%) or US (17%) for detecting venous involvement of pancreatic cancers. Yasuda et al (19) reported that EUS was as effective as angiography for diagnosing vascular involvement. In the present study, we found that EUS was more accurate for detecting venous and gastric invasions than CT or US. We also found that EUS was more effective for detecting vascular involvement of pancreatic cancers less than 3 cm than those over 3 cm in diameter. Yasuda et al (7) reported similar results: when the tumor is over 3 cm in diameter, it is difficult to evaluate the portal vein and/or splenic vein because of echoic reduction. These findings indicate that EUS in the clinical setting of pancreatic cancer staging is of great value in assessing local tumor spread in potentially resectable cancer; it might save some of these patients from unnecessary explorative laparotomy (8).

EUS is an accurate tool for diagnosis of pancreatic

cancer and assessment of its locoregional spread. However, it cannot yet be used as a screening procedure because it is still considered to be in an early stage of development compared with other imaging methods for study of pancreatic disease (20). Improvement in evaluation of EUS images as well as in the equipment will further improve the accuracy of EUS (21), and so in future EUS it should be useful as a screening procedure, like endoscopic examination of the upper gastrointestinal tract.

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