



# Preoperative CT and MRI assessment of the longitudinal tumor extent of extrahepatic bile duct cancer after biliary drainage

Seo-Bum Cho<sup>1</sup>  
 Yeun-Yoon Kim<sup>1,2</sup>  
 June Park<sup>1</sup>  
 Hye Jung Shin<sup>3</sup>

<sup>1</sup>Severance Hospital, Yonsei University College of Medicine, Department of Radiology and Research Institute of Radiological Science, Seoul, Republic of Korea

<sup>2</sup>Samsung Medical Center, Sungkyunkwan University School of Medicine, Department of Radiology and Center for Imaging Sciences, Seoul, Republic of Korea

<sup>3</sup>Yonsei University College of Medicine, Department of Biomedical Systems Informatics, Biostatistics Collaboration Unit, Seoul, Republic of Korea

## PURPOSE

To examine the diagnostic performance for the longitudinal extent of extrahepatic bile duct (EHD) cancer on computed tomography (CT) after biliary drainage (BD) and investigate the appropriate timing of magnetic resonance imaging (MRI) acquisition.

## METHODS

This retrospective study included patients who underwent curative-intent surgery for EHD cancer and CT pre- and post-BD between November 2005 and June 2021. The biliary segment-wise longitudinal tumor extent was evaluated according to the 2019 Korean Society of Abdominal Radiology consensus recommendations, with pre-BD CT, post-BD CT, and both pre- and post-BD CT. The performance for tumor detectability was compared using generalized estimating equation (GEE) method. When preoperative MRI was performed, patients were divided into two subgroups according to the timing of MRI with respect to BD, and the performance of MRI obtained pre- and post-BD was compared.

## RESULTS

In 105 patients (mean age:  $67 \pm 8$  years; 74 men and 31 women), the performance for tumor detectability was superior using both CT scans compared with using post-BD CT alone (reader 1: sensitivity, 72.6% vs. 64.6%,  $P < 0.001$ ; specificity, 96.9% vs. 94.8%,  $P = 0.063$ ; reader 2: sensitivity, 77.2% vs. 72.9%,  $P = 0.126$ ; specificity, 97.5% vs. 94.2%,  $P = 0.003$ ), and it was comparable with using pre-BD CT alone. In biliary segments with a catheter, higher sensitivity and specificity were observed using both CT scans than using post-BD CT (reader 1: sensitivity, 74.4% vs. 67.5%,  $P = 0.006$ ; specificity, 92.4% vs. 88.0%,  $P = 0.068$ ; reader 2: sensitivity, 80.5% vs. 74.4%,  $P = 0.013$ ; specificity, 94.3% vs. 88.0%,  $P = 0.016$ ). Post-BD MRI ( $n = 30$ ) exhibited a comparable performance to pre-BD MRI ( $n = 55$ ) (reader 1: sensitivity, 77.9% vs. 75.0%,  $P = 0.605$ ; specificity, 97.2% vs. 94.9%,  $P = 0.256$ ; reader 2: sensitivity, 73.2% vs. 72.6%,  $P = 0.926$ ; specificity, 98.4% vs. 94.9%,  $P = 0.068$ ).

## CONCLUSION

Pre-BD CT provided better diagnostic performance in the preoperative evaluation of EHD cancer. The longitudinal tumor extent could be accurately assessed with post-BD MRI, which was similar to pre-BD MRI.

## CLINICAL SIGNIFICANCE

The acquisition of pre-BD CT could be beneficial for the preoperative evaluation of EHD cancer when BD is planned. Post-BD MRI would not be significantly affected by BD in terms of the diagnostic performance of the longitudinal tumor extent.

## KEYWORDS

Extrahepatic cholangiocarcinoma, computed tomography, magnetic resonance imaging, biliary tract surgical procedures, drainage

Corresponding author: Yeun-Yoon Kim

E-mail: cookieks35@gmail.com

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Extrahepatic bile duct (EHD) cancer originates below the intrahepatic secondary biliary confluence and encompasses perihilar and distal bile duct cancers.<sup>1</sup> This type of cancer constitutes the majority of cholangiocarcinoma, with a mortality rate below 2 in 100,000 person-year.<sup>2</sup> Surgical resection is the sole curative treatment for it, underscoring the critical

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need for an accurate assessment of surgical resectability at the initial diagnosis.<sup>3</sup> Despite the pivotal role of the longitudinal extent of the tumor in determining the surgical approach, there is a lack of international radiologic reporting guidelines for EHD cancer. Recently, the Korean Society of Abdominal Radiology (KSAR) published consensus recommendations for the structured radiologic reporting of EHD cancer using computed tomography (CT) or magnetic resonance imaging (MRI).<sup>4</sup> Recent studies have demonstrated the utility of these recommendations in assessing resectability in EHD cancer.<sup>5,6</sup>

Approximately 90% of patients with EHD cancer initially present with cholangitis due to biliary obstruction.<sup>7</sup> Consequently, urgent endoscopic or percutaneous biliary drainage (BD) is necessary when biliary infection is suspected.<sup>7-10</sup> Moreover, BD can induce inflammation in the bile duct, mimicking or obscuring EHD cancer on CT or MRI and posing challenges in the imaging evaluation of the longitudinal tumor extent.<sup>11</sup> A previous study indicated a higher frequency of achieving no residual tumor (R0) resection in perihilar cholangiocarcinoma for patients who underwent CT before BD compared with those who underwent CT after BD. This shows the difficulty in assessing the exact longitudinal tumor extent post-BD.<sup>12</sup> While previous studies have suggested the challenges of post-BD imaging evaluation in perihilar cholangiocarcinoma,<sup>13,14</sup> there is currently no published data examining the impact of BD on the diagnostic performance of imaging studies in an intraindividual manner. Therefore, it is essential to evaluate the diagnostic performance of CT evaluation after BD to devise a more effective strategy for reporting these examinations before the curative resection of EHD cancer. Furthermore, given the limited usage of MRI compared with CT, it is crucial to investigate if BD affects tumor extent evaluation using MRI. A study involving 26 patients observed less accurate performances of MRI after BD in perihilar cholangiocarcinoma, which lacked a statistical comparison and warranted further investigation.<sup>15</sup>

This study aims primarily to examine the diagnostic performance of evaluating the longitudinal extent of EHD cancer after BD and improve performance in the preoperative setting. The secondary aim is to determine the appropriate timing of MRI acquisition concerning BD for evaluating the longitudinal extent of EHD cancer.

## Methods

### Patients

The Severance Hospital Institutional Review Board approved this study (IRB no: 4-2021-1139, date: 10.05.2021) and waived the requirement for patient consent because this study involved a retrospective review of medical records and images. This study identified potentially eligible patients with EHD cancer who underwent curative-intent surgery at our institution between November 2005 and June 2021 (Figure 1). The inclusion criteria were as follows: (a) BD performed before surgery, (b) contrast-enhanced CT scans obtained both pre- and post-BD, and (c) age of patients >18 years. The exclusion criteria were as follows: (a) preoperative embolization of the hepatic artery or portal vein causing metal artifacts on CT scans, (b) preoperative chemotherapy or chemoradiation hampering radiologic-pathologic correlation, (c) palliative surgery, and (d) lack of a reference standard for the longitudinal tumor extent.

### Image acquisition

Multiphase or single-portal venous-phase CT images were acquired according to institutional routine protocols. Patients underwent CT using either a 16- or 64-channel

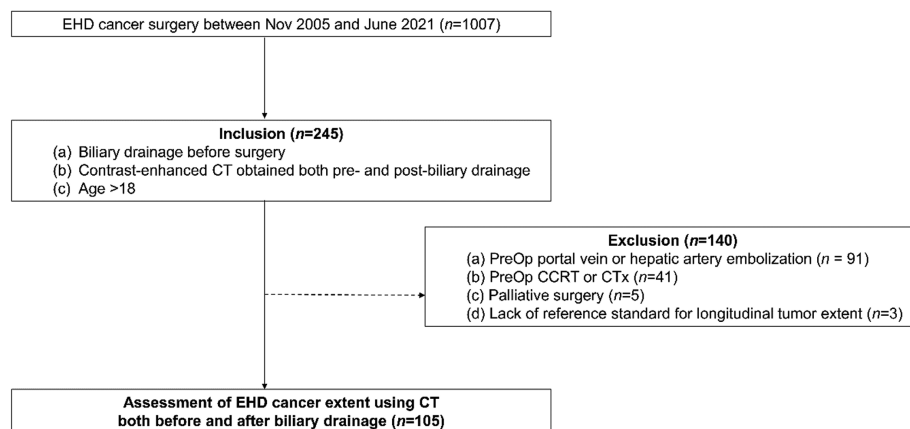
scanner (Somatom Sensation 16 or 64, Siemens, Erlangen, Germany; Brilliance iCT or 64, Philips Healthcare, Cleveland, Ohio, U.S.A.; Lightspeed VCT, GE Medical Systems, Milwaukee, Wisconsin, U.S.A.). After obtaining unenhanced images, 120–150 mL of non-ionic contrast medium was administered intravenously at a rate of 2–5 mL/sec. Using the bolus-tracking technique, the arterial phase was obtained 10–25 seconds after the attenuation value reached 100 Hounsfield units at the abdominal aorta. The portal venous and delayed phases were obtained 70–80 seconds and 3 minutes after contrast injection, respectively. The scanning parameters were as follows: beam collimation, 0.625 or 0.75 mm; slice thickness, 3 or 5 mm; reconstruction interval, 3 or 5 mm; rotation time, 0.5 seconds; effective tube current-time charge, 150–250 mAs; and tube voltage, 100–120 kVp. Coronal images were reconstructed with a slice thickness of 3 or 5 mm and a reconstruction interval of 3 or 5 mm. The routine protocol for MRI with MR cholangiopancreatography is described in the Online Resource 1.

### Computed tomography analysis

The CT images were retrospectively and independently reviewed by two readers (S.B.C., a radiology resident, and Y.Y.K., a board-certified abdominal radiologist with 5 years of practice experience) who were blinded to the surgical and pathological findings. Pre-BD CT scans, post-BD CT scans, and both pre- and post-BD CT scans were examined in each image review session with a washout period of at least 2 weeks between sessions to reduce recall bias. Image analysis was performed based on the 2019 KSAR consensus recommendations.<sup>4</sup> Moreover, the

### Main points

- Determining surgical resectability is crucial in extrahepatic bile duct cancer.
- Biliary drainage (BD) obscures the longitudinal tumor extent on cross-sectional imaging.
- Evaluation of pre-BD computed tomography improved the diagnostic performance.
- Similar performance was observed in magnetic resonance imaging pre- and post-BD.



**Figure 1.** Patient flow diagram. Out of 1,007 consecutive patients who underwent EHD cancer surgery between November 2005 and June 2021 at our institution, 245 met the inclusion criteria. After following the exclusion process, 105 patients who underwent CT both pre- and post-biliary drainage were finally included. EHD, extrahepatic bile duct cancer; Op, operation; CCRT, concurrent chemoradiotherapy; CTx, chemotherapy; CT, computed tomography.

readers recorded the presence or absence of tumors in each segment of the biliary tree (both secondary confluences, both hepatic ducts, primary confluence of the bile duct, common hepatic duct, and supra- and intra-pancreatic common bile duct) and determined the Bismuth–Corlette classification in perihilar cholangiocarcinoma.<sup>4</sup> Distal cholangiocarcinoma was classified as Bismuth–Corlette type 0. Moreover, the Bismuth–Corlette classification on the CT scan was compared with the reference standard and categorized as overestimation, correct assessment, or underestimation of the longitudinal extent of the tumor. When a Bismuth type IIIA tumor was determined to be IIIB on the CT scan or vice versa, it was categorized as incorrect. Furthermore, tumor involvement was evaluated based on the morphology (e.g., wall thickening of the bile duct, intraductal soft tissue mass, and asymmetric stricture) and degree of contrast enhancement (e.g., hyperenhancement to the liver parenchyma).<sup>4,16</sup> Hyperenhancement of the bile duct wall was assessed mainly in the arterial phase, if available, for intrapancreatic extent, and it was assessed in the portal venous phase for extrapancreatic extent.<sup>4,16</sup> Reader confidence on the longitudinal tumor extent was recorded on the 3-point Likert scale as follows: 0, 50%–75% confidence; 1, 76%–90% confidence; and 2, >90% confidence.<sup>17</sup> The location of the biliary stent was also recorded in each segment of the biliary tree to evaluate the effect of the biliary stent on the CT assessment.

### Magnetic resonance imaging analysis

When preoperative MRI was performed, the patients were divided into two subgroups according to the timing of MRI with respect to BD to compare the performance of MRI obtained pre- and post-BD. MRI scans were retrospectively and independently reviewed by two readers (S.B.C., a radiology resident, and J.P., a board-certified abdominal radiologist with one year of practice experience) who were blinded to the surgical and pathological findings. Moreover, tumor involvement was evaluated in the same manner as in the CT scan evaluation. Additional consideration was included for mild-to-moderate hyperintensity on T2-weighted images, intraductal filling defects due to a soft tissue mass using MR cholangiopancreatography, and high signal intensity of wall thickening or intraductal mass on high *b* value diffusion-weighted imaging.<sup>4,18</sup> The presence or absence of a tumor in each segment, location of the biliary stent (if obtained after BD), and reader confidence were recorded.

### Reference standard

The reference standard was determined by the surgical and pathological reports. Additionally, pathological reports were correlated with preoperative CT or MRI scans when necessary to verify the length of biliary tree segments. The presence or absence of tumors in each segment of the biliary tree and the longitudinal tumor extent were summarized using the Bismuth–Corlette classification.

### Statistical analysis

Continuous variables were summarized using either mean with standard deviation or median with interquartile range (IQR), whereas categorical variables were summarized as counts and percentages. Continuous variables were compared using the Wilcoxon signed-rank test and categorical variables by chi-squared test, according to data normality. After pooling all segments of the biliary tree in all patients, the biliary segment-wise sensitivity, specificity, and accuracy of CT scans for detecting tumors were estimated using the generalized estimating equation (GEE) method. The GEE method was used to compare the estimates, considering that the segments were nested within each patient. The comparison was also performed for segments with and without a catheter. The Bismuth–Corlette classification and reader confidence were compared using the McNemar test. Inter-reader agreement for the Bismuth–Corlette classification in each reading session was assessed using Cohen  $\kappa$  statistics. In the subgroup of patients who underwent MRI, the biliary segment-wise performance of MRI for detecting tumors was compared between patients who underwent MRI pre-BD and those who underwent MRI post-BD using the GEE. Inter-reader agreement for the Bismuth–Corlette classification on MRI was assessed using Cohen  $\kappa$  statistics. Moreover, *P* values were adjusted for multiple comparisons using the Bonferroni correction, and a two-sided *P* value of less than 0.05 indicated statistical significance. The R package (version 4.2.2; The R Foundation for Statistical Computing, Vienna, Austria) was used for analyses.

## Results

### Patient characteristics

A total of 105 patients [mean age: 67 ± 8 years; 74 men (70.5%) and 31 women (29.5%)] were included in this study (Table 1). Among the patients, 64 (61.0%) had distal cholangiocarcinoma, and 41 (39.0%)

had perihilar cholangiocarcinoma. Furthermore, BD was performed using endoscopic retrograde cholangiopancreatography in most patients (83.8%). Among the perihilar cholangiocarcinoma cases, Bismuth types I (26.8%) and IV (24.4%) were the most common. Pylorus-preserving pancreaticoduodenectomy was most commonly performed in patients with distal cholangiocarcinoma (98.4%), and hepatectomy was most commonly performed in those with perihilar cholangiocarcinoma (51.2%). Moreover, the median time interval between pre-BD CT and BD was 3 days (IQR, 1–9 days), and that between CT pre- and post-BD was 30 days (IQR, 18–40 days). The median time interval between pre-BD CT and surgery was 38 days (IQR, 28–57 days), and that between post-BD CT and surgery was 7 days (IQR, 2–23 days). Arterial phase CT images were available in 81 (77.1%) pre-BD and in 69 (65.7%) post-BD, with no statistical differences in the frequency (*P* = 0.182).

The MRI subgroup included 85 patients: 55 underwent MRI pre-BD [median time interval between MRI and BD, 1 day (IQR, 0–4 days)], and the remaining underwent MRI post-BD [median time interval between MRI and BD, 1 day (IQR, 1–3 days)]. Most MRIs (90.6%) were performed using contrast media, either a hepatobiliary (63.5%) or extracellular (27.1%) contrast agent. The median time interval between MRI and surgery was 33 days (IQR, 26–52 days), which was shorter than that between pre-BD CT and surgery (*P* < 0.001).

### Diagnostic performance of computed tomography

In all biliary segments, the performance for tumor detectability using both pre- and post-BD CTs was superior to post-BD CT and comparable with pre-BD CT for both readers (Table 2). The sensitivity and specificity for detecting the tumor segment were higher using both pre- and post-BD CTs than using post-BD CT alone (reader 1: sensitivity, 72.6% vs. 64.6%, *P* < 0.001; specificity, 96.9% vs. 94.8%, *P* = 0.063; reader 2: sensitivity, 77.2% vs. 72.9%, *P* = 0.126; specificity, 97.5% vs. 94.2%, *P* = 0.003). In biliary segments with a catheter in the lumen, the sensitivity was higher using both pre- and post-BD CTs than using post-BD CT. Moreover, the specificity was higher in reader 2 using both CTs, reducing the overestimation of the longitudinal tumor extent (reader 1: sensitivity, 74.4% vs. 67.5%, *P* = 0.006; specificity, 92.4% vs. 88.0%, *P* = 0.068; reader 2: sensitivity, 80.5% vs. 74.4%, *P* = 0.013; specificity, 94.3% vs. 88.0%,

for the Bismuth–Corlette classification was almost perfect using MRI ( $\kappa = 0.85$ ).

## Discussion

The accurate evaluation of surgical resectability is crucial in EHD cancer; however, BD poses limitations in the assessment of the longitudinal tumor extent. This study investigated the diagnostic performance of evaluating the longitudinal extent of EHD cancer after BD based on the recent KSAR consensus recommendations. It also explored the best strategy to improve CT performance in the preoperative setting. In 105 patients, reading pre-BD CT scans or the combined reading of pre- and post-BD CT scans showed better diagnostic performance than reading post-BD CT scans alone, which was supported by significantly higher reader confidence. In a subgroup of 85 patients, MRI performance was compared between those who underwent MRI pre- and post-BD, and no significant difference was found in diagnostic performance, which was similar to that of the combined CT reading.

The biliary segment-wise performance for tumor detectability was higher when both pre- and post-BD CT scans were considered compared with post-BD CT alone. These results may be attributed to the overestimation of the longitudinal tumor extent owing to post-BD cholangitis, which contributes to wall thickening and enhancement on CT scans.<sup>19–21</sup> Catheter-related beam-hardening artifacts from BD may also obscure the tumor, causing challenges in the evaluation.<sup>14,22</sup> In a previous study, the acquisition of CT post-BD was associated with decreased R0 resection rates in EHD cancer in comparison with the acquisition of CT pre-BD, which led to poorer survival rates in patients who underwent CT post-BD.<sup>12</sup> The results of that study are reinforced by the limited performance of post-BD CT scans in this study. The head-to-head comparison of the performance between pre-BD CT and post-BD CT corroborates the previous observation that the evaluation of secondary biliary confluence was less accurate in patients who underwent CT after BD than those who underwent CT before BD.<sup>13</sup> Moreover, in the biliary segment where the drainage catheter was located, post-BD CT alone showed a particularly decreased specificity. Therefore, considering pre-BD CT scans is useful for the accurate evaluation of surgical resectability even after BD.

For the Bismuth–Corlette classification evaluated on CT scans, all reading sessions showed accuracies of 66.7%–74.3%. This

**Table 1.** Clinicopathological characteristics of patients with extrahepatic bile duct cancer

Variable	Total (n = 105)	Perihilar (n = 41)	Distal (n = 64)
Age at the time of surgery (y), mean $\pm$ SD	67 $\pm$ 8	67 $\pm$ 7	68 $\pm$ 8
Male/female	74 (70.5)/31 (29.5)	33 (80.5)/8 (19.5)	41 (64.1)/23 (35.9)
<b>Biliary decompression method</b>			
PTBD	17 (16.2)	7 (17.1)	10 (15.6)
ERCP	88 (83.8)	34 (82.9)	54 (84.4)
<b>Bismuth–Corlette classification</b>			
I	NA	11 (26.8)	NA
II	NA	9 (22.0)	NA
IIIA	NA	7 (17.1)	NA
IIIB	NA	4 (9.8)	NA
IV	NA	10 (24.4)	NA
<b>Type of surgery</b>			
PPPD	75 (72.4)	12 (29.3)	63 (98.4)
Hepatectomy	21 (20.0)	21 (51.2)	0 (0.0)
Segmental resection of bile duct	5 (4.8)	4 (9.8)	1 (1.6)
Segmental resection of bile duct with hepatectomy	3 (2.9)	3 (7.3)	0 (0.0)
Hepatopancreatoduodenectomy	1 (1.0)	1 (2.4)	0 (0.0)
<b>Resection margin status</b>			
R0	64 (61.0)	20 (48.8)	44 (68.8)
R1	41 (39.0)	21 (51.2)	20 (31.3)
<b>Pathologic grade</b>			
Well differentiated	12 (11.4)	4 (9.8)	8 (12.5)
Moderately differentiated	71 (67.6)	27 (65.9)	44 (68.8)
Poorly or undifferentiated	22 (21.0)	10 (24.4)	12 (18.8)

Data are presented as numbers of patients with percentages in parentheses unless otherwise specified. SD, standard deviation; PTBD, percutaneous transhepatic biliary drainage; ERCP, endoscopic retrograde cholangiopancreatography; PPPD, pylorus-preserving pancreaticoduodenectomy; NA, not applicable.

$P = 0.016$ ) (Figures 2, 3). In biliary tree segments without a catheter, the sensitivity was higher using both pre- and post-BD CTs than using post-BD CT for reader 1 (sensitivity, 67.1% vs. 55.7%,  $P = 0.001$ ; specificity, 98.9% vs. 97.8%,  $P = 0.156$ ), yet remained comparable for reader 2 (sensitivity, 67.1% vs. 68.4%,  $P = 0.763$ ; specificity, 98.9% vs. 96.9%,  $P = 0.019$ ).

The Bismuth–Corlette classification was comparable among the three reading sessions (all  $P$ s  $> 0.05$  for both readers), but there were fewer cases of overestimating the Bismuth–Corlette classification using pre-BD CT or both pre- and post-BD CTs than using post-BD CT alone (reader 1: 4.8% vs. 11.4% vs. 13.3%; reader 2: 6.7% vs. 12.4% vs. 16.2%) (Table 3). Both readers performed one incorrect classification using post-BD CT but none using pre-BD CT or both CTs (Figure 3). Inter-reader agreement for the Bismuth–Corlette classification in each reading session was substantial ( $\kappa = 0.67$  using pre-BD CT,  $\kappa = 0.71$

using both pre- and post-BD CTs,  $\kappa = 0.79$  using post-BD CT).

Reader confidence was significantly higher using pre-BD CT or both CTs than using post-BD CT, with a higher proportion of  $>90\%$  reader confidence (reader 1: 64.8–65.7% vs. 13.3%; reader 2: 81.0–87.6% vs. 6.7%,  $P < 0.001$  for both readers) (Table 4).

### Diagnostic performance of magnetic resonance imaging

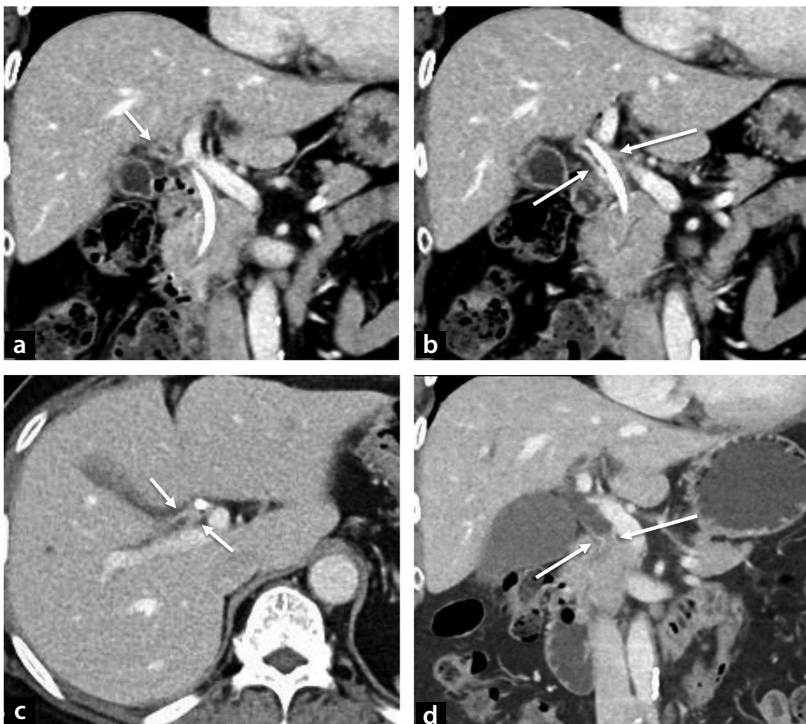
The performance for tumor detectability was not significantly different between pre- and post-BD MRIs (Supplementary Table S1, Supplementary Figures S1, S2). Post-BD MRI scans exhibited a comparable performance with pre-BD MRI scans, but the pre-BD MRI was minimally superior (reader 1: sensitivity, 77.9% vs. 75.0%,  $P = 0.605$ ; specificity, 97.2% vs. 94.9%,  $P = 0.256$ ; reader 2: sensitivity, 73.2% vs. 72.6%,  $P = 0.926$ ; specificity, 98.4% vs. 94.9%,  $P = 0.068$ ). Inter-reader agreement



**Table 2.** Diagnostic performance of CT scans for determining the longitudinal extent of the extrahepatic bile duct cancer

Reader	Examined biliary segment	Pre-BD (A)	Pre- and post-BD (B)	Post-BD (C)	<i>P</i> (A vs. B)	<i>P</i> (B vs. C)	<i>P</i> (C vs. A)
<b>Sensitivity (%)</b>							
1	All segments	72.6 (67.8–77.5)	72.6 (67.8–77.5)	64.6 (59.4–69.8)	>0.999	<0.001	<0.001
	Segments with a catheter	NA	74.4 (68.9–79.8)	67.5 (61.6–73.3)	NA	0.006	NA
	Segments without a catheter	NA	67.1 (56.7–77.5)	55.7 (44.7–66.7)	NA	0.001	NA
2	All segments	72.9 (68.1–77.8)	77.2 (72.7–81.8)	72.9 (68.1–77.8)	0.114	0.126	>0.999
	Segments with a catheter	NA	80.5 (75.5–85.4)	74.4 (68.9–79.8)	NA	0.013	NA
	Segments without a catheter	NA	67.1 (56.7–77.5)	68.4 (58.1–78.6)	NA	0.763	NA
<b>Specificity (%)</b>							
1	All segments	97.7 (96.4–99.0)	96.9 (95.4–98.4)	94.8 (92.8–96.7)	0.471	0.063	0.015
	Segments with a catheter	NA	92.4 (88.3–96.5)	88.0 (82.9–93.1)	NA	0.068	NA
	Segments without a catheter	NA	98.9 (97.8–100.0)	97.8 (96.2–99.3)	NA	0.156	NA
2	All segments	96.7 (95.2–98.2)	97.5 (96.1–98.8)	94.2 (92.2–96.2)	0.855	0.003	0.069
	Segments with a catheter	NA	94.3 (90.7–97.9)	88.0 (82.9–93.1)	NA	0.016	NA
	Segments without a catheter	NA	98.9 (97.8–100.0)	96.9 (95.1–98.7)	NA	0.019	NA
<b>Accuracy (%)</b>							
1	All segments	88.0 (85.8–90.2)	87.5 (85.3–89.7)	83.1 (80.6–85.6)	1.515	<0.001	<0.001
	Segments with a catheter	NA	81.4 (77.6–85.2)	75.5 (71.3–79.7)	NA	0.001	NA
	Segments without a catheter	NA	93.1 (90.7–95.5)	90.1 (87.3–92.9)	NA	0.001	NA
2	All segments	87.5 (85.3–89.7)	89.6 (87.6–91.7)	86.0 (83.6–88.3)	0.060	<0.001	0.600
	Segments with a catheter	NA	85.9 (82.5–89.3)	79.7 (75.8–83.6)	NA	0.001	NA
	Segments without a catheter	NA	93.1 (90.7–95.5)	91.7 (89.2–94.3)	NA	0.179	NA

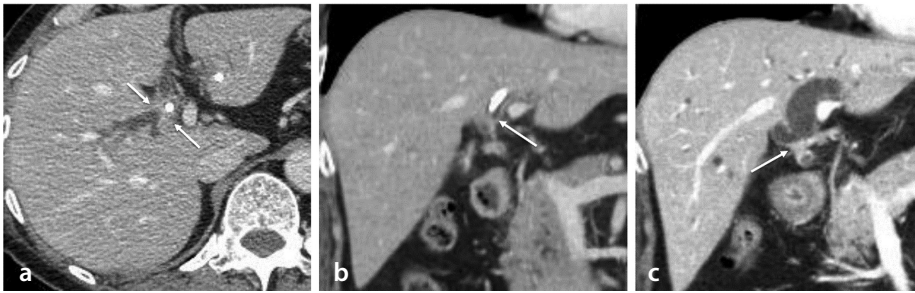
Data are performance measures with 95% confidence intervals in parentheses. CT, computed tomography; BD, biliary drainage; NA, not applicable.



**Figure 2.** Overestimation of the longitudinal extent of distal cholangiocarcinoma after biliary drainage (BD) in a 68-year-old woman. (a–c) Coronal (a, b) and axial (c) portal venous phase computed tomography (CT) images obtained one month after BD showing diffuse enhancing wall thickening (arrows) of common bile duct (CBD), common hepatic duct, primary biliary confluence, and right hepatic duct. Both readers assessed the tumor as a Bismuth–Corlette type II hilar cholangiocarcinoma using post-BD CT scan. (d) Coronal portal venous phase CT image obtained before BD depicting segmental wall thickening and luminal narrowing of the intra- and supra-pancreatic CBD (arrow). Therefore, both readers correctly determined that the tumor was a distal cholangiocarcinoma using both pre- and post-BD CT scans.

result is similar to the previously reported CT accuracy for the longitudinal tumor extent, which ranged between 56.3%–74.1%.<sup>23</sup> When both CT scans were considered, there were fewer cases of overestimation compared with using post-BD CT scans alone. This can be attributed to the limited performance of post-CT scans in differentiating between tumors and inflammation caused by BD.<sup>11</sup> Moreover, reader confidence was higher when both CT scans were considered. Therefore, when evaluating the longitudinal tumor extent using post-BD CT scans, considering pre-BD CT scans, whenever available, may improve the diagnostic performance of CT scans. Furthermore, inter-reader agreement for the Bismuth–Corlette classification was substantial for CT readings, either pre-BD or post-BD, which was comparable with the results of a prior study.<sup>23</sup> These results may be explained by the standardized evaluation of biliary tree segments based on the radiologic consensus guidelines, which supports the structured reporting approach.

A recent study showed that the performance of CT and MRI was comparable before BD for the resectability evaluation of EHD cancer.<sup>6</sup> Of note, MRI scan performance did not significantly decrease after BD in this study in contrast with the CT scan perfor-



**Figure 3.** Overestimation of the longitudinal extent of Bismuth–Corlette type IIIA perihilar cholangiocarcinoma after biliary drainage (BD) in a 64-year-old man. (a, b) Axial (a) and coronal (b) portal venous phase computed tomography (CT) images obtained one month after BD showing diffuse enhancing wall thickening (arrows) of the hilar bile duct extending to both hepatic ducts. Both readers assessed the tumor as a Bismuth–Corlette type IIIB hilar cholangiocarcinoma using post-BD CT scan (incorrect assessment), which was probably attributable to cholangitis extending to the left hilar bile duct. (c) Coronal portal venous phase CT image obtained before BD depicts segmental wall thickening and luminal narrowing of the hilar bile duct with the proximal end at the primary biliary confluence (arrow). Therefore, both readers decided that the tumor was a Bismuth–Corlette type II using both pre- and post-BD CT scans (underestimation). The involvement of the right secondary biliary confluence was not detected on the pre-BD CT scan, which was probably because of microscopic tumor extension.

**Table 3.** Results of the Bismuth–Corlette classification using CT scans

	Pre-BD (A)	Pre- and post-BD (B)	Post-BD (C)	P		
				A vs. B	B vs. C	C vs. A
<b>Reader 1</b>						
Overestimation	5 (4.8)	12 (11.4)	14 (13.3)	0.390	>0.999	0.864
Correct	78 (74.3)	70 (66.7)	70 (66.7)			
Underestimation	22 (21.0)	23 (21.9)	20 (19.1)			
Incorrect <sup>a</sup>	0 (0.0)	0 (0.0)	1 (1.0)			
<b>Reader 2</b>						
Overestimation	7 (6.7)	13 (12.4)	17 (16.2)	>0.999	>0.999	0.405
Correct	76 (72.4)	72 (68.6)	73 (69.5)			
Underestimation	22 (21.0)	20 (19.1)	14 (13.3)			
Incorrect <sup>a</sup>	0 (0.0)	0 (0.0)	1 (1.0)			

Data are numbers of patients with percentages in parentheses. <sup>a</sup>Bismuth type IIIA determined as IIIB or vice versa. CT, computed tomography; BD, biliary drainage.

**Table 4.** Comparison of reader confidence

	Pre-BD (A)	Pre- and post-BD (B)	Post-BD (C)	P		
				A vs. B	B vs. C	C vs. A
<b>Reader 1</b>						
50%–75%	4 (3.8)	6 (5.7)	57 (54.3)	>0.999	<0.001	<0.001
76%–90%	33 (31.4)	30 (28.6)	34 (32.4)			
>90%	68 (64.8)	69 (65.7)	14 (13.3)			
<b>Reader 2</b>						
50%–75%	1 (1.0)	0 (0.0)	42 (40.0)	0.723	<0.001	<0.001
76%–90%	12 (11.4)	20 (19.1)	56 (53.3)			
>90%	92 (87.6)	85 (81.0)	7 (6.7)			

Data are numbers of patients with percentages in parentheses. BD, biliary drainage.

performance. This is probably because of the higher contrast resolution of the bile duct lumen and wall on MRI scans than on CT scans.<sup>24</sup> Moreover, there was no significant difference in the diagnostic performance between MRI

scans obtained pre- and post-BD, and the sensitivity, specificity, and accuracy were similar to those of the combined reading of pre- and post-BD CT scans. The previous study by Chrissy et al.<sup>15</sup> observed a tenden-

cy toward overestimating the tumor extent after BD on MRI. However, this study, which recruited a larger number of patients, observed a comparably accurate performance of MRIs pre- and post-BD, approaching the reported near-perfect performance of pre-BD MRI.<sup>25</sup> Hence, it was assumed that even when MRI is performed after an urgent BD, there would be no significant difference in the diagnostic performance. In addition, the almost perfect inter-reader agreement for the Bismuth–Corlette classification on MRI indicates the benefits of radiologic consensus guidelines. However, another study using pre-BD MRI observed only moderate agreement for four readers, which may better reflect the real world.<sup>6</sup>

This study had some limitations. First, a selection bias might have been introduced in the surgical cohort. However, evaluating the longitudinal tumor extent would be more challenging in resectable cancers than in advanced cancers with higher T stages. Second, the validity of surgical and pathological reference standards can be suboptimal in patients with R1 resection margin status. However, the effect would be small in patients where R1 resection margins are attributable to the circumferential margin instead of the ductal margin. Third, multiphasic CT was less frequently performed after BD, albeit statistically insignificant, because single-phase CT was a preferred modality for follow-up imaging due to a lower radiation dose. This might have affected post-BD CT performance for tumors involving intrapancreatic CBD. Fourth, the diagnostic performance of pre- and post-BD MRI could not be compared in the same patient. This was because CT was the preferred imaging modality for EHD cancer, and no patient underwent MRI both pre- and post-BD. Fifth, the interval between MRI and surgery was shorter than that between pre-BD CT and surgery because MRI was the secondary imaging modality performed after CT. Nonetheless, the median interval showed approximately a one-week difference, and the longitudinal tumor extent could not have changed significantly during this interim period.<sup>26</sup> Lastly, the study results might not be generalizable to patients who undergo preoperative chemotherapy or radiotherapy, as preoperative treatment would affect the longitudinal tumor extent.

In conclusion, the consideration of pre-BD CT scans provided better diagnostic performance than reading post-BD CT scans alone. Therefore, the acquisition of pre-BD CT would be beneficial for the preoperative evaluation of EHD cancer when BD is

planned. Moreover, MRI evaluation would not be significantly affected by BD in terms of the diagnostic performance of the longitudinal tumor extent.

### Conflict of interest disclosure

The authors declared no conflicts of interest.

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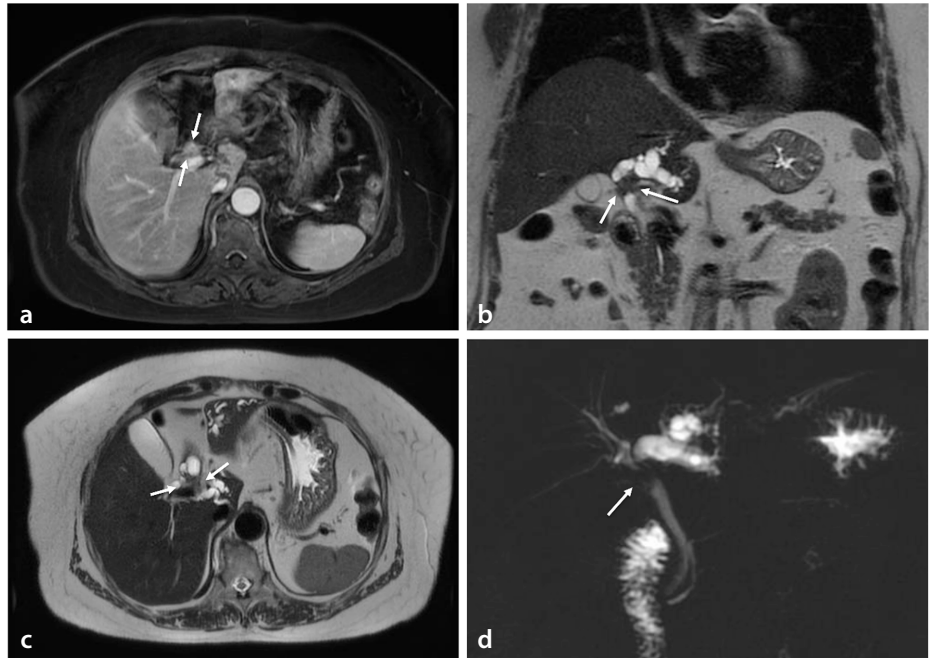
**Supplementary Table S1.** Diagnostic performance of MRI scans in determining longitudinal extent of extrahepatic bile duct cancer

Reader	Sensitivity (%)		P	Specificity (%)		P	Accuracy (%)		P
	Pre-BD MRI	Post-BD MRI		Pre-BD MRI	Post-BD MRI		Pre-BD MRI	Post-BD MRI	
1	77.9 (72.0–83.8)	75.0 (65.7–84.3)	0.605	97.2 (95.2–99.3)	94.9 (91.4–98.3)	0.256	88.9 (85.9–91.8)	87.9 (83.8–92.0)	0.256
2	73.2 (66.9–79.5)	72.6 (63.1–82.2)	0.926	98.4 (96.8–100.0)	94.9 (91.4–98.3)	0.068	87.5 (84.4–90.6)	87.1 (82.8–91.3)	0.876

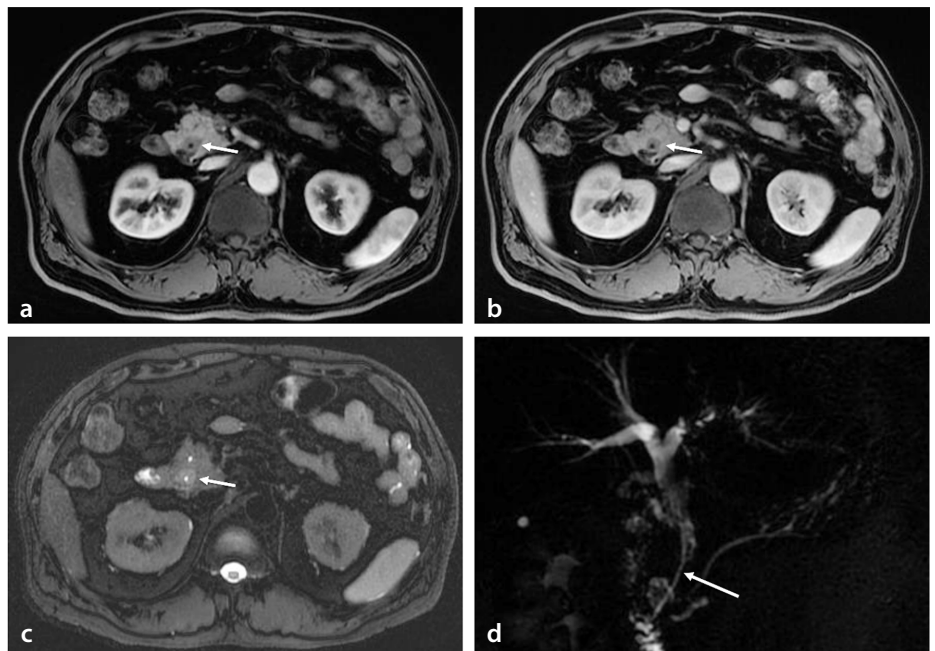
Data are performance measures in percentages, with 95% confidence intervals in parentheses. MRI, magnetic resonance imaging; BD, biliary drainage.



**Online Resource 1.** Magnetic resonance imaging (MRI) acquisition. For MRI acquisition, either a 1.5-T (Intera Achieva, Philips Medical Systems, Best, Netherlands) or 3.0-T scanner (Magnetom Trio Tim, Siemens Medical Solutions, Erlangen, Germany; Intera Achieva or Ingenia, Philips Medical Systems, Best, Netherlands; Discovery MR750w MRI unit, GE Medical Systems, Waukesha, Wisconsin, U.S.A.) with a 4-, 16-, or 32-channel torso-array coil was used. A breath-hold axial T1-weighted dual-echo gradient-recalled echo sequence was used for pre-contrast T1 images. T2-weighted single- or multi-shot turbo spin-echo with or without spectral fat suppression was performed either before or after contrast use. Magnetic resonance cholangiopancreatography was performed with a two-dimensional thick-slab single-shot turbo spin-echo or three-dimensional T2-weighted respiratory-triggered fast spin-echo sequence using the navigator technique. Dynamic contrast-enhanced T1-weighted imaging was performed after administration of either a hepatobiliary or extracellular contrast agent (Primovist, gadoxetic acid, Bayer Schering Pharma, Berlin, Germany; Dotarem, gadoterate meglumine, Guerbet, France). The contrast was injected as 0.1 mL/kg of Primovist bolus injection at a rate of 1 mL/sec or 0.2 mL/kg of Dotarem at a rate of 1 or 2 mL/sec, followed by 20 mL of saline flush. Arterial phase timing was determined using the test-bolus or bolus tracking method, 2-5 sec after peak aorta enhancement. Portal venous phase (50-60 sec) and delayed or transitional (2-3 min) phase images were obtained. Hepatobiliary phase (15-20 min) images were obtained using gadoxetic acid. Diffusion-weighted imaging was performed at b values of 0 or 50, 400, and 800 s/mm<sup>2</sup>.



**Supplementary Figure S1.** MRI evaluation of perihilar cholangiocarcinoma before biliary drainage in a 80-year-old woman. (a-c) Axial (a) T1-weighted fat-suppressed image in portal venous phase, and coronal (b) and axial (c) T2-weighted images show segmental enhancing wall thickening (arrows) of common hepatic duct, extending to primary biliary confluence, and left secondary biliary confluence. (d) Two-dimensional magnetic resonance cholangiopancreatography shows a filling defect (arrow) in biliary tree by the tumor, with dilatation of left intrahepatic bile ducts. Both readers correctly assessed the tumor as Bismuth-Corlette type IIIb perihilar cholangiocarcinoma. MRI, magnetic resonance imaging.



**Supplementary Figure S2.** MRI evaluation of distal cholangiocarcinoma after biliary drainage in a 61-year-old man. (a-c) Axial T1-weighted fat-suppressed image in arterial phase (a) and portal venous phase (b), and axial T2-weighted fat-suppressed image (c) show segmental enhancing wall thickening (arrow) of intrapancreatic CBD, and biliary stent in the center. (d) Two-dimensional magnetic resonance cholangiopancreatography shows biliary stent (arrow) located at common hepatic duct to intrapancreatic CBD, with upstream biliary tree dilatation. Both readers correctly determined the longitudinal tumor extent as distal cholangiocarcinoma. CBD, common bile duct; MRI, magnetic resonance imaging.