Staging cholangiocarcinoma by imaging studies

V. VILGRAIN

Department of Radiology, Hôpital Beaujon, Paris, France

Abstract
Cholangiocarcinoma (CCA) is an adenocarcinoma that arises from the bile duct epithelium and is observed in the entire biliary tree (intrahepatic, hilum, and extrahepatic distal). The staging of this tumor differs depending on location. The role of imaging in the staging of hilar CCA is to assess the extent of ductal involvement by the tumor, hepatic artery, or portal venous involvement, the functional status and volumetric assessment of the underlying liver, and the regional or distant tumor extension. Complete assessment is done by combining magnetic resonance (MR) cholangiography and multidetector computed tomography (CT). Multidetector CT, in particular, is accurate for resectability and the negative predictive value (patients with disease classified as unresectable and in whom unresectability has been confirmed) is quite high: 85–100%. The role of imaging in the staging of intrahepatic CCA is to evaluate resectability based on the tumor itself, vascular involvement, regional and distal extension, and volumetric assessment of the contralateral liver, and to determine the prognostic factors. These factors are mainly: tumor size, the presence of satellite nodules, vascular involvement, and lymph nodes. CT and MR imaging (MRI) are keys and their results are comparable. In distal extrahepatic CCA due to tumor location, staging is focused mainly on the adjacent vessels (portal vein and hepatic artery), the hepatoduodenal ligament, the proximal and distal biliary extent, and pancreatic invasion. CT and MRI are mandatory.

Introduction
Cholangiocarcinoma (CCA) is an adenocarcinoma that arises from the bile duct epithelium and is observed in the entire biliary tree (intrahepatic, hilum, and extrahepatic distal). Hilar CCA, which involves the biliary confluence or the right or left hepatic ducts, is the most common and accounts for 40–60% of all cases. Tumor staging of CCA is crucial, especially in hilar tumors, because most patients present with advanced disease and are not surgical candidates. Therefore, the role of preoperative imaging is the highest possible accuracy in predicting resectability.

Hilar cholangiocarcinoma
There are several staging systems for patients with hilar CCA, most of them including extent of ductal involvement by the tumor, hepatic artery, or portal venous involvement, functional status and volumetric assessment of the underlying liver, and the regional or distant tumor extension. The goal of imaging is to answer these questions in order to increase the proportion of RO resections.

Ultrasound
Despite several series recommending ultrasound (US) for staging hilar CCA, US may fail to detect hepatic artery involvement or underestimate the extent of ductal involvement. Therefore, US by itself is insufficient for staging work-up.

Helical CT
Technical advances such as multidetector technology, multiphasic scanning, and millimetric collimation have considerably improved the results of CT in the past decade. Since 1990, more than 10 original articles have been published on the role of helical CT in staging hilar CCA. Helical CT has an accuracy of 82–87% in determining portal vein involvement [1–4]. Moreover, the presence of lobar atrophy is associated with lobar portal involvement in most cases. Helical CT was considered less accurate for hepatic...
artery involvement, but recent studies have shown an accuracy of 93% [1]. Table I indicates the respective sensitivities, specificities, and accuracies of CT series using helical technology. Conversely, CT has limited sensitivity of approximately 50% for N2 metastases [1]. CT is reliable in assessing the extent of ductal involvement by the tumor at the primary and secondary confluence, but usually underestimates more proximal extension. Indeed, CT cholangiography, which includes the administration of biliary contrast material, improves this staging.

Overall, CT has an accuracy of resectability of between 60% and 87.5%, with the best results published in the past 5 years (Table II). Even more important, the negative predictive value (patients with disease classified as unresectable and in whom unresectability has been confirmed) is quite high: 85–100% [1,5–7]. CT is less accurate than vascular invasion in detecting N2 metastases, small liver metastases, and peritoneal carcinomatosis.

Magnetic resonance imaging – magnetic resonance cholangiography

Although the role of MRI in assessing vascular invasion has been emphasized (Table I), the main goal of MRI is in correctly predicting the extent of ductal involvement.

Since the 1990s, approximately 10 original papers have been published on MRCP in hilar CCAs, but these studies are difficult to compare because of varying numbers of patients and methods of reference (ERCP, PTC, or surgical exploration).

Briefly:

- MRCP is highly feasible and allows interpretation in more than 90% of cases.
- The accuracy of MRCP ranges from 81% to 96% with the exception of one study with 67% [8–14].
- MRCP seems more accurate for types 1 and 2 Bismuth–Corlette classification than the others.
- Underestimation of the extent of ductal involvement is much more common than overestimation.
- MRCP is better than ERCP, but for some teams PTC remains the best technique [15].
- MRCP is accurate for planning treatment in 72% to 83% [9,10].

PET

FDG-PET was initially evaluated for the diagnosis of CCA and even detection of this tumor in primary sclerosing cholangitis. More recently, studies have focused on staging. Today, FDG-PET has been disappointing in the detection of regional lymph node metastases, i.e. with sensitivities of just 12% to 38% [16–18]. The sensitivity of FDG-PET compared to CT is lower [17,18]. Detection of peritoneal carcinomatosis is not good with numbers of false-positive and false-negative cases [16,19]. On the other hand, FDG-PET appears the best technique in detecting distant metastases, especially when using integrated positron emission and CT (PET/CT). Two studies have reported that findings can result in a change of management in 17% to 30% of patients deemed resectable after standard work-up [18,19]. Although these results have to be confirmed by larger series, PET may hold promise in the detection of hidden metastases and can play an additional role in the evaluation of resectability [20].

Intrahepatic cholangiocarcinoma

Contrary to hilar CCA, the literature on staging in intrahepatic CCA by imaging is poor. The most important prognostic factors in intrahepatic CCA are: tumor size of 2 or 3 cm or more, lymph node metastasis, multiple tumors or intrahepatic metastasis, and vascular invasion [21–23]. Serosal invasion is not considered a prognostic factor in all studies. Multivariate analyses have shown that lymph node metastasis, multiple tumors at presentation, symptomatic tumors, and vascular invasion are independent factors associated with poor postoperative outcome
Therefore, the goal of imaging is to get the best accuracy in assessing these findings. In most cases, satellite nodules are seen at imaging (65%) [24], usually when they are larger than 1 or 2 cm in diameter [25]; however, in Okabayashi’s article, among the 51 patients who were diagnosed preoperatively with a solitary tumor, 19 (37%) had multiple satellite lesions in the resected specimen [23]. CT and MRI are comparable in the detection of satellite lesions [26].

Vascular involvement is depicted in approximately 50% of cases and more often concerns the portal branch than the hepatic veins [25]. The presence of segmental or lobar atrophy is strongly associated with ipsilateral portal vein enacement. The accuracy of CT and MRI is high, and the false-negative cases correspond to enacement of segmental portal branches. Although these two examinations are comparable, vascular involvement is considered more visible on CT [26].

The overall accuracy of detecting metastatic lymph node is 77%, and the most common error on preoperative imaging is underestimation of nodal involvement. Lymph nodes around the cardiac portion of the stomach and along the lesser gastric curvature should be examined in addition to nodes in the hepatoduodenal ligament in intrahepatic CCA of the left lobe [27]. Although rarely reported in the staging of intrahepatic CCA, PET imaging may be helpful in demonstrating extrahepatic metastases.

**Extrahepatic distal cholangiocarcinoma**

Staging of extrahepatic CCA is challenging because this tumor tends to spread outside the wall of the bile duct and attention has to be paid to the adjacent vessels (portal vein and hepatic artery), the hepatoduodenal ligament, the proximal and distal biliary extent, and pancreatic invasion. CT and MRI are mandatory. 3D angiography and multiphase fusion images using MDCT may be useful tools [28]. Endoscopic sonography and, more recently, intraductal ultrasonography using a higher frequency have been reported in small series.

In conclusion, imaging is important in staging CCAs. Indications of each modality are well established for hilar CCA but less so for the other sites.

**References**


