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Intraportal Endovascular Ultrasonography in the Diagnosis of Portal Vein Invasion by Pancreatobiliary Carcinoma

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Objective
The purpose of this study was to determine the value of intraportal endovascular ultrasonography (IPEUS) in the diagnosis of portal vein invasion by pancreatobiliary carcinoma. The authors reported their experiences with this new technique and compared it with conventional imaging technologies, such as portography and computed tomography (CT).

Summary Background Data
Pancreatobiliary carcinoma often invades the portal vein. Observation of the echogenic band of the portal vein wall by means of a high-frequency, high-resolution intravascular ultrasound catheter allows for the accurate diagnosis of the portal vein invasion.

Methods
A prospective study of 30 consecutive patients with pancreatobiliary carcinoma (16 pancreatic carcinomas, 8 bile duct carcinomas and 6 gallbladder carcinomas) was performed. In 23 cases IPEUS was performed intraoperatively from the superior mesenteric venous route with an 8 French, 20 MHz intravascular ultrasound catheter. In 7 cases IPEUS was performed before surgery from the percutaneous transhepatic route with a 6 French, 20 MHz intravascular ultrasound catheter. The finding of IPEUS was confirmed by pathologic examination of resected specimens and surgical exploration. The results of IPEUS were compared to those of portography and CT.

Results
Intraportal endovascular ultrasonography visualized the portal vein wall as an echogenic band with a thickness of 0.5 mm to 1.0 mm. The diagnostic criterion of portal vein invasion was destruction of this echogenic band. Portal vein invasion was found in 15 of 30 cases. Vascular invasion was confirmed by pathologic examination of resected specimens in 10 patients and operative findings in 5. The sensitivity, specificity, and overall accuracy of IPEUS for diagnosis of portal vein invasion was 100%, 93.3%, and 96.7%, respectively. The values were 80%, 67.7%, and 73.3% for portography and 53.3%, 80%, and 66.7%, respectively, for CT.

Conclusions
Intraportal endovascular ultrasonography provided precise information about the relationship between the pancreatobiliary tumor and the portal vein wall. It was capable of accurately detecting or excluding early invasion of the portal vein wall by pancreatobiliary carcinoma.

In patients with pancreatobiliary carcinoma, the portal vein is easily invaded. The resection of tumor with portal vein invasion has been considered by many surgeons to be impossible or not indicated. In 1983, Nakao and Kondo[1] reported a pressure gradient catheter bypass from the superior mesenteric vein to the right femoral vein for combined resection of the portal vein in pancreaticoduodenectomy. With use of a portosystemic shunt consisting of a heparinized hydrophilic catheter (Anthron tube, Toray Industries Inc., Tokyo, Japan), portal vein resection and anastomosis could be performed safely without portal blood congestion.

Increasingly aggressive radical operations with portal vein resection for pancreatobiliary carcinoma have been reported,[2-5] and the accurate diagnosis of the portal vein invasion has become crucial. Despite the progress in imaging technology, portal invasion of the tumor is sometimes difficult to visualize. When a tumor is shown to be contiguous with the portal vein by computed tomography (CT) or ultrasonography, the diagnosis of subtle invasion is extremely difficult to make,[6] and distinct diagnostic criteria for invasion or compression have not been reported. The portal phase of a superior mesenteric arteriography does not necessarily provide a sharp image, thereby making interpretation of slight changes in arterial portography difficult. With percutaneous transhepatic portography, it is also extremely difficult to distinguish between subtle invasion and compression of the tumor.[7]

In recent years, high-resolution intravascular ultrasound catheters have been developed and applied to assess coronary and peripheral angioplasty procedures.[8,9] We used an intravascular ultrasound catheter to diagnose tumor invasion of the portal vein in pancreatobiliary surgery.

In the current study, intraportal endovascular ultrasonography (IPEUS) was used to accurately diagnose portal invasion by pancreatobiliary carcinoma and to formulate the operative strategy for radical resection. The results and clinical significance of IPEUS are described and compared with those of portography, CT (including dynamic study), operative findings, and resected specimens.

PATIENTS AND METHODS

From February 1992 to December 1993, 30 consecutive patients who underwent operations for pancreatobiliary carcinomas were studied with IPEUS in a prospective clinical trial. The study group consisted of 15 men and 15 women with a mean age of 65.1 years (range, 51–78 years). Informed consent was obtained from all patients in the study. Among the patients, there were 16 pancreatic cancers, 8 bile duct cancers, and 6 gallbladder cancers. Operations were performed in all 30 cases. Twenty-three patients underwent resection, and and 15 underwent combined resection of the portal vein. Seven patients did not undergo resection. The reasons for unresectability were liver metastases (4 patients), superior mesenteric arterial invasion (1 patient), para-aortic lymph node metastases (1 patient) and peritoneal dissemination (1 patient).

Two types of intravascular ultrasound catheters were used in the current study. One consisted of a 20-MHz transducer mounted on the tip of an no. 8 French catheter equipped with a rotating mirror at a 45-degree angle that reflects the ultrasound beam perpendicular to the long axis of the catheter (CVIS, Sunnyvale, CA). This is a rotating mirror system[9] and provides axial resolution of 230 μ, lateral resolution of 130 μ, and maximum tissue penetration of 20 mm. The other type of catheter was a no. 6 or 8 French catheter with a rotating radial 20-MHz transducer (Aloka, Tokyo, Japan). The transducer was equipped at the terminus of a metallic shaft and housed and bathed in water for coupling. This is a rotating tip system[9] and provides axial resolution of 230 μ, lateral resolution of 120 μ, and maximum tissue penetration of 20 mm. Both catheters produced high-resolution, 360-degree real-time, cross-sectional images perpendicular to the intravascular ultrasound catheter.

We performed IPEUS intra-operatively from the superior mesenteric vein with the no. 8 French catheter. After laparotomy, a branch of the superior mesenteric vein was exposed and cut down. An no. 8.5 French introducer was inserted into this vein and fixed. The intravascular ultrasound catheter was gradually advanced through the introducer into the intrahepatic portal vein. The catheter was then withdrawn slowly for sequential observation of the cross-sectional images perpendicular to the portal vein axis from the intrahepatic to the intrapancreatic portion. Ultrasound images of the area under investigation were recorded on super video home system (VHS) videotape, and individual still frames were recorded with a thermal paper printer or Polaroid film (Fuji Film, Inc., Tokyo, Japan). The position of the catheter and the rotational orientation were monitored with simultaneous intra-operative ultrasonography. In cases that involved combined resection of the portal vein, the introducer was replaced by an Anthron tube. This tube bypassed the portal vein blood to the right femoral vein while the portal vein was clamped. In the cases not requiring portal vein resection, the introducer was removed and the branch of the portal vein was ligated.

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In cases in which percutaneous transhepatic portography was used, IPEUS was performed before surgery by the percutaneous transhepatic route. After percutaneous transhepatic portography, the size of the introducer was dilated to a no. 7 French introducer. A no. 6 French intravascular ultrasound catheter was inserted into the superior mesenteric vein through the introducer under fluoroscopic guidance. The catheter was then removed while the area of investigation was recorded.

We performed IPEUS on 30 patients. The portal vein was accessed through a branch of the superior mesenteric vein in 23 patients and by the percutaneous transhepatic route in 7 patients. In all cases, a preoperative CT scan (including dynamic study) and portography were performed. Computed tomography scans were obtained with a commercially available scanner (Toshiba 900S, Tokyo, Japan). A table incremental dynamic CT scan was performed. A bolus of 130 mL of contrast medium (300 mg iodine/mL) was delivered by mechanical injector with a speed of 3 mL/second through a peripheral arm vein. The first scan was obtained after the initial 60 mL of contrast material had been injected. The scanning technique used provided a 5-mm-slice contiguous section. The slice time was 1 second, and the interscan delay was 2 seconds. In 23 patients, a preoperative arterial portography was performed. In 7 patients, a preoperative direct portography from the percutaneous transhepatic route was performed. Images obtained by means of IPEUS were compared with those obtained by arterial portography, percutaneous transhepatic portography, and CT scan. The CT and angiographic studies were reviewed independently by two radiologists (S.I. and T.E.), each blinded to the results of the other examination. The diagnostic criterion for portal invasion by CT was narrowing of the lumen of the portal vein. The criterion for portal invasion by portography was unilateral or bilateral stenosis of the portal vein. In cases involving resection, the findings of IPEUS were correlated with histologic studies of the resected specimens. In nonresected cases, the results of IPEUS were confirmed by the findings of by thorough surgical exploration, and the main tumor underwent biopsy for histologic confirmation.

The results of IPEUS for portal vein invasion were compared with the results from other imaging technologies (portography and CT). Comparison of proportions for statistical significance was calculated with use of Fisher's exact probability test. A difference with a probability value of less than 0.05 was considered significant in all statistical comparisons.

RESULTS

Intraportal endovascular ultrasonography was performed without complications in all patients. The duration of each study was approximately 20 minutes. Detailed horizontal images perpendicular to the portal vein axis were obtained. The wall of the portal vein trunk had a single 0.5 mm- to 1.0 mm-thick echogenic layer. The diagnostic criterion for portal vein invasion was the destruction of the echogenic band of the portal vein wall by the hypoechoic tumor mass (Fig. 1). When the echogenic band of the portal vein was left intact, we considered there to be no portal vein invasion by the tumor (Fig. 2).

Portal vein invasion was confirmed in 15 of 30 cases. In 10 cases, portal vein invasion was confirmed histologically, and in 5 cases, pathologic results were unavailable but invasion was confirmed at surgical exploration. Of the 15 patients without portal vein invasion, 13 underwent resection and invasion was confirmed pathologically. In the two patients not receiving resection because of liver metastasis, an intact portal vein system was confirmed intraoperatively (Tables 1 and 2).

Intraportal endovascular ultrasonography detected portal vein invasion despite the negative findings of CT and portography in two cases. In cases in which tumor was in contact with the portal vein on CT, IPEUS could clearly discriminate between compression or invasion by the tumor (Figs. 3 and 4). Moreover, IPEUS could visualize intraportal tumor thrombus, which was undetectable by conventional imaging techniques (Fig. 5).

Of 16 patients with pancreatic carcinoma, 12 underwent resection with combined resection of the portal vein and 4 were ineligible for resection. The finding of portal vein invasion was confirmed pathologically in eight cases and at the time of surgery in three cases. The absence of portal vein invasion as determined by IPEUS was confirmed by pathologic findings in four cases and during surgical exploration in one case. Of 11 patients with pancreatic cancer for which portal vein invasion was diagnosed by IPEUS, one patient (patient 9) had false-positive results. In this patient, inflammation of the pancreas was so severe that the adventitia of the portal vein wall was replaced by fibrous tissue. The cause of severe pancreatitis appeared to be contrast medium injection into the pancreatic duct during preoperative endoscopic retrograde cholangiopancreatography.

In four of five pancreatic carcinoma cases in which IPEUS determined that the portal vein wall was contiguous with the tumor but intact, the diagnosis was confirmed histologically. In these four cases, the average distance between the cancer and the portal vein wall was 705 μ (range, 420–900 μ).

Of 13 patients with biliary carcinomas, 11 received resection, 3 received combined resection of the portal vein, and 3 were ineligible for resection. The IPEUS finding of portal vein invasion was confirmed in three resected specimens and in two cases at the time of surgical exploration. The absence of portal vein invasion as deter-

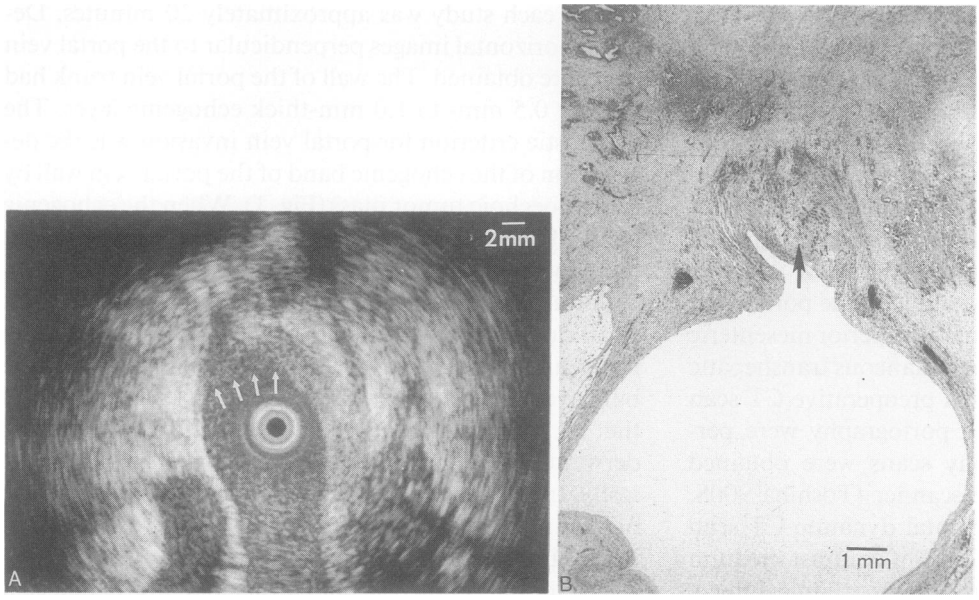

Figure 1. (A) The echogenic band of the portal vein is destroyed by the tumor (arrows). (B) The portal vein wall is invaded by the pancreatic cancer (arrow) (patient 12) (H & E, original magnification ×3).

mined by IPEUS was confirmed in eight resected specimens and in one patient at surgical exploration. In all cases, the results of IPEUS were correct.

In the diagnosis of portal invasion of the tumor, the results of IPEUS were compared with those of CT and portography (arterial portography and direct portography). The accuracy of each method was calculated from the compiled data. Sensitivity, specificity, and overall accuracy of IPEUS were 100%, 93.3%, and 96.7%, respectively; for portography, the values were 80%, 66.7%, and 73.3%, *versus* 53.3%, 80%, and 66.7%, for CT. The sensitivity of IPEUS in diagnosing portal invasion of the tumor was significantly superior to that of CT ($p < 0.01$). The sensitivity and specificity of IPEUS tended to be higher than portography without reaching statistical significance. Consequently, the overall accuracy of IPEUS was higher than that of portography ($p < 0.05$) and CT ($p < 0.01$) (Table 3).

DISCUSSION

High-frequency, high-resolution ultrasound catheters for intravascular imaging have been developed recently and have been used primarily to define intra-arterial

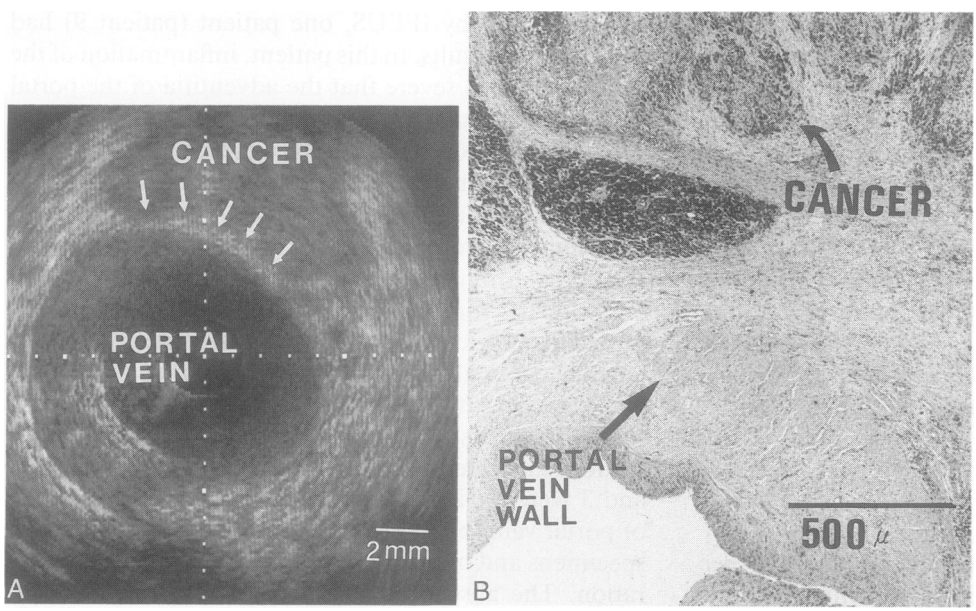

Figure 2. (A) The tumor is contiguous with the portal vein, but the echogenic band of the portal vein is not destroyed (arrows). (B) The portal vein wall is not invaded by the tumor (patient 1) (H & E, original magnification ×4).

Table 1. EVALUATION OF PORTAL VEIN INVASION IN PANCREATIC CANCER

Case No.	Diagnosis	Route	Findings by Modality			Operation	Final Results of PV Invasion
			IPEUS	Porto	CT		
1	PC (head)	SMV	(−)	(−)	(−)	PD + PV resection	(−), (420 μm)
2	PC (head)	SMV	(+)	(+)	(+)	Nonresectable (liver meta)	(+)
3	PC (head)	SMV	(+)	(+)	(+)	Nonresectable (SMA invasion)	(+)
4	PC (head)	SMV	(−)	(+)	(−)	PD + PV resection	(−), (840 μm)
5	PC (head)	SMV	(−)	(+)	(+)	PD + PV resection	(−), (660 μm)
6	PC (head)	SMV	(+)	(+)	(−)	PD + PV resection	(+)
7	PC (head)	SMV	(−)	(+)	(+)	Nonresectable, (liver meta)	(−)
8	PC (head)	SMV	(−)	(−)	(−)	PD + PV resection	(−), (900 μm)
9	PC (head)	PTP	(+)	(+)	(+)	TP + PV resection	(−)
10	PC (head)	SMV	(+)	(+)	(+)	PD + PV resection	(+)
11	PC (head)	SMV	(+)	(+)	(−)	Nonresectable (liver meta)	(+)
12	PC (head)	SMV	(+)	(+)	(+)	PD + PV resection	(+)
13	PC (body)	SMV	(+)	(+)	(−)	PD + PV resection	(+)
14	PC (head)	SMV	(+)	(−)	(−)	PD + PV resection	(+)
15	PC (head)	SMV	(+)	(+)	(+)	PD + PV resection	(+)
16	PC (head)	PTP	(+)	(−)	(+)	PD + PV resection	(+)

(+) = portal venous invasion positive; (−) = portal venous invasion negative; PD = pancreaticoduodenectomy; SMV = superior mesenteric venous route; meta = metastasis; PTP = percutaneous transhepatic portal venous route; PV = portal vein; PC = pancreatic cancer; IPEUS = intraportal endovascular ultrasonography; Porto = portography; CT = computed tomography.
Values in parentheses reflect the distance between PV and tumor.

anatomy.[10] They have been combined with balloon angioplasty catheters to provide real-time intravascular imaging during balloon dilation.[11] Applications in the urinary tract[12] and biliary tract[13] have been reported as well. Recently, application of the intravascular ultrasound catheter to assessment of the portal vein in pancreatobiliary carcinoma was reported,[14,15] as has usefulness of the intravascular ultrasound catheter for the detection of the

Table 2. EVALUATION OF PORTAL VEIN INVASION IN BILE DUCT AND GALLBLADDER CANCER

Case No.	Diagnosis	Route	Findings by Modality			Operation	Final Result of PV Invasion
			IPEUS	Porto	CT		
17	Proximal bile duct cancer	SMV	(−)	(−)	(−)	Posterior segmentectomy	(−)
18	Proximal bile duct cancer	SMV	(−)	(−)	(−)	Bile duct resection	(−)
19	Proximal bile duct cancer	PTP	(−)	(+)	(−)	Left lobe + caudate + RHA resection	(−)
20	Proximal bile duct cancer	PTP	(−)	(−)	(−)	Bile duct resection	(−)
21	Proximal bile duct cancer	SMV	(−)	(−)	(−)	Left lobe + caudate resection	(−)
22	Middle bile duct cancer	SMV	(+)	(+)	(+)	PD + PV resection	(+)
23	Middle bile duct cancer	SMV	(−)	(−)	(−)	Bile duct resection	(−)
24	Lower bile duct cancer	SMV	(−)	(−)	(−)	PD	(−)
25	Gallbladder cancer	SMV	(−)	(−)	(−)	Blle duct resection + PPPD	(−)
26	Gallbladder cancer	PTP	(+)	(+)	(−)	Extended-right lobe + PV resection	(+)
27	Gallbladder cancer	PTP	(+)	(+)	(−)	Nonresectable (lymph node meta)	(+)
28	Gallbladder cancer	PTP	(+)	(+)	(+)	Nonresectable (peritoneal meta)	(+)
29	Gallbladder cancer	SMV	(−)	(−)	(−)	Nonresectable (liver meta)	(−)
30	Gallbladder cancer	PTP	(+)	(−)	(−)	Central lobectomy + PD + PV resection	(+)

(+) = portal venous invasion positive; (−) = portal venous invasion negative; PD = pancreaticoduodenectomy; PPPD = pylorus preserving pancreaticoduodenectomy; SMV = superior mesenteric venous route; PTP = percutaneous transhepatic portal venous route; PV = portal vein; meta = metastasis; RHA = right hepatic artery; Ext = ; IPEUS = intraportal endovascular ultrasonography; Porto = portography; CT = computed tomography.

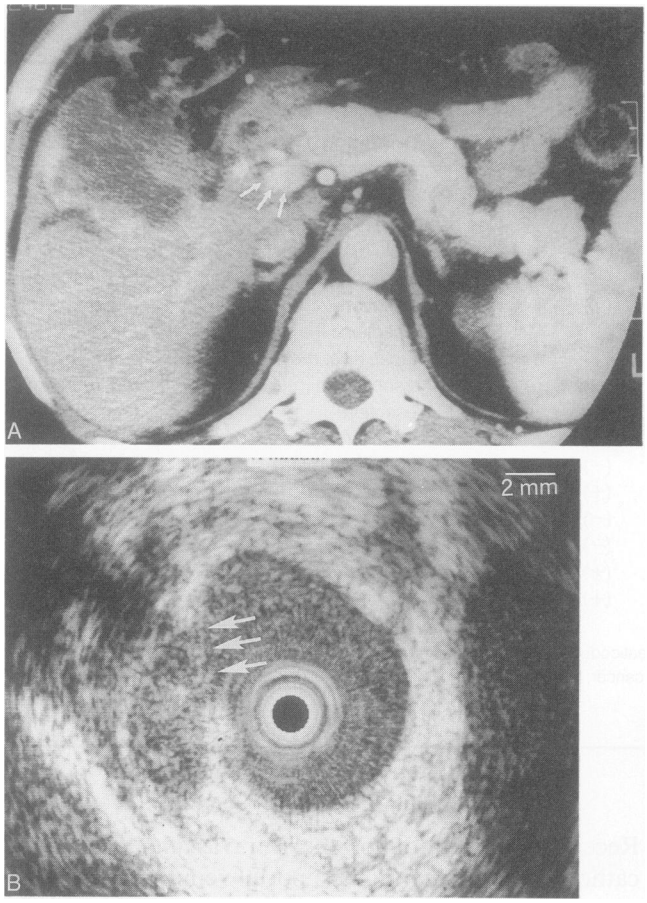

Figure 3. (A) Computed tomography demonstrating a tumor contiguous with the portal vein (arrows). (B) Detection of portal vein invasion by IPEUS (arrows) (patient 26).

intracaval tumor thrombus.[16] However, these reports were preliminary and limited to a few cases. In the current study, we have described the results of IPEUS in 30 consecutive cases and compared the results with those of angiography and CT.

In pancreatobiliary carcinoma, the portal vein wall is often invaded, so that an understanding of the spatial relationship between carcinoma and the portal vein is essential for operation. The wall of the portal vein is too thin to be visualized by conventional imaging technology, such as CT. In cases of complete occlusion of the portal vein, the diagnosis of portal invasion is easy, but CT and extracorporeal ultrasonography cannot detect subtle invasions of the portal vein wall.[7] The finding of tumor–vessel contiguity by CT and extracorporeal ultrasonography does not differentiate between subtle cancer invasion and compression. Arterial or direct portography provide only a luminal profile produced by the contrast medium in the anteroposterior direction. It does not appreciate direct tumor invasion nor differentiate between subtle invasion and compression. To overcome these limitations, we used the intravascular ultrasound catheter to evaluate of portal vein invasion.[15]

In pancreatic cancer, the resection margin of peripancreatic tissue has been reported to be an important prognostic factor.[17–19] Thorough dissection of retropancreatic tissue requires *en bloc* resection of the intrapancreatic portion of the portal vein. Correlation of IPEUS results with pathologic examination of resected specimens revealed that tumor–vessel contiguity with an intact echogenic band was indicative of tumor within 1 mm of the adventitia of the portal vein wall, though without actual invasion. Surgically, it is difficult to dissect the cancer from the portal vein, and cancer cell dissemination is a significant risk when the cancer is in contact with the portal vein by IPEUS.

In bile duct carcinoma, aggressive surgical approaches with portal vein resection have contributed to the prolongation of survival.[20] Therefore, we adopted a policy of resecting pancreatobiliary carcinoma despite portal vein invasion.

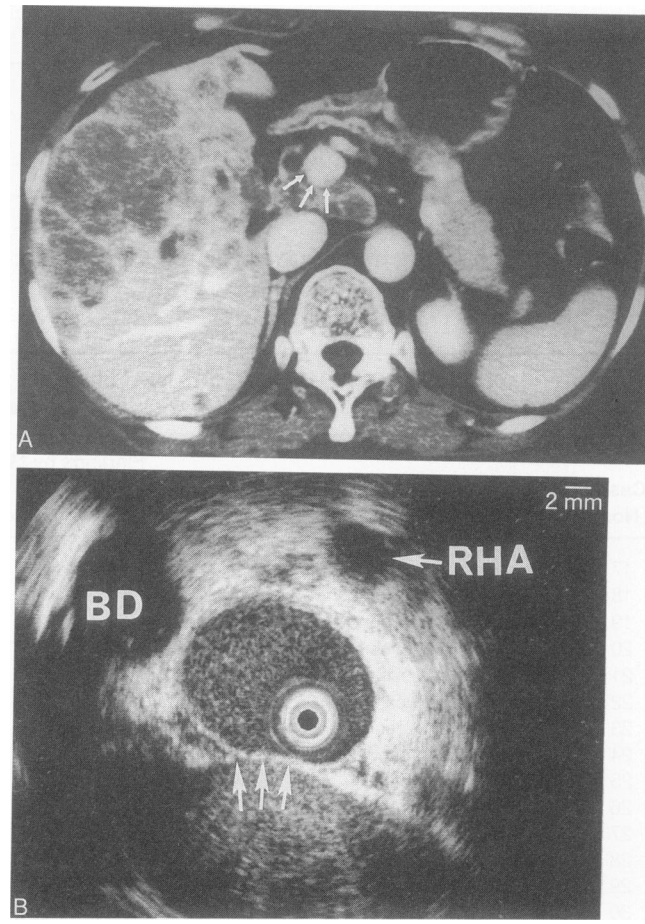

Figure 4. (A) Computed tomography demonstrating tumor contiguous with the portal vein (arrows). (B) Demonstration of the portal vein wall by IPEUS (arrows). The absence of portal vein invasion was confirmed histologically (patient 29). BD: bile duct; RHA: right hepatic artery.

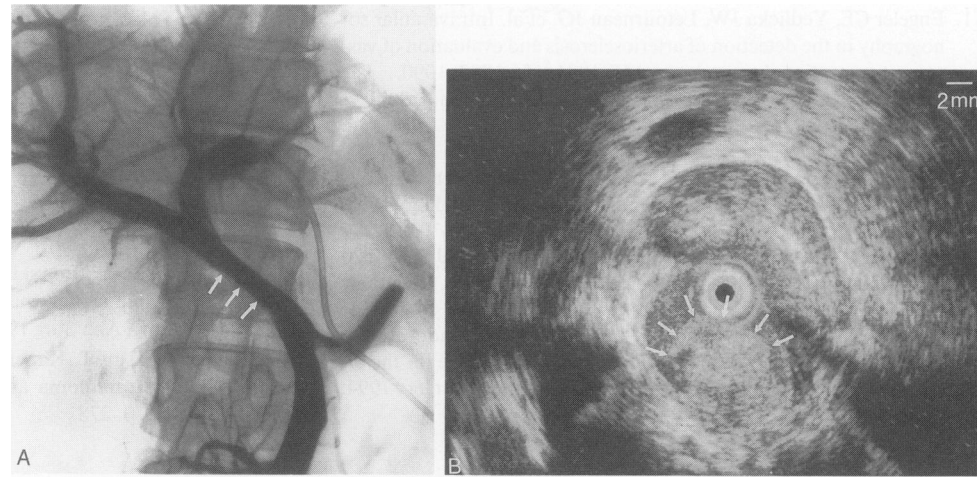

Figure 5. (A) The portal vein was smoothly compressed by the tumor (arrows). (B) Demonstration of echogenic tumor in the portal vein lumen by IPEUS (arrows) (patient 30).

In surgery for pancreatobiliary carcinoma, the cross-sectional images of IPEUS help determine operative strategy. However, because IPEUS is invasive and expensive, it should be used only in cases in which the distinction between compression and invasion cannot be made by conventional imaging techniques. In the cases in which portal vein invasion is obvious by conventional imaging diagnosis, IPEUS is unnecessary.

One limitation of IPEUS is the specificity of the test in case of pancreatitis. In the current study, one patient with a false-positive result had severe pancreatitis around the tumor. On histological examination of this case, we found that the portal vein wall was destroyed by fibrous tissue and was therefore the cause of obliteration of the echogenic band of the portal vein wall by IPEUS. In severe pancreatitis, it is difficult to differentiate between cancer and pancreatitis regarding the cause of the obliteration of the portal vein wall by IPEUS. With respect to specificity, pancreatitis around the cancer may reduce the diagnostic accuracy. Another limitation of IPEUS is its relatively poor tissue penetration. Improved tissue penetration with use of a lower-megahertz transducer can be expected. If tissue penetration exceeds 3 cm, then the diagnosis of perineural spread and perivascular lymph node metastasis of pancreatic cancer may be possible.

In conclusion, IPEUS provides more valuable and accurate information than do CT or angiography regarding portal vein invasion by tumor. This method has great potential for operative planning in pancreatobiliary carcinoma.

Table 3. COMPARATIVE ACCURACIES OF IPEUS, PORTOGRAPHY, AND CT IN ASSESSMENT OF PORTAL VEIN INVASION

	IPEUS (%)	Portography (%)	CT (%)
Sensitivity	100*	80	53.3*
Specificity	93.3	66.7	80
Overall accuracy	96.7†‡	73.3†	66.7‡

IPEUS = intraportal endovascular ultrasonography; CT = computed tomography.
* $p < 0.01$, IPEUS *versus* CT.
† $p < 0.05$, IPEUS *versus* portography.
‡ $p < 0.01$, IPEUS *versus* CT.

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