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Value of Multidetector-row Computed Tomography in Diagnosis of Portal Vein Invasion by Perihilar Cholangiocarcinoma

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Abstract
Background Although knowledge of cancer invasion of the portal bifurcation is vitally important in planning an operation for perihilar cholangiocarcinoma, the diagnostic capability of multidetector-row computed tomography (MDCT) for this purpose has not been assessed. We evaluated how well MDCT could identify cancer invasion of the portal bifurcation by perihilar cholangiocarcinoma.
Methods Between April 2003 and June 2005, perihilar cholangiocarcinoma was resected in 87 patients, 83 of whom underwent MDCT within 1 month before the surgery. Three-dimensional volume-rendered (3DVR) and multiplanar reformation (MPR) images were examined for evidence of portal vein invasion. Agreement with intraoperative and pathologic findings was assessed. Portal bifurcation findings by 3DVR and MPR were classified into no portal vein stenosis, unilateral stenosis, or more extensive stenosis, and also into tumor contact with the bifurcation in no, one of two, or two projections.
Results For macroscopic portal vein invasion, sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy were 81.5, 91.1, 81.5, 91.1, and 88.0% in 3D portography and 96.3, 92.6, 86.7, 98.1, and 94.0% in MPR, respectively. Findings by both 3DVR and MPR were significantly correlated with depth of cancer invasion ($p < 0.001$).
Conclusion MDCT is useful in assessing cancer invasion of the portal vein bifurcation by perihilar cholangiocarcinoma.

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Introduction

Only surgical resection can offer a chance of cure to patients with perihilar cholangiocarcinoma. Several authors have advocated aggressive surgical strategies such as combined portal vein and major hepatic resection, even for locally advanced cancers invading the portal bifurcation, considering a good postoperative outcome [1–14] (Fig. 1). As portal vein resection and reconstruction have proven to be required in more than 30% of patients undergoing resections [13], imaging evidence of cancer invasion of the portal bifurcation is one of the most important preoperative factors in planning resection.

Catheter angiography had been used to assess vascular involvement [15]. We have reported that percutaneous transhepatic portographic findings reliably predict the degree of microscopic cancer invasion of the portal bifurcation in patients with perihilar cholangiocarcinoma [16]. Recently, however, multidetector-row computed tomography (MDCT) has been applied to preoperative diagnosis of perihilar cholangiocarcinoma as a noninvasive modality for providing high-quality images to evaluate portal vein invasion. However, no report has clarified the value of MDCT for preoperative staging of perihilar cholangiocarcinoma.

In this study we assessed the value of MDCT in preoperatively evaluating invasion of the portal bifurcation by perihilar cholangiocarcinoma.

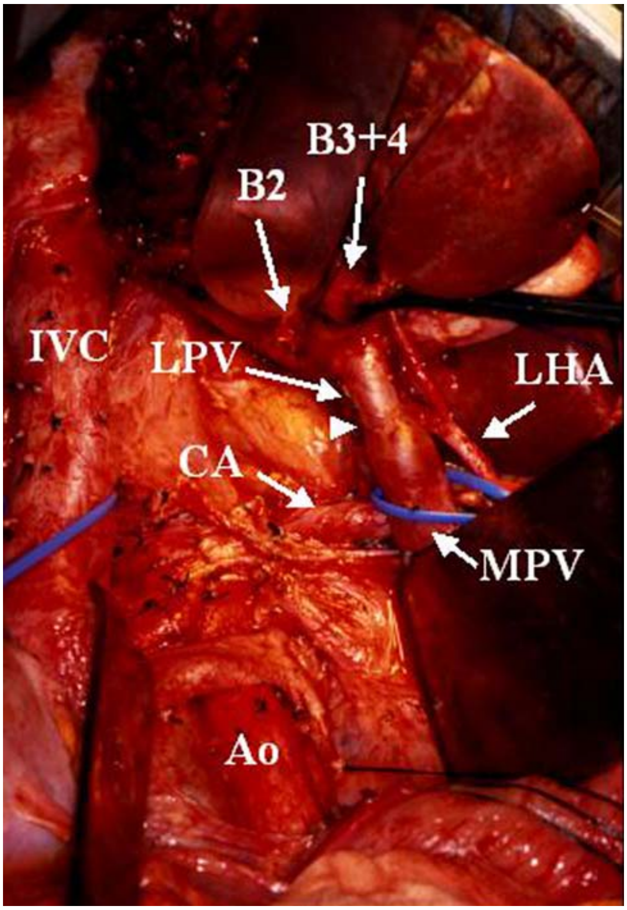

Fig. 1 Intraoperative photograph after right hemihepatectomy, caudate lobectomy, extrahepatic bile duct resection, segmental portal vein resection and end-to-end anastomosis, and extended lymphadenectomy for hilar cholangiocarcinoma. Left hepatic duct is divided proximal to the confluence of the left lateral posterior segmental hepatic duct (B2) and the trunk of the left medial segmental and the left lateral anterior segmental hepatic ducts (B3 + 4). This patient was a 65-year-old female and survived more than 9 years after the surgery. Ao, aorta; IVC, inferior vena cava; CA, celiac axis; LHA, left hepatic artery; LPV, left portal vein; MPV, main portal vein. Arrowhead indicates an anastomosis between the left and main portal vein

Patients and methods

Patients

Between April 2003 and June 2005, resection was carried out in 87 perihilar cholangiocarcinoma patients, of whom 83 underwent preoperative MDCT within 1 month before surgery and were enrolled in this study. These tumors included 48 extrahepatic cholangiocarcinomas originating from the hepatic confluence and 35 intrahepatic cholangiocarcinomas invading the hepatic confluence. The 83 patients included 57 men and 26 women with a mean age of 63 years (range = 30–80 years). The mean interval between MDCT and surgery was 20 days (range = 5–30 days). Operations performed on the 83 patients are listed in Table 1. Most patients underwent resection of three or more hepatic segments plus caudate lobectomy and extrahepatic bile duct resection [17, 18]. Percutaneous transhepatic portography (PTP) [16] was performed to embolize the portal branches in 40 of the 83 patients [19–22]. Concomitant portal vein resection and reconstruction were carried out in 27 patients (33%). Informed consent to use their data for academic studies was obtained from all patients before surgery.

Table 1 Operative procedure performed in 83 patients

Procedure	No. of patients
Left hepatectomy with/without caudate lobectomy	32 (9)
Left trisectionectomy with caudate lobectomy	17 (8)
Right hepatectomy with caudate lobectomy	29 (9)
Right trisectionectomy with caudate lobectomy	1 (1)
Central bisectionectomy with caudate lobectomy	3
Caudate lobectomy	1

All patients underwent concomitant extrahepatic bile duct resection and extended lymph node dissection

Numbers in parentheses indicate patients who underwent portal vein resection and reconstruction

Imaging techniques

All CT studies were performed using a scanner with 16 rows of detectors (Acquisition 16, Toshiba Medical Systems, Tokyo, Japan). A series of scans without a contrast agent was obtained throughout the liver and biliary tree. Then 100–150 ml of nonionic contrast material with an iodine content of 300 mg/ml was administered via the antecuboidal vein at a rate of 0.07–0.08 ml/kg/s for 30 s with a power injector before the second, third, and fourth helical scans (early arterial, late arterial, and portal phases) were obtained (24, 45, and 68 s after contrast injection). Scanning parameters for the portal phase were 16 × 1.0-mm collimation, 1.0-mm slice thickness, 0.8-mm reconstruction interval, table advancement at 30 mm/s, rotation time of 0.5 s, pitch ratio of 15:1, 120 kV, and 400 mA. All examinations were performed within approximately 10 min, without any complications.

For image analysis using Virtual Place Advance software (AZE, Tokyo, Japan), data sets were transferred to a workstation. Three-dimensional volume-rendered images (3DVR) and maximum-intensity projection images (MIP) of the portal vein were generated from portal phase data and viewed from several angles. For 3D reformating, bone, large untargeted vessels (aorta and inferior vena cava), and background tissues were eliminated interactively from images to avoid superimposition. Multiplanar reformation (MPR) images 1 mm in thickness were reconstructed from portal phase data to depict the entire liver and biliary tree.

Axial and coronal views were produced as usual. The right anterior oblique view also was obtained when necessary to examine the right and left portal veins and the bifurcation in the same image. Localization of the tumor and its relationship to the portal bifurcation were evaluated. All 3D images (3DVR and MPR) were reviewed in cine mode at the workstation.

Image analysis

MDCT and PTP images in 83 patients were reviewed in consensus by two surgeons (TS and YS) who were blinded to the other radiologic data; these authors were occupied mainly in reconstructing 3D images. Although we reconstructed both 3DVR and MIP images, findings in 3DVR images resembled those in MIP images. We therefore focused on the findings of 3DVR and MPR. Findings in 3DVR and PTP images were classified into three groups according to a classification scheme previously introduced for PTP [16] in which type A indicated no abnormal findings (Fig. 2A), type B showed stenosis or obstruction at the origin of either the right or the left portal vein (Fig. 2B), and type C exhibited additional narrowing at the opposite side of the involved vein (Fig. 2C). Types B and C were considered positive for cancer invasion of the portal bifurcation. MPR findings were evaluated in terms of presence or absence of a visible fat layer between the portal bifurcation and the adjacent tumor. Presence of a fat plane in images was deemed to indicate absence of tumor invasion (Fig. 3), while absence of a fat plane meant presence of tumor

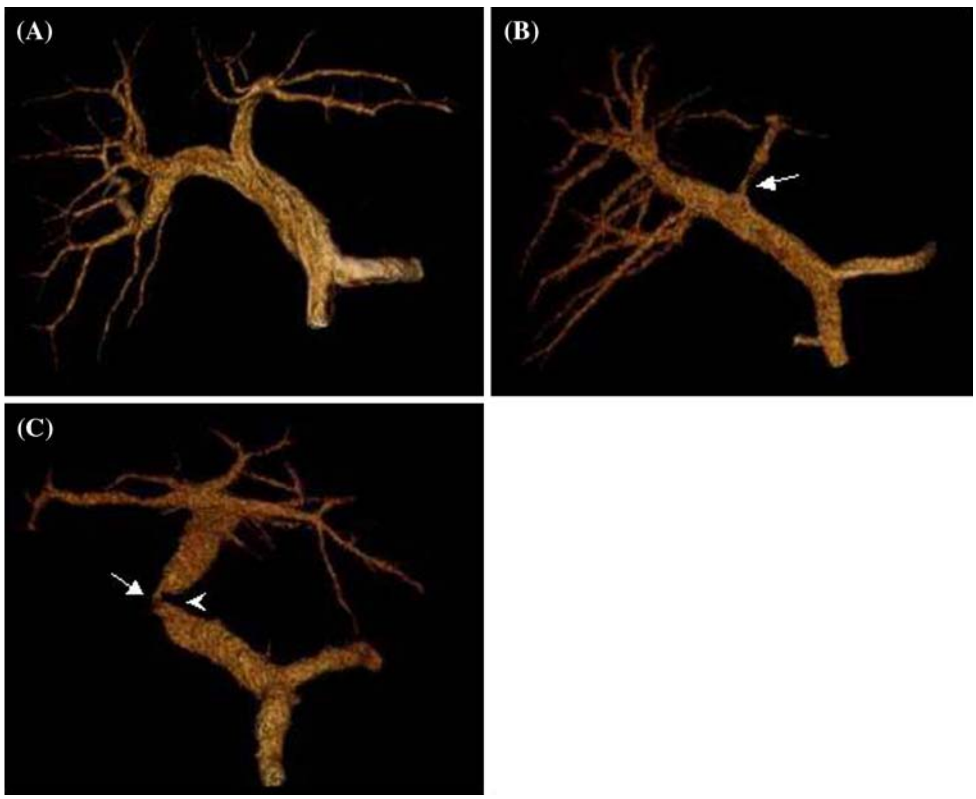

Fig. 2 Classification of portal vein bifurcation finding in 3DVR images. (**A**) Type A, no abnormal findings. (**B**) Type B, stenosis is observed at the origin of the left portal vein (arrow). (**C**) Type C, the right portal vein is obstructed at the bifurcation (arrow) and narrowing of the portal vein also is present on the side contralateral to the origin (arrowhead)

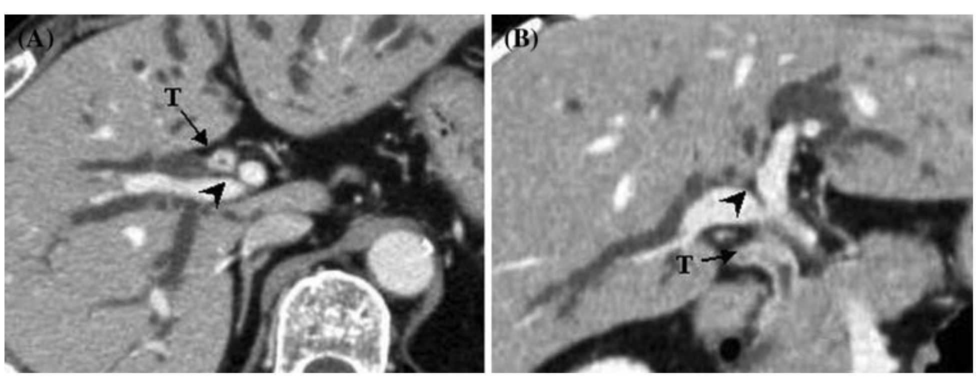

Fig. 3 MPR findings representing type 0. The fat layer between the portal bifurcation and the adjacent tumor (T) is intact in both axial and right anterior oblique views (arrowheads). (**A**) Axial view. (**B**) Right anterior oblique view

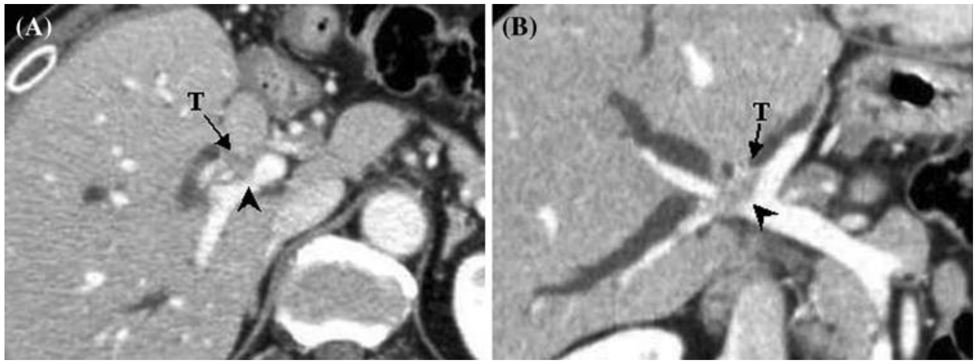

Fig. 4 MPR findings representing type II. The fat layer between the portal bifurcation and the adjacent tumor (T) is absent in both axial and oblique views (arrowheads). (**A**) Axial view. (**B**) Right anterior oblique view

invasion (Fig. 4). Fat planes were assessed in two projections, including axial and coronal or right anterior oblique projections, to examine anteroposterior and craniocaudal relationships, respectively. Finally, the relationship between the portal bifurcation and adjacent tumor was classified as type 0, with a visible fat layer in both projections; type I, with tumor contacting the bifurcation in one of two projections; or type II, with tumor contacting the bifurcation in both projections. Types I and II were considered to show cancer invasion of the portal bifurcation.

Degree of cancer invasion of the portal vein

When the portal bifurcation was macroscopically involved by tumor at the time of operation, portal vein resection and reconstruction were performed irrespective of preoperative diagnosis by MDCT. Surgical specimens were fixed in 10% formalin for several days and then cut serially at 5-mm intervals. Resulting tissue blocks were prepared by routine methods for microscopic examination using staining with hematoxylin and eosin. Degree of cancer invasion of the portal vein was classified into three grades according to depth of the invasion [16]: grade 0, no involvement; grade 1, invasion limited to the tunica adventitia or media; or grade 2, invasion reaching the tunica intima. Grade 1 and grade 2 were considered as microscopic cancer invasion. In patients without portal vein invasion (grade 0), the distance between the leading edge of the cancer and the outer layer of the tunica adventitia was measured. All patients not requiring portal vein resection were classified as grade 0.

Data analysis

Relationships between MDCT findings and the presence or absence of macroscopic and microscopic portal vein invasion by cancer were analyzed. The relationship between the MDCT findings and degree of cancer invasion of the portal vein also was assessed. Statistical analysis was performed using Spearman's rank correlation test, Kruskal-Wallis test, or McNemar test as appropriate. A p value of less than 0.05 was considered significant.

Results

3DVR and MPR findings

Findings by 3DVR in 83 patients were classified as type A ($n = 56$), type B ($n = 19$), or type C ($n = 8$) (Table 2). Type of 3DVR findings was significantly associated with both macroscopic ($p < 0.001$) and microscopic portal vein invasion ($p < 0.001$). In the six patients with macroscopically suspected but not microscopically confirmed portal vein invasion, the distance between the leading edge of the cancer and the adventitia ranged from 0.3 to 1.1 mm (median = 0.55).

Correlation between type of 3DVR findings and degree of cancer invasion of the portal bifurcation also was significant ($r = 0.8128$, $p < 0.001$). The more extensive the 3DVR findings appeared, the deeper the tumor invaded to the portal bifurcation.

Table 2 Correlation between type of 3DVR findings and portal vein invasion

Type of 3DVR findings	No. of patients	No. of patients				
		Macroscopic PV invasion*	Microscopic PV invasion**	Degree of cancer invasion***		
				grade 0	grade 1	grade 2
A	56	5	1	55	1	0
B	19	14	12	7	7	5
C	8	8	8	0	2	6

3DVR = three-dimensional volume rendering; PV = portal vein

* $p < 0.001$; ** $p < 0.001$, *** $r = 0.8128$, $p < 0.001$

Table 3 Correlation between type of MPR findings and portal vein invasion

Type of MPR findings	No. of patients	No. of patients				
		Macroscopic PV invasion*	Microscopic PV invasion**	Degree of cancer invasion***		
				grade 0	grade 1	grade 2
0	53	1	1	52	1	0
I	13	10	4	9	2	2
II	17	16	16	1	7	9

MPR = multiplanar reformation; PV = portal vein

* $p < 0.001$; ** $p < 0.001$; *** $r = 0.7942$, $p < 0.001$

Fine MPR images could show intrahepatic cholangiocarcinoma as a massive tumor and extrahepatic cholangiocarcinoma as a thickened bile duct wall. The presence or absence of fat tissue between portal vein and the tumor was easily evaluated.

The MPR findings in the 83 patients were classified as type 0 ($n = 53$), type I ($n = 13$), or type II ($n = 17$) (Table 3). Type of MPR findings was significantly associated with macroscopic ($p < 0.001$) and microscopic portal vein invasion ($p < 0.001$) and degree of cancer invasion ($r = 0.7942$, $p < 0.001$).

Diagnostic ability of 3DVR and MPR

For macroscopic invasion of portal bifurcation, sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy were 81.5, 91.1, 81.5, 91.1, and 88.0% in 3D portography and 96.3, 92.6, 86.7, 98.1, and 94.0% in MPR, respectively. The difference of overall accuracy between 3DVR and MPR was not significant ($p = 0.125$). For microscopic invasion of portal bifurcation, sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy were 95.2, 88.7, 74.1, 98.2, and 90.3% in 3D portography and 95.2, 83.9, 66.7, 98.1, and 86.7% in MPR, respectively. The difference of overall accuracy between 3DVR and MPR was not significant ($p = 0.453$).

Discordance between 3DVR findings and MPR findings

Of 56 patients with a type A 3DVR portogram, 5 had a type I MPR image (Table 4). Of these 5 patients, 4 underwent portal vein resection because of macroscopically suspected portal vein invasion, but none proved to have microscopic cancer invasion of the portal bifurcation. Of 19 patients with a type B 3DVR portogram, 2 had a type 0 MPR image. Both patients underwent portal vein resection because of macroscopically suspected portal vein invasion, but none proved to have microscopic cancer invasion of the portal bifurcation.

Table 4 Correlation between types of 3DVR and MPR findings

Type of 3DVR findings	Type of MPR findings		
	0	I	II
A	51	5	0
B	2	8	9
C	0	0	8

3DVR = three-dimensional volume rendering; MPR = multiplanar reformation

$r = 0.8618$, $p < 0.001$

Comparison between PTP and MDCT

PTP findings in the 40 patients were classified as type A ($n = 29$), type B ($n = 10$), or type C ($n = 1$). PTP findings were identical to 3DVR findings in 39 of the 40 patients. In the remaining patient PTP findings were classified as type A, while 3DVR findings represented type B. Although portal vein resection was performed in this patient, cancer did not microscopically invade the portal bifurcation.

On the other hand, PTP findings were the same as MPR findings in 36 of the 40 patients. In the remaining 4 patients, PTP showed type A findings, whereas MPR images revealed type I findings. Three of the 4 patients underwent portal vein resection and none had microscopic cancer invasion of the portal bifurcation.

Discussion

Hepatic angiography had been considered the best method for determining vascular invasion and vascular anatomy. However, transarterial portography [15] or PTP [16], commonly used for this purpose, are invasive. Although endovascular ultrasonography has been reported to be useful in diagnosing portal vein invasion by pancreatobiliary cancer [23], the special equipment needed, knowledge of novel techniques, and additional operative time have limited its use. In contrast, MDCT is far less invasive than transarterial portography, PTP, and endovascular ultrasonography, while both 3DVR and MPR provide much better images than conventional CT [24, 25]. Nowadays, MDCT has surpassed those invasive modalities and PTP is performed in our hospital only for portal vein embolization.

However, no report has clarified the value of MDCT for perihilar cholangiocarcinoma.

In this study we investigated two different types of three-dimensional MDCT images, 3DVR and MPR. The 3DVR images were useful in determining the three-dimensional configuration of the portal vein [26] but could provide only an intraluminal profile opacified by the contrast medium. This was also true for arterial portography and PTP. Actually, the PTP findings were the same as those of 3DVR except for one patient. In contrast, MPR images showed the relationship between the tumor and the portal bifurcation. Despite a lack of significant difference, MPR images were more accurate than 3DVR images in predicting macroscopic cancer invasion of the portal bifurcation, which, as opposed to microscopic cancer invasion, provides the final piece of information needed for completing the surgical procedure. Although six patients who proved not to have microscopic cancer invasion of the portal bifurcation underwent portal vein resection because of macroscopically suspected cancer invasion, the distance between the tumor and the portal vein wall was minute. The surgical dissection margin would be considered positive for cancer if portal vein resection had not been performed in these patients [13, 16]. Furthermore, macroscopic cancer invasion has been shown to be important in predicting outcome; it is a demonstrated negative prognostic factor in hilar cholangiocarcinoma [13]. Taking all the results of this study into consideration, presence or absence of cancer invasion of the portal bifurcation first should be assessed using MPR images. Next, the 3DVR images should be used to evaluate the configuration of the portal system and the extent of tumor invasion for planning the portal vein resection and reconstruction (e.g., wedge vs. segmental resection and direct end-to-end anastomosis vs. autogenous vein grafting) when MPR images detect portal vein invasion. Both MPR and 3DVR images are needed to delineate portal vein invasion by perihilar cholangiocarcinoma.

Apart from the invasive examinations, magnetic resonance imaging (MRI) potentially has the ability comparable to that of MDCT for assessing portal vein invasion by perihilar cholangiocarcinoma, because MRI can offer noninvasive 2D and 3D imaging. However, we could not include such imaging modalities in the current study because MRI was not the routine preoperative evaluation method for perihilar cholangiocarcinoma used in our hospital. Although several authors have emphasized the usefulness of magnetic resonance angiography, only Lee et al. [27] have evaluated this modality in diagnosing portal vein invasion by hilar cholangiocarcinoma, reporting sensitivity, specificity, and accuracy of 78% (14 of 18), 91% (82 of 90), and 89% (96 of 108), respectively. This performance is very similar to what we obtained with 3DVR. In contrast, however, our results with MPR images represented a higher diagnostic capability than magnetic resonance angiography despite the lack of statistical significance for these differences. We stress that magnetic resonance angiography or 3DVR alone is insufficient to evaluate portal vein invasion. MPR images for assessing the relationship between the tumor and the portal vein are required to reliably diagnose portal vein invasion by perihilar cholangiocarcinoma.

In hilar and suprapancreatic cholangiocarcinoma, Uchida et al. [28] recently reported the value of multiphase fusion images of the hepatic artery, portal vein, hepatic vein, and bile duct obtained by 3D angiography using MDCT. The color images were very helpful in identifying vascular structures and their relationship in the hepatoduodenal ligament. However, the tumor itself was not shown in these color images. The quality of the images depends on the capabilities of the CT equipment and 3D rendering techniques. Even though future advances will provide better images, MPR images at present are the best modality for assessing the relationship between perihilar cancer and portal bifurcation.

Aggressive surgery offers a better outcome than conservative therapy [29]. Although portal vein invasion is a negative independent predictor of survival for locally advanced perihilar cholangiocarcinoma, portal vein resection and reconstruction increase the resectability rate and can offer a better chance of long-term survival [1–14]. Therefore, we have been performing surgery even for patients with locally advanced perihilar cholangiocarcinoma invading the portal bifurcation. Recently, Neuhaus et al. [8, 10] emphasized the clinical significance of right trisectionectomy with concomitant portal vein resection to complete the no-touch technique. In contrast, our strategy is a local resection with minimal lymphadenectomy to achieve a curative resection, which means that the portal vein should be resected only in cases with macroscopic cancer invasion of portal bifurcation [13]. This approach may risk the dissemination of cancer. In this study MPR images showed a high affinity with macroscopic portal vein invasion. Therefore, the portal vein can be resected without the dissection maneuver around the portal bifurcation when MPR images reveal cancer invasion of the portal bifurcation. Conversely, if MPR images show no cancer invasion, portal bifurcation can be skeletonized.

In conclusion, MDCT may be a valuable tool for assessing cancer invasion of the portal bifurcation in patients with perihilar cholangiocarcinoma. Presence or absence of cancer invasion of the portal bifurcation should be estimated using MPR images. Portal vein resection and reconstruction should be planned using 3DVR images. Both MPR and 3DVR images are mandatory for evaluating cancer invasion of the portal bifurcation by perihilar cholangiocarcinoma.

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