J Gastroenterol 2000; 35:919–923

Journal of Gastroenterology

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Limitations of three-dimensional intraductal ultrasonography in the assessment of longitudinal spread of extrahepatic bile duct carcinoma

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Abstract: We investigated the utility and limitations of three-dimensional intraductal ultrasonography (3D-IDUS), for the assessment of the extent of longitudinal cancer spread to the hepatic side by extrahepatic bile duct carcinoma. In eight patients with extrahepatic bile duct carcinoma, 3D-IDUS was used to assess longitudinal cancer extension to the hepatic side prior to resection. When the linear dimension of 3D-IDUS showed bile duct wall thickening that was connected to the tumor and which became thin at a point, it was determined to be the front formation of longitudinal cancer extension. The findings were examined in relation to histologic information from the resected specimen. Although 3D-IDUS showed front formation of wall thickening in two patients, it accurately reflected the histological margin of the longitudinal cancer extension in only one patient. In the other patient, the wall thickening was longer than the histological margin. When 3D-IDUS showed bile duct wall thickening without front formation ($n = 2$), the wall thickening was longer than the histological margin of the longitudinal cancer extension. Even when 3D-IDUS did not show wall thickening ($n = 4$), one of these patients showed cancer spread histologically. As a result, the accuracy in assessing longitudinal cancer extension by 3D-IDUS was only 50%. Even if the linear dimension of 3D-IDUS demonstrated front formation of thickening of the bile duct, it reflected not only cancer extension but also inflammatory wall thickening.

Key words: three-dimensional, intraductal ultrasonography, bile duct cancer, bile duct carcinoma, longitudinal cancer extension

Received: March 21, 2000 / Accepted: July 7, 2000
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Introduction

Extrahepatic bile duct carcinoma shows longitudinal spread to the hepatic side along the bile duct,[1–9] often resulting in residual tumor at the surgical margin. However, many investigators have reported that cholangiography failed to accurately assess the extent of longitudinal spread.[1–9] Although longitudinal spread of bile duct cancer has been assessed by mapping biopsy, using percutaneous transhepatic cholangioscopy (PTCS),[1,2,5,8,9] this required invasive techniques. Intraductal ultrasonography, using a high-frequency probe, is a promising modality in this area.[7,9–28] However, distinguishing of bile duct wall thickening caused by cancer spread from that caused by inflammation was difficult with conventional two-dimensional intraductal ultrasonography (2D-IDUS).[7,9,13,15,18] Recently, we have been able to use an apparatus for three-dimensional intraductal ultrasonography (3D-IDUS),[27–28] which can represent the tumor and the continuous bile duct on the same images. We expected that 3D-IDUS could demonstrate the continuity of the tumor and the thickened bile duct, and that the linear dimension of 3D-IDUS could represent the front formation of longitudinal cancer extension. In this study, we analyzed the utility and limitations of 3D-IDUS in this area.

Methods

Patients

Between December 1997 and September 1998, eight consecutive patients (six men, two women) with extrahepatic bile duct carcinoma underwent tumor staging by 3D-IDUS prior to surgical resection. The mean patient age was 66.1 years (range, 56 to 84 years). Four patients had proximal bile duct cancer, two had middle bile duct cancer, and two had distal bile duct

cancer. Written informed consent was obtained from all patients prior to percutaneous transhepatic biliary drainage (PTBD), endoscopic retrograde cholangiography (ERC), and IDUS.

Methods

The 3D-IDUS system (Fujinon, Saitama, Japan) we used consists of thin-diameter ultrasonic probes (diameter, 2.0 mm; 12 and 20 MHz), a probe translator (SP-501), an ultrasound unit (SP-701), and a 3D unit (TP-101). Probes with a 20-MHz frequency provided an axial resolution of 0.1 mm, and a maximum penetration of approximately 20 mm. Probes with a 12-MHz frequency provided an axial resolution of 0.3 mm, and a maximum penetration of approximately 30 mm. The 3D-IDUS system showed radial and linear scans imaged in real time. Radial images were created by a 360° scan perpendicular to the tip of the probe. The linear dimension was produced by integrating 40 serial radial scan images obtained at uniform intervals during one scanning, and storing these digitally. To obtain the linear images, the ultrasonic probe was moved lengthwise for 20 mm over a period of about 3 s, using the translator during scanning. Although the translator was moved manually, the linear images were constructed automatically and uniformly according to the length of scanning, even when the bile duct was not scanned at uniform speed. Three-dimensional images were produced automatically as stereographic views within a few seconds after the procedure by selecting a region of interest from the radial and linear images.

When a percutaneous approach was used ($n = 7$), a few days after PTBD, the bile duct was canalized using a presharpened catheter (Catex, Tokyo, Japan) and a polymer-coated guidewire (Terumo, Tokyo, Japan). A sheath (9-Fr, 250 mm in length; Terumo) was introduced into the bile duct over the guidewire, and the probe was inserted into the bile duct through the sheath under fluoroscopic guidance. During evaluation, a sufficient amount of contrast medium (30% meglumine sodium amidotrigoate) was injected through the side port of the sheath. The transpapillary approach ($n = 1$) was performed using a standard duodenoscope (model JF-230; Olympus Optical, Tokyo, Japan). The probe was inserted into the bile duct through the papilla, without endoscopic sphincterotomy.

Study design

Two experts, including the first author, prospectively reviewed IDUS images by selecting a region of interest from the radial and linear images, with no information from other imaging tests, except for transcutaneous ultrasonography and cholangiography. When the linear dimension of 3D-IDUS showed bile duct wall thickening that was connected to the tumor and which became thin at a point, it was determined to be the front formation of longitudinal cancer extension. A typical case is presented in Fig. 1. After fixation with 10% formalin, the surgically resected bile ducts were cut transversely into 3-mm slices. Each slice was sectioned, stained with hematoxylin and eosin, and the cancer extension was analyzed by two experienced pathologists.

Results

Complications

No patients suffered from acute pancreatitis, biliary bleeding, acute peritonitis, or septic shock.

Accuracy of IDUS

As summarized in Table 1, the histologic findings of the resected specimen showed longitudinal cancer extension to the hepatic side in five of the eight patients. Although 3D-IDUS showed front formation of wall thickening in two patients, it accurately reflected the histological margin of the longitudinal cancer extension in only one of these patients. In the other patient, the wall thickening was longer than the histological margin. When 3D-IDUS showed bile duct wall thickening

Table 1. Accuracy in assessing the extent of longitudinal spread of extrahepatic bile duct carcinoma to the hepatic side ($n = 8$)

	Intraductal ultrasonography		
Histology	Wall thickening	Front formation	Assessment of extent
Spread (+) ($n = 5$)	Negative ($n = 1$)	Negative ($n = 1$)	Under ($n = 1$)
	Positive ($n = 4$)	Negative ($n = 2$)	Over ($n = 2$)
		Positive ($n = 2$)	Over ($n = 1$)
			Accurate ($n = 1$)
Spread (−) ($n = 3$)	Negative ($n = 3$)	Negative ($n = 3$)	Accurate ($n = 3$)

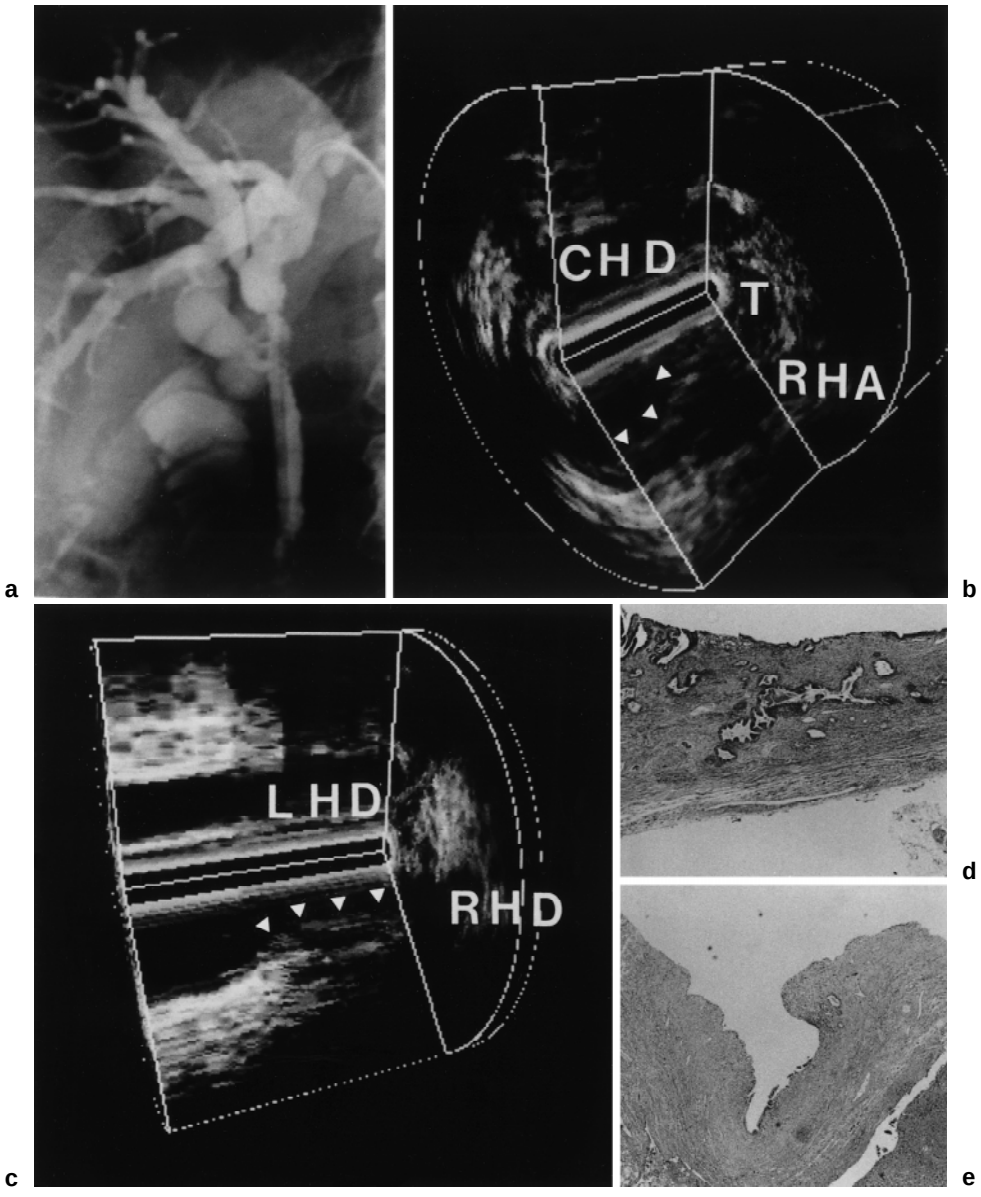

Fig. 1a–e. Findings in a 64-year-old man with cancer of the proximal bile duct who underwent surgical resection. **a** Cholangiography showed stenosis in the proximal bile duct and irregularity of the common hepatic duct. **b** Frame from three-dimensional intraductal ultrasonography at the common hepatic duct (*CHD*) showed bile duct wall thickening (*arrowheads*) which was connected to the tumor (*T*). **c** Three-dimensional intraductal ultrasonography showed continuous wall thickening (*arrowheads*) and front formation 10 mm on the hepatic side of the bifurcation of the left hepatic duct (*LHD*) and the posterior segmental branch of the right intrahepatic bile duct (*RHD*). **d** The histologic findings of the specimen resected in the common hepatic duct showed wall thickening caused by cancer spread. **e** However, the histologic findings in the left hepatic duct showed wall thickening caused by inflammatory, change, and not by cancer spread. *RHA*, right hepatic artery. **d** HE, ×4; **e** HE, ×4

without front formation ($n = 2$), the wall thickening was longer than the histological margin of the longitudinal cancer extension. Even when 3D-IDUS did not show wall thickening ($n = 4$), one of these patients showed cancer spread histologically. As a result, the accuracy of IDUS in assessing longitudinal cancer extension was only 50%.

Effect of drainage period on IDUS findings

When IDUS was performed 7 days after the biliary drainage ($n = 3$), IDUS did not show wall thickening, although the histologic findings of the resected specimen showed longitudinal cancer extension in one of these patients. In the patient with histological cancer extension, the histological findings showed mucosal surface spread without apparent projection of the mucosa. On the other hand, when IDUS was conducted 10 to 22 days (mean, 13.8 days) after the biliary drainage ($n = 5$), four of these patients showed wall thickening. However, in three of these four patients, 3D-IDUS did not indicate the accurate surgical margin because of associated inflammatory wall thickening.

Discussion

IDUS has been used to obtain high-quality cross-sectional images of the bile ducts in real time. Our research group, and others, have previously reported the utility and limitations of 2D-IDUS in the staging of bile duct cancer.[7,9–26] Recently, Kanemaki et al.[27] and our research group[28] have reported the utility of 3D-IDUS

in assessing tumor invasion to adjacent structures. However, no previous report has investigated the utility and limitations of 3D-IDUS in assessing longitudinal cancer extension along the bile duct by bile duct carcinoma, which is clinically important for determining the appropriate surgical line.

Because 3D-IDUS can represent cross-sectional images of adjacent structures and longitudinal images of the bile duct on the same images, if this modality can demonstrate front formation of cancer spread, we felt it could be possible to estimate the length of the longitudinal extension using the cystic duct, right hepatic artery, portal vein, or the bifurcation of the right and left hepatic ducts as the landmark. However, to our regret, the ultrasonographic findings showed front formation (the margin of the width of the wall thickening) caused not only by cancer spread but also that caused by inflammatory change as shown in Fig. 1. Therefore, in our study, 3D-IDUS did not show useful information that would indicate its superiority to conventional IDUS.

We have already reported that when IDUS was performed 14 to 35 days after biliary drainage, the bile duct wall thickness on IDUS images showed a significant increase after drainage.[15,18] In contrast, when IDUS was performed 6 to 8 days after biliary drainage, there was no significant difference between the bile duct wall thickness measured on the IDUS images obtained prior to catheter drainage and the images obtained after catheter drainage. Therefore, we must perform IDUS to assess longitudinal cancer extension as soon as possible after biliary drainage to minimize the inflammatory wall thickening due to the influence of the biliary catheter. Transpapillary IDUS prior to biliary drainage is a method that minimizes this artifact.[18] In one patient in our study, IDUS failed to demonstrate wall thickening, although the histologic results showed longitudinal cancer spread. As previously reported, when the histologic findings show mucosal surface spread without apparent projection of the mucosa, IDUS cannot demonstrate cancer spread.[9,13] We consider this to be a limitation of this modality.

In summary, even when the linear dimension of 3D-IDUS demonstrated front formation of thickening of the bile duct, it reflected not only longitudinal cancer extension but also inflammatory wall thickening. Because our current study had only a small number of patients, further studies are necessary to clarify the usefulness of these findings.

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