Hilar cholangiocarcinoma: Diagnostic accuracy and tumor extent with MR Cholangiography

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INTRODUCTION

Hilar cholangiocarcinoma is an adenocarcinoma arising from the hepatic duct or near its bifurcation. Hilar cholangiocarcinoma involving hepatic bifurcation progresses along the main hepatic ducts and leadsto infiltration of intrahepatic ducts. In most instances, hilar cholangiocarcinoma is lethal, but recent reports have suggested that aggressive surgery for hilar cholangiocarcinoma can improve the prognosis. The overall 5-year survival rate in a recent report was 56% after curative resection, compared...
with only 1% after non-curative resection. Infiltration of the tumor beyond the second-order branches on both sides is considered incurable because surgical resection becomes impossible. The precise evaluation of tumor extension, therefore, is very important in hilar cholangiocarcinoma. This is because the determination of the resectability and choice of treatment modalities depend on the status of tumor extension.

Several studies have emphasized the values of non-invasive imaging. According to these studies, ultrasound and computed tomography have a wide range of accuracy in the evaluation of tumor extent ranged from 40% to 94%. However, these studies have limitations of small number of patients and most of them compared with endoscopic retrograde cholangiography (ERC).

Recent, MR cholangiography has improved for the evaluation of bile ducts. There have been a few studies reporting the usefulness of MR cholangiography in the evaluation of biliary diseases, but most of them had been done in comparison with ERC and not enough consideration has been paid to extent of hilar cholangiocarcinoma into the bile duct with small number of patients.

So far, percutaneous transhepatic cholangioscopy (PTCS) has been regarded as the most accurate preoperative diagnostic modality in assessing tumor extension of hilar cholangiocarcinoma, because PTCS provides direct visualization of biliary tract mucosa and permits biopsy. To our knowledge, there is little report about the accuracy of MR cholangiography with reference to PTCS for tumor extension of hilar cholangiocarcinoma.

The purpose of this study was to determine the accuracy of MR cholangiography in evaluating the tumor extension of hilar cholangiocarcinoma with reference to PTCS and surgical findings.

MATERIALS AND METHODS

Patients
By a computerized search of pathology records, 198 patients with pathologically proven hilar cholangiocarcinoma were identified during 2-year. Among them, 97 underwent MR cholangiography for the evaluation of operability of hilar cholangio carcinoma. 89 of these 97 patients had undergone both MR cholangiography and PTCS to evaluate the extent of hilar cholangiocarcinoma and were included in this study. There were 72 men and 17 women. Patients ranged in age from 30 to 72 years (mean, 56 years). Hilar cholangiocarcinoma were proved by means of surgery (n=17) or PTCS guided biopsy (n=72). Written informed consent was obtained from all patients before both MR cholangiography.

MR cholangiography was performed prior to percutaneous transhepatic biliary drainage (PTBD) in most patients (n=74). However, when the patients manifested with acute cholangitis, emergency PTBD was performed prior to MR cholangiography (n=15). The time interval between the MR cholangiography and PTBD was less than 2 days.

MR Cholangiography
MR cholangiography was performed on a 1.5-T MR system (Magnetom Vision; Siemens, Erlangen, Germany). A circular polarized, phased-array body coil with four elements was used. No premedication or contrast
medium was administered. Before MR cholangiography, T1-weighted axial and coronal gradient-echo imaging (repetition time, 149 msec; echo time, 4.8 msec; flip angle, 70°; section thickness, 8 mm; 18 sections in a 20-second breath hold) was performed to localize the biliary system. These images were then used as guides to perform MR cholangiography. Two different MR cholangiography techniques were applied: single-slab rapid acquisition with relaxation enhancement (RARE) and multislice half-Fourier acquisition single-shot turbo spin-echo (HASTE). The slabs of a single-shot RARE sequence were obtained at various angles (coronal, axial, and oblique planes) that allow optimal visualization of the bile ducts; the number of thick-slab acquisitions per patient ranged from three to 10 (mean, six acquisitions). Next, multislice HASTE images were obtained in the coronal and oblique planes. Each examination was performed during a single breath-hold.

The imaging parameters for the single-shot RARE sequence were the following: repetition time, msec; effective echo time, 1200 msec; echo spacing, 11.5 msec; echo train length, 240; flip angle, 150°; slab thickness, 70-96 mm; field of view, 300 mm; number of signals acquired, one; matrix, 240 256; and acquisition time, 6.32 sec. The imaging parameters for the multislice HASTE sequence were the following: repetition time, msec; effective echo time, 95 msec; echo spacing, 11.9 msec; echo train length, 128; flip angle, 150°; section thickness, 4 mm with no gap; number of slices, 13-15 (range of coverage, 52-60 mm); field of view, 300 mm; number of signals acquired, one; matrix, 240 256; and acquisition time, 20-23 sec. Fat saturation was used to reduce strong fat signal during image acquisition. It takes about 15 minutes to take all examination. It performed by special radiologist to determine the proper slabs of a MR cholangiography to properly fit the common bile duct, hilum, and both intrahepatic ducts.

**Cholangioscopic Examination**

Cholangioscopic examination was performed via a percutaneous transhepatic tract. For PTCS, initial PTBD was carried out by using a pigtail catheter (7.5 to 8.0 F; Cook, Bloomington, Ind.) under fluoroscopic guidance. Two or three days after PTBD, the sinus tract was dilated up to 16 or 18 F in one session. PTCS was then performed 7 to 10 days after tract dilatation. This waiting period is required for stabilization and maturation of the sinus tract. Morphological types of hilar cholangiocarcinoma were classified into stenotic type, diffuse sclerosing type, and polyoid type based on selective cholangiographic findings obtained during PTCS examination. The extent of hilar cholangiocarcinoma at PTCS was determined histologically with mapping biopsy and occasionally combined with pathognomonic cholangioscopic findings such as tumor vessels. Usually more than four times PTCS-guided biopsy per one lesion were performed, and in infiltrative type seven to eight times were taken in each lesion.

**Imaging interpretation**

MR cholangiography retrospectively analyzed by two radiologists who were unaware of the final results with consensus. An interpretation of the PTCS was made by the two experienced biliary endoscopists by consensus, who were unaware of the MR cholangiography findings.
The extent of hilar cholangiocarcinoma was determined by MR cholangiography with following known criteria for cholangiocarcinoma: loss of continuity of bile duct or ductal separation, an abrupt and irregular narrowing of distal segment and a proportionally dilated proximal biliary tree, and an irregularly shaped intraluminal filling defects. The tumor extension of hilar cholangiocarcinoma was classified according to the Bismuth-Corlette classification. Type I was obstruction of the common hepatic duct within 2 cm of the hilum. Type II was obstruction involving the hilus with no communication between the main right and left hepatic ducts. Type III indicated extension of the tumor to involve secondary and tertiary radicles on one side only with IIIa denoting right branch ducts and IIIb left branch ducts, with absence of ductal obstruction on the contralateral side. Type IV denoted bilateral obstruction with tumor extension to secondary and tertiary radicles. The efficacy of both MR cholangiography in the assessing the Bismuth classification was compared with PTCS and surgical findings. The Fisher exact test was used to compare the MR cholangiography findings with PTCS and surgical findings.

**RESULTS**

We compared Bismuth types evaluated by MR cholangiography with reference to those evaluated by PTCS and surgical findings. The overall agreement of MR cholangiography was 76/89 (85%). The agreement of MR cholangiography in each Bismuth classification with reference to PTCS and surgical findings were as follows: Bismuth type I (n=16), 12/16 (75%); Bismuth type II (n=17), 14/17 (82%); Bismuth type IIIa (n=19), 15/19 (79%); Bismuth type IIIb (n=15), 15/15 (100%); Bismuth type IV (n=22), 20/22 (91%).

The morphologic types of hilar cholangiocarcinoma based on selective cholangiographic findings were classified into stenotic type (n=55, 62%), diffuse sclerosing type (n=14, 16%), and polypoid type (n=20, 22%).

Table 1 summary diagnostic performances of MR cholangiography for hilar cholangiocarcinoma on Bismuth classification in 89 patients comparison with PTCS and surgical findings. The diagnostic accuracy ranged between 93% and 96%; the sensitivity, specificity, and diagnostic accuracy of the MR cholangiography were 75%, 97% and 93% in Bismuth classification I (Fig. 1), 82%, 96%, and 93% in Bismuth classification II, 79%, 99% and 94% in Bismuth classification IIIa, 100%, 95%, and 96% in Bismuth classification IIIb (Fig. 2), 91%, 94%, and 93% in Bismuth classification IV. MR cholangiography was correct in 76 cases (85%), over stage in nine (10%) and under stage in four (5%) when compared to PTCS and surgical findings (Table 2).

**DISCUSSION**

The preoperative assessment of the extent of hilar cholangiocarcinoma is very important to determine the management plan. Recent reports have suggested that curative resection can improve the prognosis. The overall 5-year survival rate in a recent report was 56% after curative resection, compared with only 1% after non-curative resection. Because surgical resection of the tumor is regarded as the only method for curative treatment, it is important to determine the resectability of the tumor by accurate staging in terms of tumor extent in the bile ducts.

There have been a few studies reporting the usefulness of MR cholangiography in evaluating hilar
cholangiocarcinoma. The degree of agreement on tumor extension was from 63 to 96% in these studies. Yeh TS et al.\textsuperscript{10} reported that the present and extent of malignant biliary obstruction was determined in 81%. But, most of the previous reports had been done in comparison with ERC with small number of patients. There has been, however, few literature comparing MR cholangiography with PTCS in tumor extension of hilar cholangiocarcinoma.

We compared MR cholangiography with reference to PTCS and surgical findings in the evaluation of tumor extension in hilar cholangiocarcinoma. Of course, evaluating the accuracy of MR cholangiography with completely resected surgical specimen would be ideal but it was impossible because at most 19% out of enrolled patients with hilar cholangiocarcinoma underwent curative resection in our study. We evaluated therefore the accuracy of MR cholangiography with reference to PTCS that is accepted as the most accurate preoperative examination of tumor extension in hilar cholangiocarcinoma until now.\textsuperscript{13-16}

We take two different MR cholangiography techniques: single-slab rapid acquisition with relaxation enhancement (RARE) and multislice half-Fourier acquisition single-shot turbo spin-echo (HASTE). In previous reports, these two MR cholangiography techniques is a sensitive modality for detection and evaluation of the biliary system.\textsuperscript{13,21-24} Lopera JE et al.\textsuperscript{21} reported that overall accuracy in assessing the extent of biliary duct involvement was 96% in patients with malignant hilar and parahilar obstruction.

In our study, In MR cholangiography, the diagnostic accuracy ranged between 93% and 96%. In Bismuth class I, the overall sensitivity, specificity and diagnostic accuracy of MRC were 75%, 97 %, and 93 %, respectively. In Bismuth class II, the overall sensitivity, specificity and diagnostic accuracy of MRC were 82 %, 96%, and 93 %, respectively. In Bismuth class IIIa, the overall sensitivity, specificity and diagnostic accuracy of MRC were 79%, 99 %, and 94 %, respectively. In Bismuth class IIIb, the overall sensitivity, specificity and diagnostic accuracy of MRC were 100 %, 95 %, and 96 %, respectively. In Bismuth class IV, MR cholangiography is the ability to correct diagnosis in 76 cases (85%). We believe that the MR cholangiography is the ability to preoperative evaluates the extent of hilar cholangiocarcinoma with a very high sensitivity, specificity and diagnostic accuracy as compared with PTCS and surgical findings.

In our study, MR cholangiography was correct in 76 cases (85%). The results of MR cholangiography and PTCS differed in thirteen patients (15%). There have been a few studies reporting the usefulness of MR cholangiography in evaluating hilar cholangio carcinoma. The degree of disagreement on tumor extension was from 4% to 22% in these studies (10,11,21). Zidi SH et al.\textsuperscript{15} reported that the extent of malignant biliary obstruction was differ in four (22%) patients. In our study, The extent of hilar cholangiocarcinoma was overestimated with MR cholangiography in nine patients (10%) because of a hemobilia, air bubble, pus after PTBD in four patients, papillary type cholangiocarcinoma with large amount of mucin in two patients, a congenital anomaly in one patient including a right posterior branch directly inserted into the left main duct, and fail to identify the confluence in two patients. The level was underestimated with MR cholangiography in four patients (5%) because of superficial spread of the tumor in three patients, and failure to identify nonuniting duct in one.
Still yet, PTCS is considered to be the most accurate examination in the preoperative tumor extension of hilar cholangiocarcinoma. However, it has some limitations. PTCS is very invasive and has substantial complications related to PTBD and sinus tract dilatation. Furthermore, PTCS is a time-consuming procedure. From the results of the present study, MR cholangiography provided good overall agreement with PTCS and surgical findings on tumor extension of hilar cholangiocarcinoma. These findings ultimately affect the determination of the resectability and choice of treatment modality for the disease. MR cholangiography has some advantages, including noninvasiveness without using contrast enhancement and possible opacification of isolated bile duct. MR cholangiography is therefore suggested as very useful noninvasive diagnostic method in the evaluation of tumor extension in hilar cholangiocarcinoma. There are a few limitations of this study, such as the fact that surgical confirmation of bile duct was not available in all patients. We believe that the MR cholangiography can provide comprehensive information needed for the diagnosis and assessment of resectability in hilar cholangiocarcinoma. In the future, MRC may almost replace the diagnostic role of PTCS in the determination of tumor extension. Using a MR cholangiography may reduce the expenses and the length of hospital stay, with the additional attractive feature of being completely noninvasive. In conclusion, MR cholangiography may play as effective diagnostic modality as one of preoperative diagnostic modality of tumor extension of hilar cholangiocarcinoma.

References


Table 1. Diagnostic Performances of MRC for Klatskin tumor on Bismuth classification in 89 Patients
## Table 2. Diagnostic accuracy of MRC for Klatskin tumor on Bismuth classification in 89 Patients

<table>
<thead>
<tr>
<th>Bismuth classification</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Diagnostic accuracy</th>
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<tr>
<td>II (n=17)</td>
<td>82%</td>
<td>96%</td>
<td>82%</td>
<td>96%</td>
<td>93%</td>
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<tr>
<td>IIIa (n=19)</td>
<td>79%</td>
<td>99%</td>
<td>94%</td>
<td>95%</td>
<td>94%</td>
</tr>
<tr>
<td>IIIb (n=15)</td>
<td>100%</td>
<td>95%</td>
<td>79%</td>
<td>100%</td>
<td>96%</td>
</tr>
<tr>
<td>IV (n=22)</td>
<td>91%</td>
<td>94%</td>
<td>83%</td>
<td>97%</td>
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</table>

Note: PPV = positive predict value, NPV = negative predict value

### MR cholangiography

<table>
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<tr>
<th>PTCS</th>
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<th>IIIa</th>
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Note: PTCS = percutaneous transhepatic cholangioscopy
Fig. 1. MR cholangiography of Klatskin tumor of Bismuth type II. A: Oblique coronal thick-section RARE MR cholangiography shows bile duct obstruction at the hilum with no communication between the main right and left hepatic ducts. B-D: Thin-section HASTE MR cholangiography shows separation of the intrahepatic ducts at the hilum.
Fig. 2. MR cholangiography of Klatskin tumor of Bismuth type IIIb. A: Oblique coronal thick-section RARE MR cholangiography shows hilar obstruction. There is no communication between the right and left intrahepatic ducts with separation of left medial intrahepatic ducts and lateral intrahepatic ducts. B-D: Thin-section HASTE MR cholangiography clearly demonstrates ductal separation of left medial intrahepatic ducts and lateral intrahepatic ducts.