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Radiologic Evaluation and Structured Reporting Form for Extrahepatic Bile Duct Cancer: 2019 Consensus Recommendations from the Korean Society of Abdominal Radiology

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Radiologic imaging is important for evaluating extrahepatic bile duct (EHD) cancers; it is used for staging tumors and evaluating the suitability of surgical resection, as surgery may be contraindicated in some cases regardless of tumor stage. However, the published general recommendations for EHD cancer and recommendations guided by the perspectives of radiologists are limited. The Korean Society of Abdominal Radiology (KSAR) study group for EHD cancer developed key questions and corresponding recommendations for the radiologic evaluation of EHD cancer and organized them into 4 sections: nomenclature and definition, imaging technique, cancer evaluation, and tumor response. A structured reporting form was also developed to allow the progressive accumulation of standardized data, which will facilitate multicenter studies and contribute more evidence for the development of recommendations.

Keywords: Extrahepatic bile duct cancer; Common bile duct neoplasms; Klatskin tumor; Structured reporting form; Consensus

INTRODUCTION

Extrahepatic bile duct (EHD) cancer is an uncommon devastating disease. It is more common among Asians, and its incidence is approximately between 0.5 to 2 cases/100000 person-years (1-3). The only curative treatment for EHD cancer is surgical resection. Surgery for EHD cancer is complex due to the need for a wide surgical field; consequently, comprehensive preoperative evaluations of tumor extent, major vessel involvement, and remnant liver function, among others, are prerogative (2, 4). If curative surgical resection is not possible, palliative treatment such as systemic chemotherapy and/ or radiotherapy is recommended over cytoreductive surgery

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(2). An accurate preoperative imaging assessment is critical for the prevention of unnecessary procedures and successful RO resection. Guidelines for EHD cancer that have been confirmed by national organizations or expert groups are limited because of its low incidence and an insufficient amount of evidence from studies. Most of the existing guidelines do not focus on EHD cancer only; they cover intrahepatic cholangiocarcinoma and EHD cancer or gallbladder cancer, which require different staging systems and treatment methods, and have different prognoses. Although some guidelines cover diagnostic imaging, the presented recommendations are general guidelines for diagnosis, treatment, and prognosis, and they are not concerned with specific technical aspects or diagnostic criteria for evaluating EHD cancer (4). Recently, the Korean Society of Abdominal Radiology (KSAR) developed consensus recommendations on controversial issues in abdominal radiology (5-7). South Korea has a high incidence of EHD cancer, and consequently, many of the KSAR members have gained extensive experience in the evaluation of EHD cancer. Hence, the KSAR study group for EHD cancer leveraged the pool of experts and developed consensus recommendations focused on the imaging-driven diagnosis of EHD cancer. Structured reporting forms can also visualize the essential characteristics that need to be evaluated on imaging, which allow easy and accurate communication between multidisciplinary team members and straightforward collection and analysis of uniform reporting data. Until now, there had been no unanimously accepted structured reporting forms for EHD cancer due to its complexity; in the few that were suggested, reporting categories were descriptive rather than specific (8). The KSAR study group for EHD cancer also presented a ready-touse structured reporting form for EHD cancer based on its consensus recommendations.

MATERIALS AND METHODS

Organization and Overall Workflow of the KSAR Study Group for EHD Cancer

The KSAR study group for EHD cancer was composed of 13 board-certified abdominal radiologists from eight tertiary hospitals in South Korea. All of the radiologists were KSAR members, and they were experienced with biliary images from CT, MRI, and ultrasonography. Each member was assigned to one of four subgroups that focused on subjects related to EHD cancer: 'Nomenclature and definition,' 'Imaging technique,' 'Cancer evaluation,' and 'Tumor response.' Each subgroup searched and evaluated the references, and they developed and refined key questions and statements. The first subgroup was tasked with determining appropriate nomenclature and definitions, which would be used throughout the consensus recommendations. The second subgroup was tasked with ascertaining the usefulness and effectiveness of different imaging modalities for evaluating EHD cancer. The third subgroup focused on the approaches for evaluating EHD cancer using imaging studies, while the last subgroup was tasked with developing guidelines on tumor response after treatment. Key questions and statements were developed through discussions that took place within each study group and between the subgroups.

Literature Search

We searched for reference articles using Medline (PubMed). Literature searches were carried out by a radiologist and a subject specialist librarian. Before performing the literature search, we classified the candidate issues into four sections, which were nomenclature and definition, imaging technique, cancer evaluation, and tumor response. One to five members were assigned to each section as investigators, and they performed the literature review, developed key questions and statements, analyzed the voting results, and wrote a draft of consensus recommendations for their assigned sections. Because various terms have been used for EHD cancer, a sensitive search query was developed to ensure that no relevant articles were missed. The search query used ("Klatskin Tumor"[Mesh]) OR (Hilar Cholangiocarcinoma*[TIAB] OR Perihilar Cholangiocarcinoma*[TIAB] OR Klatskin Tumor*[TIAB]) OR ("Common Bile Duct Neoplasms"[Mesh]) OR ((("Common bile duct" [TIAB] OR "Common hepatic duct"[TIAB]) AND (cancer[TIAB] OR Neoplasm*[TIAB] OR Carcinoma*[TIAB] OR Cholangiocarcinoma*[TIAB])) OR "CBD-cancer"[TIAB]) OR ("Bile Ducts, Extrahepatic"[Mesh] AND "Bile Duct Neoplasms" [Mesh]) OR ((Extrahepatic[TIAB] OR Extra-hepatic[TIAB]) AND ("Bile duct"[TIAB] OR "Bile ducts"[TIAB]) AND (cancer[TIAB] OR Neoplasm*[TIAB] OR Carcinoma*[TIAB] OR Cholangiocarcinoma*[TIAB])). After searching 10420 eligible articles for patients with EHD cancer, additional literature searches were done for the four specific sections. The specific search queries are summarized in Supplementary Table 1. We found 2026 eligible articles: nomenclature and definition (n = 277),

imaging technique (n = 1092), cancer evaluation (n = 416), and tumor response (n = 241). All investigators of the KSAR study group for EHD cancer assessed potentially relevant articles for eligibility. The decision to include or exclude a study was hierarchical, and it was initially based on the study title, followed by the abstract and finally the complete manuscript.

Drafting Key Questions and Statements and Initial Presentation

In each section, key questions essential to the imaging evaluation of EHD cancer were developed, and the assigned members brainstormed for all possible recommendations for each key question. Initially, 64 recommendation statements were developed, and they were presented at the annual KSAR meeting on April 26, 2019, with approximately 120 participating KSAR members. The reasons for developing consensus recommendations for EHD cancer and the first draft of statements to be included in the KSAR recommendations were presented at this meeting. An open discussion followed, and all KSAR members commented on each statement and the approach used to develop the consensus recommendations.

Amendment of Key Questions

Statements were refined after the annual KSAR member meeting, followed by offline and online group meetings. Duplicated or redundant items were deleted or merged, and items deemed essential for the imaging evaluation of EHD cancer were maintained. Finally, 13 key questions with 24 statements were chosen.

Development of a Structured Reporting Form

Imaging studies are essential for initial decisions on patients with EHD cancer by radiologists. Although most radiologists currently do freestyle dictation to report imaging findings, it is limited by inter-reader variability, non-standardized descriptive terms, and possible omission of key findings, among others. Therefore, there is an increasing clinical need for structured reporting forms. Several societies have suggested structured reporting forms for pancreas cancer and rectal cancer (5, 9-11). However, no structured reporting forms have been published for EHD cancer, from the perspective of radiologists, with special emphasis on consistent terminology and image interpretation. Therefore, the KSAR study group for EHD cancer was determined to develop a structured reporting form for EHD cancer based on key questions and corresponding recommendation statements.

Agreement Voting

After the key questions and statements were finalized, a consensus voting for all statements was held at the KSAR annual organ-based meeting on July 20, 2019. Before voting, participants were asked about their experience in biliary imaging, and only the results of those who had more than two years of experience were used for the analysis. The six-point modified Delphi method was used to collect the opinions of the participants. The participants replied to each statement using one of six choices: "strongly agree," "agree with minor reservations," "agree with major reservations," "disagree with minor reservations," "disagree with major reservations," and "strongly disagree" (7). If more than 80% of the participants with more than 2 years of experience in biliary imaging chose "strongly agree" or "agree with minor reservations" for a given statement, it was considered to have reached consensus. Additionally, two issues on the structured reporting form were heavily debated within the KSAR study group before the annual meeting, and participants voted on their inclusion in the consensus recommendations.

Determination of Evidence Level

After a consensus was reached on all statements, relevant literature was reviewed again by the KSAR study group for EHD cancer, and the evidence level of each statement was graded based on the criteria of the Oxford Centre for Evidence-Based Medicine from I (highest) to V (lowest) (12, 13).

RESULTS

Voting Results

Among the KSAR members who voted on each statement (mean: n = 79; range: 74–91), approximately 90% (n = 71; range: 67–79) had more than two years of experience in biliary imaging. After voting, 23 of 24 statements reached consensus (Table 1). For the structured reporting form, the two heavily debated issues did not reach consensus, and they were not included in the final structured reporting form. The first issue, "Length of main portal vein (MPV) invasion should be included in the structured form," got an agreement of 51.4%; thus, it was excluded from the structured reporting form. The length of MPV invasion is



Table 1. Consensus Key Questions and Recommendation Statements

Key Questions and Recommendation Statements	Agreement Level
Section 1. Nomenclature and definition	
KQ 1. What are the criteria for classifying perihilar bile duct cancer and distal bile duct cancer?	
S1. EHD cancer can be classified as perihilar bile duct cancer or distal bile duct cancer based on the insertio	on 80.0%
site of the cystic duct.	09.970
KQ 2. How is the gross morphology of EHD cancer categorized?	
S2. EHD cancer can be classified into the mass-forming, periductal-infiltrating, or intraductal-growing type	02 5%
based on growth patterns.	52.570
Section 2. Imaging technique	
KQ 3. Which imaging modality is recommended for patients suspected of EHD cancer, and when do we perform a imaging study if biliary intervention is needed?	an
S3. Contrast-enhanced CT and/or contrast-enhanced MRI with MRCP are recommended to evaluate EHD cance	er. 100%
S4. Imaging studies are recommended before any biliary interventional procedure whenever possible.	98.6%
KQ 4. What is the optimal CT protocol to evaluate EHD cancer?	
S5. Multiphase imaging, which includes the precontrast, arterial, and portal venous phase, is recommended.	97.1%
S6. A slice thickness of 3 mm or less is recommended.	95.7%
S7. Multiplanar reconstruction can aid the evaluation of relationships between EHD cancer and adjacent structures.	98.6%
S8. Including the pelvis in at least one phase is recommended.	85.9%
KQ 5. Which MR sequences are needed to evaluate bile duct cancer?	
S9. T1-weighted images, T2-weighted and heavily T2-weighted images, MRCP, and contrast-enhanced dynam	
images are recommended as MR sequences for bile duct cancer.	97.3%
S10. DWIs can help radiologists characterize bile duct lesions and detect extra-bile duct lesions.	89.7%
Section 3. Cancer evaluation	
KQ 6. Which imaging features indicate the presence of EHD cancer?	
S11. On contrast-enhanced CT or MRI, EHD cancer is indicated by irregular ductal wall thickening with upstre	am
ductal dilatation, hyper-enhancement of the ductal wall relative to the liver, and/or obliteration of the	e 100%
lumen by an intraductal soft-tissue mass or thickened ductal wall.	
S12. On cholangiography, EHD cancer is indicated by the abrupt and/or irregular narrowing of the bile duct and irregularly shaped filling defects within the lumen.	94.5%
KQ 7. How is the biliary tree classified when evaluating the longitudinal extent of EHD cancer?	
S13. Longitudinal involvement of EHD cancer can be assessed by classifying the presence/absence of tumor	
involvement in the right secondary confluence, right hepatic duct, primary confluence, left hepatic duc	ct, oo ov
left secondary confluence, common hepatic duct, suprapancreatic common bile duct, and intrapancreat	
common bile duct.	
S14. The Bismuth-Corlette classification is recommended for the imaging assessment of bile duct involvement	t in 97.3%
S15 Provimal and dictal extensions of parihilar hile duct cancer and provimal extensions of dictal hile duct	
cancer are included in the imaging assessment of hile duct involvement	95.8%
K0.8. How do we evaluate tumor vascular invasion on MDCT and MRT for FHD cancer?	
S16. The henatic artery PV and their branches as well as variant henatic vessels should be evaluated for the	
presence of tumor invasion, depending on the anatomic location of the EHD cancer.	97.2%
S17. Tumor vascular invasion is indicated by the tumor encasement of vessels, vessel deformity, occlusion, o tumor thrombus.	or 92.6%
S18. The degree of tumor-vessel contact is classified as no contact (preserved tumor-vessel fat plane), abutm	ent
(tumor involvement up to 50% of the vessel circumference), or encasement (tumor involvement more th	nan 95.7%
50% of the vessel circumference).	
KQ 9. How do we evaluate LN metastasis in EHD cancer?	
S19. LNs are considered suspicious for metastatic involvement if they are greater than 1 cm along the short	02 0%
axis or have abnormal round morphology, heterogeneous enhancement, or central necrosis.	52.570



Table 1. Consensus Key Questions and Recommendation Statements (Continued)

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Key Questions and Recommendation Statements	Agreement Level		
KQ 10. How do we evaluate distant metastasis in EHD cancer?			
S20. MRI or 18F-FDG PET-CT is recommended to evaluate indeterminate or suspicious findings for distant metastasis on CT.	92.6%		
KQ 11. How do we assess the resectability of EHD cancer beyond the tumor staging/extent?			
S21. The future remnant liver volume and biliary/vascular anatomic variations need to be evaluated to determine the resectability of perihilar bile duct cancer.	98.5%		
S22. A multidisciplinary team consultation is recommended when deciding or assessing resectability.	91.7%		
Section 4. Tumor response			
KQ 12. How do we evaluate treatment response through imaging after chemotherapy for patients with EHD cancer?			
S23. Contrast-enhanced CT or contrast-enhanced MRI with MRCP according to the RECIST criteria is recommended	90.5%		

CT = computed tomography, DWI = diffusion-weighted image, EHD = extrahepatic bile duct, KQ = key questions, LN = lymph node, MDCT = multidetector CT, MRCP = MR cholangiopancreatography, MRI = magnetic resonance imaging, PET = positron emission tomography, PV = portal vein, RECIST = response evaluation criteria in solid tumors, S = statements, 18F-FDG = 18F-fluorodeoxyglucose

important in some patients because a shorter invasion of MPV is advantageous for vascular reconstruction. However, it is challenging to measure MPV invasion accurately and consistently with routine axial and coronal reconstructed images. Moreover, in perihilar bile duct cancer, the invasion site of portal vein (PV) (ipsilateral/contralateral PV or MPV) is more important than the length. This may account for the exclusion of this item after it did not reach a consensus.

Subsequently, the final assessment of resectability was excluded from the structured reporting form. The statement, "Final assessment (resectability) should be included in the structured reporting form," was agreed to by only 45.5%. To determine the resectability of EHD cancer, factors such as tumor extent, major vascular invasion, vascular or biliary anatomy, ability to reconstruct vessels, and future remnant liver volume need to be considered. Furthermore, decisions regarding tumor resectability may vary between surgeons and institutions without established criteria. Therefore, we concluded that it would be better not to include a standardized resectability assessment in the structured reporting form for EHD cancer.

Section 1. Nomenclature and Definition

KQ 1. What Are the Criteria for Classifying Perihilar Bile Duct Cancer and Distal Bile Duct Cancer?

Statement 1: EHD cancer can be classified as perihilar or distal based on the insertion site of the cystic duct (agreement level, 89.9%; evidence level, not applicable [n/a]).

The EHD is composed of the right extrahepatic duct, left



Fig. 1. Anatomy of the EHD. EHD = extrahepatic bile duct

extrahepatic duct, common hepatic duct, and common bile duct. Based on the cystic duct insertion site, the EHD can be subdivided into the perihilar area, which includes the right/left extrahepatic duct and the common hepatic duct, and the distal bile duct, which extends from the confluence of the cystic and common hepatic ducts to the ampulla of Vater (excluding the ampulla itself) (Fig. 1) (3, 14-16). EHD cancers originating from these two compartments are marked by various names: 'hilar cholangiocarcinoma' and 'distal cholangiocarcinoma' in National Comprehensive Cancer Network (NCCN) guidelines version 2.2019 (17), 'perihilar (proximal) cholangiocarcinoma' and 'distal bile duct tumors (cancers)' in the 8th American Joint Committee



on Cancer (AJCC) cancer staging manual (18), or 'perihilar bile duct cancer' and 'distal extrahepatic bile duct cancer' in the National Cancer Institute's dictionary (15). The KSAR study group for EHD cancer discussed and agreed to use the terms 'perihilar bile duct cancer' and 'distal bile duct cancer' throughout the consensus recommendations, as these terms were intuitive and consistent for distinguishing the two parts of the EHD. EHD cancer is classified into these two categories because surgical techniques and surgical fields differ significantly between them. Furthermore, the T staging of tumors is also different, probably because the distribution of smooth muscles differs with location (19). The KSAR study group for EHD cancer also discussed how to establish a reference point for classifying the perihilar area and distal bile duct. According to previous studies. only 51-75% of cystic duct insertion sites are located in the middle third of the EHD (20, 21). Therefore, the KSAR members debated on whether dividing the perihilar area and the distal bile duct by the cystic duct insertion site was appropriate even when the cystic duct insertion site was not located in the middle of the EHD. Although new criteria were suggested, the KSAR study group for EHD cancer finally agreed to follow traditional standards, because the location of the cystic duct insertion site is not of clinical importance for treatment plans, and creating a new reference point can also create controversy. Perihilar bile duct cancer can extend into the intrahepatic bile duct or even the liver parenchyma, and EHD cancer may involve both the perihilar area and distal bile duct. In this case, the location of the tumor epicenter can be a reference point for categorization. However, describing the area of tumor involvement is more important because treatment plans are mainly determined based on tumor extent.

KQ 2. How is the Gross Morphology of Extrahepatic Bile Duct Cancer Categorized?

Statement 2: EHD cancer can be classified into the massforming, periductal-infiltrating, or intraductal-growing type based on growth patterns (agreement level, 92.5%; evidence level, n/a).

Because the gross morphology of EHD cancer can present with different imaging findings and tumor biology, descriptions of the gross tumor morphology can help in determining treatment plans and prognosis (22). Various terminologies have been suggested for the gross morphology of EHD cancer, such as mass-forming/nodular/ small fibrous nodules, periductal infiltrating/flat/sclerosing/ segmental stenosis, and intraductal growing/papillary or papillary growth (22, 23). The KSAR study group for EHD cancer aimed at determining appropriate terms that were intuitive, representative, and familiar to radiologists, and it recommended the mass-forming, periductal-infiltrating, and intraductal-growing type to classify the gross morphology of EHD cancer (Fig. 2) (22, 24). EHD cancer usually presents as the periductal-infiltrating type or intraductal-growing type. The periductal-infiltrating type spreads longitudinally through the periductal or perineural connective tissue and lymphatics even with intact mucosa, whereas the intraductal-growing type spreads superficially along the mucosa. Lymph node (LN) metastasis is more common and the periductal-infiltrating type shows a worse prognosis than the intraductal-growing type (22). Sometimes, EHD cancer can also present as a mixed type with two or more gross morphologies.

Section 2. Imaging Technique

KQ 3. Which Imaging Modality is Recommended for Patients Suspected with Extrahepatic Bile Duct Cancer, and When Do We Perform an Imaging Study If Biliary Intervention Is Needed?

Statement 3: Contrast-enhanced CT and/or contrastenhanced MRI with MR cholangiopancreatography (MRCP) are recommended to evaluate EHD cancer (agreement level, 100%; evidence level, IV).

Statement 4: Imaging studies are recommended before any biliary interventional procedure whenever possible (agreement level, 98.6%; evidence level, IV).

With recent advances in multidetector CT (MDCT) technology, CT provides rapid temporal resolution as well as high spatial resolution. Therefore, contrast-enhanced abdominopelvic CT is recommended when staging malignant diseases. In regards to EHD cancer, CT could facilitate the assessment of the extent of the primary EHD cancer and the relationship between the tumor and adjacent vascular structures, including the hepatic artery and PV, which is very important for tumor resectability. CT also provides information on distant metastases such as liver or distant LN metastasis and/or peritoneal seeding. Thus, contrastenhanced abdominopelvic CT has been regarded as the initial and standard imaging modality for patients suspected of EHD cancer (25-28). Contrast-enhanced MR has been

regarded as an alternative imaging modality to contrastenhanced CT for malignant diseases; however, it may be the initial imaging modality for patients who are hypersensitive to iodinated contrast media. In addition, MRCP can provide detailed information about the bile duct anatomy as well as the extent of EHD cancer. Several studies have



Fig. 2. Gross morphology of EHD cancer.

A, **B**. Mass-forming type: **(A)** on T1-weighted axial image, an enhancing nodular mass is noted within the CBD; **(B)** on T2-weighted coronal image, a nodular lesion is seen (arrow) within the distal CBD with upstream bile duct dilatation. **C**, **D**. Periductal-infiltrating type: **(C)** contrast-enhanced T1-weighted axial image shows circumferential bile duct wall thickening with luminal narrowing at the EHD (arrow); **(D)** on MRCP, segmental narrowing (arrow) with upstream biliary dilatation is seen at the distal EHD. **E**, **F**. Intraductal-growing type: **(E)** on T1-weighted axial image, a polypoid mass (arrowheads) is seen within the EHD; **(F)** on MRCP, multiple polypoid lesions (arrowheads) are seen within the EHD. These polypoid tumors involved the right secondary confluence of the bile duct (Bismuth-Corette type IIIA) while extending into the intra-pancreatic common bile duct. CBD = common bile duct, MRCP = MR cholangiopancreatography



reported that contrast-enhanced MR with MRCP can provide diagnostic accuracy that is comparable to that of contrastenhanced abdominopelvic CT with direct cholangiography when assessing the longitudinal tumor extent, vascular involvement, and tumor resectability of EHD cancer (29, 30). It is also important to distinguish distal bile duct cancer from pancreatic cancer because chemotherapy regimens and prognoses differ, especially in unresectable cases. MRI with MRCP may help in ascertaining the origin of periampullary cancer (31). Hence, we recommend contrastenhanced CT and/or contrast-enhanced MR with MRCP to evaluate EHD cancer.

Patients with EHD cancer usually present with jaundice due to bile duct obstruction, and a substantial portion of EHD cancer patients suffer from cholangitis and biliary sepsis as bile flow is blocked off. When biliary infections result from EHD cancer, an endoscopic or percutaneous biliary drainage procedure has to be urgently performed. However, biliary interventions such as the insertion of drain catheters can cause inflammatory changes in the bile duct. This can mimic tumor involvement and negatively affect the diagnostic performance of imaging studies that assess the extent of EHD cancer (32, 33). Taking this into consideration, we recommend imaging studies before any biliary interventional procedures whenever possible. However, no studies have accurately evaluated how biliary drainage procedures affect the diagnostic performance of imaging studies for assessing the tumor extent of EHD cancer. Additionally, no data has conclusively demonstrated the extent of reduction in diagnostic accuracy after biliary drainage procedures. The effect of biliary drainage procedures on the diagnostic performance of imaging studies for EHD cancer should be evaluated in a future study.

KQ 4. What is the Optimal CT Protocol for Evaluating Extrahepatic Bile Duct Cancer?

Statement 5: Multiphase imaging, which includes the precontrast, arterial, and portal venous phase, is recommended (agreement level, 97.1%; evidence level, IV).

Statement 6: A slice thickness of 3 mm or less is recommended (agreement level, 95.7%; evidence level, V).

Statement 7: Multiplanar reconstruction can aid the evaluation of relationships between EHD cancer and adjacent structures (agreement level, 98.6%; evidence level, IV).

Statement 8: Including the pelvis in at least one phase is recommended (agreement level, 85.9%; evidence level, V).

Multiphase images with contrast enhancement are usually obtained to evaluate EHD cancer (34). By acquiring multiphase images before and after the administration of contrast media, it is possible to adequately evaluate radio-opague stones, vascular structures, and abdominal organs (35). Precontrast images help clinicians to detect intraductal stones and differentiate them from tumors (26, 28). Although some studies showed that routine acquisition of the arterial phase is not necessary for the detection and evaluation of EHD cancer and its extent (36, 37), the AJCC guidelines recommend that dynamic imaging be performed during the arterial and portal venous phases (1). The arterial phase is useful for enhancing the conspicuity of the distal bile duct cancer against the background. The portal venous phase is useful for judging the extrapancreatic extent of the distal bile duct cancer and detecting liver metastases (1). The delayed phase, which is usually observed 3-5 minutes after the injection of contrast agent, is not commonly acquired for EHD cancer (8). Detailed imaging findings of EHD cancer are described in Key Question 6 and its statements.

Thin-section imaging is recommended for EHD cancer (1, 8, 38, 39). No studies have conducted a head-to-head comparison between thin- and thick-section CT imaging to evaluate EHD cancer. Several studies use CT images with a slice thickness between 1.5 and 3 mm to distinguish benign papillary strictures from malignant ampullary tumors or determine the resectability of EHD cancers (40-43). The AJCC guidelines suggest 2- to 3-mm thicknesses for thinsection CT imaging (1). Thus, we recommend a CT slice thickness of 3 mm or less.

Although axial CT is useful for evaluating biliary trees, cross-sectional images have limited value in demonstrating complex anatomical relationships. In this regard, multiplanar reformation (MPR) images are better at demonstrating the relationships between tumors and adjacent structures (28, 40, 41, 44-49). Longitudinal and vertical extensions of tumors can be identified with MPR images (49-52). MPR images can also help radiologists to assess vascular invasion of the primary tumor (49, 53, 54). Curved planar reformation along the course of specific anatomic structures such as bile ducts and vessels is also useful when evaluating the longitudinal extent of the bile duct tumor (55-57).

MDCT should facilitate the assessment of distant metastases in addition to the primary EHD tumor (1, 28, 38). Peritoneum and LNs are among the most common metastatic sites in both perihilar and distal bile duct cancers (1, 38, 41). Hence, MDCT that involves the abdomen and pelvis at initial staging is recommended to detect distant metastases such as peritoneal seeding, as this knowledge is critical for appropriate treatment plans and prognostic predictions.

KQ 5. Which MR Sequences Are Needed to Evaluate Bile Duct Cancer?

Statement 9: T1-weighted, T2-weighted and heavily T2weighted, MRCP, and contrast-enhanced dynamic images are recommended as MR sequences for bile duct cancer (agreement level, 97.3%; evidence level, IV).

Statement 10: Diffusion-weighted images (DWIs) may help radiologists characterize bile duct lesions and detect extra-bile duct lesions (agreement level, 89.7%; evidence level, IV).

To evaluate EHD cancer, precontrast images should always include cross-sectional T2-weighted and T1-weighted sequences as well as heavily two-dimensional (2D) and/or three-dimensional (3D) T2-weighted MRCP, which has been accepted as an effective imaging modality for demonstrating the presence and level of biliary obstruction (58). 3D MRCP has superior image quality and ductal conspicuity than 2D MRCP, although no significant difference was observed when evaluating tumor extent (59). When gadolinium-based contrast agents are used, multiphasic dynamic fat-saturated 3D gradient-echo T1-weighted imaging (T1WI), involving the arterial and portal venous phases, is recommended. For hepatobiliary agent (HBA)-enhanced MRI, T2-weighted sequences and DWI can be performed after contrastenhanced dynamic phases to shorten examination times (60-63). However, heavily T2-weighted MRCP should be performed before the contrast agent is excreted into the biliary tree (60, 64). With higher concentrations of contrast agent in the biliary ductal system, the signal intensity of the bile appears darker on T2-weighted images (T2WIs) owing to the T2-shortening effect (64).

DWI, typically using 0 to 100 sec/mm² and 800 to 1000 sec/mm² for low and high b values, respectively, can provide additional information for patients with EHD cancer. The application of a 3T MRI system and parallel imaging techniques to DWI can enhance the signal-tonoise ratio and lesion-to-liver contrast by improving image quality (65, 66). Some studies have reported that adding DWI to conventional MRI shows a high sensitivity for bile duct cancer (67), and it helps differentiate benign from malignant bile duct strictures (68, 69). DWI may also facilitate the evaluation of tumor extent and liver invasion as well as help differentiate liver metastases from biliary abscesses (70-73).

Section 3. Cancer Evaluation

KQ 6. Which Imaging Features Indicate the Presence of Extrahepatic Bile Duct Cancer?

Statement 11: On contrast-enhanced CT or MRI, EHD cancer is indicated by irregular ductal wall thickening with upstream ductal dilatation, hyper-enhancement of the ductal wall relative to the liver, and/or obliteration of the lumen by an intraductal soft-tissue mass or thickened ductal wall (agreement level, 100%; evidence level, III).

Statement 12: On cholangiography, EHD cancer is indicated by the abrupt and/or irregular narrowing of the bile duct and irregularly shaped filling defects within the lumen (agreement level, 94.5%; evidence level, III).

On cross-sectional imaging and cholangiography, scarlike fibrosis and/or intraductal tumors can result in irregular ductal wall thickening, luminal narrowing, and luminal obliteration, causing upstream bile duct dilatation (28, 74-76). EHD tumors show increased enhancement to the liver on the arterial and/or portal venous phase; fibrosis and scirrhous tissue are better visualized on later phases (76, 77). EHD cancer also more commonly presents with thicker bile duct wall, longer involved segment, luminal irregularity, asymmetric narrowing, and high signal intensity on DWI, compared to benign strictures (68, 78, 79). However, these features are also found in benign biliary diseases, including but not restricted to primary sclerosing cholangitis, AIDSrelated cholangiopathy, immunoglobulin G4-related sclerosing cholangitis, recurrent pyogenic cholangitis, and ischemic cholangitis (80). Thus, further histologic evidence is often required to confirm the diagnosis of bile duct abnormalities.

KQ 7. How Is the Biliary Tree Classified When Evaluating the Longitudinal Extent of Extrahepatic Bile Duct Cancer?

Statement 13: Longitudinal involvement of EHD cancer can be assessed by classifying the presence/absence of tumor involvement in the right secondary confluence, right hepatic duct, primary confluence, left hepatic duct, left secondary confluence, common hepatic duct, suprapancreatic common

bile duct, and intrapancreatic common bile duct (agreement level, 89.0%; evidence level, V).

Statement 14: The Bismuth-Corlette classification is recommended for the imaging assessment of bile duct involvement in perihilar bile duct cancer (agreement level, 97.3%; evidence level, V).

Statement 15: Proximal and distal extensions of perihilar bile duct cancers and proximal extensions of distal bile duct cancers are included in the imaging assessment for bile duct involvement (agreement level, 95.8%; evidence level, V).

Various terminologies have been proposed to describe the longitudinal extent of bile duct cancers. The modified Bismuth-Corlette classification is one of the most widely accepted systems, which uses primary confluence and right or left secondary confluence to describe tumor extent (81, 82). The Bismuth-Corlette system defines the longitudinal extent of the tumor relative to the biliary confluences, which may roughly yield the estimated extent of surgery (81, 83). However, the applicability of the system is limited by biliary variation, and the potential resectability or scope of surgery may vary even among patients with the same Bismuth-Corlette type (82, 84). Therefore, when reporting Bismuth-Corlette classifications, the anatomic variation of the bile duct should be described in detail as well, if present.

The longitudinal extent of the tumor dictates the type of curative surgery, such as pancreaticoduodenectomy, hepatopancreaticoduodenectomy, hepatobiliary resection, or segmental bile duct resection, to be performed (83, 85, 86). Hepatobiliary resection, with or without pancreaticoduodenectomy, is regarded as the standard curative surgery for perihilar bile duct cancer (83). Hepatopancreaticoduodenectomy is a challenging procedure with high morbidity and mortality rates, but it gives patients a chance for long-term survival when curative resection is feasible. Thus, an accurate description of the proximal and distal extent of the perihilar bile duct cancer as well as the proximal extent of the distal bile duct cancer may help in determining appropriate treatment.

In retrospective studies, the accuracy of enhanced CT for the longitudinal tumor extent ranged from 75–96% (29, 87-90). In a meta-analysis, the pooled accuracy for CT was 86% (25). MR cholangiography showed a similar accuracy of 71–80% (91-93), and adding enhanced MRI increased accuracy to 87–93.3% (29, 92). However, imaging studies may underestimate the longitudinal extent of the tumor; microscopic tumors that spread through the mucosa or submucosa are unnoticeable on imaging, although this results in positive resection margins (94).

KQ 8. How Do We Evaluate Tumor Vascular Invasion on MDCT and MRI for Extrahepatic Bile Duct Cancer?

Statement 16: The hepatic artery and PV, as well as their branches, and the variant hepatic vessels should be evaluated for tumor invasion, depending on the anatomic location of the EHD cancer (agreement level, 97.2%; evidence level, V).

Statement 17: Tumor vascular invasion is indicated by the tumor encasement of vessels, vessel deformity, occlusion, or tumor thrombus (agreement level, 92.6%; evidence level, III).

Statement 18: The degree of tumor-vessel contact is classified as no contact (preserved tumor-vessel fat plane), abutment (tumor involvement up to 50% of the vessel circumference), or encasement (tumor involvement more than 50% of the vessel circumference) (agreement level, 95.7%; evidence level, V).

The evaluation of tumor vascular invasion is crucial when determining the resectability of EHD cancer, especially for perihilar bile duct cancer. In a previous meta-analysis (25), the pooled sensitivity and specificity of MDCT for assessing the vascular invasion of perihilar bile duct cancer was 89% (95% confidence interval [CI], 80–94%) and 92% (95% CI, 85–96%), respectively, for PV invasion, and 84% (95% CI, 63–94%) and 93% (95% CI, 69–99%), respectively, for hepatic artery invasion.

Tumor vascular invasion on MDCT and MRI is determined by the degree of tumor contact with vessels, vessel deformity, and vessel occlusion or tumor thrombus (Fig. 3). We recommend classifying the degree of tumor-vessel contact as no contact (preserved tumor-vessel fat plane), abutment (tumor involvement up to 50% of the vessel circumference), or encasement (tumor involvement more than 50% of the vessel circumference), following the NCCN guidelines for pancreatic cancer (95) (Fig. 3).

Although previous studies evaluated imaging criteria for the vascular invasion of EHD cancer (25, 29, 41, 49, 53, 88, 96-100), all of them were retrospective with small to moderate study populations. Another point of consideration is that perivascular infiltration may not always be a tumor; it may be an inflammatory infiltration. In most of these cases, surgery was not performed and, hence, perivascular infiltration was not pathologically confirmed.







(A) No contact: a fat plane is preserved between tumor and vessel. (B) Abutment: tumor involves up to 50% of the vessel circumference, (C-F) vascular invasion. (C) Encasement: tumor involves more than 50% of the vessel circumference, (D) occlusion, (E) contour deformity, (F) tumor thrombosis. Green circle, bile duct; red circle, vessel.

Despite the low evidence level of past study findings, they consistently demonstrated that vessel encasement in EHD cancer strongly indicates vessel invasion, with reported specificities of 93–97% and sensitivities of 70–88% (29, 41, 88, 96, 99, 100). On the other hand, the absence of tumor-vessel contact may reliably rule out vessel invasion. The negative predictive value of this finding for excluding tumor invasion was reported as 93–100% (49, 53). However, tumor abutment is considered inconclusive. Previous studies reported that tumor abutment of vessels resulted in a sensitivity of 100%, with only a moderate specificity

of 77–90% for detecting vessel invasion (49, 53). Thus, radiologists cannot arrive at a confident diagnosis of vessel invasion using only tumor abutment. However, this finding should be reported in radiologic reports for doctors to consider when planning surgery or considering surgical resectability through multidisciplinary discussions.

KQ 9. How Do We Evaluate Lymph Node Metastasis in Extrahepatic Bile Duct Cancer?

Statement 19: LNs are considered suspicious for metastatic involvement if they are greater than 1 cm

along the short axis or have abnormal round morphology, heterogeneous enhancement, or central necrosis (agreement level, 92.9%; evidence level, III).

Only a few reports on the diagnostic accuracy of LN metastasis in EHD cancer are available (25, 101, 102). Previous studies have used various combinations of characteristics such as a short diameter of 1 cm, abnormal round morphology, heterogeneous enhancement, or central necrosis to diagnose LN metastasis. A meta-analysis for hilar bile duct cancer vielded a sensitivity of 61% and a specificity of 88% for detecting LN metastases (25). In terms of LN size, a cutoff of 1 cm for the short diameter is the diagnostic criterion for LN metastasis for other malignancies: metastatic LNs are significantly larger than their non-metastatic counterparts. However, a previous study reported that only 23% of LNs larger than 1 cm were associated with metastatic cells, and 10% of LNs smaller than 1 cm harbored metastatic cells (102). Furthermore, enlarged reactive regional LNs are more frequent in EHD cancer than in other malignancies because of the accompanying obstructive cholangitis. Therefore, the size criterion should be used with other imaging criteria to provide a reliable diagnosis of LN metastasis on imaging studies (102). Combinations of the size criterion and round morphology or internal heterogeneity demonstrated an increased positive predictive value for LN metastasis, compared with the size criterion alone (101). However, the low prevalence of such characteristic LNs is a limitation of this approach. For the preoperative assessment of LN metastasis, similar limitations have been reported for other malignancies as well (103, 104). Although imaging studies do not show enough accuracy to assess LN metastasis, LNs greater than 1 cm along the short axis with abnormal round morphology, heterogeneous enhancement, or central necrosis are more likely to be metastatic. According to findings from recent studies, 18F-fluorodeoxyglucose (18F-FDG) positron emission tomography (PET)-CT may help radiologists in differentiating LN metastasis from its differentials (105, 106).

KQ 10. How Do We Evaluate Distant Metastasis in Extrahepatic Bile Duct Cancer?

Statement 20: MRI or 18F-FDG PET-CT is recommended for evaluating indeterminate or suspicious findings of distant metastasis on CT (agreement level, 92.6%; evidence level, V).

The liver is the most common (11.9-23.2%) site of metastasis, followed by the lung (2.7-5.8%) and distant LNs (3.0-4.4%) (107). The peritoneum is also a common site of metastasis; however, the exact prevalence of metastasis is unknown. Diagnosing liver metastasis is a challenge in EHD cancer patients because small biliary abscesses frequently coexist due to biliary obstruction. The findings from previous studies suggest that patchy parenchymal enhancement, arterial rim enhancement persistent through portal venous phase and perilesional hyperemia on CT and MR, and size discrepancy between T1WI and T2WI as well as T1WI and the hepatobiliary phase on MR are indicative of biliary abscess rather than liver metastasis (108, 109). Short-term follow-up with imaging can also help radiologists to assess lesional size changes. An ultrasound-quided biopsy may also aid differential diagnosis if technically feasible.

The extent and location of regional LNs are defined differently for perihilar bile duct cancer and distal bile duct cancer. Hilar, cystic duct, choledochal, portal, hepatic arterial, and posterior pancreaticoduodenal LNs are classified as regional LNs in perihilar bile duct cancer, whereas the common bile duct, hepatic artery, the posterior and anterior pancreaticoduodenal, and the right lateral wall of the superior mesenteric artery LNs are classified as regional LNs in distal bile duct cancer (18). The differential diagnoses of reactive and metastatic LNs are described in detail in Statement 19.

Peritoneal metastases are frequently underestimated on CT (110, 111). In a meta-analysis of peritoneal metastases in all cancers, 18F-FDG PET-CT demonstrated good sensitivity (87%) and specificity (92%) for the detection of peritoneal metastasis (112).

KQ 11. How Do We Assess the Resectability of Extrahepatic Bile Duct Cancer beyond the Tumor Staging/Extent?

Statement 21: The future remnant liver volume as well as biliary and vascular anatomic variations has to be evaluated to determine the resectability of perihilar bile duct cancer (agreement level, 98.5%; evidence level, VI).

Statement 22: A multidisciplinary team consultation is recommended when deciding or assessing resectability (agreement level, 91.7%; evidence level, n/a).

For perihilar bile duct cancer, preoperative assessment of biliary and vascular anatomy variations and tumor extent to the intrahepatic bile duct is important because resectability depends on hilar biliary and vascular anatomy (84, 113). For example, the anterior and posterior sectional branches of the right hepatic duct drain directly into the main hepatic duct at a 20% frequency; hence, this case may be misdiagnosed as the Bismuth classification type IV, which is an unresectable case, when the hilar tumor involves the right anterior and posterior hepatic ducts with a segmental involvement of the left side (84, 113). However, if diagnosed properly, radical resection with an extended left hepatectomy may be preferred as a curative treatment. Various anatomic variations may exist, but the important consideration is whether blood flow to the remaining liver can be preserved. The availability of surgical techniques, such as vascular reconstruction, should also be considered (114).

Because extended hepatic resections are usually required for curative treatment, it is important to estimate the future remnant liver volume in patients with perihilar bile duct cancer (84). According to previous studies, a future remnant liver volume of > 25–30% is considered a safe cutoff for patients with healthy liver parenchyma, whereas > 40% is considered in patients with compromised livers such as cholestatic livers (115, 116). CT and MRI are standard techniques for assessing future remnant liver volume.

The diagnosis and management of EHD cancer are challenging, and it requires skilled experts. As diagnosis and management of EHD cancer are complex and the availability of surgical resection or liver transplantation depends on surgical expertise, an optimal assessment and decision on resectability require a multidisciplinary collaboration between hepatobiliary surgeons, endoscopists, radiologists, medical oncologists, and pathologists (117, 118).

Section 4. Tumor Response

KQ 12. How Do We Evaluate Treatment Response through Imaging after Chemotherapy for Patients with Extrahepatic Bile Duct Cancer?

Statements 23: Contrast-enhanced CT or MRI with MRCP, according to the response evaluation criteria in solid tumors (RECIST), is recommended (agreement level, 90.5%; evidence level, V).

According to previous literature, most researchers use their follow-up protocols for patients with EHD cancer placed on chemotherapy (119-143). There is currently no "standard" follow-up strategy for assessing patients after We recommend contrast-enhanced CT and contrastenhanced MRI with MRCP as imaging modalities for assessing tumor response using the RECIST criteria. A universal follow-up schedule has not been discussed in these guidelines; schedules should be determined by clinicians according to chemotherapy regimen, complications such as biliary obstruction or infection, and disease stage.

The Key Questions and Statement Which Did Not Reach Consensus

KQ. Which Type of MRI Contrast Agent Can Be Used to Evaluate Bile Duct Cancer?

Statement: For bile duct cancer, extracellular agents (ECAs) are preferred over gadoxetate disodium, among MRI contrast agents (agreement level, 61.4%; evidence level, IV).

This statement on the optimal contrast media for EHD cancer did not reach a consensus because there was not enough data to support the diagnostic superiority of MRI with ECA (ECA-MRI) over MRI with gadoxetate disodium (HBA-MRI) for EHD cancer. So far, only a few publications have evaluated the clinical applications of HBA-MRI when assessing EHD cancer (72, 144).

There are several drawbacks to using HBA-MRI in the preoperative evaluation of bile duct cancer. First, there are concerns about transient motion artifacts that appear during the arterial phase (145, 146) and less vascular enhancement due to the lower amount of administered gadoxetate disodium (0.025 mmol/kg vs. 0.1 mmol/kg for extracellular gadolinium chelates) (147). Second, the uptake of HBA into hepatocytes and its excretion into the biliary tree can be hindered by high bilirubin related to biliary obstruction (64, 148). In addition, the increased signal intensity of the liver may hinder the evaluation of bile duct wall enhancement. Third, the cost of performing HBA-MRI is higher than that of ECA-MRI (149, 150). The statement may not have reached a consensus because of these reasons. The advantages and disadvantages of HBA-MRI should be understood before it is used to evaluate bile duct cancer, and without further guidelines, an MRI contrast agent should be chosen based on the clinical setting of



Table 2. Suggested Structured Report Form for EHD Cancer

1. Imaging quality	
Appropriate	
$\hfill\square$ Not appropriate, but diagnosable	\square Not appropriate, hard to diagnose
Additional description:	
2. Location	
Perihilar bile duct cancer	Distal bile duct cancer
Additional description:	
3. Biliary intervention	
 Absent Performed, but not disturbing diagnosis 	$\hfill\square$ Performed with disturbing diagnosis
4. Bile duct evaluation	
1) Bile duct involvement	
Right secondary confluence	Left secondary confluence
Right hepatic duct	□ Left hepatic duct
Primary confluence	Common hepatic duct
 Suprapancreatic common bile duct Bile duct anatomy variation 	Intra-pancreatic common bile duct
Not evaluable	
□ No	
□ Yes:	
Trifurcation	
\square Right posterior duct inserted to the le	eft hepatic duct
\square Right posterior duct inserted to the c	ommon bile duct
Other (please specify):	
3) Bismuth classification	
□ I □ II □ IIIa □ IIIb	\Box IV
4) Gross morphology (based on the dominan	t component)
□ Mass-forming (maximum size: cm)	
Periductal-infiltrating	
Intraductal-growing	
Additional description:	
5. Vessel evaluation	
1) Artery anatomy variation	
Not evaluable	
□ No	
□ Yes:	
\square Replaced or \square accessory right hepatic	artery from
\Box Replaced or \Box accessory left hepatic a	artery from
Replaced common hepatic artery from	۱
Other (please specify)	
2) PV anatomy variation	
Not evaluable	
□ No	
□ Yes:	
PV trifurcation	
\square Right posterior PV as the first branch	of MPV
\Box Other (please specify):	- · ·



Table 2. Suggested Structured Report Form for EHD Cancer (Continued)

5. Vessel evaluation

3) Evaluation of tumor vascular invasion

No contact	Abutment	Invasion
No contact	Abutment	Invasion
	 No contact 	No contactAbutmentNo contactAbutment

Additional description:

6. Regional LN metastasis evaluation

□ Absent □ Indeterminate* □ Present

*LN (\leq 1 cm along short axis) with suspicious findings of metastasis (abnormal round morphology, heterogeneous enhancement, central necrosis, increased 18F-FDG uptake) or LNs (> 1 cm) without suspicious findings of metastasis.

Additional description:

7.	Distant	metastasis	evaluation
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1) Liver lesion			
Absent	Indeterminate (specify location)	
2) Peritoneal carcinomatosis			
Absent	Indeterminate*	t	
*Consider diagnostic laparoscopy.			
3) Distant LNs			
Absent	Indeterminate (specify location)	
4) Other (organ involved:)			
Absent	□ Indeterminate □ Present		

Additional description:

MPV = main portal vein

each patient.

Structured Reporting Form

This structured reporting form was developed to provide a common reporting form for EHD that could be readily used in daily clinical practice. If a structured reporting form is complicated, it will be inconvenient to incorporate it into clinical practice, and it will eventually be shunned by the medical community. Therefore, a structured reporting form for EHD should be as simple as possible; however, it should include essential items such as bile duct involvement, vessel invasion, regional LN metastasis, and distant metastasis evaluation, while noting whether the EHD cancer is located on the perihilar bile duct or distal bile duct (Table 2). The starting questions of the structured reporting form should

be on imaging guality and if image guality is not sufficient for accurate diagnosis, re-examinations or additional examinations are recommended. Biliary intervention may also affect the diagnostic accuracy of imaging, so biliary intervention procedures should also be recorded. Essential items are listed under each section title and users can select the items that correspond to their observations by marking the matching checkboxes. If multiple items are observed, users can select all of the concerned items in that particular section. Items with low incidence such as certain variations of blood vessels or bile ducts have to be filled out directly. Additional descriptions can be recorded under each section (in the 'additional description') if required. This structured reporting form focuses on the evaluation of initially diagnosed EHD cancer before treatment and does not intend to evaluate treatment response. We hope to validate the diagnostic performances and inter-reader agreements of this structured reporting form for EHD cancer in future studies.

SUMMARY

Twelve key questions and 23 statements on the imaging analysis of EHD cancer were confirmed through consensus at several meetings. A structured reporting form was developed based on these key questions and recommendation statements, which included essential items to be evaluated such as bile duct involvement, vessel invasion, and LN and distant metastasis. Although the evidence levels of most recommendations were low due to insufficient research, the consensus recommendations and the structured reporting form were developed to summarize existing findings and clarify future research topics. Furthermore, the proposed structured reporting form can be used to accumulate standardized data progressively; based on newly collected data, quidelines may be revised when answers are found to questions that are currently unresolved. This will increase the evidence levels of the current recommendations.

Supplementary Materials

The Data Supplement is available with this article at https://doi.org/10.3348/kjr.2019.0803.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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