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Preoperative evaluation of Klatskin tumor: accuracy of spiral CT in determining vascular invasion as a sign of unresectability

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Abstract

Background: To assess the accuracy of spiral computed tomography (CT) in predicting the resectability of Klatskin tumor as determined by vascular invasion.

Methods: Twenty-one consecutive patients with Klatskin tumor who had undergone laparotomy were included in this study. The preoperative thin-section (5-mm-thick) spiral CT scans of these patients were assessed for the surgical resectability of tumor by evaluating the vascular invasion. The criterion for vascular invasion indicating unresectability was the tumoral invasion of the proper hepatic artery or main portal vein or simultaneous invasion of one side of the hepatic artery and the other side of the portal vein.

Results: All nine patients with tumors thought to be unresectable on the basis of CT findings had tumors that were unresectable at surgery (positive predictive value, 100%). Of 12 patients with tumors thought to be resectable, six had resectable tumors (negative predictive value, 50%). Spiral CT failed to detect small hepatic metastasis ($n = 1$), lymph node metastasis ($n = 1$), extensive tumor ($n = 2$) and variation of bile duct ($n = 2$), which precluded surgical resection.

Conclusion: Spiral CT is a reliable method for detecting vascular invasion and unresectable tumors. However, it has limitations in detecting variations of the bile duct or the intraductal extent of tumor.

Key words: Bile ducts—Bile ducts, CT—Bile ducts, neoplasm.

Hilar cholangiocarcinoma is an adenocarcinoma arising from the hepatic duct or near its bifurcation [1]. This tumor is generally divided into three types: infiltrative, exophytic, and polypoid [2]. In most instances, hilar cholangiocarcinoma is lethal, with an overall 1% 5-year survival rate. Even after curative resection, the 5-year survival rate is approximately 20% [3]. Thus, nonsurgical management such as insertion of expandable metallic stents has been common practice.

Recently, however, radical, extensive surgery such as extended left or right lobectomy with caudate lobectomy and hepaticojejunostomy aiming to cure has been attempted with this tumor [4–7]. Before radical surgery, it is necessary to ascertain not only the presence of tumors but also the extent of the disease to know whether it is resectable and to plan which side of the liver is to be resected [8].

With spiral computed tomography (CT), continuous volume data acquisition is possible in a very short period. Thus, we can not only detect a small tumor more effectively but also obtain more information on the hepatic circulation, reflecting the status of the hepatic artery or the portal vein. There have been several reports on the conventional and spiral CT findings of hilar cholangiocarcinoma [2, 9–11] and preoperative staging or assessment of resectability with CT [3, 11]. The purpose of this study was to evaluate the value of two-phase spiral CT in predicting the resectability of infiltrative hilar cholangiocarcinoma as determined by vascular invasion.

Materials and methods

CT findings of 21 patients with Klatskin tumor were retrospectively reviewed. Thirteen were male and eight were female (age range = 34–69 years, mean = 56.3 years). One patient had stone disease, but no patient had other predisposing factors such as primary sclerosing cholangitis. Inclusion criteria for this study were the surgical exploration

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Table 1. Hilar cholangiocarcinoma: vascular invasion assessed by computed tomography

	Main PV	Right PV	Left PV	None	Total
Proper HA	U	U	U/2[a]	U	2
Right HA	U/2		U/1[b]	1[c]	4
Left HA	U	U			
Middle HA	U		1		1
None	U/3[b]		2	9	14
Total	5		6	10	21

HA, hepatic artery; PV, portal vein; U, unresectable finding
[a]Two also had simultaneous right and left HA invasion
[b]One of the three patients with main PV involvement and one with right HA and left PV involvement also had simultaneous right PV invasion
[c]The patient had celiac and retropancreatic lymphadenopathy as another finding of unresectability

and pathologic confirmation of malignancy and preoperative thin-section spiral CT scans available for the review at our institution between January 1993 and December 1997.

In all patients, two-phase (arterial- and portal-dominant) spiral CT was done with a Somatom Plus-S (Siemens, Erlangen, Germany) or a Hi-speed (GE Medical Systems, Milwaukee, WI, USA). Diluted contrast material was orally administered to all patients. We injected 120 mL nonionic contrast material (Ultravist 370, Schering, Berlin) into an antecubital vein with an automated injector at a rate of 2.5 mL/s. Spiral CT was performed with 5-mm-thick collimation and a table speed of 5 mm/s (1:1 pitch) from the porta hepatis to the lower margin of the pancreas two times, in the arterial- and portal-dominant phases at 30 and 65 s, respectively, after the start of contrast material injection. Images were reconstructed at 5-mm intervals. Afterward, the images from the upper part of the liver and the lower abdomen were scanned with 10-mm axial sections at 10-mm intervals.

CT scans were interpretated by the consensus of two radiologists (J.K.H., J.H.C.) who had no knowledge of the patient's surgical findings. The observers determined whether the tumor was resectable on the basis of vascular invasion of tumor. The criterion for vascular invasion indicating unresectability was (a) the invasion of the proper hepatic artery or main portal vein or (b) simultaneous invasion of one side of the hepatic artery and the other side of the portal vein. Vascular invasion was diagnosed when there was (a) a soft tissue infiltration around the vascular structure and (b) focal luminal narrowing of the portal vein or its branches in serial images. In this study, the intraductal extent of the tumor was not analyzed because the prediction is usually not sufficiently accurate [10], but contralateral bile duct involvement, hepatic and lymph nodal metastasis, and the spread to contiguous ligaments were also analyzed as signs of unresectability other than vascular involvement.

All patients had undergone laparotomy 3–63 days (mean = 29.1 days) after CT. The surgical findings were reviewed in all cases to determine resectability. In cases of disagreement between the assessment of resectability based on CT findings and the surgical findings, the radiologic and surgical findings were analyzed further to investigate the discrepancy.

Results

Tumor invasions of portal vein, hepatic artery, and their branches on CT in all 21 patients are reported in Table 1.

All nine patients thought to have unresectable tumors on the basis of CT findings had unresectable tumors at surgery (positive predictive value, 100%). Eight of nine patients had vascular invasions, indicating unresectability (Figs. 1, 2). One had only right hepatic arterial involvement but had celiac and retropancreatic lymphadenopathy on CT as another finding of unresectability. Findings other than vascular invasion indicating unresectability were also detected in seven out of eight patients with unresectable vascular invasion, such as hepatoduodenal ligament infiltration in four patients and distant lymph node enlargement in five patients.

Of 12 patients with tumors thought to be resectable on the basis of CT findings, six patients had resectable tumors (negative predictive value, 50%; Fig. 3) and six had unresectable tumors at surgery. The causes of unresectability were tumor extension far beyond the secondary confluence of the bile duct ($n = 2$; Fig. 4), anatomical variation of the bile duct ($n = 2$; Fig. 5), small paraaortic lymph node metastasis (N2 by UICC TNM stage, $n = 1$), and multiple small hepatic metastasis ($n = 1$).

Discussion

The role of preoperative imaging studies in patients with hilar cholangiocarcinoma is the same as that in other malignancies: detection, characterization, and staging for resectability. The resectability of hilar cholangiocarcinoma depends on the level of bile duct obstruction, the presence of vascular invasion, the extent of parenchymal invasion, and the presence of metastatic disease. Direct cholangiogram through either retrograde endoscopic or percutaneous approach is the definitive method of detecting biliary obstruction and assessing intraductal extent of this tumor [10, 12]. However, it is limited in assessing the extrabiliary extent of the tumor, which is also an essential feature in determining resectability.

Hepatic arteriography and indirect portal venography have long been considered the best method for determining vascular invasion and vascular anatomy. Therefore, angiography is usually included in the preoperative study of hilar cholangiocarcinoma [2, 13]. However, because the detection of vascular invasion at angiography depends on the change in the diameter of the involved vessel, it is natural to assume that angiography cannot depicit vascular invasion without luminal change. Recently, the dominant role of angiography has been challenged by noninvasive imagings. For example, duplex sonography can depicit severe vascular stenosis or occlusion and can be used as a preliminary screening tool before a more invasive study such as angiography [11, 14, 15]. Feydy et al. [11] reported that helical CT and hepatic angiography for assessing portal vein invasion are of similar usefulness and have a similar error rate. However, both methods failed to accurately detect arterial invasion. Loosers et al. [14] reported that the vascular patency or involvement in 22 patients with hilar cholangiocarcinoma was correctly

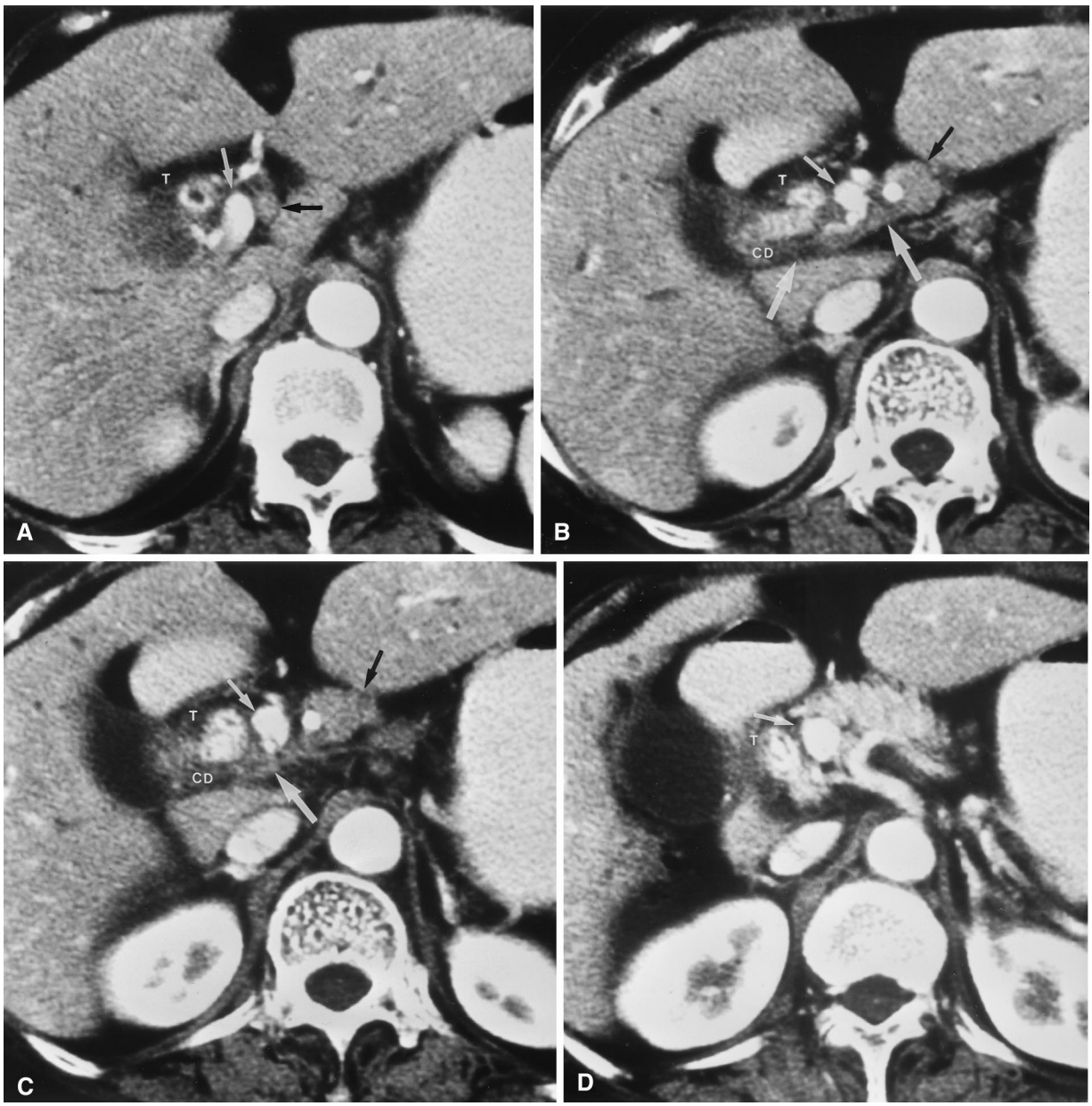

Fig. 1. A 47-year-old female with unresectable Klatskin tumor (Bismuth type IIIa) due to extensive hepatoduodenal ligament and portal vein invasion. On serial CT images, the diameter of the portal vein (*small white arrow*) in **B** and **C** is smaller than that shown in **A** and **D**, suggesting encasement and narrowing of the portal vein in the corresponding area. Also, there is soft tissue infiltration around the portal vein (*large white arrows*). During surgery, extensive tumor infiltration along the hepatoduodenal ligament and portal vein invasion were noted. There are multiple lymph nodes along the course of the hepatic artery (*black arrows*). The tumor is seen as a high attenuation lesion on right side of portal vein (*T*). In **B** and **C**, the mucosa of the cystic duct (*CD*) also shows strong enhancement, which is another finding indicating tumor involvement.

predicted in 86% by duplex sonography and that it was comparable to arteriography in the assessment of hilar vessels.

There have been several reports on CT findings of hilar cholangiocarcinoma [2, 11, 16] and on preoperative assessment of resectability [2, 3, 11, 17]. Choi et al. [2] reported that CT showed hilar cholangiocarcinoma in 40% of cases, but small tumors were usually not demonstrable with conventional CT scans. Nesbit et al. [3] reported that the accuracy of conventional CT in helping predict unresectability of cholangiocarcinoma was 54% and that the negative predictive value was only 44%. However, their data were obtained from a conventional CT scanner.

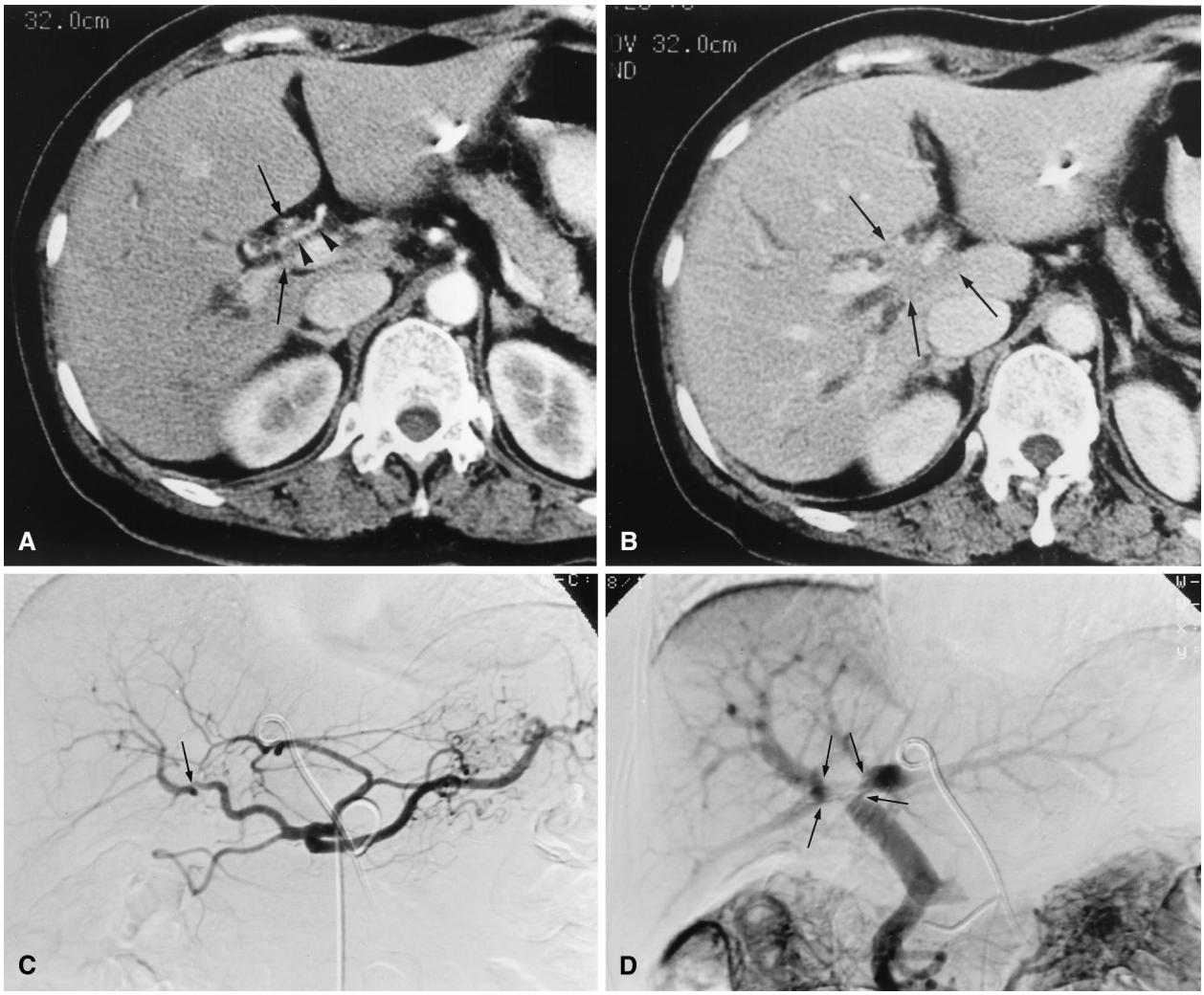

Fig. 2. A 56-year-old female with unresectable tumor correctly diagnosed on the basis of CT findings. **A** Spiral CT scan obtained during the arterial-dominant phase shows a soft tissue mass (*arrows*) encasing right hepatic artery (*arrowheads*). **B** CT during the portal-dominant phase also shows encasement of the right and left portal veins by the tumor (*arrows*). **C** Hepatic arteriography shows segmental narrowing of the right hepatic artery (*arrow*). **D** Portography shows narrowing of the portal vein bifurcation, at the right and left portal veins (*arrows*). At surgery, metastatic adenocarcinoma in the celiac lymph node was detected at exploration, so the surgeon did not try to confirm the vascular invasion.

Recent advances in CT technology have enabled the spiral scanning of the biliary tree. With spiral CT, the continuous volume data acquisition is possible in a very short period, the misregistration artifact can be eliminated, and dynamic study of liver is possible. Therefore, we can detect small tumors more effectively with careful tracing of individual ducts. Another advantage of spiral CT is the ability to evaluate vascular invasion. Spiral CT can demonstrate vascular invasion more effectively by better contrast enhancement of vessels and show the compensatory hyperperfusion reflecting the significant obstruction of the portal vein. Han et al. [10] reported that small soft tissue mass was identified with thin-section spiral CT at the confluence in all 27 patients with hilar cholangiocarcinoma. Also, Feydy et al. [11] reported that helical CT aids in tumor localization and in the assessment of parenchymal, biliary intrahepatic, and portal involvement in hilar cholangiocarcinoma.

Although there is some disagreement concerning the criteria of resectability among surgeons, the unresectable hilar cholangiocarcinoma is suggested by the following findings: (a) cholangiographic evidence of severe bilateral involvement of secondary confluence (Bismuth type IV), (b) involvement of the main trunk of the portal vein or hepatic artery, (c) involvement of both branches of the portal vein or bilateral involvement of the hepatic artery and portal vein, and (d) a combination of vascular involvement on one side of the liver with extensive cholan-

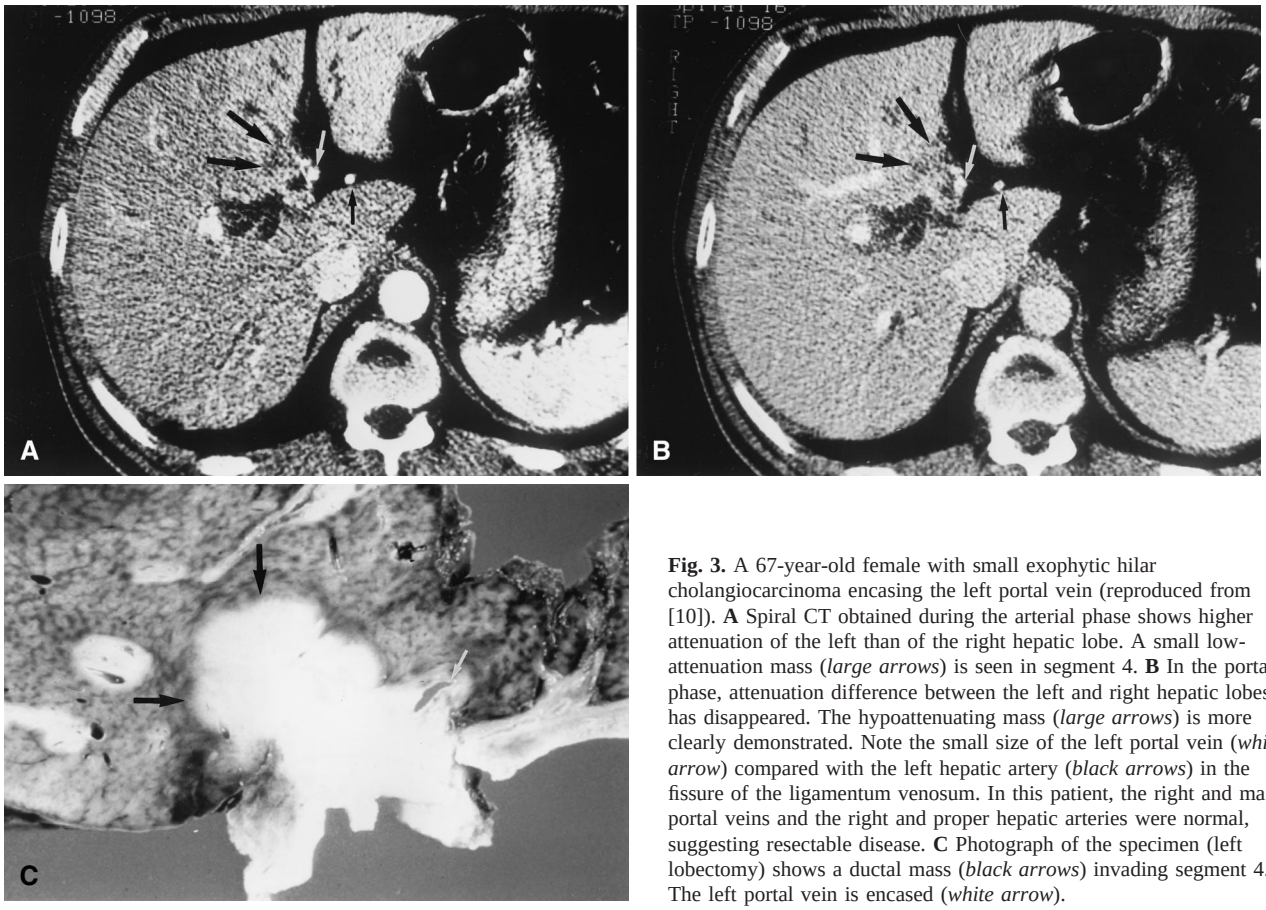

Fig. 3. A 67-year-old female with small exophytic hilar cholangiocarcinoma encasing the left portal vein (reproduced from [10]). **A** Spiral CT obtained during the arterial phase shows higher attenuation of the left than of the right hepatic lobe. A small low-attenuation mass (*large arrows*) is seen in segment 4. **B** In the portal phase, attenuation difference between the left and right hepatic lobes has disappeared. The hypoattenuating mass (*large arrows*) is more clearly demonstrated. Note the small size of the left portal vein (*white arrow*) compared with the left hepatic artery (*black arrows*) in the fissure of the ligamentum venosum. In this patient, the right and main portal veins and the right and proper hepatic arteries were normal, suggesting resectable disease. **C** Photograph of the specimen (left lobectomy) shows a ductal mass (*black arrows*) invading segment 4. The left portal vein is encased (*white arrow*).

giographic involvement on the other side. Unilateral involvement of the artery, the vein, or both is not a sign of unresectability [6, 8]. Because even thin-section spiral CT has been reported to have limitations in accurately depicting the intraductal extent of the tumor [10], we planned to use vascular invasion as the criterion for the unresectable disease.

In our study, spiral CT had a positive predictive value of 100% in the detection of unresectable disease by using vascular invasion as the criterion for unresectability. However, in the detection of resectable disease, the negative predictive value was only 50%. In six patients with resectable disease, all the vessels except one left portal vein were free from tumor invasion at CT, and surgery confirmed the CT findings. In six patients with unresectable disease, whose preoperative CT diagnoses were incorrect, the documented causes of unresectable disease were not vascular invasion. Our data suggest that, although CT is accurate in detecting vascular invasion, in particular portal veins, spiral CT is limited in detecting small hepatic or lymph node metastasis. Tumor spread to normal-sized lymph nodes and hepatic metastases smaller than 1 cm size are well-recognized problems with current imaging techniques [3, 15, 18]. Also, the extent of ductal invasion could not be assessed with CT only. In some patients, bile duct cancer spreads superficially along the surface, far beyond the level of biliary obstruction. On CT, these areas show a thin line of mucosal enhancement along the surface, which is indistinguishable from cholangitis. Therefore, spiral CT tends to underestimate the intraductal extent of the tumor [10]. However, combined with direct cholangiogram and sometimes with choledochoscopy, more accurate assessment of intraductal extent of the tumor is possible. In two patients who had extensive intraductal spread, we could accurately predict the extent of tumor and the unresectable disease with the additional information provided by cholangiography (Fig. 5). With combined use of spiral CT and cholangiography, positive and negative predictive values are 100% and 60%, respectively, with an overall accuracy of 80.9%.

Our data suggest that spiral CT is highly effective in determining unresectability. However, it has limited value in confirming resectable disease (negative predictive value, 50%). It may be possible to use spiral CT as a screening tool. If spiral CT clearly shows unresectable disease, patients may be managed nonsurgically. If spiral CT and direct cholangiography suggest resectable disease, more definite surgical treatment can be tried.

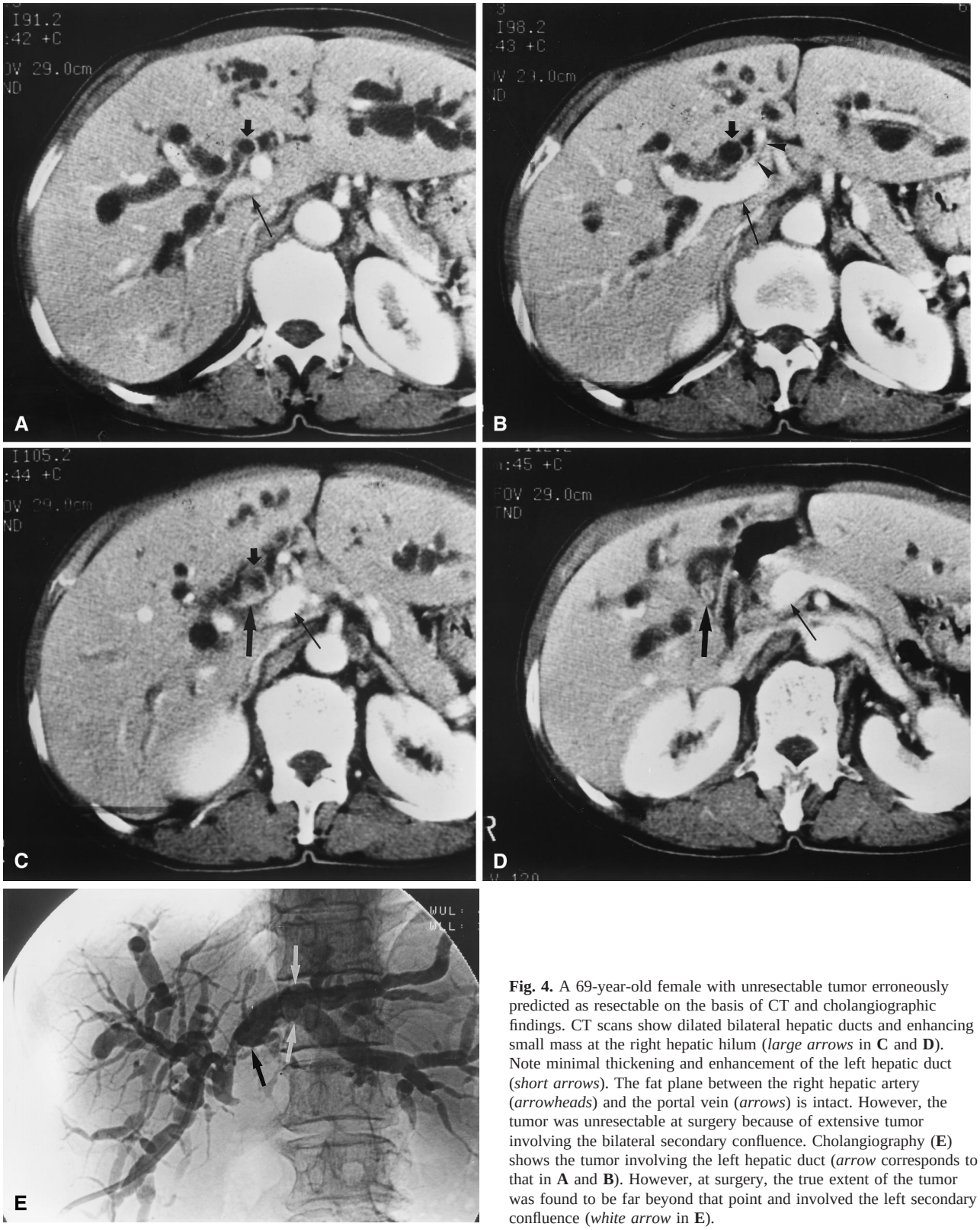

Fig. 4. A 69-year-old female with unresectable tumor erroneously predicted as resectable on the basis of CT and cholangiographic findings. CT scans show dilated bilateral hepatic ducts and enhancing small mass at the right hepatic hilum (*large arrows* in **C** and **D**). Note minimal thickening and enhancement of the left hepatic duct (*short arrows*). The fat plane between the right hepatic artery (*arrowheads*) and the portal vein (*arrows*) is intact. However, the tumor was unresectable at surgery because of extensive tumor involving the bilateral secondary confluence. Cholangiography (**E**) shows the tumor involving the left hepatic duct (*arrow* corresponds to that in **A** and **B**). However, at surgery, the true extent of the tumor was found to be far beyond that point and involved the left secondary confluence (*white arrow* in **E**).

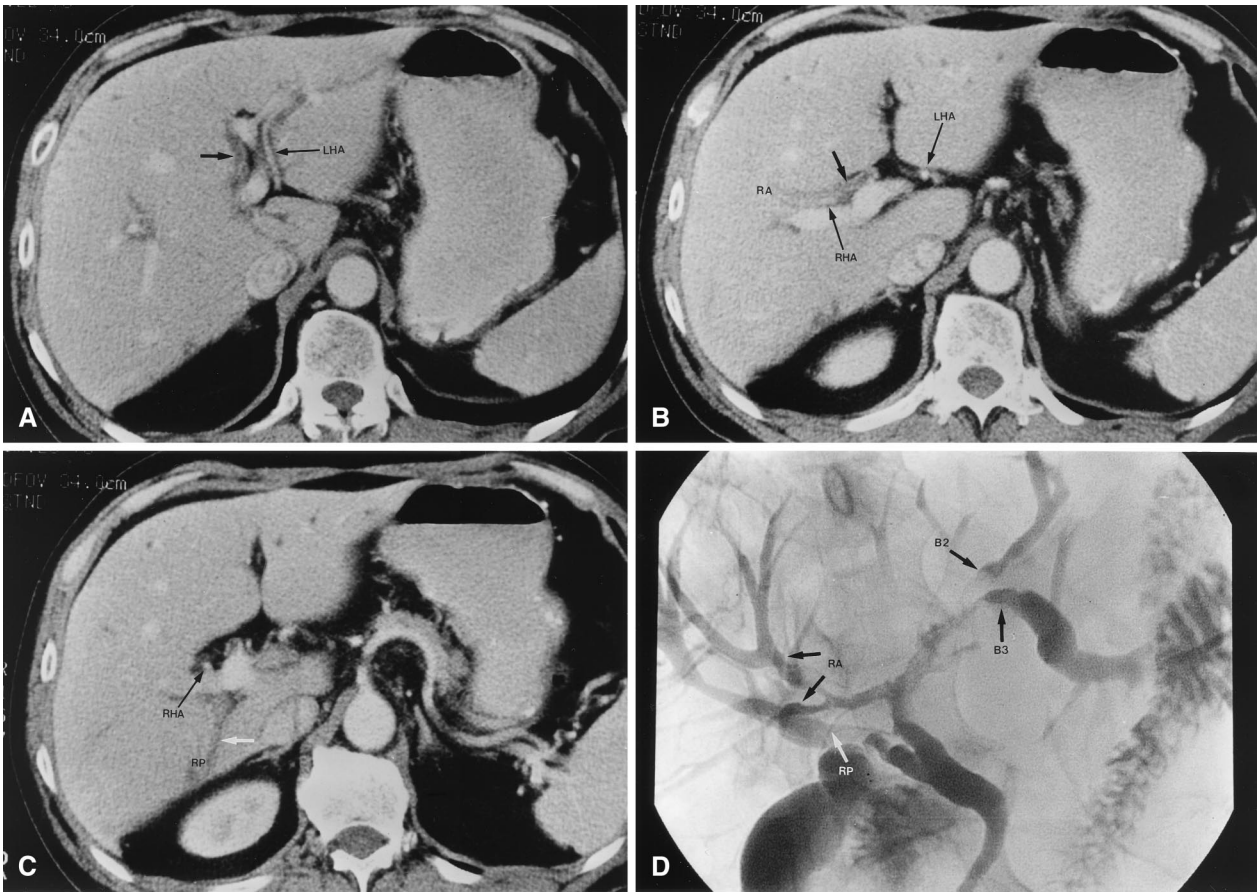

Fig. 5. A 63-year-old male with unresectable tumor because of normal variation of the bile duct and lobar atrophy. CT scans show an atrophic posterior segment of the right hepatic lobe and its bile duct (*white arrow* in **C**). In this patient, there was dilatation of the left intrahepatic duct (IHD) at CT. Only minimally thickened bile ducts are visible (*arrows* in **A** and **B**). The portal vein and the hepatic arterial branches are not invaded by the tumor. **D** At cholangiography, papillary tumors involving bifurcation to the left secondary confluence (*arrows*) are noted. Only the atrophic right posterior segmental duct (*white arrow*) is saved. Because of this anatomic variation, surgical resection could not be done.

There is one limitation in our study. When the surgeon sees the findings of unresectable disease, such as hepatic metastasis, peritoneal implants, or paraaortic lymph node metastasis during laparotomy, that surgeon does not try to confirm vascular invasion, which requires extensive, time-consuming hilar dissection. Of 15 patients with unresectable disease, 13 had such findings of unresectable disease other than vascular invasion. The causes of unresectability in therese 13 patients were hepatic metastasis or seeding ($n = 5$), lymph node metastasis ($n = 3$), extensive tumor ($n = 3$), and bile ductal variation ($n = 2$). In only two patients was vascular invasion the sole cause of unresectability. Therefore, although CT showed high positive predictive value, the true status of vascular invasion may not be known in many patients. However, definite vascular invasion at spiral CT may suggest locally extensive and biologically aggressive disease, with possible distant metastasis that preclude curative (or even palliative) resection.

In conclusion, thin-section spiral CT may be a valuable tool in preoperative staging of hilar cholangiocarcinoma in predicting resectability by assessing the vascular invasion.

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