

Imaging of Cholangiocarcinoma

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Abstract

Keywords

- ▶ cholangiocarcinoma
- ▶ magnetic resonance imaging
- ▶ cholangiography
- ▶ computed tomography

Cross-section imaging plays an increasingly important role in the evaluation and diagnosis of cholangiocarcinoma (CC). CCs can have varied radiological appearances, depending on their location, morphology, as well as their histological characteristics. An awareness of the varied imaging manifestations of CC and its accurate diagnosis are necessary to direct appropriate management. Recent advances in imaging techniques, histological assessment, molecular imaging, surgical techniques, and radiation therapy have all revitalized interest in the diagnosis and management of CCs.

Cholangiocarcinoma (CC) originates from epithelial cells of the biliary tree. They account for approximately 10 to 15% of all hepatobiliary malignancies, second only to hepatocellular carcinoma (HCC).¹ The incidence rates of CC vary among different geographic locales, according to diverse risk factors in different parts of the world.² The development of CC is associated with conditions that result in hepatobiliary inflammation and cholestasis, including primary sclerosing cholangitis, choledochal cysts, hepatolithiasis, and parasitic infections.^{2–5} The vast majority (95%) of CCs are adenocarcinomas, but less common histologic types have also been reported.⁶ Men tend to be affected 1.5 times more commonly than women.²

CCs are classified into two anatomically distinct subtypes: intrahepatic CC (ICC) and extrahepatic CC (ECC).⁷ ICCs are further characterized as either perihilar or peripheral.⁸ Recent studies have suggested further subtyping of ICC into two distinct histological types, based on mucin production and immunophenotypes.⁹ As the name implies, perihilar CC develops at the level of bifurcation of the left and right hepatic ducts, whereas peripheral CC arises more distally, usually from more peripherally located ducts.^{10,11} Growth patterns have been described as mass forming (most common), periductal, intra-ductal, or mixed.^{12–14} Various staging systems have been

developed in an attempt to either describe disease extent and/or surgical candidates. The Bismuth–Corlette's classification focuses on the extent of tumor invasion into the biliary tree.¹⁵ The American Joint Committee on Cancer/International Union Against Cancer system is based on the pathological TNM staging.¹³ The Memorial Sloan Kettering system attempts to classify tumors based on factors related to local extension of tumor, location of bile duct involvement, and presence of portal vein invasion.¹⁴

The overall prognosis of CC is poor, and surgery offers the only potential for cure. Surgical resection with microscopically negative margins is the objective for cure and offers the best long-term survival.^{16–19} Unfortunately, up to 20 to 50% of patients are deemed unresectable at presentation due to advanced disease. Factors that preclude surgical resection include bilateral ductal involvement to the level of the second order bile ducts, tumor involvement of the proper hepatic artery, bilateral hepatic arteries, main portal vein, metastatic lymphadenopathy, or peritoneal carcinomatosis.^{20,21} Nonsurgical treatment options differ depending on the location, stage, and extent of disease. Because many patients present clinically with advanced disease, treatment goals are often directed toward mitigating the consequences of biliary obstruction. Relief of biliary obstruction can be achieved by biliary drainage

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(endoscopic or percutaneous), biliary stenting, and surgical bypass. Emerging technologies such as photodynamic therapy, transarterial chemo- or radioembolization, and thermal ablation may be considered in select cases.²²⁻²⁶ Liver transplantation for CC is controversial, though recent studies suggest it may have a role for selected patients with early stage disease.²⁷⁻²⁹ Adjuvant chemotherapy may extend survival following surgical resection or in cases of macroscopic residual disease or recurrence.³⁰ Because the ideal strategy for management of CC begins with accurate diagnosis, this review will primarily focus on the imaging features of CC.

Imaging Modalities

Ultrasound

Transabdominal ultrasound is a valuable and widely available screening tool for evaluating patients with suspected biliary pathology (►Fig. 1).^{8,31-33} Sonographic findings commonly encountered in CC included biliary dilatation, often associated with lobar atrophy. Dilatation of the biliary tree with abrupt cutoff in duct calibers the most common sonographic finding of CC. Owing to their location at the confluence of the left and right ducts, Klatskin's tumors cause segmental dilatation of the left and hepatic ducts, often in association with lobar atrophy. Although ultrasound is often helpful to establish the level of intrahepatic biliary obstruction, a discrete mass is infrequently identified.³³

The sonographic appearances of CCs are variable, ranging from hypoechoic to mixed or hyperechoic echogenicity.^{34,35} When a mass is detected, US alone cannot provide the specificity for detecting CC, as mass-forming lesions may mimic other tumors such as hepatoma or metastases.³⁶ Color Doppler imaging is helpful in distinguishing vessels from dilated ducts and in establishing the patency of intrahepatic vessels, especially the portal vein.³³

Computed Tomography

Computed tomography (CT) is the preferred noninvasive diagnostic tool for evaluation of CC (►Fig. 2).³⁷ CT offers

anatomic resolution that is superior to ultrasound and allows evaluation of the level and extent of biliary obstruction. Furthermore, CT allows assessment of nonbiliary/hepatic structures, such as regional lymph nodes or omentum which can be involved by carcinomatosis.³⁸⁻⁴¹ Optimal contrast-enhanced CT (CECT) images are obtained using a triphasic imaging protocol including arterial, portal venous, and delayed phases. Intravenous (IV) contrast is injected at the rate of approximately 3 to 5 mL/s, with arterial phase images obtained at 20 to 30 seconds following the administration of IV contrast. Subsequently, portal-venous phase images are obtained 60 to 70 seconds later, followed by acquisition of delayed images 5 minutes after the contrast bolus. In contrast to HCC, CCs are typically hypoattenuating during arterial phase imaging. On portal-venous phases, CCs become hyperattenuating relative to normal hepatic parenchyma on delayed phase imaging.⁴²⁻⁴⁴ Associated lobar retraction is a common CT finding of CC.⁴⁴ In addition, multiplanar reconstructions in coronal and sagittal planes provide additional information regarding variant vascular anatomy and presence or absence of vascular encasement.^{45,46} CT cholangiography with IV agents allows noninvasive assessment of the biliary tree.⁴⁷⁻⁵⁰ Volume-rendered CT cholangiography offers a noninvasive opportunity to assess the biliary tree but is limited in patients with obstructive hyperbilirubinemia.^{51,52} Newer magnetic resonance imaging (MRI) contrast agents may be better suited for cholangiography analysis.

Magnetic Resonance Imaging

MRI is another valuable diagnostic imaging tool for assessment of CC.⁵³ On T1-weighted imaging (T1WI), mass-forming CCs are hypo- to isointense relative to normal hepatic tissue and hyperintense on T2-weighted imaging (T2WI). Following IV contrast administration, CCs follow an enhancement pattern similar to CECT with little tumoral enhancement on arterial phase images followed by delayed enhancement on delayed phase images.⁵⁴⁻⁵⁸ The presence of satellite nodules confers a poor prognosis and usually renders a patient inoperable.^{59,60} Intraductal CC shows a variety of

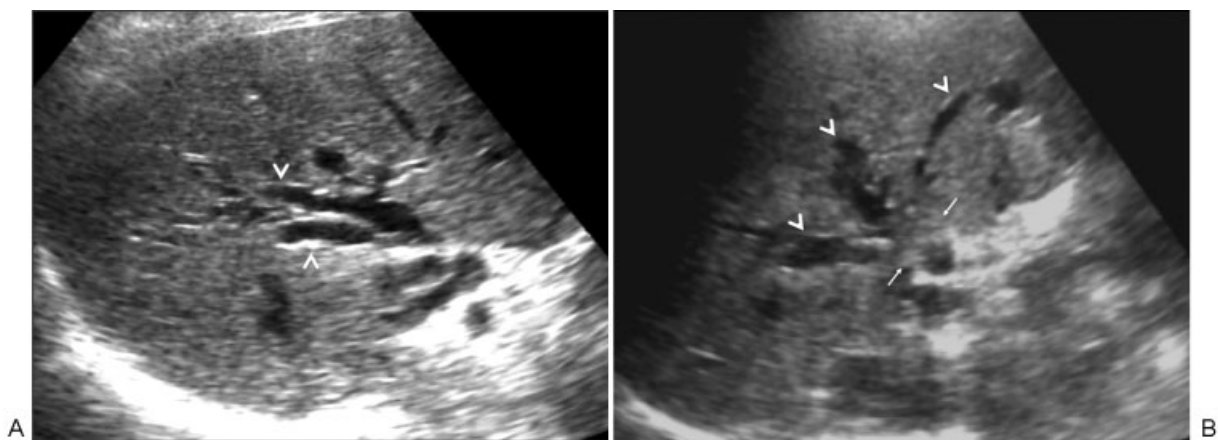


Fig. 1 (A) Transabdominal ultrasound image that shows intrahepatic biliary duct dilatation (white arrowheads). (B) Transabdominal ultrasound image that shows isoechoic soft tissue mass at the porta hepatis (white arrows), consistent with cholangiocarcinoma. Arrowheads indicate dilated bile ducts.



Fig. 2 Contrast material-enhanced CT scan of the liver that demonstrates dilatation of the left and right biliary radicals (white arrows). CT, computed tomography.

imaging features depending on its growth characteristics and can manifest on MRI as diffuse infiltrating with severe duct ectasia, an intraductal polypoid-like mass with focal duct dilatation, cast-like lesions, or as a focal stricture.^{59,61,62} Intraductal lesions are hypo- to isointense on T1WI and are usually slightly hyperintense on T2WI. Magnetic resonance cholangiopancreatography (MRCP) supplements standard MRI by providing noninvasive evaluation of the biliary anatomy^{63,64} (→**Fig. 3**). MRCP is associated with high sensitivity and specificity for localizing the location of biliary obstruction.^{65,66} Magnetic resonance angiography, similar to CECT, offers detailed assessment of the anatomic relationship of tumors to hepatic vasculature (→**Fig. 4**).^{67–69} Diffusion-weighted imaging also adds higher sensitivity and diagnostic accuracy for assessing biliary obstruction or bile duct injury following liver transplant.^{70,71}

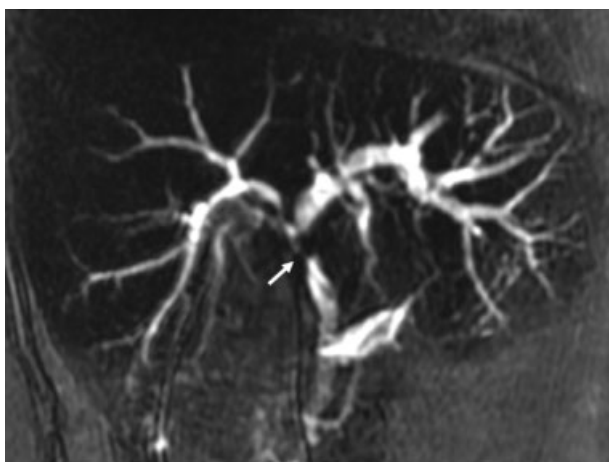


Fig. 3 Magnetic resonance cholangiogram that demonstrates malignant hilar strictures (white arrow).

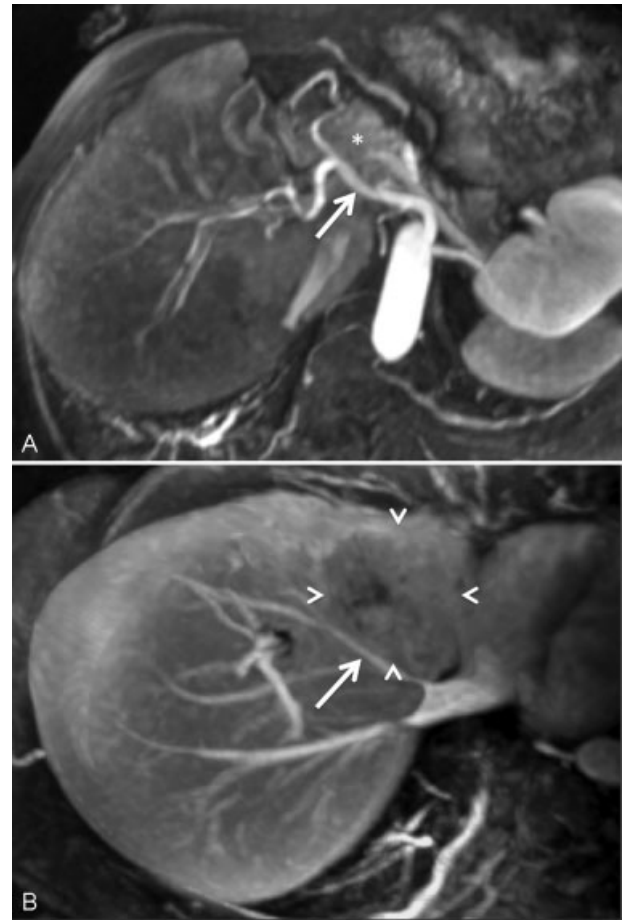


Fig. 4 (A) Contrast material-enhanced MRI that demonstrates relationship of cholangiocarcinoma (asterisk) to hepatic artery (white arrow). (B) Contrast material-enhanced MRI that demonstrates relationship of cholangiocarcinoma (white arrowheads) to middle hepatic vein (white arrow). MRI, magnetic resonance imaging.

Endoscopic Ultrasound

Endoscopic ultrasound (EUS) is commonly used to establish the diagnosis of CC especially when fine needle aspiration (FNA) biopsy is employed.^{72,73} The high-resolution image quality allows assessment of local tumor characteristics such as depth, stricture length, and ability to target liver lesions and regional lymph nodes inaccessible by percutaneous techniques.^{74,75} When combined with endoscopic retrograde cholangiopancreatography fine needle aspirates, EUS-FNA shows increased diagnostic accuracy (86%) when compared with EUS-FNA (70%) or endoscopic retrograde cholangiography biopsy (67%) alone.⁷⁶ The value of EUS-FNA is limited by restricted needle penetration, cases of significant desmoplastic reaction, diminished cellularity, external compression of the bile duct by the tumor.

Positron Emission Tomography and PET-Computed Tomography

The role of positron emission tomography/CT (PET/CT) with 2-deoxy-[¹⁸F]fluoro-D-glucose (¹⁸F-FDG) is somewhat controversial, but emerging data suggest that they have a

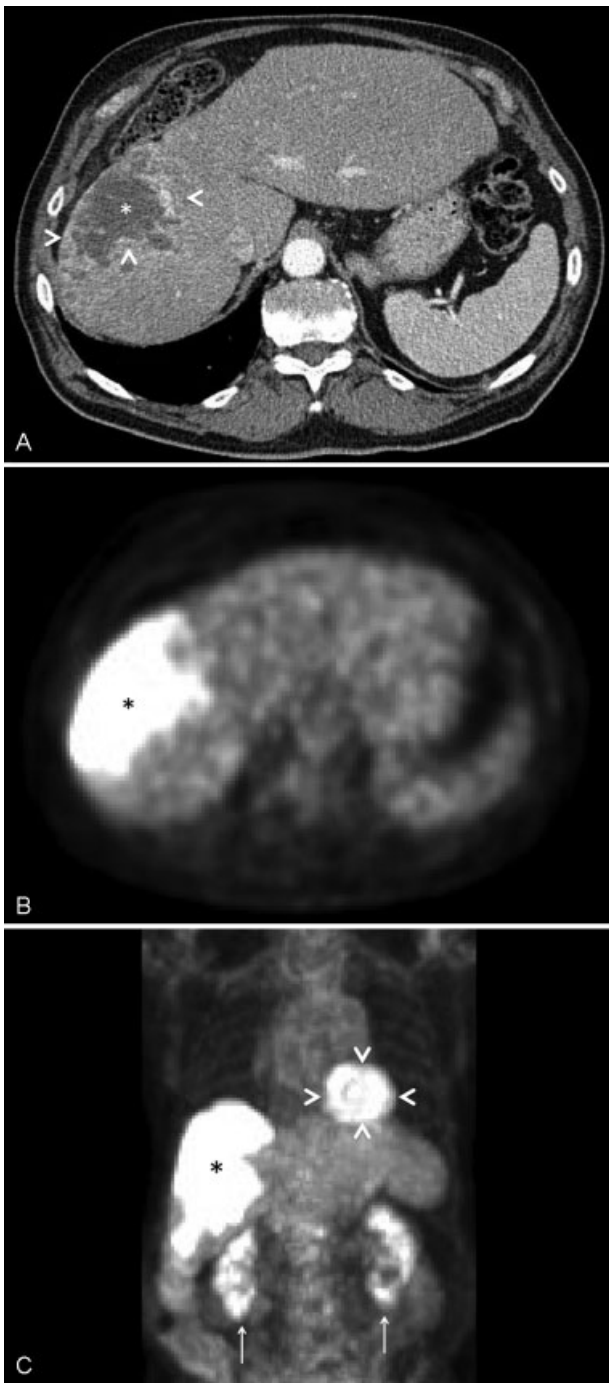


Fig. 5 (A) Contrast material-enhanced CT scan of the liver that demonstrates cholangiocarcinoma involving the right hepatic lobe (asterisk). The scan was obtained during the early portal-venous phase, when the enhancement is predominantly along the tumor margins (white arrowheads). (B) Axial positron emission tomography scan of the liver that demonstrates intense FDG activity of cholangiocarcinoma. (C) Coronal positron emission tomography scan of the liver that demonstrates intense FDG activity of cholangiocarcinoma (black asterisk). Normal FDG activity is noted in the heart (white arrowheads) and kidneys (white arrows). CT, computed tomography; FDG, fluoro-D-glucose.

potential role in the diagnosis and staging of CCs (► **Fig. 5**). Elias et al recently compared the diagnostic performance of FDG-PET/CT and CECT in patients with CC and found that FDG-PET/CT detected more intrahepatic malignant and

extrahepatic metastases and had significant higher sensitivity, negative predictive value, and accuracy than CECT.⁷⁷ PET/CT also adds value in assessing the FDG activity outside the liver. In a recently published study by Jiang et al, the sensitivity, specificity, and accuracy of PET/CT and MRI in the diagnosis of regional lymph node metastases were 70/0 versus 50%, 91.7 versus 83.3%, and 81.8 versus 68.2%, respectively.⁷⁸ Other studies have found that FDG-PET is helpful in identifying regional and distant metastases but performed poorly in detecting mucinous variant of CC.⁷⁹ Choi et al have shown that PET/CT is useful in differentiating extrahepatic biliary malignancy from benign disease.⁸⁰

Conclusion

CC is a disease with various imaging features based on multiple factors, including causative agents, growth pattern, and location within the hepatobiliary tree. Accurate detection, characterization, and assessment of the resectability of the tumor are the primary goals of imaging.

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