Preoperative Imaging

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B.I. Choi and J.M. Lee

5.1 Introduction

Cholangiocarcinomas (CC) are relatively rare tumors, although their incidence is increasing worldwide [1]. CC is classified anatomically as intrahepatic (5–10 % of cases), perihilar (60–70 %), or distal (20–30 %) [2, 3]. Hilar cholangiocarcinoma (HCCA) originally described by Klatskin, is defined as adenocarcinoma of the extrahepatic biliary tree, arising from the biliary confluence and/or the main left or right hepatic ducts, whereas intrahepatic CC arises from the bile ducts peripheral to the secondary bifurcation of the left or right hepatic duct [4, 5]. Cancers arising in the perihilar region have been further classified according to the pattern of involvement of the hepatic ducts (the Bismuth-Corlette classification) (Fig. 5.1) [6]. Despite a great increase in knowledge and major improvements in diagnostic methods as well as surgical techniques, these tumors still are a problematic issue [7]. Preoperative histological confirmation of an HCCA can be difficult to obtain. Percutaneous needle biopsies and endoscopic brush biopsies are reliable only if they identify a malignancy (sensitivity, 50 %), and excessive reliance on negative results may miss the opportunity to resect an early lesion [8, 9]. Whereas the vast majority of hilar strictures are the result of an HCCA, histological diagnosis is not mandatory before exploration. Accurate detection and differentiation from other bile duct pathologies on imaging, such as inflammatory lesions or stone disease, are highly important [7].

Surgical resection remains the only potentially curative treatment modality [10–12]. However, HCCA is a disease characterized by frequent locoregional invasion into porta hepatis structures, and although not necessarily indicative of unresectability, they are associated with both locally advanced tumors and metastatic disease [12]. Therefore, the majority of patients, nearly two-thirds in some series, present with disease that is beyond surgical correction [13]. In general, operation for HCCA requires a supraduodenal bile duct excision, portal lymphadenectomy, cholecystectomy, bilioenteric reconstruction, and, in most cases, a partial hepatectomy, which carry significant risk of morbidity [14–16]. Therefore, accurate disease staging is clearly critical for identifying patients who would benefit from an operation and for avoiding a non-therapeutic laparotomy [12].

Recently, cross-sectional imaging modalities such as multi-row detector computed tomography (MDCT) and magnetic resonance imaging (MRI) with magnetic resonance cholangiopancreatography(MRCP) have made considerable advances, and have contributed to robust biliary imaging with higher temporal and spatial resolution. Therefore, currently, those noninvasive cross sectional imaging modalities are more frequently used for diagnosis and tumor staging, whereas invasive examinations, including diagnostic endoscopic retrograde cholangiography (ERC) or percutaneous cholangiography or endoscopic ultrasound (EUS), have become less important [2, 7]. If HCCAs is diagnosed on preoperative imaging study, the next step is to exclude the established criteria for unresectable tumors, and then to define the tumor spread, and to identify any other combined findings [17]. The diagnosis and staging of CC require a multimodality approach involving laboratory, radiologic, endoscopic, and pathologic analysis [18]. Despite the variety of techniques used, determining the extent of disease still poses a challenge and is often underestimated [19]. Given that these tumors are usually very small, although these imaging tests can suggest the diagnosis, the major issue of imaging with this tumor is to determine whether the tumor is resectable [4]. In the absence of clear evidence of unresectability, all suspected HCCA should be considered for resection [13].

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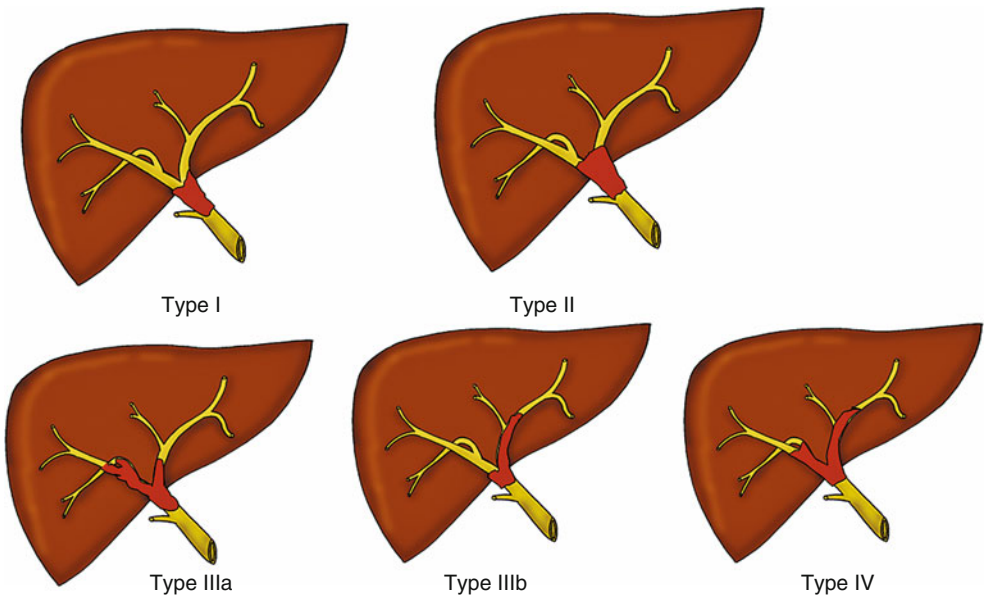

Fig. 5.1 Classification of biliary extent of hilar cholangiocarcinoma according to Bismuth-Corlette

5.2 Imaging Techniques

Imaging studies are essential in establishing the cause of jaundice, whether bile duct strictures are benign or malignant, and planning management in patients with suspected CC. The appropriate selection of radiological tests necessary to evaluate a patient with a suspected HCCA has undergone significant evolution in recent years. The diagnostic procedures include the traditional procedures of diagnosing bile duct pathologies such as transabdominal and endoscopic ultrasonography and ERC or percutaneous cholangiography as well as the modern cross-sectional imaging modalities such as MDCT, MRI with MR angiography (MRA) or MRCP, and positron emission tomography (PET) [7]. Until recently, invasive techniques such as transhepatic percutaneous cholangiography, ERC, and visceral angiography, combined with CT scanning were required to establish the diagnosis and determine resectability. However, besides being invasive in nature, recent studies have found that preoperative biliary instrumentation, particularly when combined with biliary stenting, increases perioperative infectious complications [20, 21]. Advances in imaging technology such as CT or MRI, combined with a philosophical approach aimed at limiting biliary instrumentation, have led us to more frequent use of MDCT with CT angiography, and/or MRI with MRCP with good determination of the disease extent and the potential respectability [22–25].

5.2.1 Ultrasonography

Ultrasound (US) is one of the first-line imaging modalities chosen for the evaluation of biliary disease [19]. At many centers, most jaundiced patients undergo initial transabdominal US to confirm biliary ductal dilatation, localize the site of the obstruction, and exclude gallstones [26]. Although US can effectively demonstrate dilatation of the bile duct, it has only limited value in demonstrating the obstructing lesion in this type of tumor [4]. Most common findings of HCCA on US include nonspecific indirect signs such as intrahepatic bile duct dilatation with an abrupt change in bile duct caliber and nonunion of the right and left ducts. Although perihilar cancers may not be detected, especially if small, indirect signs (ductal dilatation throughout the obstructed liver segments) may point toward the diagnosis of HCCA. With state-of-the-art equipment, an excellent view even of the central hepatic parts with high spatial resolution is possible [27]. With regard to detection of intrahepatic bile duct dilatation, ultrasound reveals up to 100 % sensitivity for experienced examiners [28]. Color Doppler and spectral Doppler are helpful tools for detecting compression and tumor encasement of the portal vein or hepatic artery. However, for direct tumor assessment and differentiation between benign or malignant biliary lesions in the course of the common bile duct, it often has only limited value because of the image degradation from bowel gas and difficult anatomy [28]. In addition, US has poor sensitivity for detecting metastases in the lymph nodes (LN) (37 %), liver (66 %), and peritoneum (33 %) [29]. Overall, the sensitivity and specificity of ultrasound is poor in the diagnosis of HCCA, and staging generally relies on other imaging modalities [26, 30]. On the other hand, EUS is able to provide detailed information about pathologies in the hepatic porta, although it is invasive and its quality also depends on the experience of the examiner [28, 31, 32]. In addition, EUS seems to be more accurate at determination of regional LN and vascular involvement, and has the ability to perform direct-guided, fine-needle aspiration (FNA) on primary tumors as well as

local LNs with sensitivity, specificity, and accuracy of 86–89, 100, and 88–91 %, respectively [31, 33, 34]. More recently, intraductal US has been developed and it uses small-diameter probes that can be inserted over a 9-mm guide wire at the time of direct cholangiography, providing US views that are 89 % accurate at determining the benign or malignant nature of biliary strictures and 82 % accurate at determining respectability [31, 35]. As with any US procedure, the accuracy of IDUS is again operator dependent [36].

5.2.2 Direct Cholangiography

Cholangiography through a retrograde endoscopic or percutaneous transhepatic approach may provide the most accurate anatomic information pertaining to which segmental branches are involved [4, 37]. Preoperative cholangiography may be indicated either diagnostically or therapeutically for patients with biliary obstruction.

The choice between ERCP and percutaneous cholangiography (PTC) is dictated by institutional experience and anatomic characteristics of the tumor: hilar and intrahepatic lesions typically can be viewed better with PTC [36]. However, ERCP is preferred in patients with primary sclerosing cholangitis (PSC) since the marked stricturing of the intrahepatic biliary tree makes a percutaneous approach difficult. Both modalities carry an overall sensitivity of 75–85 %, a specificity of 70–75 %, and an accuracy of 95 % in identifying the presence and extent of CC [2, 28, 36]. However, the invasiveness of both procedures is a notable limiting factor, favoring routine use of MRCP with or without EUS during the diagnostic stage of most cases unless the development of cholangitis demands early interventional therapy [38, 39]. Furthermore, direct cholangiography provides information only on the ductal system as a filling defect in the lumen, whereas any data on extraductal extension or the cause of the biliary obstruction cannot be obtained (Fig. 5.2) [7]. Other diseases that can cause hilar obstruction indistinguishable from HCCAs are metastases to periportal lymph nodes, gallbladder cancer invading the hepatoduodenal ligament, lymphadenopathy due to other inflammation, and idiopathic benign focal stricture of the bile duct [4]. However, direct cholangiography affords the opportunity of obtaining brush cytology and/or biopsy specimens, which can assist with making a definitive diagnosis [36]. Although these sampling methods carry sensitivities ranging from 10 to 80 % in the diagnosis of CC, the experience of most authorities has been at the lower end of this range, reflective of the substantial associated desmoplastic reaction and low cellularity seen in many CCs [32, 40]. This limitation has frequently led to the need to make definitive treatment decisions without the advantage of tissue diagnosis [36].

Nevertheless, in some centers, particularly in Japan, direct cholangiography of segmental ducts and cholangioscopy are still used in the evaluation of respectability [41–45]. This approach generally involves placement of multiple percutaneous biliary drainage catheters to allow complete access to the biliary tree. This is frequently combined with preoperative portal vein embolization in an effort to lower the risk of postoperative hepatic failure. Such an aggressive diagnostic evaluation may increase resectability but requires a prolonged hospital stay, and its ultimate value is unclear [46].

5.2.3 MDCT

Because of its widespread availability, CT is commonly obtained in patients with suspected biliary malignancy. It is useful for detecting biliary tumors, the level of biliary obstruction, and the presence of liver atrophy. In addition, MDCT has greatly enhanced the capabilities of CT in the assessment of HCCA. With state-of-the art scanners, the entire upper abdomen can be covered with a sub-millimeter collimation in one breath hold (<5 s). With these data, high-quality multiplanar reconstructions (MPR) in sagittal, coronal, oblique coronal or curved planes can be acquired, which are helpful for assessing the complex anatomy of the biliary system (Fig. 5.2) [47–49]. Moreover, the arterial and portovenous enhancement phases are clearly separated. The detail representation of the hepatic artery or portal vein as well as possible tumor invasion of these vessels at the porta hepatis can be demonstrated adequately [7]. CT can image the primary site of HCCA in 70–90 % of cases as lesions that are hypo- or hyper-attenuating relative to normal hepatic parenchyma during arterial and portal venous phases before showing gradual enhancement during delayed phase images [4, 47]. Although HCCA sometimes is not well demonstrated on CT, ductal dilatation in both hepatic lobes with a contracted gallbladder or nonunion of the right and left hepatic ducts suggest a Klatskin tumor.

Although previous reports have shown only a limited value of CT in diagnosing tumors of the biliary system with tumor detection rates of only 69 % and correct assessment of resectability in only 54 % [50], when performed with modern technology, the detection rate of biliary tumors is much better, with accuracies up to 100 % in hepatic arterial dominant phase scans and 86 % in portovenous phase scans [51]. The overall accuracy of CT for assessing resectability ranges between 60 and 86 % with sensitivities between 56 and 76 % [7, 47, 51–58].

5.2.4 MRI

For many years, biliary MRI was limited by poor spatial resolution as well as motion artifacts related with breathing. However, recently introduced technical improvements including parallel imaging and rapid sequences such as

gradient echo, and half Fourier acquired single-shot turbo spin echo (HASTE), and respiratory independent sequences navigator triggering, have contributed to increasing use of MRI, including MRCP for evaluation of biliary tumors [7, 59]. Each of these techniques or in combination, have substantially increased the spatial and temporal resolution as a critical parameter in biliary imaging with reduced blurring. It is important to use sequences with thin-slice thickness (3–4 mm) that provide sufficient signal to obtain good quality images and are sufficiently thin to detect subtle abnormalities. For MRCP, the latest developments are 3D-triggered T2-weighted fast spin echo sequences with a voxel size of approximately 1.5 mm, by which high quality MPR images and maximum intensity projections (MIP) can be obtained

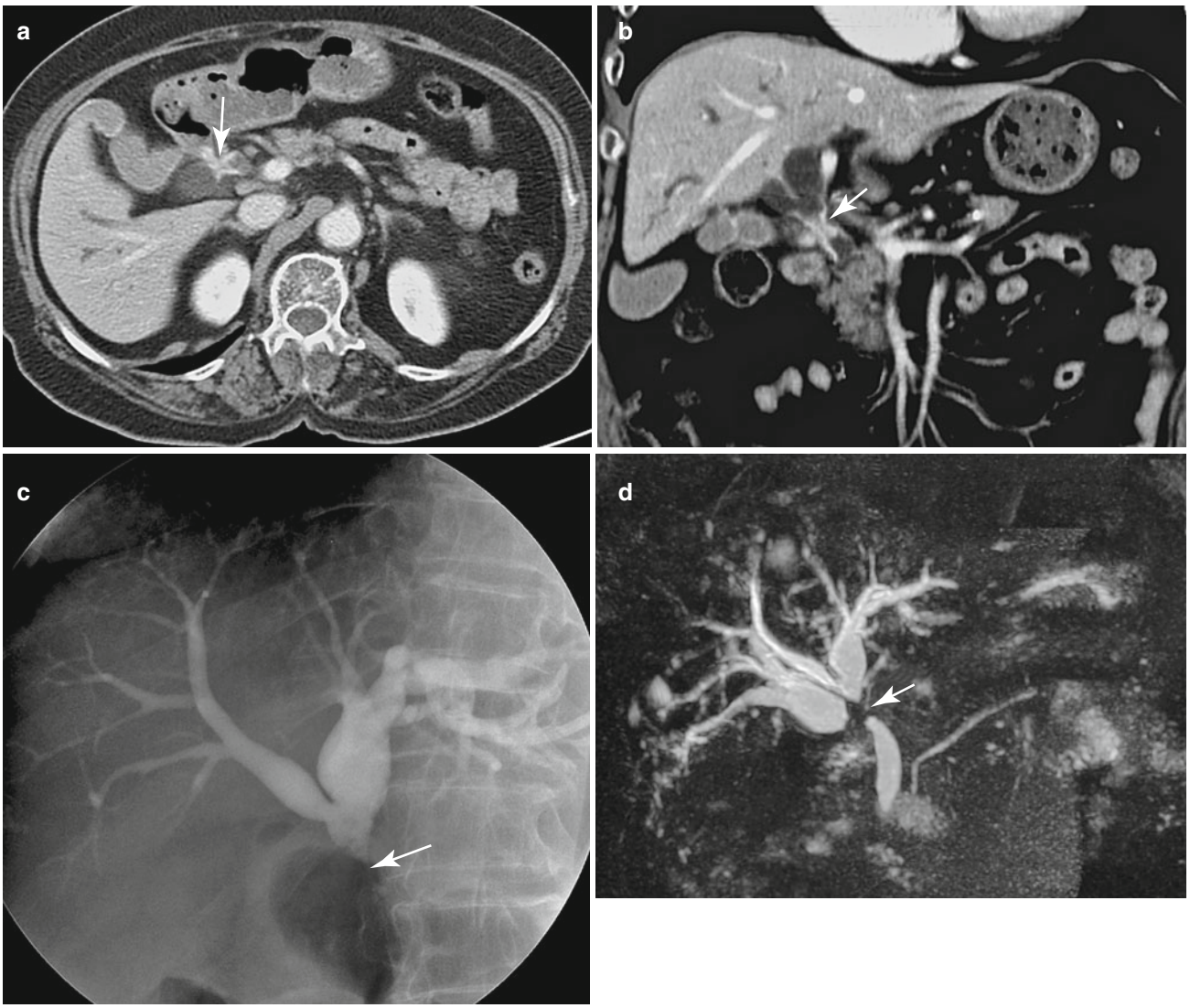

Fig. 5.2 Surgically proven periductal infiltrating type, hilar cholangiocarcinoma (Bismuth-Corlette type II). (**a**) Contrast-enhanced axial CT scan shows a hilar cholangiocarcinoma, which is depicted as a thickened and strongly enhancing wall of the hilar duct (*arrow*), and dilatation of the intrahepatic bile duct. (**b**) Coronal multiplanar reformatted image better demonstrates a longitudinal extent of the hilar cholangiocarcinoma than axial CT (**a**). Note that a hilar cholangiocarcinoma presents as a thickened bile duct wall with enhancement (*arrow*) during the portal venous phase. (**c**) On direct cholangiogram obtained by contrast injection through the percutaneous transhepatic biliary drainage, the proximal common bile duct is obliterated by the tumor. However, bilateral secondary confluences are intact. (**d**) MR cholangiography also demonstrates a stricture (*arrow*) involving hilar duct and proximal common bile duct, with dilatation of upstream intrahepatic bile duct. (**e** and **f**) Axial T2-weighted image (**e**) and T1-weighted image (**f**) show a focally thickened ductal wall (*arrow*) obliterating the lumen. On both T1- and T2-weighted images, the tumor appears slightly hypointense to the liver. (**g**) On contrast-enhanced axial T1-weighted image, the tumor is appreciated as a thickened and strongly enhancing wall of the hilar duct (*arrow*), anterior to the right portal vein branch. (**h**) On coronal T1-weighted image, the tumor involves the hilar portion as well as the proximal common bile duct (*arrow*). (**i**) The macroscopic picture of the resected specimen shows an irregular mucosal lesion (*arrows*) involving the primary biliary confluence as well as right and left intrahepatic bile duct

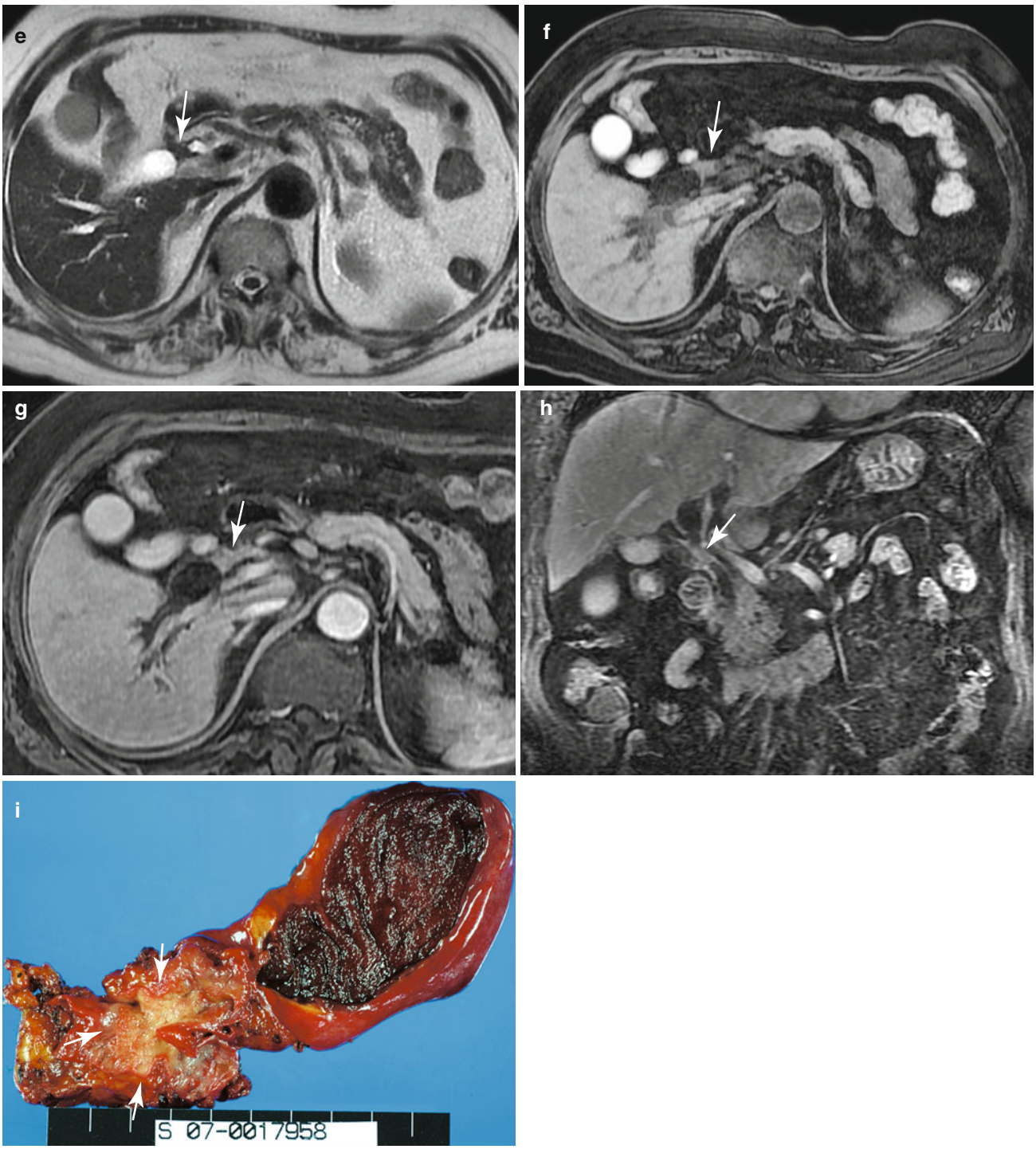

Fig. 5.2 (continued)

(Figs. 5.2 and 5.3). In addition, the axial thick-slab TSE T2-weighted cholangiographic views obtained at the hilum are the most informative about the number of strictures and the involvement of the different liver segments, including the caudate lobe (Fig. 5.4) [59]. MRCP can be very useful in visualization of the exact biliary tree map regarding extent of HCCA, in a non-invasive manner.

The principle sequences used for imaging the biliary system are T2-weighted imaging, MRCP, and pre- and postgadolinium-enhanced volumetric fat-suppressed gradient echo T1-weighted imaging [59]. MRI, in conjunction with MRCP, has proved helpful in diagnosing HCCA and in determining respectability [7, 60, 61]. This is due to MR imaging and MRCP being able to investigate all different

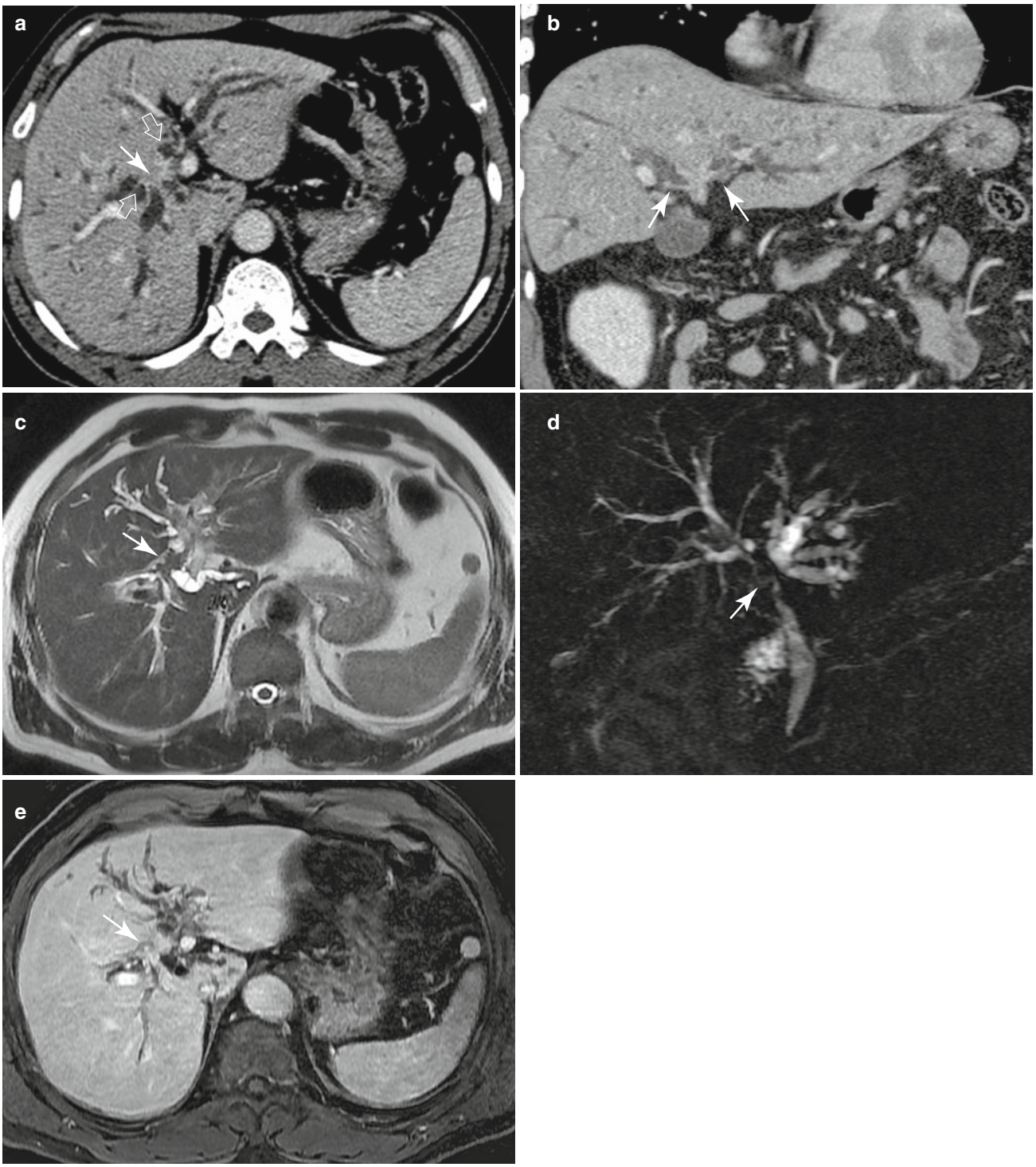

Fig. 5.3 Surgically proven periductal infiltrating type, hilar cholangiocarcinoma (Bismuth-Corlette type IV). (**a**) Contrast enhanced axial CT scan shows a slightly hyperattenuated mass (*arrow*) with heterogeneous enhancement, involving both secondary biliary confluences (*open arrows*). Note that there is a dilatation of the bile duct branches of the caudate lobe. Thus, CT diagnosis was Bismuth-Corlette type IV. (**b**) Coronal multiplanar reformatted image also demonstrates an irregular thickening of the hilar duct with hyperenhacement (*arrows*). (**c** and **d**) Axial T2-weighted image (**c**) and MR cholangiography (**d**) show an obliteration of the hilar duct (*arrow*) by the tumor with a hypointensity compared with adjacent liver parenchyma. (**e**) Contrast-enhanced axial T1-weighted image demonstrates an irregular shaped tumor (*arrow*) with hyperenhancement and upstream ductal dilatation, near the lobar branches of the portal vein

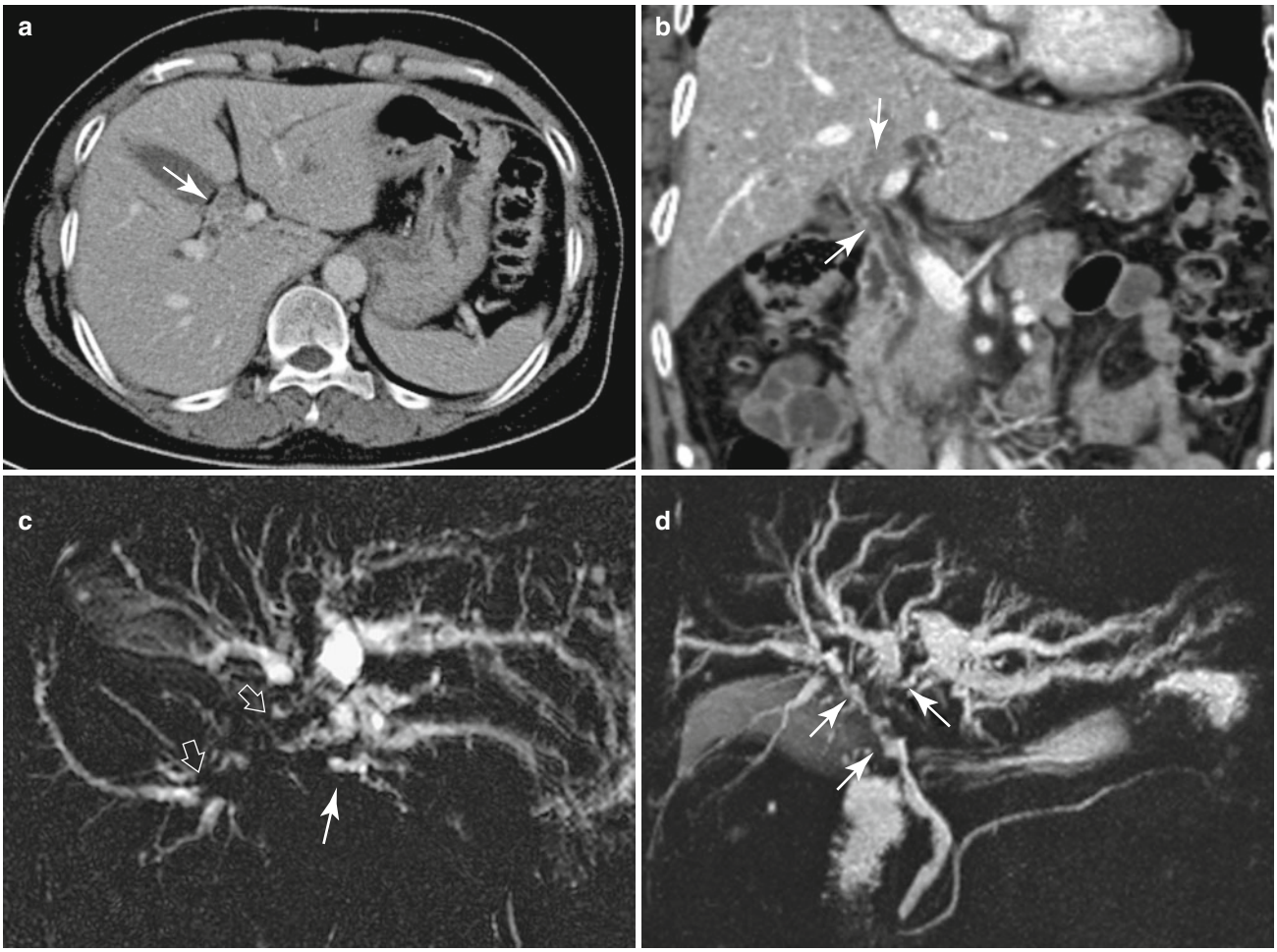

Fig. 5.4 Histolgically proven intraductal polypoid hilar cholangiocarcinoma (Bismuth-Corlette type IV). (**a**) Portal venous phase CT scan shows an intraductal mass (*arrow*) with slight hypoattenuation as compared with the adjacent hepatic parenchyma. (**b**) Coronal multiplanar reformatted image demonstrates multiple intraluminal filling defects (*arrows*) in the left and right intrahepatic ducts, hilar duct, and the common bile duct. (**c**) Axial slab MRCP also demonstrates a long stricture involving hilar duct and bilateral secondary biliary confluences (*open arrows*), and dilatation of intrahepatic bile duct in caudate lobe (*arrow*). Note that axial slab MR cholangiography con provide the most informative about the number of strictures and the involvement of the different liver segments, including caudate lobe. (**d**) Coronal multiplanar reformatted image of 3D-T2-weighted MRC shows irregular narrowing of both intrahepatic bile ducts and hilar duct, caused by multiple polypoid intraductal lesions (*arrows*)

components: bile ducts, vessels, and invasion of adjacent liver parenchyma [17]. The morphology of bile duct stricture detectable on MRCP closely reflects the gross morphologic changes occurring along the biliary ductal walls [4, 62, 63]. In addition, combined use of MRCP and dynamic MRI can display the overall extent of biliary tree involvement and the correct diagnosis of biliary malignancies (Fig. 5.3) [4, 17, 61, 64]. This capability of obtaining both cross sectional MRI and MRCP results in nearly 100 % sensitivity in diagnosing biliary obstruction, 98 % accuracy in identifying the level of obstruction, and an 88–95 % accurate assessment of the cause of obstruction; performance equivalent to that of direct cholangiography [28, 36, 60, 61, 65]. Given this cholangiographic performance, the ability to concurrently evaluate for intra-abdominal local or distant metastasis and its noninvasive nature, MRCP has become the imaging modality of choice in evaluation of biliary strictures and CC [15, 36, 60, 61]. Until now, the place of MRCP in the preoperative evaluation of suspected CC is evolving and somewhat center-dependent [66]. Some consider that the combination of MRCP and spiral CT have largely supplanted invasive cholangiography in patients with obstructive jaundice thought to be due to a proximal lesion. However, one of the disadvantages of MRCP is that current technology does not allow any intervention to be performed, such as stent insertion, or biopsy [28]. An accurate assessment of resectability of CC is rendered by MRI with MRCP in 70–80 % of cases, a rate equivalent to that provided by the combination of CT and direct cholangiography in prospective comparison [67].

From a strategic standpoint, it is important to recognize that stenting and percutaneous drainage procedures cause mild bile duct wall inflammation that is indistinguishable on MRI from CC spread [17]. Consequently, MRCP should be performed before interventional procedures whenever possible [17, 36]. For preoperative assessment of resectability of HCCA, however, several types of invasive imaging such as cholangiography and angiography are sometimes required, when the tumor size is too small to demonstrate its extent clearly on MRI with MRCP [4].

5.2.5 FDG-PET

Evaluation of metastatic disease from several neoplasms has recently been aided with the development of positron emission tomography (PET) scanning, particularly when fused with CT [36]. FDG-PET scan permits visualization of CCs because of the high glucose uptake of bile duct epithelium [68]. PET scans can detect nodular CCs as small as 1 cm but is less helpful for infiltrating tumors [68, 69]. However, the role of FDG-PET in the management of HCCA is yet less clear [70]. Most studies addressing the use of FDG-PET have included few patients and have combined CC with other biliary cancers, making interpretation of these studies difficult. Nonetheless, these studies suggest a potential benefit of FDG-PET; it can be helpful when there is a question of possible metastatic disease [32, 36, 71, 72]. In a study of 62 patients with CC who underwent preoperative PET staging at the Memorial Sloan-Kettering Cancer Center, 78 % of the tumors were PET-avid, and PET identified occult metastatic disease that altered management in 24 % of patients [71]. However, pending further data, PET does not currently have a routine role in preoperative evaluation of HCCA.

5.3 Imaging Findings

HCCAs can be classified as exophytic, infiltrative, polypoid, or a combination of these based on their typical growth pattern [73–75]. At the hilar portion, CCs are most commonly of the infiltrative type (>70 %) and less frequently they manifest as exophytic or polypoid lesions [59, 74]. Radiologic studies can show different imaging features of HCCAs based on their growth pattern [63, 76, 77]. Those of unusual histologic type (e.g., mucin-hypersecreting CC, squamous adenocarcinoma, biliary cystadenocarcinoma, and mucinous carcinoma) show a different growth pattern compared with that of the typical ones (i.e., ductal), and also may show different imaging features [78]. For example, mucin-producing intraductal papillary neoplasm (adenocarcinoma/adenoma) in the bile duct bears a striking similarity to intraductal papillary mucinous neoplasms of the pancreas with regard to its histopathologic features and is becoming recognized as a specific type of neoplasm [79]. CCs frequently develop in patients with any of a variety of preexisting bile duct diseases, some of which are considered precursors of CC (e.g., biliary lithiasis, clonorchiasis, recurrent pyogenic cholangitis, and primary sclerosing cholangitis) [75]. Although imaging tests can suggest the diagnosis of a HCCA, in some patients with those precursors, early diagnosis of a HCCA can be difficult [74]. In patients with primary sclerosing cholangitis, early diagnosis of a CC can be challenging, because CCs or significant intrahepatic biliary dilatation are infrequently identified on imaging. Similarly, in patients with recurrent pyogenic cholangitis in whom severe periductal fibrosis and hepatolithiasis have developed, diagnosis of a CC can be very difficult, due to the presence of severe biliary stricture and ductal wall thickening [80]. Therefore, a high index of suspicion and multidisciplinary investigative procedures are needed in those patients.

5.3.1 Periductal-Infiltrating Hilar Cholangiocarcinoma

Periductal infiltrating CA is the most common type of HCCA (70 % of cases). At pathologic analysis, infiltrating HCCA manifests as a sclerotic lesion with abundant fibrous tissue [74, 80]. US shows dilatation of the intrahepatic bile duct and normal-size extrahepatic bile ducts, as well as nonunion of the right and left ducts. This association suggests the diagnosis of HCCA. Although the tumor can appear as a mural thickening or an encircling mass along the bile duct wall, a definite mass is rarely seen on sonograms [81]. On CT and MRI, the key diagnostic features of periductal infiltrating hype HCCA include a long segment stricture with an irregular margin, asymmetric narrowing and peripheral ductal dilatation, ductal enhancement, and periductal soft tissue lesion (Figs. 5.2 and 5.3) [59]. Benign stenoses usually appear as regular, symmetric, and smooth-shaped narrowing of the lumen [82]. Although it is not a sensitive feature, thickening of the ductal wall more than 5 mm is suggestive of CCs [61]. Nonunion of the right and left hepatic ducts with or without a visibly thickened wall is a typical finding of infiltrating HCCA [83]. On contrast-enhanced CT, infiltrating tumors are seen as an asymetrically thickened ductal wall obliterating the lumen, and approximately 80 % of these tumors are hyperattenuating relative to the liver on arterial or portal phase or both (Fig. 5.2) [77, 84]. On either direct cholangiography or MRCP, HCCA frequently shows a long segment stricture with an irregular margin, asymmetric narrowing and peripheral ductal dilatation (Fig. 5.3). The involved bile duct lumen may be completely obstructed or markedly narrowed. On cross-sectional MR images, the lesion appears hypointense to the liver on T1-weighted images and slightly or moderately hyperintense on T2-weighted images.

5.3.2 Mass-Forming Exophytic Hilar Cholangiocarcinoma

Mass-forming exophytic HCCA manifests as hilar ductal stricture and a parenchymal mass with connection to the hilar duct. The parenchymal mass frequently present as a low-attenuation mass with peripheral rim enhancement during the arterial dominant phase, and homogeneous hypoattenuation in the portal dominant phase, findings that are similar to those for peripheral intrahepatic CC [47, 63, 75, 83]. It can be difficult or even impossible to ascertain whether the carcinoma arises at the main hepatic juncture or represents a peripheral CC that secondarily obliterates the hilar area [4, 86].

5.3.3 Intraductal Polypoid Hilar Cholangiocarcinoma

On pathology, intraductal papillary CCs can present as an polypoid mass or cast-like intraductal growth, superficial spreading growth or cyst-forming bile duct dilatation [73, 76, 78]. Variable degrees of bile duct dilatations may be observed. On CT or MRI with MRCP, intraductal HCCAs manifest as single or multiple intraductal soft tissue masses that are hypoattenuating or hypointense relative to the hepatic parenchyma or cast-like filling defects in bile duct on either CT or dynamic MRI (Fig. 5.4) [63, 77, 86]. On cross-sectional MR images, the lesion appears hypointense to the liver on T1-weighted images and moderately hyperintense with a high signal on T2-weighted images [59, 63]. The tumors are frequently multiple or disseminated within the biliary system and involve the intrahepatic and extrahepatic bile ducts [67, 84, 87]. A subtype of intraductal papillary CCs is intraductal papillary mucin producing neoplasm of the bile duct, which can secrete mucin. This tumor often demonstrates dilatation of the upstream bile duct as well as the downstream bile duct, or entire biliary tree because of excessive mucin discharge or compression by the primary tumor [79]. When bile duct dilatation is prominent and associated aneurismal dilatation occurs, mucin production and consequent bile flow obstruction should be suspected [59]. At MR imaging, mucin may have the same signal intensity as bile or manifest as multiple cordlike filling defects that are better diagnosed at ERCP.

5.4 Preoperative Evaluation and Staging

The surgical management of HCCA and the indications for operative exploration are complex. Precise preoperative staging is necessary to determine whether the patient's disease is potentially resectable and warrants operative exploration and to guide the surgeon in planning the operation [46]. Comprehensive preoperative imaging of biliary tumors should: (1) show the size and location of a primary lesion and assess the longitudinal and radial extent of bile duct involvement; (2) show involvement of the hepatic artery (main and lobar branches) and portal vein (main and lobar branches) with the tumor, for the purpose of surgical planning; (3) Depict the presence and extent of liver invasion and lobar atrophy or hypertrophy; and (4) enable the detection of regional lymph nodes and metastases [59, 62]. Despite that several staging systems for CC have been proposed based on pathologic evaluation of the surgical specimen, for surgical planning, preoperative staging based on the information that is garnered from imaging of patients with HCCA is necessary. The two most commonly used are the tumor, node, metastasis staging system, devised by the American Joint Committee on Cancer (AJCC), and the modified Bismuth-Corlette classification for HCCA (Fig. 5.1) [88–91]. Both systems are based mainly on the extent of primary tumor involvement within the hepatic ductal system. In an attempt to improve the preoperative clinical and prognostic usefulness of the AJCC tumor, node, metastasis system, modified T-stage criteria for HCCA have been proposed by Memorial Sloan-Kettering Cancer Center [14, 92]. This modified T staging that takes into consideration of both vascular involvement by local tumor extension and the presence or absence of liver atrophy. This proposed T staging system is predictive of resectability, the likelihood of nodal or distant metastases, and overall survival [92].

The major determinants of resectability are the extent of tumor within the biliary tree, the amount of hepatic parenchyma involved, vascular invasion, hepatic lobar atrophy, and metastatic disease. The infiltrative growth pattern and the close proximity to the portal vein and the hepatic artery of HCCA result in a low resectability rate, ranging between 20 and 40 % [18, 40, 93]. Although there is some disagreement about the criteria for resectability among surgeons, unsectability of HCCA is suggested by (a) cholangiographic evidence of severe bilateral involvement of the secondary confluence, (b) involvement of the main trunk of the portal vein, (c) involvement of both branches of the portal vein or bilateral involvement of the hepatic artery and portal vein, or (d) vascular involvement on one side of the liver and extensive bile duct involvement on the other side [4, 13, 62].

Understaging of CCs on preoperative imaging may frequently occur due to a lack of recognition of submucosal spread in involved bile ducts on imaging or limitation of imaging for detection of metastases [32, 94–96]. Even multiphasic CT is limited in its ability to establish the extent of intraductal tumor spread and resectability. In one report of 29 patients with histologically-proven HCCA, all of whom underwent multiphasic CT (arterial and portal venous phase), resectability was correctly predicted in only 60 % [51]. In the study by Park and colleagues, overall accuracy rates for predicting involvement of the bilateral secondary biliary confluences were 90.7 and 85.1 %, respectively, for MR imaging with MRCP and MDCT compared with direct

cholangiography [67]. However, in general, the relationship of the tumor to the vessels and surrounding organs is regarded as being more easily evaluated on CT as opposed to MRI [97]. However, precise preoperative evaluation of tumor extent often requires several imaging or combined use of imaging with endoscopy such as cholangioscopy or laparoscopy [2, 46, 98]. Despite the enhanced diagnostic capability of newer radiologic studies such as MRI with MRCP and dynamic CT, unless there is clear evidence of metastatic disease, true resectability can be determined only by operative evaluation [96, 99].

References

1. Shaib YH, Davila JA, McGlynn K, El-Serag HB, et al. Rising incidence of intrahepatic cholangiocarcinoma in the United States: a true increase? J Hepatol. 2004;40(3):472–7.
2. Aljiffry M, Walsh MJ, Molinari M. Advances in diagnosis, treatment and palliation of cholangiocarcinoma: 1990–2009. World J Gastroenterol. 2009;15(34):4240–62.
3. Nakeeb A, Pitt HA, Sohn TA, et al. Cholangiocarcinoma—a spectrum of intrahepatic, perihilar, and distal tumors. Ann Surg. 1996;224(4):463–73.
4. Choi BI, Lee JM, Han JK. Imaging of intrahepatic and hilar cholangiocarcinoma. Abdom Imaging. 2004;29(5):548–57.
5. Klatskin G. Adenocarcinoma of hepatic duct at its bifuration within porta hepatis—an unusual tumor with distinctive clinical and pathological features. Am J Med. 1965;38(2):241–56.
6. Bismuth H, Castaing D, Traynor O. Resection or palliation: priority of surgery in the treatment of hilar cancer. World J Surg. 1988; 12(1):39–47.
7. Zech CJ, Schoenberg SO, Reiser M, et al. Cross-sectional imaging of biliary tumors: current clinical status and future developments. Eur Radiol. 2004;14(7):1174–87.
8. Wetter LA, Ring EJ, Pellegrini CA, et al. Differential diagnosis of sclerosing cholangiocarcinomas of the common hepatic duct (klatskin tumors). Am J Surg. 1991;161(1):57–62; discussion 62–53.
9. Ryan ME. Cytologic brushings of ductal lesions during ERCP. Gastrointest Endosc. 1991;37(2):139–42.
10. Nagorney DM, Kendrick ML. Hepatic resection in the treatment of hilar cholangiocarcinoma. Adv Surg. 2006;40:159–71.
11. Nakeeb A, Tran KQ, Black MJ, et al. Improved survival in resected biliary malignancies. Surgery. 2002;132(4):555–63.
12. Rocha FG, Matsuo K, Blumgart LH, et al. Hilar cholangiocarcinoma: the memorial Sloan-Kettering Cancer Center experience. J Hepatobiliary Pancreat Sci. 2010;17(4):490–6.
13. Chamberlain RS, Blumgart LH. Hilar cholangiocarcinoma: a review and commentary. Ann Surg Oncol. 2000;7(1):55–66.
14. Jarnagin WR, Fong Y, DeMatteo RP, et al. Staging, resectability, and outcome in 225 patients with hilar cholangiocarcinoma. Ann Surg. 2001;234(4):507–17.
15. Khan SA, Thomas HC, Davidson BR, et al. Cholangiocarcinoma. Lancet. 2006;366:1303. Lancet. 2006;367(9523):1656.
16. Jonas S, Benckert C, Thelen A, et al. Radical surgery for hilar cholangiocarcinoma. Eur J Surg Oncol. 2008;34(3):263–71.
17. Masselli G, Manfredi R, Vecchioli A, et al. MR imaging and MR cholangiopancreatography in the preoperative evaluation of hilar cholangiocarcinoma: correlation with surgical and pathologic findings. Eur Radiol. 2008;18(10):2213–21.
18. Blechacz B, Gores GJ. Cholangiocarcinoma: advances in pathogenesis, diagnosis, and treatment. Hepatology. 2008;48(1):308–21.
19. Blechacz BR, Gores GJ. Cholangiocarcinoma. Clin Liver Dis. 2008;12(1):131–50, ix.
20. Heslin MJ, Brooks AD, Hochwald SN, et al. A preoperative biliary stent is associated with increased complications after pancreatoduodenectomy. Arch Surg. 1998;133(2):149–54.
21. Hochwald SN, Burke EC, Jarnagin WR, et al. Association of preoperative biliary stenting with increased postoperative infectious complications in proximal cholangiocarcinoma. Arch Surg. 1999;134(3):261–6.
22. Hochwald SN, Dobryansky MB, Rofsky NM, et al. Magnetic resonance cholangiopancreatography accurately predicts the presence or absence of choledocholithiasis. J Gastrointest Surg. 1998;2(6): 573–9.
23. Hochwald SN, Rofsky NM, Dobryansky M, et al. Magnetic resonance imaging with magnetic resonance cholangiopancreatography accurately predicts resectability of pancreatic carcinoma. J Gastrointest Surg. 1999;3(5):506–11.
24. Kim HJ, Lee DH, Lim JW, et al. Multidetector computed tomography in the preoperative workup of hilar cholangiocarcinoma. Acta Radiol. 2009;50(8):845–53.
25. Uchida M, Ishibashi M, Tomita N, et al. Hilar and suprapancreatic cholangiocarcinoma: value of 3D angiography and multiphase fusion images using MDCT. Am J Roentgenol. 2005;184(5):1572–7.
26. Foley WD, Quiroz FA. The role of sonography in imaging of the biliary tract. Ultrasound Q. 2007;23(2):123–35.
27. Bloom CM, Langer B, Wilson SR. Role of US in the detection, characterization, and staging of cholangiocarcinoma. Radiographics. 1999;19(5):1199–218.
28. Rosch T, Meining A, Fruhmorgen S, et al. A prospective comparison of the diagnostic accuracy of ERCP, MRCP, CT, and EUS in biliary strictures. Gastrointest Endosc. 2002;55(7):870–6.
29. Neumaier CE, Bertolotto M, Perrone R, et al. Staging of hilar cholangiocarcinoma with ultrasound. J Clin Ultrasound. 1995; 23(3):173–8.
30. Slattery JM, Sahani DV. What is the current state-of-the-art imaging for detection and staging of cholangiocarcinoma? Oncologist. 2006;11(8):913–22.
31. Varadarajulu S, Eloubeidi MA. The role of endoscopic ultrasonography in the evaluation of pancreatico-biliary cancer. Surg Clin North Am. 2010;90(2):251–63.
32. Weber A, Schmid RM, Prinz C. Diagnostic approaches for cholangiocarcinoma. World J Gastroenterol. 2008;14(26):4131–6.
33. Eloubeidi MA, Chen VK, Jhala NC, et al. Endoscopic ultrasound-guided fine needle aspiration biopsy of suspected cholangiocarcinoma. Clin Gastroenterol Hepatol. 2004;2(3):209–13.
34. Fritscher-Ravens A, Broering DC, Sriram PV, et al. EUS-guided fine-needle aspiration cytodiagnosis of hilar cholangiocarcinoma: a case series. Gastrointest Endosc. 2000;52(4):534–40.
35. Menzel J, Poremba C, Dietl KH, et al. Preoperative diagnosis of bile duct strictures – comparison of intraductal ultrasonography with conventional endosonography. Scand J Gastroenterol. 2000; 35(1):77–82.
36. Reitz S, Slam K, Chambers LW. Biliary, pancreatic, and hepatic imaging for the general surgeon. Surg Clin North Am. 2011; 91(1):59–92.
37. Yu SA, Zhang C, Zhang JM, et al. Preoperative assessment of hilar cholangiocarcinoma: combination of cholangiography and CT angiography. Hepatobiliary Pancreat Dis Int. 2010;9(2):186–91.
38. Andriulli A, Loperfido S, Napolitano G, et al. Incidence rates of post-ERCP complications: a systematic survey of prospective studies. Am J Gastroenterol. 2007;102(8):1781–8.
39. Loperfido S, Angelini G, Benedetti G, et al. Major early complications from diagnostic and therapeutic ERCP: a prospective multicenter study. Gastrointest Endosc. 1998;48(1):1–10.
40. Lazaridis KN, Gores GJ. Cholangiocarcinoma. Gastroenterology. 2005;128(6):1655–67.

41. Nimura Y. Preoperative biliary drainage before resection for cholangiocarcinoma (Pro). HPB (Oxford). 2008;10(2):130–3.
42. Nimura Y. Staging cholangiocarcinoma by cholangioscopy. HPB (Oxford). 2008;10(2):113–5.
43. Nimura Y. Radical surgery: vascular and pancreatic resection for cholangiocarcinoma. HPB (Oxford). 2008;10(3):183–5.
44. Nimura Y. Extended surgery in bilio-pancreatic cancer: the Japanese experience. Semin Oncol. 2002;29(6 Suppl 20):17–22.
45. Nimura Y, Kamiya J, Kondo S, et al. Aggressive preoperative management and extended surgery for hilar cholangiocarcinoma: Nagoya experience. J Hepatobiliary Pancreat Surg. 2000;7(2):155–62.
46. Miller G, Schwartz LH, D'Angelica M. The use of imaging in the diagnosis and staging of Hepatobiliary malignancies. Surg Oncol Clin N Am. 2007;16(2):343–68.
47. Choi JY, Kim MJ, Lee JM, et al. Hilar cholangiocarcinoma: role of preoperative imaging with sonography, MDCT, MRI, and direct cholangiography. AJR Am J Roentgenol. 2008;191(5):1448–57.
48. Endo I, Shimada H, Sugita M, et al. Role of three-dimensional imaging in operative planning for hilar cholangiocarcinoma. Surgery. 2007;142(5):666–75.
49. Tamm EP, Balachandran A, Bhosale P, et al. Update on 3D and multiplanar MDCT in the assessment of biliary and pancreatic pathology. Abdom Imaging. 2009;34(1):64–74.
50. Nesbit GM, Johnson CD, James EM, et al. Cholangiocarcinoma: diagnosis and evaluation of resectability by CT and sonography as procedures complementary to cholangiography. AJR Am J Roentgenol. 1988;151(5):933–8.
51. Tillich M, Mischinger HJ, Preisegger KH, et al. Multiphasic helical CT in diagnosis and staging of hilar cholangiocarcinoma. AJR Am J Roentgenol. 1998;171(3):651–8.
52. Akamatsu N, Sugawara Y, Osada H, et al. Diagnostic accuracy of multidetector-row computed tomography for hilar cholangiocarcinoma. J Gastroenterol Hepatol. 2010;25(4):731–7.
53. Cho ES, Park MS, Yu JS, et al. Biliary ductal involvement of hilar cholangiocarcinoma: multidetector computed tomography versus magnetic resonance cholangiography. J Comput Assist Tomogr. 2007;31(1):72–8.
54. Choi JY, Lee JM, Lee JY, et al. Assessment of hilar and extrahepatic bile duct cancer using multidetector CT: value of addingmultiplanar reformations to standard axial images. Eur Radiol. 2007;17(12):3130–8. Epub 8 May 2007.
55. Senda Y, Nishio H, Oda K, et al. Value of multidetector row CT in the assessment of longitudinal extension of cholangiocarcinoma-correlation between MDCT and microscopic findings. World J Surg. 2009;33(7):1459–67.
56. Unno M, Okumoto T, Katayose Y, et al. Preoperative assessment of hilar cholangiocarcinoma by multidetector row computed tomography. J Hepatobiliary Pancreat Surg. 2007;14(5):434–40.
57. Watadani T, Akahane M, Yoshikawa T, et al. Preoperative assessment of hilar cholangiocarcinoma using multidetector-row CT: correlation with histopathological findings. Radiat Med. 2008;26(7):402–7.
58. Cha JH, Han JK, Kim TK, et al. Preoperative evaluation of klatskin tumor: accuracy of spiral CT in determining vascular invasion as a sign of unresectability. Abdom Imaging. 2000;25(5):500–7.
59. Matos C, Serrao E, Bali MA. Magnetic resonance imaging of biliary tumors. Magn Reson Imaging Clin N Am. 2010;18(3):477–96, x.
60. Manfredi R, Masselli G, Maresca G, et al. MR imaging and MRCP of hilar cholangiocarcinoma. Abdom Imaging. 2003;28(3):319–25.
61. Manfredi R, Barbaro B, Masselli G, et al. Magnetic resonance imaging of cholangiocarcinoma. Sem Liver Dis. 2004;24(2):155–64.
62. Lee HY, Kim SH, Lee JM, et al. Preoperative assessment of resectability of hepatic hilar cholangiocarcinoma: combined CT and cholangiography with revised criteria. Radiology. 2006;239(1):113–21.
63. Kim JE, Lee JM, Kim SH, et al. Differentiation of intraductal growing-type cholangiocarcinomas from nodular-type cholangiocarcinomas at biliary MR imaging with MR cholangiography. Radiology. 2010;257(2):364–72.
64. Kim HJ, Lee JM, Kim SH, et al. Evaluation of the longitudinal tumor extent of bile duct cancer: value of adding gadolinium-enhanced dynamic imaging to unenhanced images and magnetic resonance cholangiography. J Comput Assist Tomogr. 2007;31(3):469–74.
65. Varghese JC, Farrell MA, Courtney G, et al. A prospective comparison of magnetic resonance cholangiopancreatography with endoscopic retrograde cholangiopancreatography in the evaluation of patients with suspected biliary tract disease. Clin Radiol. 1999;54(8):513–20.
66. Freeman ML, Sielaff TD. A modern approach to malignant hilar biliary obstruction. Rev Gastroenterol Disord. 2003;3(4):187–201.
67. Park HS, Lee JM, Choi JY, et al. Preoperative evaluation of bile duct cancer: MRI combined with MR cholangiopancreatography versus MDCT with direct cholangiography. AJR Am J Roentgenol. 2008;190(2):396–405.
68. Kim YJ, Yun M, Lee WJ, et al. Usefulness of 18F-FDG PET in intrahepatic cholangiocarcinoma. Eur J Nucl Med Mol Imaging. 2003;30(11):1467–72.
69. Anderson CD, Rice MH, Pinson CW, et al. Fluorodeoxyglucose PET imaging in the evaluation of gallbladder carcinoma and cholangiocarcinoma. J Gastrointest Surg. 2004;8(1):90–7.
70. Poultsides GA, Zhu AX, Choti MA, et al. Intrahepatic cholangiocarcinoma. Surg Clin North Am. 2010;90(4):817–37.
71. Corvera CU, Blumgart LH, Akhurst T, et al. F-18-fluorodeoxyglucose positron emission tomography influences management decisions in patients with biliary cancer. J Am Coll Surg. 2008;206(1):57–65.
72. Wakabayashi H, Akamoto S, Yachida S, et al. Significance of fluorodeoxyglucose PET imaging in the diagnosis of malignancies in patients with biliary stricture. Eur J Surg Oncol. 2005;31(10):1175–9.
73. Lim JH, Kim YI, Park CK. Intraductal mucosal-spreading mucin-producing peripheral cholangiocarcinoma of the liver. Abdom Imaging. 2000;25(1):89–92.
74. Lim JH, Park CK. Pathology of cholangiocarcinoma. Abdom Imaging. 2004;29(5):540–7.
75. Lim JH. Cholangiocarcinoma: morphologic classification according to growth pattern and imaging findings. AJR Am J Roentgenol. 2003;181(3):819–27.
76. Kim H, Lim JH, Jang KT, et al. Morphology of intraductal papillary neoplasm of the bile ducts: radiologic-pathologic correlation. Abdom Imaging. 2010;36(4):438–46.
77. Kim NR, Lee JM, Kim SH, et al. Enhancement characteristics of cholangiocarcinomas on mutiphasic helical CT: emphasis on morphologic subtypes. Clin Imaging. 2008;32(2):114–20.
78. Lee WJ, Lim HK, Jang KM, et al. Radiologic spectrum of cholangiocarcinoma: emphasis on unusual manifestations and differential diagnoses. Radiographics. 2001;21(Spec No):S97–116.
79. Takanami K, Yamada T, Tsuda M, et al. Intraductal papillary mucininous neoplasm of the bile ducts: multimodality assessment with pathologic correlation. Abdom Imaging. 2011;36(4):447–56.
80. Park HS, Lee JM, Kim SH, et al. CT differentiation of cholangiocarcinoma from periductal fibrosis in patients with hepatolithiasis. AJR Am J Roentgenol. 2006;187(2):445–53.
81. Hann LE, Greatrex KV, Bach AM, et al. Cholangiocarcinoma at the hepatic hilus: sonographic findings. AJR Am J Roentgenol. 1997;168(4):985–9.
82. Kim JY, Lee JM, Han JK, et al. Contrast-enhanced MRI combined with MR cholangiopancreatography for the evaluation of patients

with biliary strictures: differentiation of malignant from benign bile duct strictures. J Magn Reson Imaging. 2007;26(2):304–12.
83. Han JK, Choi BI, Kim TK, et al. Hilar cholangiocarcinoma: thin-section spiral CT findings with cholangiographic correlation. Radiographics. 1997;17(6):1475–85.
84. Seo H, Lee JM, Kim IH, et al. Evaluation of the gross type and longitudinal extent of extrahepatic cholangiocarcinomas on contrast-enhanced multidetector row computed tomography. J Comput Assist Tomogr. 2009;33(3):376–82.
85. Han JK, Choi BI, Kim AY, et al. Cholangiocarcinoma: pictorial essay of CT and cholangiographic findings. Radiographics. 2002; 22(1):173–87.
86. Lee JW, Han JK, Kim TK, et al. CT features of intraductal intrahepatic cholangiocarcinoma. AJR Am J Roentgenol. 2000;175(3): 721–5.
87. Jung AY, Lee JM, Choi SH, et al. CT features of an intraductal polypoid mass: differentiation between hepatocellular carcinoma with bile duct tumor invasion and intraductal papillary cholangiocarcinoma. J Comput Assist Tomogr. 2006;30(2):173–81.
88. Nathan H, Pawlik TM. Staging of intrahepatic cholangiocarcinoma. Curr Opin Gastroenterol. 2010;26(3):269–73.
89. Farges O, Fuks D, Le Treut YP, et al. AJCC 7th edition of TNM staging accurately discriminates outcomes of patients with resectable intrahepatic cholangiocarcinoma: by the AFC-IHCC-2009 study group. Cancer. 2010;117(10):2170–7.
90. Edge SB, Compton CC. The American joint committee on cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. Ann Surg Oncol. 2010;17(6):1471–4.
91. Bismuth H, Corlette MB. Intrahepatic cholangioenteric anastomosis in carcinoma of the hilus of the liver. Surg Gynecol Obstet. 1975;140(2):170–8.
92. Burke EC, Jarnagin WR, Hochwald SN, et al. Hilar cholangiocarcinoma – patterns of spread, the importance of hepatic resection for curative operation, and a presurgical clinical staging system. Ann Surg. 1998;228(3):385–92.
93. Blechacz BR, Sanchez W, Gores GJ. A conceptual proposal for staging ductal cholangiocarcinoma. Curr Opin Gastroenterol. 2009;25(3):238–9.
94. Zidi SH, Prat F, Le Guen O, et al. Performance characteristics of magnetic resonance cholangiography in the staging of malignant hilar strictures. Gut. 2000;46(1):103–6.
95. Weber SM, DeMatteo RP, Fong Y, et al. Staging laparoscopy in patients with extrahepatic biliary carcinoma. Analysis of 100 patients. Ann Surg. 2002;235(3):392–9.
96. Callery MP, Strasberg SM, Doherty GM, et al. Staging laparoscopy with laparoscopic ultrasonography: optimizing resectability in Hepatobiliary and pancreatic malignancy. J Am Coll Surg. 1997;185(1):33–9.
97. Zhang Y, Uchida M, Abe T, et al. Intrahepatic peripheral cholangiocarcinoma: comparison of dynamic CT and dynamic MRI. J Comput Assist Tomogr. 1999;23(5):670–7.
98. Fishman DS, Tarnasky PR, Patel SN, et al. Management of pancreaticobiliary disease using a new intra-ductal endoscope: the Texas experience. World J Gastroenterol. 2009;15(11): 1353–8, 21.
99. Su CH, Tsay SH, Wu CC, et al. Factors influencing postoperative morbidity, mortality, and survival after resection for hilar cholangiocarcinoma. Ann Surg. 1996;223(4):384–94.