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Assessment of hilar and extrahepatic bile duct cancer using multidetector CT: value of adding multiplanar reformations to standard axial images

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Abstract To retrospectively assess the value of multiplanar reformations (MPRs) compared with standard axial images in the assessment of hilar and extrahepatic bile duct cancer. Forty-eight patients with confirmed bile duct cancer were included as preoperative work-ups; all of these patients underwent contrast-enhanced multidetector CT consisting of axial and MPR images. Two radiologists independently assessed the axial images alone and the combined axial and MPR images in the coronal and sagittal planes for the presence of tumor, its extent, vascular involvement, and resectability. The results were compared with surgical and pathologic findings. For tumor presence and conspicuity, combined axial and MPR images had higher values than the axial only images. For evaluation of tumoral extent, there was no difference between the two image sets for either reader. The accuracy for tumor extent was lower in hilar cancer than in extrahepatic bile duct cancer. For evaluation of vascular involvement and resectability, the area under the receiver operating characteristic curve of axial images was not significantly different from that of the reformatted images.The addition of MPR images to the standard axial images did not significantly improve the diagnostic performance of MDCT in the evaluation of the bile duct cancer.

Keywords Bile duct cancer · Hilar cholangiocarcinoma · Multiplanar reformat · Multidetector CT

Introduction

Tumors originating from a large bile duct are in a critical location and are discovered early due to the presence of jaundice or cholangitis. Surgical resection is the only curative treatment for cholangiocarcinoma [1]. Accordingly, preoperative assessment of the resectability of bile duct cancer has increased in importance in recent years because more aggressive surgeries are currently accepted by many surgeons as possible curative options [2–4]. Recently, multidetector-row CT has been introduced into clinical practice. It allows faster scanning, which decreased motion and respiratory artifacts as well as allowing thinner scanning [5]. Although axial CT is useful for evaluation of the biliary tree in patients with bile duct cancer, the cross-sectional orientation of the CT scans makes it difficult to reveal complex anatomic relationships [6–8]. The extent of bile duct and vascular involvement by tumor are closely related and are crucial for determinating resectability. MDCT collects volumetric data that lead to improved three-dimensional assessment of vascular structure and the biliary tree. Furthermore, recent studies have shown that coronal reformations from scans obtained along the length of the pancreatic duct and common bile duct, were a useful supplement to routine axial scans in the local staging of pancreatic carcinoma and in the diagnosis of suspected biliary tract disease [7, 9]. The purpose of this study is to evaluate the utility of multiplanar reformations (MPRs) compared with standard axial images in the assessment of hilar and extrahepatic bile duct cancer.

Materials and methods

Patients

The institutional review board approved this retrospective study and waived the requirement for informed consent. Between August 2003 and December 2005, we identified patients with a diagnosis of bile duct cholangiocarcinoma and who received surgical treatment at our institution from a database maintained by the hepatobiliary section of the department of surgery and from pathologic reports. Criteria for inclusion of patients were as follows: patients with hilar and extrahepatic bile duct cancer who had undergone surgical resection at our institution; preoperative imaging with MDCT; and diagnosis of cholangiocarcinoma at pathologic examination of surgically resected tumor. Of the 140 patients (94 men and 46 women) initially found, 92 were excluded from the study due to: (1) peripheral cholangiocarcinoma (n=45); (2) incomplete pathologic examination, i.e. cases with incomplete lymph node or vascular assessment in pathology) (n=10); (3) patients who did not undergo preoperative contrast-enhanced biphasic MDCT (n=37).

The remaining 48 consecutive patients, 30 men and 18 women (age range 38–87 years; mean age 64 years), comprised our study population. Twenty patients had hilar bile duct cancer and 28 patients had extrahepatic bile duct cancer. Twenty-one patients underwent percutaneous transhepatic biliary drainage (PTBD) before undergoing CT scanning.

Imaging technique

All patients underwent contrast-enhanced biphasic CT consisting of precontrast, arterial-dominant, and portal-venous phases using a Somatom Sensation 16 scanner (Siemens, Erlangen, Germany; n=27) or a LightSpeed 8 channel scanner (GE Medical Systems, Milwaukee, Wis.; n=21). After the administration of 120 ml of nonionic contrast material (iopromide, Ultravist 70; Schering, Berlin, Germany) at a rate of 2.5–3.0 ml/s using a power injector, arterial and portal venous phase helical CT scans were obtained. The scanning parameters for multidetector CT scanners included a gantry rotation time of 0.5– 0.8 s with 1.25 mm×8-detector array or 0.75 mm×16-detector array, pitch of 1.0 –1.5, 150 mAs, 120 kVp, and a 512×512 matrix. The reconstruction parameters were 3-mm slice thickness, 3-mm reconstruction interval ,which were standard for axial images. For MPR image production, another axial image set was reconstructed using 1.25-mm or 1-mm slice thickness and a 0.7 mm reconstruction interval. For arterial phase scanning, a 15-s delay was used after the maximal HU of the aorta reached 100 HU using bolus tracking. After completion of arterial phase scanning, a 24-s delay was used for portal venous phase imaging. Using these scanning parameters, volumetric data could be acquired from the liver dome to the end of the pancreas.

MPRs

The reconstructions were performed on a commercially available separate console system with three-dimensional software (Wizard; Siemens Medical Systems, Iselin, N.J.; or Advantage Windowing; GE Medical Systems, Buc, France) devoted to rapid reconstruction. The entire process was performed by the technologist at the operator's console. The 3-mm-thick coronal, sagittal images were transferred to a PACS workstation (Marotech, Seoul, Korea) for interpretation as a separate series of images. The reason why we choose 3-mm-thick MPR images was that too thinner slices make images noisy [10, 11]. Dedicated CT technologists in our three-dimensional laboratory who have undergone physician-directed training in delineating vascular and bile and pancreatic ductal anatomy, produced the MPRs.

Image analysis

Images were reviewed retrospectively by two abdominal radiologists (J.Y.L., S.H.K.). The two radiologists had 7 and 10 years of experience in abdominal imaging, respectively. In the first session, they were presented with standard axial images alone and in the second session, with the combined axial and MPR images in coronal and sagittal planes. Between these sessions, we required a minimum of 4 weeks to minimize recall bias.

Axial only images and combined axial and MPR images were analyzed for the presence of tumor, tumor conspicuity and confidence level for assessing the tumor extent. The tumor conspicuity was rated using a four-point scale based on subjective assessment: 1=not visible; 2=barely visible; 3=adequately visible; 4=clearly visible. The confidence level of the tumor extent was rated using a five-point scale: 1=assessment definitely not possible; 2=assessment probably not possible; 3=assessment possibly possible; 4=assessment probably possible; 5=assessment definitely possible. Schematic templates of the biliary anatomy were provided to the readers so they could mark the location of the lesion in order to make an accurate correlation of the lesions detected by each reader.

Biliary ductal involvement was determined using the classification proposed by Bismuth and Corlette [12], in which type I involves distal to the confluence of the right and left hepatic ducts (primary confluence), type II involves the primary confluence but not the secondary confluences, type III involves the primary confluence and either the right (type IIIa) or left (type IIIb) secondary confluence, and type IV involves the secondary confluence of both the right and left hepatic ducts. Extrahepatic bile duct cancers were divided into intrapancreatic and extrapancreatic common bile duct (CBD) because intrapancreatic CBD involvement by tumor can lead to pancreaticoduodenectomy. If a lesion extended across more than one defined ductal segment, the most proximal part of the extrahepatic duct involved by the lesion was used to define the anatomic location [13].

Each reader also indicated the vascular involvement and resectability of the tumors. The suspected vessel involvement was recorded for the celiac artery, right and left hepatic artery, portal vein and superior mesenteric vein. Criteria for unresectable vascular involvement included vessel occlusion, stenosis or contour deformity associated with tumor contact or greater than 50% perimeter contact with tumor [14, 15]. The vascular involvement was rated using a five-point scale: 1= definitely not invaded; 2= probably not invaded; 3= possibly invaded; 4= probably invaded; 5= definitely invaded.

Due to the retrospective review nature of this study and a lack of pathologic analysis regarding tumoral extension to the intrahepatic vasculature of the lobar resection side of the liver, we could not obtain accurate information of the ipsilateral tumor extension or the vascular invasion following surgical resection. However, in the preoperative evaluation of bile duct cancer, the extent of the intrahepatic tumoral involvement determines the surgery type. Therefore, we asked each reader to record the suggested surgery type in patients with hilar bile duct cancer, i.e., right lobectomy with hilar bile duct excision, left lobectomy with hilar bile duct excision or bile duct excision only. The suggested surgery type was compared with the surgery type performed by our surgeons.

Criteria for unresectability were: contralateral hepatic artery invasion; segmental main or contralateral portal vein invasion longer than 2 cm; biliary extension to contralateral secondary confluence farther than 2 cm from hepatic hilum; enlarged lymph nodes on the right side of the celiac axis and portocaval area; peritoneal seeding; and liver parenchymal atrophy [16]. The confidence level for tumor resectability was rated (1=definitely unresectable, 2= probably unresectable, 3=possibly resectable, 4=probably resectable, and 5=definitely resectable) and evaluated in each case. The CT findings were compared with the surgical findings and with the final pathologic report.

Statistical analysis

The Wilcoxon signed rank test was used to compare the axial only group and the combined axial and MPR group to determine the confidence level of tumor presence and conspicuity. The level of significance was indicated by a P value less than 0.05. The McNemar test for each reader was performed to compare the sensitivities and specificities of the axial only and combined axial and MPR images with regard to vascular involvement and resectability.

Receiver operating characteristic (ROC) curve analysis was performed to compare the results of the readings of the axial only images versus the results of the readings of the combination axial and MPR images. Binormal ROC curves were fitted using the MedCalc program (version 6.15.000; MedCalc Software, Mariakerke, Belgium). The diagnostic capability was determined by calculating the area under the ROC curve (A_z) for each reader. Calculation of the statistical significance of the difference between the areas under the ROC curves for the two readers, was performed using the univariate z score test using the same software.

Interobserver agreement between the two readers for the vascular invasion, biliary involvement, and resectability of the axial alone group and the combined axial and MPR groups was quantified using κ statistics. A κ value less than 0.20 was considered to indicate poor agreement; a κ value of 0.20 – 0.39, fair agreement; a value of 0.40 – 0.59, moderate agreement; a κ value of 0.60 – 0.79, substantial agreement; and a value of 0.80 or greater, excellent agreement.

Results

Tumor detection and extent

The mean confidence level of the presence and conspicuity of the mass for readers 1 and 2 are given in Table 1. Analysis of the presence and conspicuity of the mass revealed that combined axial and MPR images had higher values than the axial only images from both readers.

To determine the tumor extent, hilar bile duct cancer (n= 20) was divided into five types according to the Bismuth-Corlette classification, type II in one case, type IIIa in seven

Table 1 Comparison of the axial alone group and the combined axial and MPR groups to determine the confidence level of the presence and conspicuity of a mass

	Reader 1		Reader 2	
	Axial alone	Combined axial and MPR	Axial alone	Combined axial and MPR
Presence of mass	4.43 ± 0.98	4.64±0.72	4.62±0.67	4.85±0.46
P value	0.007		0.035	
Conspicuity of mass	3.37±0.84	3.50±0.74	3.58±0.67	3.83±0.47
P value	0.054		0.001	

cases, type IIIb in three cases, and type IV in nine cases. Extrahepatic bile duct cancer was classified into involvement of the extrapancreatic and the intrapancreatic CBD: extrapancreatic CBD in 22 cases and intrapancreatic CBD in six cases.

The accuracy of the tumor extent according to location is given in Table 2. In hilar cancer, the accuracy of axial only images for the two readers was 60.0%, 45.0%, respectively, and the accuracy of the combined axial and MPR images for the two readers was 60.0%, 50.0%, respectively (Fig. 1). The accuracy of determining the tumor extent in extrahepatic bile duct cancer was very high, which was 92.8% for both readers in the axial only and the combined axial and MPR groups.

Vascular involvement and resectability

The McNemar test revealed no significantly different sensitivities or specificities between axial only and combined axial and MPR images in regard to vascular involvement and resectability ($P>0.05$).

The area under the curve of the axial only group and of the combined axial and MPR group for vascular involvement and resectability of tumor for the two readers, is given in Table 3. For vascular involvement, A_z values with 95% confidence intervals (CIs) of axial only and combined axial and MPR images, were 0.858 (95% CI: 0.727, 0.942) and 0.867 (95% CI: 0.738, 0.948), respectively, for reader 1 and 0.688 (95% CI: 0.538, 0.814) and 0.665 (95% CI: 0.514, 0.795), respectively, for reader 2 (Fig. 2). There was no significant difference between the A_z values of the axial only and the combined axial and MPR images for both readers ($P=0.910$ for reader 1 and $P=0.882$ for reader 2). For resectability, the A_z values with 95% CIs of the axial only and of the combined axial and MPR images, were 0.691 (95% CI: 0.541, 0.816) and 0.691 (95% CI: 0.541, 0.816), respectively, for reader 1 and 0.707 (95% CI: 0.558, 0.829) and 0.686 (95% CI: 0.536, 0.812), respectively, for reader 2 (Fig. 3). There was no significant difference between the A_z values of the axial only images and of the combined axial and MPR images for either reader ($P=1.000$ for reader 1 and $P=0.817$ for reader 2).

The accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the vascular involvement and resectability for readers 1 and 2, are given in Table 4.

The patients with hilar bile duct cancer underwent right lobectomy ($n=8$), left lobectomy ($n=4$) or palliative segmental resection ($n=8$). The accuracy for determinating the surgical procedure was 70.0% (14/20) and 70.0% (14/20), respectively, for reader 1 and 70.0% (14/20) and 90.0% (18/20), respectively, for reader 2.

Interobserver agreement

Interobserver agreement was increased in the combined axial and MPR images group compared with the axial only images group in the assessment of vascular involvement and tumor resectability; however, there was no statistical significance. For vascular involvement, values were 0.21 for the axial only images and 0.48 for the combined axial and MPR images. The values for biliary ductal involvement were 0.79 for the axial only images and 0.74 for the combined axial and MPR images, which was not statistically significant ($P=0.52$). The values for tumor resectability were 0.36 and 0.56 for the axial only images and the combined axial and MPR images, respectively. Interobserver agreement for vascular involvement and tumor resectability showed fair to moderate agreement, whereas interobserver agreement for biliary ductal involvement revealed substantial agreement.

Comparison between the PTBD insertion and the non-PTBD insertion group

The mean confidence level of the tumor extent for readers 1 and 2 are given in Table 5. Wilcoxon signed rank test revealed that there was no significant difference of the confidence level between the PTBD insertion group and the non-PTBD insertion group ($P>0.05$).

Discussion

Our results indicate that a scan obtained in the coronal and sagittal planes does not improve the diagnostic accuracy of the preoperative evaluation of bile duct cancer. The

Table 2 Accuracy of axial alone group and combined axial and MPR groups to determine tumor extent according to location. Data presented are the number of patients, followed *in parentheses* by the percentage

	Reader 1		Reader 2	
	Axial alone	Combined axial and MPR	Axial alone	Combined axial and MPR
Hilar cancer	12/20 (60.0)	12/20 (60.0)	9/20 (45.0)	10/20 (50.0)
Extrahepatic cancer	26/28 (92.8)	26/28 (92.8)	26/28 (92.8)	26/28 (92.8)

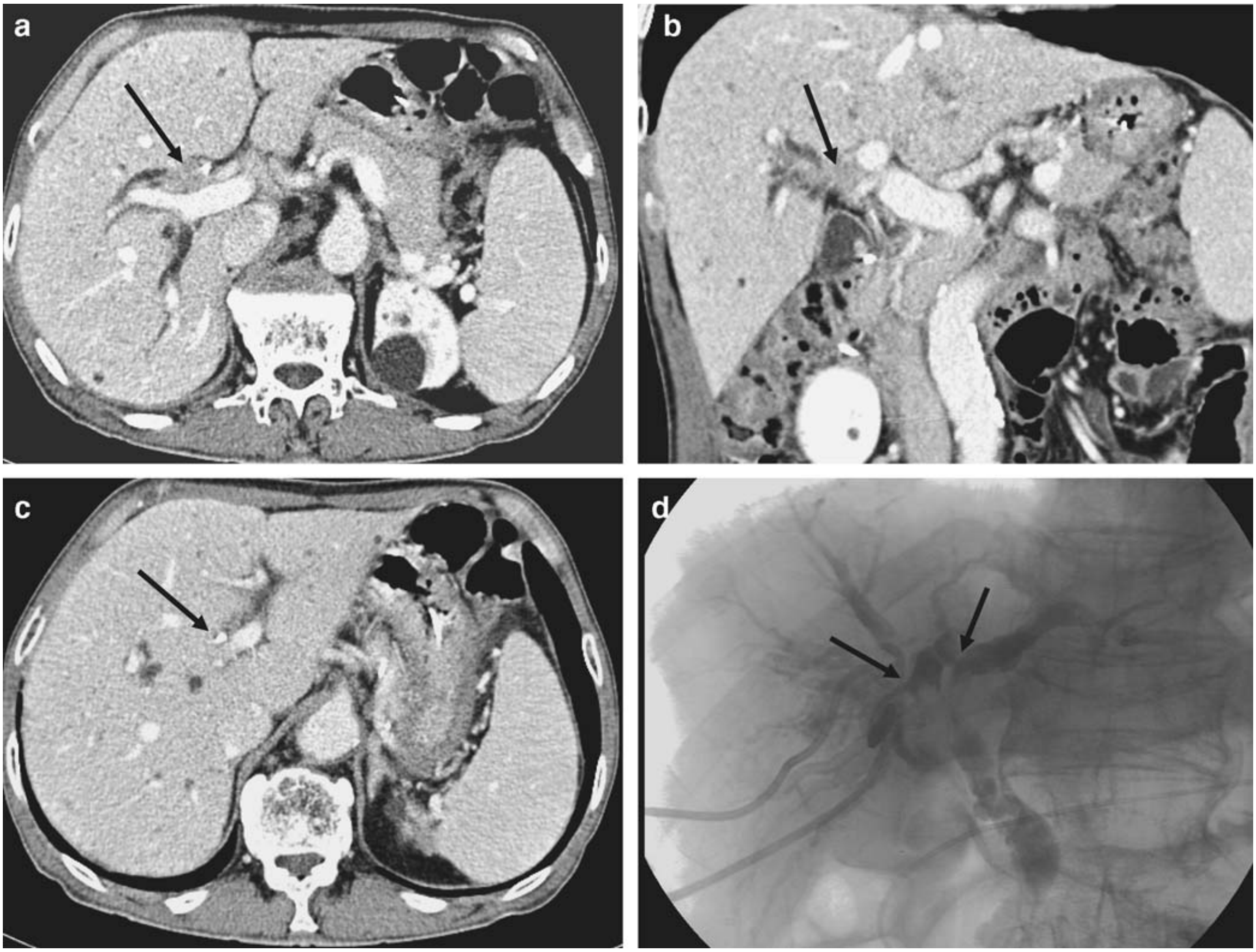

Fig. 1a–d A 65-year-old male with hilar cholangiocarcinoma (Bismuth type IV). **a**, **b** Axial and coronal images during the portal phase show an ill-defined soft tissue mass in the hilar area (*arrows*). The right anterior and posterior duct are separated by the tumor. **c** Axial image shows no tumor involvement around the percutaneous transhepatic biliary drainage (PTBD) catheter in the left hepatic duct (*arrow*). Both readers interpreted that it was Bismuth type IIIa hilar duct cancer. **d** Percutaneous cholangiogram depicts the tumor extension to the bilateral second confluence level (*arrows*)

sensitivity and specificity for the axial-only images and the combined axial and MPR images, were not significantly different for evaluating tumor extent, vascular involvement or resectability. However, the confidence level of the presence and conspicuity of the mass were raised when the MPR images were added to the standard axial only images.

There have been many reports that MPRs are helpful for the diagnosis of intraabdominal diseases in the pancreas,

Table 3 AUC (area under the curve) of the axial alone group and the combined axial and MPR groups to determine vascular involvement and tumor resectability. Data presented are A_z values,followed *in parentheses* by the 95% CI

	Reader 1		Reader 2	
	Axial alone	Combined axial and MPR	Axial alone	Combined axial and MPR
Vascular involvement	0.858 (0.727,0.942)	0.867 (0.738,0.948)	0.688 (0.538,0.814)	0.665 (0.514,0.795)
P value	0.910		0.882	
Resectability	0.691 (0.541,0.816)	0.691 (0.541,0.816)	0.707 (0.558,0.829)	0.686 (0.536,0.812)
P value	1.000		0.817	

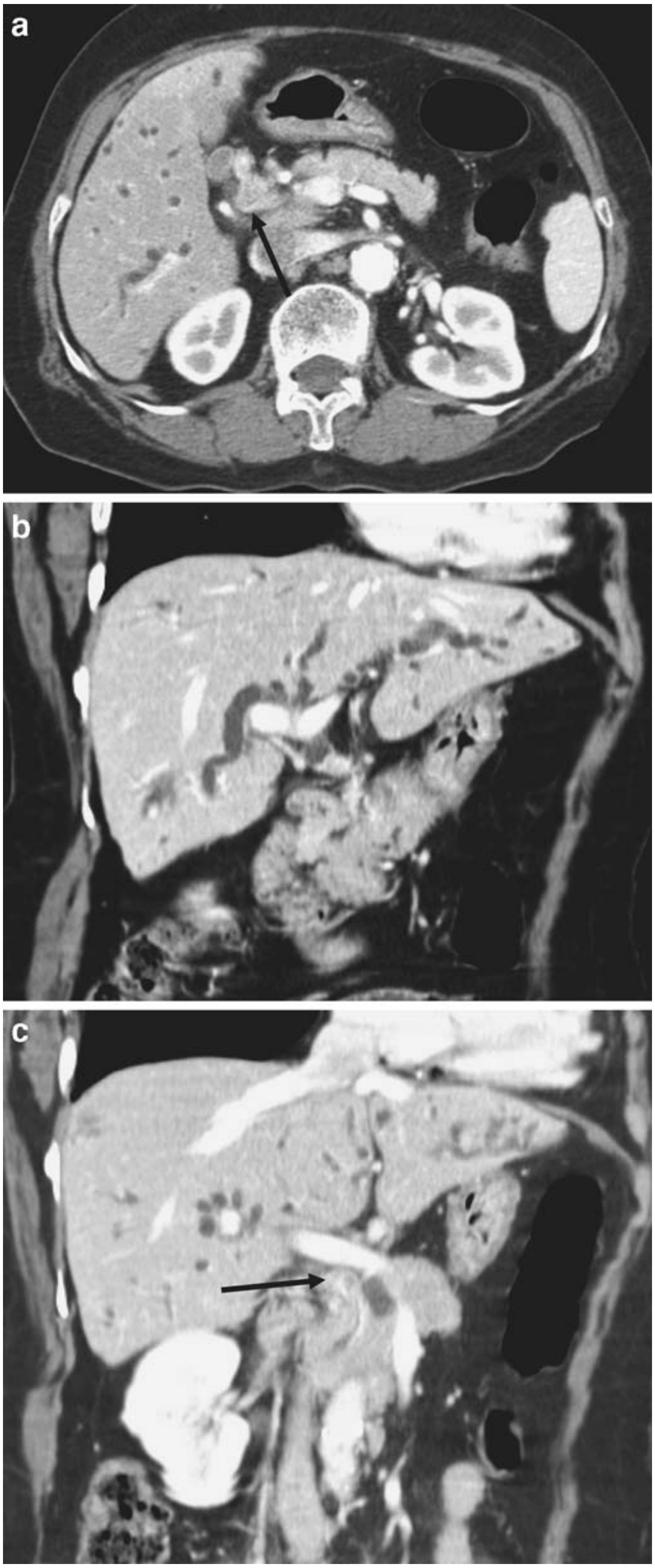

Fig. 2a–c A 72-year-old male with hilar CBD cancer. **a** Axial CT during the arterial phase shows a soft tissue tumor in the mid-CBD abutting the right hepatic artery (*arrow*). **b** Coronal reformation shows a soft tissue tumor in the mid-CBD and depicts its length along the CBD. Although the readers interpreted that the right hepatic artery was not invaded by the tumor, pathologic findings suggested vascular invasion by tumor. **c** Coronal reformatted image shows CBD cancer abutting the main portal vein (*arrow*). Two readers estimated that the portal vein was not invaded by the tumor. However, the surgical findings revealed that the hepatoduodenal ligament was infiltrated by the tumor and the portal vein invasion by the tumor was confirmed by the histopathologic examination

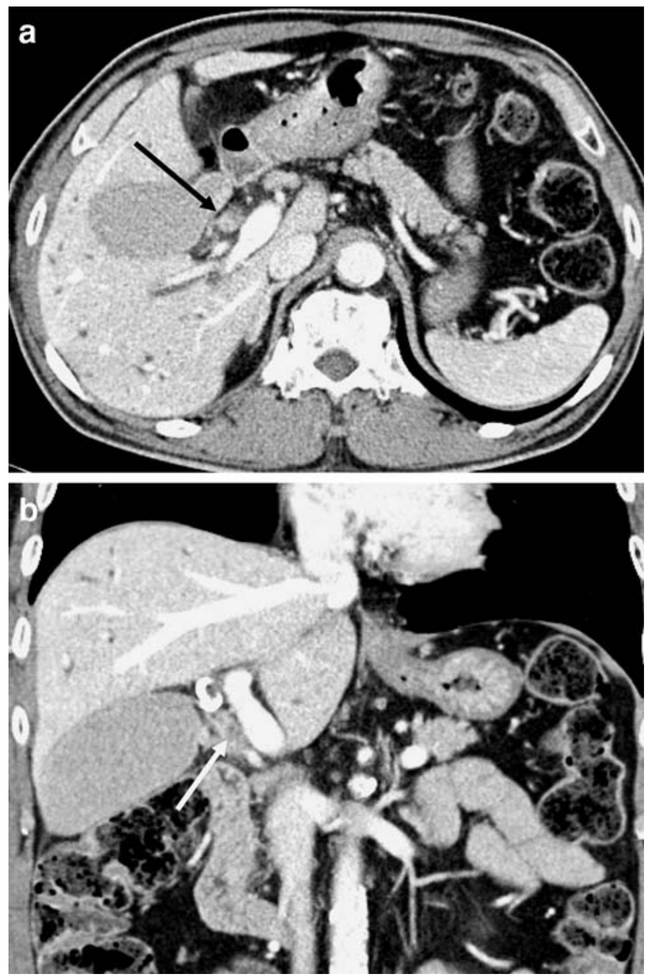

Fig. 3a,b A 68-year-old male with CBD cancer. **a** Axial CT during the portal venous phase shows a soft tissue tumor in the mid-CBD (*arrow*). Reader 2 interpreted that CBD cancer was resectable with a confidence level 3 (possibly resectable). **b** Coronal reformation reveals the entire length of the tumor extent (*white arrow*) and its relationship with the vascular structure. The confidence level of reader 2 was elevated to a confidence level 4 (probably resectable) with this reformatted image. The surgical findings revealed that the tumor was resectable

stomach, liver, and bowel [17–20]. However, there have been no reports that focused on the usefulness of MPR in the biliary tree of patients with bile duct cancer. According to our results, we cannot expect significantly improved diagnostic performance when adding MPR images to the standard axial images in complex structures like the hepatic

Table 4 Prediction of vascular involvement and resectability of the axial alone group and the combined axial and MPR groups. Data presented are the number of patients, followed *in parentheses* by percentages

	Reader 1		Reader 2	
Parameter	Axial alone	Combined axial and MPR	Axial alone	Combined axial and MPR
Vascular involvement				
Sensitivity (%)	4/5 (80.0)	4/5 (80.0)	3/5 (60.0)	3/5 (60.0)
Specificity (%)	41/43 (95.3)	41/43 (95.3)	37/43 (86.0)	38/43 (88.4)
Accuracy (%)	45/48 (93.7)	45/48 (93.7)	40/48 (83.3)	41/48 (85.4)
PPV (%)	4/6 (66.7)	4/6 (66.7)	3/9 (33.3)	3/8 (37.5)
NPV (%)	41/42 (97.6)	41/42 (97.6)	37/39 (94.8)	38/40 (95.0)
Resectability				
Sensitivity (%)	33/34 (97.1)	31/34 (91.2)	30/34 (88.2)	31/34 (91.2)
Specificity (%)	4/14 (28.6)	6/14 (42.8)	4/14 (28.6)	6/14 (42.8)
Accuracy (%)	37/48 (77.1)	37/48 (77.1)	34/48 (70.8)	37/48 (77.1)
PPV (%)	33/43 (76.7)	31/39 (79.5)	30/40 (75.0)	31/39 (79.5)
NPV (%)	4/5 (80)	6/9 (66.7)	4/8 (50.0)	6/9 (66.7)

hilum. Although MPRs do not increase diagnostic performance in patients with bile duct cancer, they are still valuable. MPRs display the entire length of the bile duct and show ductal thickening and intraductal masses. Also, MPRs allow the opportunity for a second look at the tumor and give intuitive images as well as a roadmap to the surgeons. These are beneficial to the surgeon in planning therapeutic options and also give confidence in surgical decision-making. Furthermore, MPRs are expected to be more beneficial for radiologists with limited experience in hepatobiliary imaging by providing intuitive images and different view angles. Also, inter-observer agreement was increased in the combined axial and MPR images group compared with the axial-only images group in assessing vascular involvement and tumor resectability.

In our results the diagnostic accuracies for the evaluation of CBD cancer were high in both readers but their accuracy for evaluating hilar duct cancer was low in both readers. The reason for this low accuracy in patients with hilar bile duct cancer is that the hepatic hilum is a more compact complex anatomic structure than the head of the pancreas and therefore the ductal extension tends to be underestimated. There may be some reasons for not improving diagnostic performance despite adding the combined MPR images to standard axial images. One reason is that the reviewers in our study are very experienced in hepatobiliary imaging skilled in the interpretation of axial images and have a systematic approach to reading such images. Therefore, there is a chance that their diagnosis was not very influenced by the MPR. Another reason is that the cine-view picture archiving and communication system) has made it easy to trace vascular structures and the ductal system even with axial-only images. Furthermore axial images are perpendicular to the course of the bile duct. The third reason is that we cannot obtain the ideal plane to display each confluent portion of the bile duct at the same time on axial coronal and sagittal planes.

In our study, two readers showed low diagnostic accuracy, ranging from 33.3% to 58.3%, for the evaluation of tumor extent of hilar cancer, whereas the diagnostic accuracy for the evaluation of tumor extent of CBD cancer was high in both readers. The most common reason for inaccurate preoperative assessment with MDCT was underestimation of the proximal ductal tumor extent.

Table 5 Comparison of the confidence level of the tumor extent between prior PTBD insertion group and non-PTBD insertion group

	Reviewer 1		Reviewer 2	
	Axial only	Combined axial and MPR	Axial only	Combined axial and MPR
PTBD group	4.00±0.77	4.38±0.66	3.47±0.67	4.09±0.70
Non-PTBD group	4.29±0.77	4.66±0.48	3.66±0.67	4.29±0.82
P value	0.211	0.184	0.280	0.329

Assessment of tumor extension along the bile duct is not promising, even with multiphasic MDCT. Percutaneous transhepatic cholangiography or endoscopic retrograde cholangiography still remains the "gold standard" for the preoperative assessment of ductal involvement in the MDCT era. Therefore, a further refined strategy, such as the combined reading of cholangiography and CT, will be needed for accurate biliary ductal evaluation.

For determining tumor resectability, previous reports on the resectability of hilar cholangiocarcinoma using multiphasic helical CT have shown a range of 60–86% with sensitivities of 56–76% [10, 11, 21, 22]. For tumors in the periampullary region, MDCT allows 95% detection of these tumors. In our results, the overall accuracy for resectability ranged from 70.8 to 77.1%. Because of the infiltrating growth pattern of bile duct cancer, its exact proximal extent along the bile duct tends to be underestimated on CT. Therefore, MDCT is not accurate for determining resectability even with MPR images.

There were several limitations of this study. One possible bias was that because patients with potentially resectable disease underwent surgery, limiting our patient group to surgical patients introduced a selection bias toward resectable disease. However, this selection bias might be reduced to some extent because the readers were informed that some patients who have unresectable criteria on preoperative CT scanning underwent surgery for palliative purposes. The second limitation is that some patients with bile duct cancer have a PTBD catheter inserted before undergoing MDCT. Therefore, bile duct extension could be underestimated. We believe that many tertiary referral hospitals, such as our institution, have the same situation in that as patients with biliary obstruction are referred for biliary drainage, CT scanning is obtained with the biliary drainage catheter still in place. In our results, there was no significant difference for confidence level of tumor extent between the PTBD insertion group and the non-PTBD insertion group. Thirdly, in patients with hilar ductal cancer tumor, extension and vascular invasion of resected liver are not clearly evaluated surgically or pathologically. Because surgeons and pathologists are not concerned with the resected ipsilateral side of the lesion, we cannot obtain a standard of reference for the ipsilateral tumor extension or the vascular invasion. Therefore, we did not have the standard of reference regarding ipsilateral tumor extension and vascular invasion for the hilar bile duct cancer.

In conclusion, the addition of MPR images to the standard axial images does not significantly improve the diagnostic performance of MDCT in the preoperative evaluation of bile duct cancer. Nevertheless, MPRs are still beneficial for the clinicians and radiologists with limited experience in hepatobiliary imaging, and the benefit of MPR should be further investigated prospectively.

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