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Original article

Perihilar cholangiocarcinoma: accuracy of 16-detector-row computed tomography in evaluating tumor extension and resectability

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Background: Management of perihilar cholangiocarcinoma is mainly by surgery. Computed tomography is the imaging choice by which to evaluate tumor extension and resectability. However, reports concerning the accuracy of computed tomography for this purpose differ.
Objective: To retrospectively assess the accuracy of 16-detector-row computed tomography in evaluating tumor extension and tumor resectability of perihilar cholangiocarcinoma.
Method: Sixty-two patients attending our hospital from January 2004 to June 2011were included in this study. Tumor extension and resectability were retrospectively reviewed. Pathological results, diagnostic laparoscopy, and surgical findings were used as references.
Result: The accuracy for predictability of resectability was 80.7%. The accuracy of 16-detector-row computed tomography in evaluating tumor extension was; 95.2% for prediction of ductal involvement, 85.7% for prediction of hepatic artery invasion, 79.1% for prediction of portal vein invasion, 67.3% for prediction of N1 nodal involvement and 90.9% for prediction of N2 nodal involvement.
Conclusion: Good accuracy was found using 16-detector-row computed tomography in overall evaluation of tumor resectability. For tumor extension, 16-detector-row computed tomography has good accuracy except for evaluating N1 nodes.

Keywords: Accuracy, MDCT, perihilar cholangiocarcinoma, tumor extension, 16-detector-row computed tomography

Cholangiocarcinoma is a primary malignancy of the biliary system and is the second most common primary hepatic cancer. The incidence of cholangiocarcinoma in Thailand is high, particularly in the northeastern region and correlates with liver fluke infestation (e.g. *Opisthorchis viverrini*) [1-3].

About 50%–60% of cholangiocarcinomas are located around the perihilar region. The definition of perihilar tumor implies that the tumor arises directly from the hepatic duct confluence or initially arises from a unilateral intrahepatic bile duct, and then invades the confluence of the liver [4]. The tumor has been classified into four groups based on longitudinal extension. Type I: tumor is below the junction of the left and right hepatic ducts; Type II: tumor is reaching the junction, but does not involve the left or right hepatic ducts; Type III: tumor occludes the common hepatic duct and either the right (IIIa) or left (IIIb) hepatic ducts; Type IV: tumors are multicentric or involve the junction and both right and left hepatic ducts [4-6].

Invasion of hilar cholangiocarcinoma is classified into longitudinal extension and vertical invasion. The longitudinal extension refers to a tumor that spreads along the mucosa or submucosa of the biliary tree and vertical invasion refers to direct invasion of tumor into the hepatic parenchyma, infiltration into the hepatoduodenal ligament, including the adjacent hepatic artery and portal vein, or invasion of the pancreas and duodenum. Lymph node metastasis and distant metastasis could be an extension of vertical invasion. Longitudinal spread determines the type of radical operation indicated and vertical infiltration

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determines resectability and potential curability of the tumor. Both of these predict prognosis [7].

Multidetector computed tomography (MDCT) is now widely available. It plays an important role in preoperative planning for evaluation of tumor extension and the feasibility of tumor resection. MDCT is used to identify the extent of the ductal tumor, vascular involvement, liver morphology, nodal involvement, and distant metastases. Variable results and pitfalls of CT in evaluating tumor extension and tumor resectability have been published [8-10]. However, these studies are combinations of the results of single and multidetector CT scanners.

The purpose of this study was to retrospectively assess the accuracy of 16-detector-row CT in the evaluation of tumor extension and tumor resectability of perihilar cholangiocarcinoma using imaging criteria. Pathological results or surgical findings, or both, were used as endpoints.

Materials and methods

Patient selection

After approval from the Research Ethics Committee of the Faculty of Medicine, Chulalongkorn University, we retrospectively reviewed patients with cholangiocarcinoma (C22.1: ICD 10: International Statistical Classification of Diseases and Related Health Problems: 10th Revision) by searching the hospital information system from January 2004 to June 2011. We included patients with perihilar cholangiocarcinoma who underwent preoperative MDCT and had diagnostic laparoscopic records, surgical records or pathology reports. The exclusion criterion was patients who had other coexisting malignancies.

CT technique

CT was performed on a Siemens Somatom Sensation 16 system (Siemens, Forchheim, Germany). The protocol parameters were 16 × 1.5 mm collimator, 24.0 mm feed per rotation and 0.5 s gantry rotation time. After a precontrast scan of the upper abdomen, a bolus-tracking technique was performed by placing the region of interest (ROI) at the abdominal aorta at the middle level of the liver using threshold of 100 HU. The rate of the bolus injection was 3 mL/s of 100 mL nonionic monomeric contrast media. The arterial phase was obtained at 10 seconds after bolus tracking and 90 seconds after the contrast injection for the portovenous phase. A 5 to 15 minute delay study was performed after the contrast injection. The scan was started at the level above the diaphragm to the level of the lower poles of both kidneys.

Image analysis

A radiologist and the first author (resident) retrospectively reviewed all images using criteria described below. Images were reviewed on our Picture Archiving and Communication System (PACS). The latest CT study before the surgical operation was reviewed. CT studies with a preoperative intervention procedure (such as PTBD, PVE or internal stent placement) were also reviewed. The CT images were viewed in the axial, coronal and sagittal planes with slice thickness of 5–8 mm. Radiological interpretation focused on four main areas: parenchymal and ductal extension of tumor, hepatic vascular involvement (hepatic artery, portal vein, hepatic vein, intrahepatic IVC), lymphadenopathy, and peritoneal nodules.

Tumor unresectability was based on the following criteria: bilateral involvement of hepatic ducts to the level of secondary biliary radicals, atrophy of one liver lobe with encasement of branches of the contralateral portal vein, atrophy of one liver lobe with contralateral secondary biliary radical involvement, hepatic artery invasion, encasement or occlusion of the main portal vein proximal to bifurcation, bilateral involvement of hepatic arteries, extrahepatic adjacent local invasion, nodal metastases beyond the hepatoduodenal ligament, and disseminated disease [11, 12].

Bile duct involvement was interpreted by irregular wall thickening of the bile duct of more than or equal to 5 mm with proximal dilatation of the intrahepatic bile ducts or intraluminal nodule or mass or intraluminal filling defects or tapering end of the bile duct or stretched and narrowed of lumen [10, 13].

Vascular involvement was indicated by vessel occlusion, stenosis or contour deformity associated with the tumor, or tumor contact greater than 50% of the vessel circumference [14-16]. We analyzed hepatic arteries, hepatic veins, the main portal vein and its branches, and the inferior vena cava.

Positive lymph nodes were considered as a short axis diameter larger than 10 mm; or smaller than 10 mm with internal low attenuation (necrosis), or a short axis diameter larger than 6 mm for retrocrural or porta hepatis nodes, or enhancement on post contrast studies (portovenous and delayed phase studies). We divided lymph nodes into two groups following the TNM classification: N1 (not beyond hepatoduodenal ligament such as cystic duct, pericholedochal, and/or hilar lymph nodes) and N2 (other regional nodes such as peripancreatic, periduodenal, periportal, celiac, superior mesenteric and/or posterior pancreaticoduodenal nodes) [17-19].

Peritoneal metastases were considered when there were nodules or masses in the greater omentum or in the peritoneum or sheet-like soft tissue attenuation or thickening of intra-abdominal ligament [20].

Standard references

We reviewed surgical records and pathological reports. Surgical records and/or pathological reports were the standard references. In case of any conflict between a surgical record and a pathological report, the pathological report had precedence.

Statistical analysis

The sensitivity, specificity, predictive values and accuracy to predict ductal involvement, vascular involvement, nodal metastases, and peritoneal metastases were calculated using 2×2 tables. The accuracy in evaluating tumor resectability was also calculated using 2×2 tables.

Results

Sixty-two patients met the inclusion criteria (43 men and 19 women). The mean age of the patients was 58 ± 10 years with range of 37 to 82 years. Patients were from the northeastern, central, eastern, and the northern part of Thailand: 48%, 34%, 11%, and 7%, respectively. Jaundice presented in 52 of 62 patients (84%). Six patients presented with upper abdominal pain and tumor was found incidentally in four patients during regular health checks. CA19-9 was obtained from 52 patients with the range of 0.8 to more than 1,000 IU/mL. MDCT was performed in all patients within 1–83 days before surgery (mean; 29 ± 20 days). Two different slice thicknesses were used in this study: 5-mm thickness in 32 patients and 8-mm thickness in the remaining 30 patients.

Tumor resectability

Eighteen of 62 patients (29%) underwent diagnostic laparoscopy. Among them, 11/18 patients showed findings of unresectability, 10/11 underwent peritoneal or nodal biopsy, and the other underwent palliative surgery. Seven of the 18 patients were confirmed as resectable by diagnostic laparoscopy and underwent surgical exploration with curative surgical treatment. In another 44 patients, diagnostic laparoscopy was not done before exploratory laparotomy; 22 patients showed surgical findings of unresectability, and the remaining 22 patients showed surgical findings of resectability. In the unresectable group; 2 patients underwent biopsy, 12 patients underwent palliative surgery and 8 patients underwent attempted curative surgery. The patients in the resectable group, all underwent curative surgery. **Figure 1** summarizes as a diagram of resectable and unresectable cases.

CT correctly predicted all 29 resectable cases (100%) and 21 of 33 unresectable cases (63.6%). Twelve cases were inaccurately grouped because of underestimation in 2 cases with bile duct extension; 1 case had inferior vena cava involvement; 5 cases had main portal vein involvement; 1 case had N2 nodal metastases; 2 cases had undetected peritoneal metastases, and 1 case had combined conditions (tumor in the left hepatic lobe with right portal vein involvement). Sensitivity, specificity, positive predictive value, negative predictive value and overall accuracy were 63.6%, 100%, 100%, 70.7%, and 80.7%, respectively. **Table 1** shows the percentage of the CT scans that predicted the resectable and unresectable cases based on diagnostic laparoscopy, exploratory laparotomy, and pathological results. **Table 2** shows the percentage of the CT scan that predicted tumor resectability.

Bile duct extension

There were 42 of 62 patients who had adequate records concerning bile duct involvement. MDCT accurately evaluated ductal extension in 40 out of 42 patients. Underestimation was noted in 2 out of 42 patients (**Figure 2**). Sensitivity, positive predictive value and overall accuracy were 95.2%, 100%, and 95.2%, respectively.

Hepatic artery involvement

Thirty-five of 62 patients had adequate records about hepatic artery involvement. MDCT accurately evaluated those who had no hepatic artery involvement in 25 of 30 patients and those who had hepatic artery involvement in 5 out of 5 patients. Overestimation was noted in 5 of 35 patients (**Figures 3 and 4**). Sensitivity, specificity, positive predictive value, negative predictive value and overall accuracy were 100%, 83.3%, 50.0%, 100% and 85.7%, respectively.

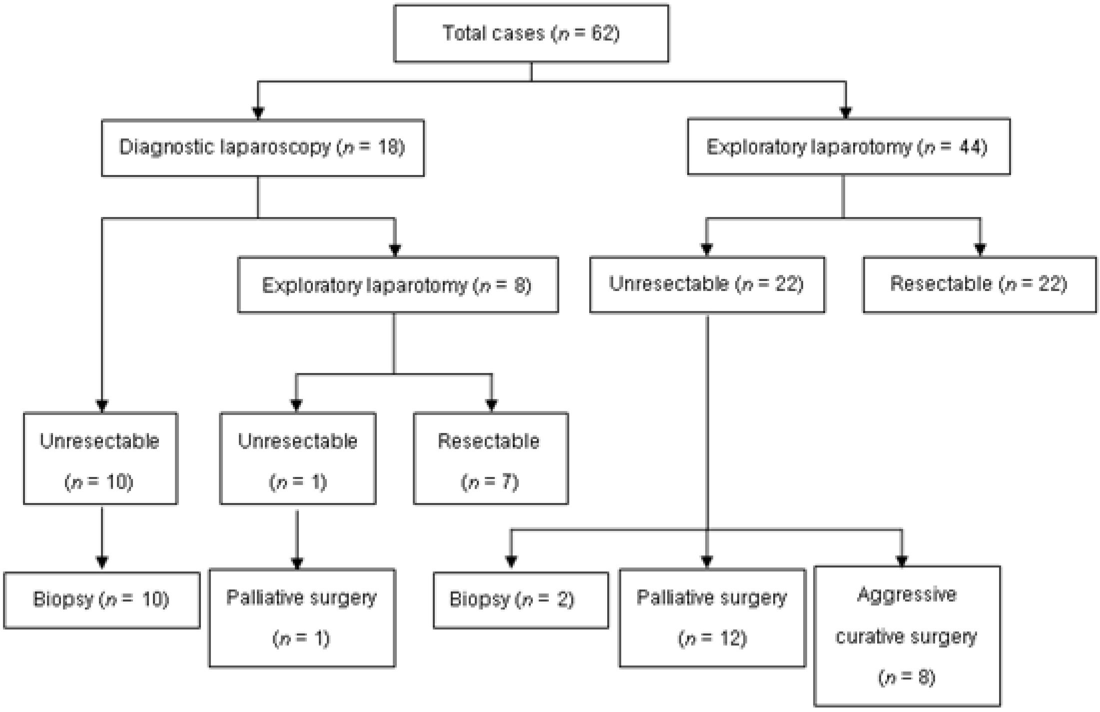

Figure 1. Diagram showing numbers of resectable and unresectable cases from diagnostic laparoscopy and exploratory laparotomy including final management in each group.

Table 1. The number and percentage of predicting tumor resectability of the CT scan in the resectable and unresectable cases

	Number of predicting tumor resectability (%)
Diagnostic laparoscopy	
Resectable	7/7 (100%)
Unresectable	9/11 (81.8%)
Exploratory laparotomy	
Resectable	22/22 (100%)
Unresectable	12/22 (54.5%)

Table 2. Summary of number and percentage of predicting tumor resectability between resectable and unresectable cases

CT findings	Operative findings	
	Resectable	Unresectable
Resectable	29	12
Unresectable	-	21
Number and percentage of predicting tumor resectability	29/29 (100%)	21/33 (63.6%)

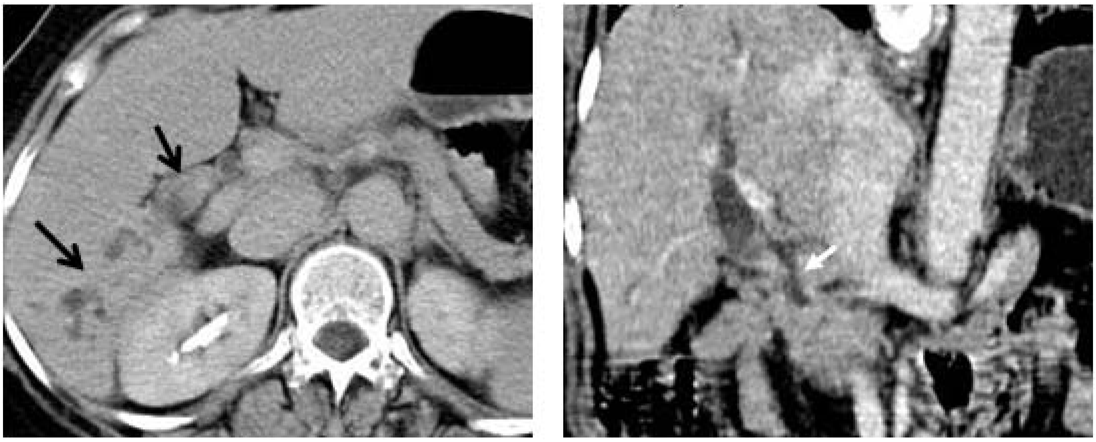

Figure 2. **A:** axial: delayed phase and **B:** coronal: portovenous phase. There was irregular thickening with delayed enhancement of the right hepatic duct and its posterior branch (black arrow in A). The common bile duct appears as a smooth thin wall (white arrow in B). The patient underwent right hepatectomy. The pathological result shows positive tumor at the right hepatic duct, common hepatic duct and common bile duct.

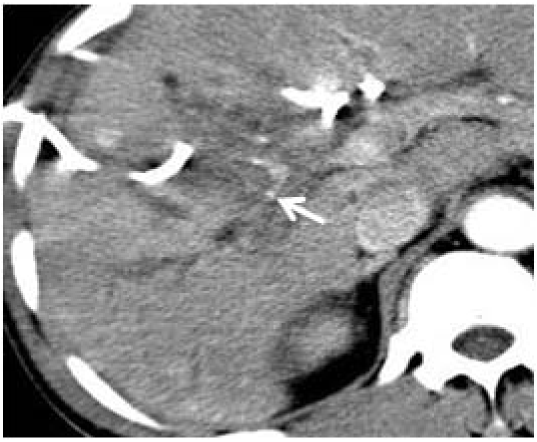

Figure 3. Axial CT image of the arterial phase study at the level of branches of right hepatic artery. The right hepatic artery and its branches were encased (white arrow). The patient underwent extended right hepatectomy. The pathological result is negative for right hepatic artery invasion. This mismatch could be the difference between imaging and pathological criteria to diagnosis of the tumor extension.

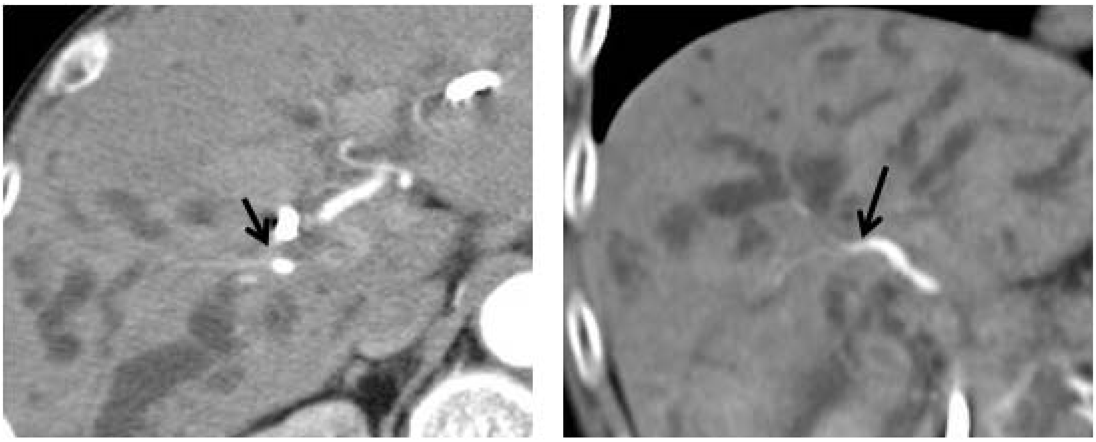

Figure 4. **A:** Axial and **B:** coronal arterial phase CT images at the level of branches of right hepatic artery in a 55-year-old man with a periductal tumor involving hepatic duct bifurcation and right hepatic duct (type IIIa). The right hepatic artery showed abrupt narrowing (black arrow). The patient underwent a right hepatectomy. The pathological result was negative for right hepatic artery invasion. This could be the difference between imaging and pathological criteria to diagnosis of the tumor extension.

Portal vein involvement

Forty-three of 62 patients had adequate records concerning portal vein involvement. In these 43 patients, portal vein involvement occurred in 18 patients and no portal vein involvement in 25 patients. This was confirmed by pathology findings. CT accurately depicted portal vein involvement in 14 of 18 patients. Four cases showed false negative results (**Figure 5**). CT showed 5 false positive cases in 25 patients whose pathology reports showed intact portal vein (**Figure 6**). Sensitivity, specificity, positive predictive value, negative predictive value and the overall accuracy were 77.8%, 80.0%, 73.7%, 83.3%, and 79.1%, respectively.

Other major vascular involvement

Forty-four of 62 patients had adequate records about other major vascular involvement. CT accurately evaluated those who had no major vascular involvement in 40 of 44 patients. Four patients showed inferior vena cava (IVC) involvement. CT accurately depicted three of these. One case was underestimated (**Figure 7**). Sensitivity, specificity, positive predictive value, negative predictive value and overall accuracy were 75.0%, 100%, 100%, 97.6%, and 97.7%, respectively.

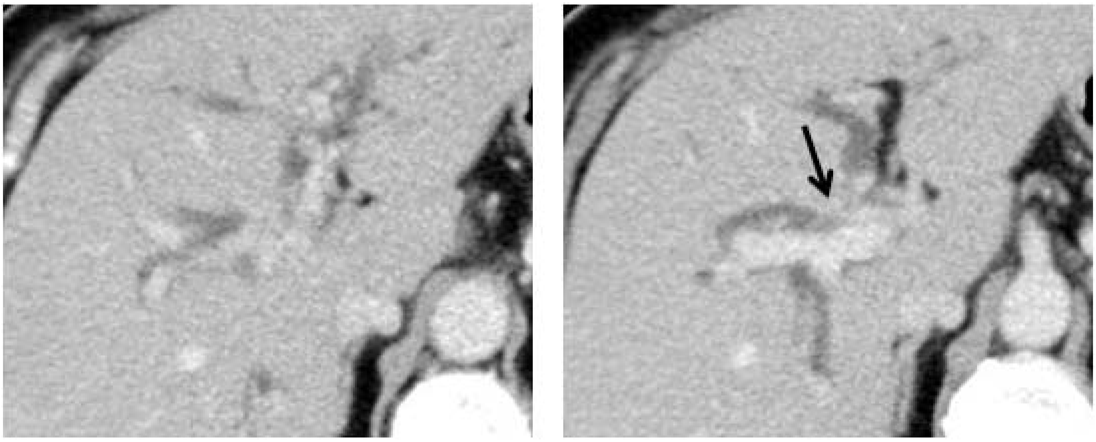

Figure 5. Axial CT images of the portovenous phase study (**A** was more cranial in position than **B**). The tumor abutted proximal right portal vein less than 50%. No tortuousness or narrowing of the portal vein was observed. Imaging was interpreted as no invasion. The patient underwent left hepatectomy, partial right hepatectomy and caudate lobe resection. The operative finding was the tumor had involved right portal vein.

Figure 6. Axial CT image of the portovenous phase study. The right portal vein was obliterated. Right lobe atrophy was also observed. The patient underwent right hepatectomy. The pathological result was negative for right portal vein invasion. This could be the difference between imaging and pathological criteria to diagnose the tumor extension.

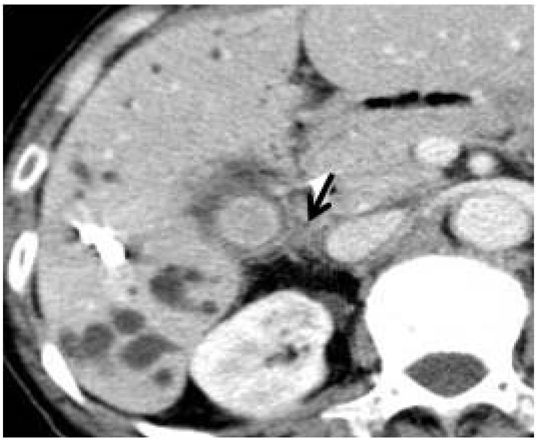

Figure 7. Axial CT image of the portovenous phase study. The tumor involves hepatic duct bifurcation and right hepatic duct with infiltrating the adjacent gallbladder. There is minimal fat haziness at anterior aspect of the IVC without a pressure effect (black arrow). Imaging is interpreted as no invasion. Operative findings show that the tumor has infiltrated the hilum, and extended to the gallbladder and anterior aspect of IVC.

Lymph node metastases

Forty-nine of 62 patients had adequate records concerning N1 metastases. Twenty-seven of these 49 patients had N1 metastases. CT failed to detect N1 node in 8/27 patients. In the remaining 22 patients, overestimation by CT was found in 8 patients (**Figure 8**). Sensitivity, specificity, positive predictive value, negative predictive value and overall accuracy were 70.4%, 63.6%, 70.4%, 63.6%, and 67.3%, respectively for N1 node metastases.

Forty-four of 62 patients had adequate records about N2 metastases. Nine of the 44 patients had N2 metastases. CT failed to detect N2 nodes in 3/9 patients. In the remaining 35 patients, overestimation by CT was found in 1 patient. Sensitivity, specificity, positive predictive value, negative predictive value and overall accuracy were 66.7%, 97.1%, 85.7%, 94.4% and 90.9%, respectively for N2 node metastases.

Figure 8. Axial CT image of the portovenous phase study of a patient with cholangiocarcinoma of the hepatic confluence (type II). The imaging showed positive node metastasis with 11 mm in short diameter (black arrow). The patient underwent a right extended hepatectomy. Pathological results were negative for nodal metastasis (0/2 common hepatic node, 0/1 cystic node, and 0/7 hilar node).

Peritoneal metastases

Fifty-eight of 62 patients had adequate records concerning peritoneal metastases. Peritoneal metastases were proven in 14 out of 58 patients. CT failed to detect peritoneal metastases in 4 of 14 patients. No false positives were found. Sensitivity, specificity, positive predictive value, negative predictive value and overall accuracy were 71.4%, 100%, 100%, 91.7%, and 93.1%, respectively.

A summary of bile duct extension, hepatic arterial involvement, portal vein involvement, other major vascular involvement, lymph nodes metastases, peritoneal metastases and tumor resectability is shown in **Table 3.**

Discussion

The accuracy of 16-detector-row computed tomography in evaluating tumor resectability was evaluated in all 62 patients. However in evaluating about the details of tumor extension (bile duct, hepatic artery, portal vein, other major vessels and lymph nodes), not all patients could be studied because many were found unresectable by diagnostic laparoscopy and exploratory laparotomy, then biopsy and/or palliative surgery was done.

There are prior studies showing that helical CT was ineffective in the assessment of distal extrahepatic duct, artery, and lymph node involvement [8, 9]. Other retrospective studies revealed that the sources of inaccuracies in CT were an underestimation of bile duct involvement, hepatoduodenal infiltration, and vascular involvement [10].

In our study, there was a very high percentage of predicting tumor resectability in resectable cases. However in the unresectable cases, the percentage was not so high. These cases were considered resectable, but they were in fact unresectable. This could have been from microinvasion of the tumor to adjacent structures and that the 16-detector-row computed tomography had not enough sensitivity to detect small amounts of tumor. The other possibility was that thickness of slices (5–8 mm) may not be enough to evaluate tumor extension in some cases. Our PACS did not store the raw data, we could not reconstruct the images with thicknesses of less than stored data of 5 or 8 mm in problematic cases.

Regarding the evaluation of tumor extension, we found many false positives of vascular involvement: 5 of 43 patients for portal vein involvement and 5 of 35 patients for hepatic artery involvement. Imaging showed significant involvement of portal vein with ipsilateral atrophic changes of the affected hepatic lobe. We discussed this with the pathologist and it was thought that this could be the result of different criteria used for tumor extension. Regarding lymph node metastases, our findings agreed with prior studies [10, 21, 22], showing both false positive and false negatives. Much less accuracy in N1 nodes was noted when compared with N2 nodes. The size of the lymph nodes was not sufficient to differentiate benign from malignant nodes. However, increased diameter with abnormal enhancement of nodes, predicted malignancy.

A limitation of this study is its retrospective nature. Some cases showed significant differences because of the difference between imaging and pathological criteria in diagnosis of the tumor extension. However, the results of this study were based on surgical and pathology reports.

Table 3. Summary of tumor resectability, bile duct extension, hepatic arterial involvement, portal vein involvement, other major vascular involvement, lymph nodes metastases, and peritoneal metastases

	N	Sensitivity	Specificity	PPV	NPV	Accuracy
Resectability	62	63.6%	100%	100%	70.7%	80.7%
Duct extension	42	95.2%	–	100%	–	95.2%
Hepatic artery invasion	35	100%	83.3%	50.0%	100%	85.7%
Portal vein invasion	43	77.8%	80.0%	73.7%	83.3%	79.1%
Major vascular invasion	44	75.0%	100%	100%	97.6%	97.7%
N1 metastasis	49	70.4%	63.6%	70.4%	63.6%	67.3%
N2 metastasis	44	66.7%	97.1%	85.7%	94.4%	90.9%
Peritoneal metastases	58	71.4%	100%	100%	91.7%	93.1%

N = number of cases, PPV = positive predictive value, NPV = negative predictive value

Conclusion

Sixteen-detector-row computed tomography shows a better percentage of predicting tumor resectability in resectable cases as compared with the unresectable cases. This computed tomography shows good accuracy in detecting tumor extension except in evaluating N1 nodes. To improve accuracy, setting of definite radiological and pathological criteria for evaluation of tumor extension should be considered.

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The authors declare that there is no conflict of interest in relation to this article.

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